Symposium SFRMS – Sleep and Neuro-Psychiatric Disorders

S31

Sleep disturbances and depression in the elderly

Y. DAUVILLIERS and I. JAUSSENT
University of Montpellier, Montpellier, FR

Insomnia and excessive daytime sleepiness (EDS) are frequent sleep complaints, whose prevalence increases with age. Some studies reported that insomnia and EDS may predict depression in adults. However, none of them have examined these associations specifically in community-dwelling elderly and none took into account together the phenotype of insomnia symptom (IS) in terms of its component symptoms i.e. sleep quality (SQ), difficulty in initiating sleep (DIS), difficulty in maintaining sleep (DMS) and early morning awakening (EMA), EDS, and sleep medication.

The aim of our present study was to examine the relationships between sleep disturbances and the incidence of depressive symptoms (DEPs) over 4-year in community-dwelling elderly (3824 subjects aged 65 years) free of depressive symptoms at baseline, and taking into account sleep disturbance characteristics, sleep medication and multiple independent and interacting causes of depressive symptoms.

Sleep disturbances were assessed at baseline by a face-to-face clinical interview followed by the completion of a sleep questionnaire. DEPs were assessed using the Center for Epidemiologic Studies-Depression scale at baseline, at 2- and 4-year follow-up. Logistic regression models controlling for potential confounders were generated to determine whether sleep disturbances were associated with depressive symptoms and to determine the effect of individual IS.

Insomnia and EDS increased independently the risk of incident DEPs (Odds Ratio (OR) = 1.69, 95% Confidence Interval (CI) = 1.26–2.26 and OR = 3.06, 95% CI = 1.99–4.73, respectively). Poor sleep quality, difficulty in initiating and in maintaining sleep but not early morning awakening were identified as risk factors of DEPs, with risk increasing with the severity and the frequency of IS. Sleep medication was also a risk factor for DEPs independently of sleep disturbances (OR = 1.87, 95% CI = 1.46–2.38 for insomnia, OR = 2.03, 95% CI = 1.59–2.58 for EDS).

To conclude, insomnia, EDS and the use of medication increase independently the risk of subsequent depression in elderly. Physicians should carefully consider sleep disorders or durable prescription of sleep medications to prevent late depression.

S32

Sleep and circadian rhythms in Parkinson's disease: from bench to bedside

C. GRONFIER
University of Lyon, Lyon, FR

Although Parkinson disease (PD) is mainly known for its classical motor features of resting tremor, rigidity, slowness, freezing, bradykinesia, and postural instability, nonmotor symptoms are increasingly recognized as key components of this neurodegenerative disorder. Nonmotor impairments are even often more detrimental on the quality of life than motor symptoms in PD. Sleep disorders are among the most frequent nonmotor features in PD, and are believed to affect almost all patients, with different expressions (insomnia, REM sleep behavior disorder (RBD), excessive daytime sleepiness). Their precise origins are unknown, but they are thought to be multifactorial, and to involve degeneration of several neuronal structures involved in the control of sleep and wakefulness. Although less consensual, disturbances of 24 h biological rhythms in PD have also been observed in few studies, including: a decrease in the amplitudes of body temperature, motor activity, blood pressure, cortisol and prolactin rhythms. Anatomical studies have suggested that cellular degeneration in the suprachiasmatic nucleus may be an underlying substrate for the changes in rhythmicity in Alzheimer disease, but such a degeneration hasn't been reported in PD. Therefore, whether the circadian timing system is involved in the chronobiological symptoms observed in PD is still unknown. In this presentation, we will review the recent literature in animal models of PD and in patients. We will discuss the possible alterations of circadian and homeostatic drives in PD. We will address the hypothesis that sleep disorders maybe early features of PD and not necessarily the consequence of motor symptoms.

Vezoli J, Fifel K, Leviel V, Dehay C, Kennedy H, Cooper HM, Gronfier C, Procyk E (2011) Early presymptomatic and long-term changes of rest activity cycles and cognitive behavior in a MPTP-monkey model of Parkinson's disease. PLoS One 6: e23952. doi:10.1371/journal.pone.0023952.

S33

Sleep and circadian rhythm disturbances in autism

C. SCHRÖDER
University of Strasbourg, Strasbourg, FR

Though highly prevalent in Autism Spectrum Disorders (ASD), sleep and circadian rhythm disturbances are not systematically assessed, and comprehensive treatment approaches are often lacking.

In this symposium, we will address sleep and circadian rhythm disorders in children with ASD both from a research as well as a clinical perspective. We will discuss in detail (i) the most common sleep and circadian rhythm disturbances in ASD as well as (ii) their impact on cognitive and behavioral development and their relationship to the autistic symptomatology; (iii) the neurobiological factors that might contribute to these disturbances; (iv) the range of diagnostic tools used to refine their assessment; and finally (v) a comprehensive treatment approach developed for children with ASD and their families at the Strasbourg University Hospital, targeting neurobiological, psychodynamic and environmental factors through a multi-component treatment approach. Among others, we will detail herein sleep hygiene measures, cognitive-behavioral therapy of sleep disturbances geared to the functioning of children with ASD, as well as complementary pharmacological treatment options.

S34

Sleepiness, sleep deprivation and accidents

P. PHILIP
University of Bordeaux, Bordeaux, FR

Drowsiness and falling asleep at the wheel are now identified as the reasons for many fatal crashes and traffic accidents. For years, fatigue has been associated with risk of accidents but the causes of fatigue were unclear. Extended hours and nocturnal driving have

been associated with accidents but few reports differentiate fatigue from sleepiness. In the early 1990s, researchers using epidemiological data began investigating sleepiness and sleep deprivation as causes of accidents. Falling asleep at the wheel associated with sleep restriction and nocturnal driving have been incriminated in 20% of traffic accidents. Drugs affecting the central nervous system (i.e., benzodiazepines, narcotic analgesics, and antihistamines), nocturnal breathing disorders, and narcolepsy have also been associated with an increased risk of accidents. Several articles show that objective measures of sleepiness such as the Multiple Sleep Latency Test or Maintenance of Wakefulness Test can predict accident rates or deteriorated driving performance. Further studies before and after treatment are required in patients with obstructive sleep apnea as well as other types of sleep disorders involving drowsy driving (e.g. ADHD, periodic leg movement syndrome, hypersomnia, insomnia, circadian rhythm disorders). This issue of evaluation is particularly crucial because studies show a major inter-subject variability in response to sleep loss or sleep fragmentation. Treatments improving daytime vigilance (e.g., Continuous Positive Airway Pressure in obstructive sleep apnea) significantly reduce the risk of traffic accidents for a reasonable cost. On the other hand, alerting drugs have never been evaluated regarding their protective effects with respect to sleep-related accidents. Many countries systematically evaluate medical disorders in professional drivers but the criteria are still very heterogeneous and an effort towards harmonization would be very beneficial, especially in continents like Europe or United States where drivers can cross several countries or states each of which applies different rules. Drowsy driving is still under-diagnosed and sleep disorders are not well enough explored and treated in the exposed population of sedentary males. Sleep physicians also tend to pay insufficient attention to the problem of road safety in their clinical evaluation of non-professional drivers and better awareness by the health community should help in reducing accident risk.

Symposium SFRMS - Role of hypothalamus in sleep/wake regulation

S35

Hypothalamic regulation of REM sleep

P.-H. LUPPI, O. CLEMENT, E. SAPIN, P.-A. LIBOUREL, S. ARTHAUD and P. FORT
University of Lyon, Lyon, FR

More than fifty years after paradoxical sleep (PS) discovery, the mechanisms responsible for PS onset and maintenance are still a matter of debates. Nevertheless, it is generally accepted that the pontine sublaterodorsal tegmental nucleus (SLD) is responsible for muscle atonia and cortical activation characterizing PS. Strong evidence also demonstrate that SLD activation, and thus PS onset, is due to the removal of a tonic GABAergic input from the ventrolateral periaqueductal gray (VLPAG) and the dorsal deep mesencephalic reticular nucleus (dDpMe) just ventral to it. Despite their essential role in PS genesis, the mechanisms controlling the cessation of activity of these GABAergic neurons at the onset and during PS are not fully understood.

To determine which structure(s) could inhibit(s) VLPAG/dDpMe GABAergic neurons during PS, and thus control(s) this state, we first exhaustively mapped all afferents to the VLPAG/dDpMe activated during PS. To do so, we combined the immunodetection of c-FOS, a marker of neuronal activation, with cholera-toxin b subunit (CTb) retrograde tracing from VLPAG/dDpMe in three groups of rats (control, PS deprived and PS hypersomniac, $n = 4$ in each group). We found that the lateral hypothalamic area (LH) was the only brain structure containing a very large number of neurons activated (c-FOS positive) during PS hypersomnia and projecting to the VLPAG/dDpMe. Moreover, 44% of these neurons expressed the neuropeptide melanin concentrating hormone (MCH) in triple labelled sections (MCH, CTb, c-FOS).

To confirm that the LH could be responsible for the inhibition of VLPAG/dDpMe GABAergic neurons during PS, eight additional rats were then bilaterally implanted with guide cannula targeting the LH. The sleep-waking cycle of these animals was analyzed during 16 h following injection in the LH of NaCl, clonidine (an alpha2 adrenergic agonist) or muscimol (a GABAa agonist). We showed that bilateral inhibition of LH neurons by clonidine or muscimol injection induced an inhibition of PS compared to saline.

Finally, combining c-FOS, CTb (injected in the SLD) and glutamate decarboxylase 67 (GABA synthesizing enzyme) double stainings, we further showed that VLPAG/dDpMe GABAergic neurons projecting to the SLD were strongly activated by muscimol inhibition of the LH.

Altogether, our data strongly suggest that LH PS-on neurons, in part MCH positive, control PS onset by means of their inhibitory projections to PS-off GABAergic neurons of the VLPAG/dDpMe.

S36

The multiple faces of wakefulness, hypothalamic control

J. S. LIN, C. ANACLET, C. ZHAO, E. GONDARD, K. OUK and Y. ZHAO
University of Lyon, Lyon, FR

Despite the presence of variable behavioural and cognitive activities during wakefulness (W), this vigilance state has long been regarded as relatively homogeneous in terms of EEG phenomenology. Recent studies have shown, however, that cortical oscillation and neuronal properties undergo major changes from quiet to active W. We hypothesize that each brain arousal system exerts a distinct control of different behavioural contexts of W and have investigated the role of histamine (HA) and orexins (Ox), two W-promoting systems located in the posterior hypothalamus.

KO mice lacking HA, or Ox or both were prepared for chronic EEG and sleep-wake monitoring under baseline conditions and after pharmacological dosing or behavioural tests, including locomotion, exploration, motivation, anticipation and sexual arousal.

We found that (i) Ox KO but not HA-deficient mice showed impaired W when they were subjected to a voluntary wheel test, indicating that Ox but not HA promotes W by enhancing locomotion. (ii) HA-deficient mice were unable to remain awake in a new environment while Ox KO mice preserved their W enhancement. (iii) In a test of motivation, wild type (WT) and Ox KO mice were motivated enough to catch difficult-to-reach palatable food and maintained highly awake, while HA deficient mice, though interested by the food, made no effort to catch it and slept as usual. The two last tests show that as compared to Ox, HA is more involved in the cognitive aspects of W. (iv) When WT mice were fed with a predictable restricted schedule (11 am–17 pm) instead of ad libitum, they displayed an anticipatory W of 70 ± 9 min before the meal time. This anticipatory W was significantly reduced in both Ox KO or HA-deficient mice. Moreover, Ox KO, but not HA-deficient mice exhibited W deficit during the feeding period. Finally, the anticipatory W disappeared completely in double KO mice lacking both HA and Ox; (v) In sexual arousal test, defined as increased W in a male mouse facing a female, acute inhibition of HA synthesis or antagonism of Ox1-receptor abolished sexual arousal while this function was intact in Ox KO or HA-deficient mice, indicating a compensation under long term loss of HA or Ox. This compensation became ineffective when both HA and Ox were deficient as sexual arousal was severely impaired in KO mice lacking both HA and Ox.

These data support our hypothesis according to which, W is a heterogeneous state with multiple faces. Each arousal system contributes complementarily and synergistically to the maintenance of cortical activation during W, while in different behavioural and cognitive contexts, their individual participation and specific functional role are fundamentally distinct.

Symposium SFRMS – Role of Hypothalamus in Sleep/Wake Regulation

S37

Hypocretin neurons at the interface of sleep an mood regulation

V. FABRE
University of Paris, Paris, FR

Impaired sleep is a symptom that often associates with affective disorders including depression and anxiety. Indeed, a high percentage of depressed patients present sleep alterations including insomnia, sleep fragmentation and increased rapid eye movement (REM) sleep pressure. Conversely, sleep disorders may impact mood as recently evidenced in narcoleptic patients who exhibit high rate of depression. However, the mechanisms underlying both mood and sleep regulation and their link remain to be determined. Here, we propose that hypocretin (orexin) neurons act as integrators to modulate both sleep and emotional behaviour in tight relation with the serotonergic system.

To investigate the role of hypocretin-serotonin interactions, a special attention was brought to animal models with impaired serotonergic or hypocretinergic neurotransmissions under depressogenic and/or stressful experimental conditions. To this goal, we studied mutant mice (i) lacking the serotonin transporter (5-HTT-/-) and (ii) that do not express the hypocretin precursor preprohypocretin (ppHcrt-/-). Firstly, anxio-depressive-like behaviours were evaluated by using validated tests. Secondly, sleep-wake cycles were monitored by polysomnographic recordings in control conditions and after 90 min of restraint stress. Finally, we used biochemical approaches to assess the activity of hypocretinergic and serotonergic systems under basal condition and after stress.

5-HTT-/- mice display a depression-like syndrome with a rapid eye movement (REM) sleep increase, enhanced helplessness and an altered response to stress. Thus, in contrast to wild-type mice, 5-HTT-/- mice fail to exhibit the delayed increase in REM sleep after restraint stress. We have shown that this impaired sleep response to stress is causally related to an enhanced hypocretinergic neurotransmission. Conversely, ppHcrt-/- mice display a narcoleptic-like phenotype which includes sleep fragmentation and cataplectic-like attacks. Interestingly, these mice exhibit a depressive-like behaviour in the forced-swimming test and an impaired response to stress. Such alterations might be accounted for, at least in part, by decreased serotonergic neurotransmission as suggested by a decrease in brain serotonin turn-over in ppHcrt-/-mice.

Taken together, these data strengthen the hypothesis that interactions between hypocretin and serotonin neurons modulate in a convergent manner sleep homeostasis and emotional related-behaviour.

S38

Role of hypothalamic peptides in central hypersomnias

Y. DAUVILLIERS
University of Montpellier, Montpellier, FR

Narcolepsy with cataplexy (NC) is a disabling disorder characterized by excessive daytime sleepiness and abnormal rapid eye movement (REM) sleep manifestations, due to a deficient hypocretin/orexin neurotransmission. However whether the sleepiness in NC is a direct consequence of hypocretin deficiency or low hypocretin tone reduces activity in other wake-promoting systems such as the histaminergic neurons remained unclear. Little is known regarding the pathophysiology of non-hypocretin deficient central hypersomnia, including mainly narcolepsy without cataplexy, and idiopathic with long or without long sleep time. Data on histamine (HA) activity in sleep disorders just came out in the recent years. Despite the absence of clear-cut threshold for pathological CSF histamine levels, results mainly revealed low levels in patients with narcolepsy and idiopathic hypersomnia, and especially in hypocretin deficient and non-medicated subjects. We report the results of CSF HA and tele-methylhistamine (t-MHA) using a sensitive liquid chromatographic-electrospray/tandem mass spectrometric assay together with hypocretin-1 levels in patients with confirmed central hypersomnias [narcolepsy-cataplexy NC (n = 56), narcolepsy without cataplexy NwC (n = 27), idiopathic hypersomnia IH (n = 11), secondary narcolepsy (n = 3)], with a complaint of daytime sleepiness but with unspecified diagnosis (n = 17), and in neurological controls (n = 50). In contrast to previous studies, we failed to detect significant between-group differences on CSF HA levels and any association with hypocretin-1 deficiency. We also report, for the first time, the measurements of CSF t-MHA levels in patients affected with hypersomnia, with the absence of between-group differences. No association was found between CSF HA, t-MHA or HA + t-MHA, sleepiness, treatment intake, and frequency of cataplexy. A slight negative correlation was found between age and HA levels. CSF histamine and tele-methylhistamine did not significantly differ between patients with narcolepsy-cataplexy, other etiologies of non-hypocretin-1 deficient central hypersomnias from neurological controls, being therefore not informative tools to differentiate etiologies of central hypersomnia or to assess the severity of centrally-mediated hypersomnia.

To conclude, we report the results of the first use of a method that provides a highly sensitive and selective quantification of both CSF histamine and its metabolite t-MHA in a large population of patients affected with narcolepsy-cataplexy, other etiologies of non-hypocretin-1 deficient central hypersomnia, and neurological controls, but without between group significant differences.

Young Scientist Symposium

S56

You snooze, you lose: adaptive sleep loss in polygynous pectoral sandpipers

J. A. LESKU[1], N. C. RATTENBORG[1], M. VALCU[1], A. L. VYSSOTSKI[2], S. KUHN[1], F. KUEMMETH[3], W. HEIDRICH[3] and B. KEMPENAERS[1]

[1]Max Planck Institute for Ornithology, Seewiesen, DE, [2]University of Zurich, Zurich, CH, [3]e-obs GmbH, Gruenwald, DE

Objectives: Sleep is thought to perform restorative processes that sustain adaptive waking brain function. Accordingly, sleep restriction and fragmentation can diminish neurobehavioural performance in animals, including humans. However, here we provide the first evidence that sleep loss can be beneficial.

Methods: Pectoral sandpipers (Calidris melanotos) are birds that migrate annually from South America to Alaska to breed in the summer under continuous daylight. Males are polygynous and engage in intense male-male competition in order to copulate with fertile females during a 3-week period. We measured activity levels in mature males and the number of male-female interactions. The parentage of virtually all chicks on the study site was determined genetically. In a separate year, we implanted electrodes using standard techniques to measure EEG/EMG activity in free-roaming birds on the tundra. Collectively, these data were used to quantify (i) the relationship between activity and brain state, (ii) variation in the amount of wakefulness/activity and (iii) the relationship between sleep and reproductive output.

Results: Activity levels varied considerably across males. Some males were active >95% of the time for periods lasting up to 19 day. EEG-defined wakefulness and sleep were associated with high and low EMG activity, respectively, and birds rapidly transitioned from active wakefulness to sleep, such that activity is a good proxy for wakefulness in these animals. Accordingly, there was great variation in the amount of sleep, with extremes at <10% and >30% of the 24-h day. The total time males spent sleeping correlated positively with the number, and mean and maximum duration of sleep episodes. Despite having more fragmented sleep, males that slept the least showed the greatest slow wave activity during non-REM sleep, suggesting that they compensated, at least partially, for sleep loss by sleeping more deeply. Most importantly, males that slept the least interacted with more females and sired the most offspring.

Conclusion: Males that slept more performed worse on the most important measure of performance from an evolutionary perspective. Thus, reduced neurobehavioural performance is not a universal outcome of sleep restriction and fragmentation as generally thought. As such, these results challenge notions on the adaptive value of sleep.

S57

Age-related differences in cerebral activation for motor sequence learning are correlated with sleep spindles

S. FOGEL[1], G. ALBOUY[1], C. VIEN[1], B. KING[1], R. HOGE[1], S. JBABDI[2], H. BENALI[3], A. KARNI[4], P. MAQUET[5], J. CARRIER[1] and J. DOYON[1]

[1]University of Montreal, Montreal, CA, [2]University of Oxford, Oxford, UK, [3]INSERM, Paris, FR, [4]University of Haifa, Haifa, IL, [5]University of Liège, Liège, BE

Objectives: Sleep is necessary for the efficient consolidation of motor sequence learning (MSL). Older adults exhibit normal MSL, but do not consolidate this type of skill, as they show no sleep-dependent gains in performance. With age, sleep becomes fragmented and sleep spindles are reduced. The present study was thus designed to determine whether age-related changes in sleep, and in spindle activity in particular, do explain the motor memory consolidation deficit observed with normal aging. It was hypothesized that age would be associated with a deficit in performance gains and that sleep spindles would be correlated with the neural substrates involved in MSL consolidation in young but not older individuals.

Methods: We investigated, through behavioural and magnetic resonance imaging (fMRI) studies in young (Y: 20–35 year, $n = 13$) and older (O: 55–70 year, $n = 15$) healthy adults, the effects of sleep (90-min daytime nap) on MSL (5-item sequence, 12 sequences/block, 14 blocks per session). MSL was measured using time between key-presses. fMRI blood-oxygen-level dependent (BOLD) signals at 3T were acquired during training and retest. For each subject, a general linear model estimated cerebral BOLD changes. Group-level contrasts were used to investigate the interaction across training session (retest-training) and age condition (Y versus O) that related to the conjunction of spindle duration, amplitude and density. A region of interest approach including brain regions involved in MSL and consolidation (cerebellum, striatum, hippocampus, parietal, motor and supplementary motor cortex) was used. Peak cluster values for independent t-tests were reported using uncorrected *P*-values ($P < 0.005$, $k = 3$).

Results: Bonferroni-corrected t-tests revealed that the Y ($P = 0.016$) but not O ($P = 0.764$) group had gains in asymptotic versus predicted performance at re-test. Increased cerebral activation (retest-training) was modulated by sleep spindles, and correlated significantly with age differences in the left putamen (Y>O: $P = 0.002$), motor cortical regions (O>Y: $P < 0.001$), left caudate (O>Y: $P = 0.002$) and cerebellum (O>Y: $P < 0.001$).

Conclusions: These results indicate that spindle activity in Y subjects is related to increased activation in the striatal-cortical network implicated in the later stages of MSL, whereas spindle activity in the O subjects is associated with increased activation in the cerebellar-cortical network, implicated in the earlier stages of MSL.

S58

The effect of intranasal hypocretin-1 on glucose tolerance in normal weighted and obese narcolepsy patients

S. L. WEINHOLD, M. SEECK-HIRSCHNER, A. NOWAK, R. GÖDER and P. C. BAIER

Christian-Albrechts-University, Kiel, DE

Objectives: Narcolepsy is an intrinsic sleep disorder typically caused by a deficiency of hypocretin-1 (hcrt-1), also called Orexin-A. Hcrt-1 is essentially involved in not only sleep regulation, but also energy homeostasis. There is evidence that its absence might lead to obesitas and a diabetogenic state in part of the patients. This, and the observation that whereas most of the narcoleptic patients are overweighted some are underweighted, indicates two types of narcolepsy with respect to glucose metabolism and regulation.

Aim of this study was to investigate the effect of intranasal hcrt-1 on oral glucose tolerance in patients with narcolepsy with cataplexy with normal weight and obesity.

Methods: We investigated in a double blind, placebo-controlled experiment the effect of hcrt-1 on glucose tolerance in 14 patients

with narcolepsy with cataplexy. All patients received in randomized order hcrt-1 and placebo intranasally with an interval of approximately 2 weeks. Immediately after substance administration the participants were subjected to a standard procedure of an oral glucose tolerance test (OGTT; administration of 75 g glucose in solution, measurement of blood glucose before and 30, 60, 90 and 120 min after glucose intake). Patients were divided into a group with normal weight (n = 5, BMI < 26) and one with obesity (n = 9, BMI ≥26). For the decision of the relevance of group differences paired t-tests were calculated and the alpha was set to 5%. The area under the curve defined blood glucose over the time.

Results: Whereas the area under the curve in the normal weighted group shows no differences after hcrt-1 (M = 73.1; SD = 41.9) and placebo (M = 83.4; SD = 36.8; P = 0.305), obese narcoleptics had a significant higher glucose level after hcrt-1 administration (M = 109.4; SD = 41.1) compared to placebo condition (M = 84.9; SD = 21.3; P = 0.049).

Post hoc tests showed a significantly increased blood glucose level in OGTT in obese narcoleptics 90 min after hcrt-1 and glucose administration (M = 156.9, SD = 30.6) compared to the placebo condition (M = 130.2; SD = 20.0; P = 0.024).

Conclusion: Our results indicate that exogenous hcrt-1 has an impact on oral glucose tolerance in obese but not in normal weighted patients with narcolepsy. These findings confirm the assumption of two different types of narcolepsy in view of the glucose metabolism. Further studies with lager sample sizes and hcrt-1 measurements are necessary to elucidate the underlying mechanisms.

This study was supported by the Deutsche Forschungsgemeinschaft (DFG, SFB 654).

S59

Polysomnographic measures of sleep in adolescents and young adults with delayed sleep phase disorder and healthy controls on a self-chosen sleep schedule

I. W. SAXVIG, A. WILHELMSEN-LANGELAND, S. PALLESEN, Ø. VEDAA, I. H. NORDHUS and B. BJORVATN

University of Bergen, Bergen, NO

Objective: Delayed sleep phase disorder (DSPD) is characterised by a delay in the major sleep period in relation to societal norms. Sleep quality has traditionally been described as normal, but this has not been thoroughly confirmed by polysomnographic studies (PSG). Hence, the aim of the present study was to examine objective measures of sleep in patients with DSPD by means of PSG, and to compare it to that of healthy controls.

Methods: PSG data from 54 adolescents and young adults were analysed, 35 diagnosed with DSPD and 19 healthy controls. The DSPD group consisted of 25 females and 10 males with a mean age of 20.6 years (SD = 3.1) whereas the control group consisted of 14 females and five males, mean age 21.1 (SD = 2.3, P = 0.465). Participants slept on a self-chosen schedule from 3 days prior to- and throughout the experiment to rule out effects of prior sleep deprivations and/or enforced asynchrony. Sleep measures used for further calculations included measures on sleep timing (lights on and off, sleep onset and offset), time in bed (TIB), total sleep time (TST), sleep onset latency (SOL = the interval between lights off and sleep onset), wake after sleep onset (WASO), sleep efficiency (SE = TST expressed as percentage of TIB) and amount of each sleep stage. We also calculated amount of slow wave sleep (N3) during the last 3 h of the sleep period.

Results: Results show that the timing of sleep was delayed in the participants with DSPD, confirming the sleep phase delay. Although participants were allowed to choose their own bed-time, SOL was longer in the DSPD group than in the control group (36 ± 49.7 versus 17 ± 12.6 min, P = 0.037). Also TIB was longer in the DSPD group (622 ± 112.2 versus 551 ± 67.2 min, P = 0.005). Once sleep was initiated, no obvious differences in sleep quality were observed in terms of TST, WASO, SE, or time spent in each sleep stage. Similar amounts of N3 during the last 3 h of the night indicate that there were no differences between the groups in the distribution of slow wave sleep (11.8 ± 7.5% in the DSPD group compared to 12.0 ± 9.9% in the control group, P = 0.918).

Conclusion: In conclusion, timing of the sleep period was delayed in the DSPD group. Participants with DSPD spent more time in bed, and SOL was slightly longer than in the control group. Sleep quality was otherwise not reduced.

Video Session – Paroxysmal Episodes in Adults

60

Paroxysmal episodes in adults

C. SCHENCK[1], R. MANNI[2] and G. PLAZZI[3]

[1]Minnesota Regional Sleep Disorders Center, Minneapolis, MN, US, [2]IRCCS C. Mondino Foundation, Pavia, IT, [3]University of Bologna, Bologna, IT

Objectives: Show video examples of a broad spectrum of abnormal, sleep-related paroxysmal events.

Methods: Patients clinically evaluated at academic sleep centers and who provided consent for the educational presentation of videotaped episodes during their video-PSG or home video.

Results:

These video examples will be shown: 1. Atypical headbanging with rhythmic and quasi-rhythmic punching and slapping of the head in three normal, well-adjusted patients without neurologic or psychiatric disorders [1].

2. Violent, prolonged body-rolling–young adult.

3. Typical sleep paralysis with body-rolling[2].

4 Rhythmic movements (head and leg banging) in an iRBD patient: two episodes recorded by v-PSG [3].

5. 'Atypical sleep terrors' referral who was documented to have nocturnal frontal lobe epilepsy (NFLE) (4).

6. Violent sleep terror episode–to distinguish from the violent, screaming NFLE episodes just described.

7. Stereotypic nocturnal screaming followed by very strange verbal violence.

8) NFLE seizures with so-called 'Salamander-like' motor patterns seen on home video and v-PSG.

9. Example of epileptic nocturnal wandering in a published case (5) with updated history involving a change in the semiology of the seizures with age, subsequent surgery, development of psychosis, and eventual discovery of the gene affecting his family (not yet published).

10. Example of injurious behaviors in a case of iRBD that ultimately responded to sodium oxybate.

11. V-PSG examples of cases with violent behaviors arising from unequivocal NREM sleep in PD patients (6).

12. Abrupt SW during v-PSG in a 23 year female.

13. Very prolonged sleep paralysis with v-PSG documentation during the paralysis and upon recovery (7). The patient appears to be in a mixed REM/wake state of mind during the paralysis.

14. Very prolonged cataplectic attacks arising in adulthood, with an 'astasia' pattern that can be discussed concerning different cataplectic features in childhood versus adult onset NC.

15. V-PSG of visual hallucinations upon arousal from NREM sleep and persisting into W in PD (6).

Conclusion: The wide heterogeneity of the presented videos & their challenging differential diagnoses pinpoint the utility of v-PSG in the diagnosis of behavioral sleep disorders.

References:

1. Yeh S-B, Schenck CH. J Clin Sleep Med 2012 (in press).
2. Pizza F, et al. Sleep Med 2010;11 (4):423–5.
3. Manni R, Terzaghi M. Mov Disord 2007;22:1797- 800.
4. Boursoulian LJ, et al. J Clin Sleep Med 2012; 8:108–12.
5. Plazzi G, et al. Sleep 1995;18:749–56.
6. Ratti PL, et al. Sleep Med 2012; June 13.
7. Terzaghi M, et al. Neurol Sci 2012;33:169–72.

Case Discussion – Insomnia

67

Co morbid insomnia: insomnia and polyarthritis a reciprocal

A. METLAINE and D. LÉGER
Hospital Hotel-Dieu, Paris, FR

Chronic pain and insomnia are frequent complains in insomniacs patients coming to our sleep centre in the Hotel Dieu de Paris, while we have a common consultation between sleep and pain specialists. However it is often difficult to decide which one of pain or insomnia has to be considered first. Some treatments of pain may have sleep consequences. Based on the case of one 51 old male with polyarthritis and insomnia we discuss the interaction between sleep and inflammatory osteo-articular disorders.

68

Co morbid insomnia: depression and anxiety

D. RIEMANN
Freiburg University Medical Center, Freiburg, DE

In classical psychopathology, insomnia was typically interpreted as a symptom of depression, anxiety or any other mental disorder. Recent years have seen a change of paradigm, as evidence from epidemiological studies pointed out that insomnia can be an independent predictor or even risk factor for depression and anxiety. DSM-V will suggest 'Insomnia Disorder' as a new category instead of the concept of primary/secondary insomnias. Several case vignettes highlighting the intriguing and bi-directional relationships between insomnia and depression/anxiety will be presented.

69

Insomnia at the workplace: exploring insomnia in minors and drivers in Brazil

S. B. VIEIRA
Unit for Research in Sleep Disorders, Vitoria, BR

Insomnia is a sleeping disorder of great occurrence in general population, with great impact on the life quality, supporting the absenteeism, the appearance of psychiatric disorders and increaseing the risk of accidents at work. The clinical case presented here is a part of a Sleep Medicine Program implanted about 12 years ago in a passenger transportation company in southeastern Brazil.

Male, 42-year-old patient, working for 20 years, in a varied shift work regime of about 8 h a day, with 11-h-regular breaks and 2 days off every six worked days. In the beginning of the clinical picture the patient presented difficulties in starting and keeping his sleep in a persistent way, showing significant impact in his personal and family relationships, decrease of his behavioral and working performances. The importance of the detection and treatment of the insomnia picture presents two factors of great relevance: the quality of life and the prevention of work accidents.

70

Insomnia in adolescence and young adults - Impact of modern life style

G. BADER
University of Göteborg, Göteborg, SE

There are increased reports of insomnia among adolescents and young adults yielding to an alarming increase of drug prescriptions and over-consumption of hypnotics, sedatives and anti-depressive medicine.

Insomnia in adolescents and young adults may differ from insomnia in adults. The clinical picture can be quite complex. While difficulties in falling asleep are common to both, difficulties in maintaining sleep are initially rare with adolescents and young adults.

Daytime consequences of insomnia as reported by adults, such as subjective fatigue, worsened performances, mood variations, lack of energy etc… are missing, often replaced by hyperactivity, dissociative emotional state, aggressiveness and over-reactive attitudes in adolescents. As long as these remain motivated there is no failure in performance, on the contrary they often have very satisfactory results. These young people present a resilience not encountered in adults.

Multiple factors can initiate and maintain this condition; physiological ones, such as the delayed sleep phase occurring at puberty, worsened by permanent inter-connectivity (internet…); environmental and social factors with hectic, irregular life style and demands for continuous availability; mental with constant stress and multi-processing, anxiety to be rebuffed or bullied as well as existential and emotional experiences.

Furthermore it is not uncommon that these subjects over consume products containing caffeine and, even at this age, indulge in binge drinking, tobacco and substance abuse - leading to co-morbid symptoms and making the clinical picture even more confusing and complex - therefore yielding to wrong diagnosis (e.g. bi-polar disorders…) and inadequate treatments.

It is essential to recognise the multiple facets of the condition for appropriate approach and adequate, often combined treatment.

We illustrate with two case studies, a 16-year old boy and a young university student.

Symposium – Local Sleep – its Origin and Function

S80

Multiunit recordings during sleep and waking in the rat

V. VYAZOVSKIY
University of Surrey, Guildford, UK

Objectives: Prolonged wakefulness or a lack of sleep lead to cognitive deficits, but little is known about the underlying cellular mechanisms. When we fall asleep, brain activity changes dramatically, but our understanding of the functional significance of different patterns of brain activity during sleep remains in its infancy. Whereas it was once thought that sleep is a whole brain phenomenon, an emerging current view is that sleep develops locally at the level of individual neurons or specific neuronal networks and plays a fundamental role in the local synaptic function and neural plasticity. The aim of this study was to investigate whether local neuronal sleep is regulated homeostatically and whether it can account for behavioural deficits incurred during sleep deprivation.

Methods: Spontaneous and evoked cortical neuronal activity, EEGs, LFPs and EMGs were recorded chronically in freely-behaving rats during sleep, wakefulness and 4 h sleep deprivation. The recordings were performed from 1–2 cortical locations. Spiking activity of the individual neurons was analysed offline. Behavioural performance was measured with a sugar-pellet reaching task.

Results: We found that as wake time increases, cortical neurons tend to go briefly 'OFF line,' as they do in sleep, and the incidence of OFF periods increases, accompanied by slower waves in the local EEG. Such neuronal OFF period often occurred in one cortical area and not in another. During these periods of 'local sleep' rats displayed a wake EEG and appear awake and behaving. The occurrence of neuronal OFF periods was associated with a progressive impairment in a sugar pellet reaching task. By applying local electrical microstimulation to the frontal area of the neocortex, we found that after a 4-h period of waking the initial neuronal response in the contralateral frontal cortex was stronger and more synchronous, and was followed by a more profound inhibition of neuronal spiking as compared to the control condition.

Conclusions: The changes in cortical neuronal activity during sleep deprivation suggest increased neuronal excitability and/or efficacy of cortico-cortical connections, and indicate that after staying awake cortical neurons become transiently bistable. We propose that some of the detrimental effects of sleep deprivation on the behaviour and cognition are a result of altered neuronal responsiveness to incoming intrinsic and extrinsic inputs.

S81

Local aspects of avian sleep

N. C. RATTENBORG, J. A. LESKU and G. J. L. BECKERS
Max Planck Institute for Ornithology, Seewiesen, DE

Despite being a derived type of reptile, birds exhibit electrophysiological sleep states that more closely resemble those of their distant mammalian relatives than those of their close reptilian relatives. As in mammals, sleeping birds alternate between two distinct states, rapid eye movement (REM) and non-REM (NREM) sleep. In addition to engaging in similar sleep states, several local aspects of sleep described in mammals also occur in birds. In this symposium we will discuss four local features of sleep shared by mammals and birds. (i) Unlike other birds, ostriches – members of an early evolutionary branch of modern birds – engage in a sleep state that combines brainstem-mediated aspects of REM sleep with NREM sleep-related EEG slow waves in the forebrain, a mixed state previously only described in the most 'ancient' group of living mammals, the monotremes. The presence of this mixed state in ostriches and monotremes, suggests that it reflects an early stage in the evolution of REM and NREM sleep. Moreover, it suggests that REM sleep with concurrent activation of the brainstem and forebrain is a derived trait among mammals and birds that presumably supports new sleep functions. (ii) As in several aquatic mammals, birds often sleep with one eye open, a state associated with an interhemispheric asymmetry in the level of NREM sleep slow wave activity. This form of local sleep allows birds to keep an eye out for predators and may allow them to sleep during long non-stop flights, although the latter has not been confirmed. (iii) The local intensity of NREM sleep (slow wave activity) is homeostatically regulated in a use-dependent manner, as in the mammalian cortex. Consequently, functional hypotheses linked to local sleep homeostasis in mammals may also apply to birds and therefore reflect a fundamental function of NREM sleep. (iv) Recent high-density depth recordings in anesthetized birds have revealed that, as in the mammalian cortex, slow waves and associated multiunit activity propagate as traveling waves in the avian forebrain. Although slow waves tend to appear first in certain brain regions, the propagation pattern is diverse, in some cases apparently occurring in 3 dimensions as expanding plumes of activity. Collectively, the study of local sleep in birds can provide insight into the function of sleep in mammals by revealing evolutionary convergences in sleep and potential functionally interrelated traits.

S82

Intracranial recordings of dissociated vigilance states in humans

L. NOBILI
Niguarda Hospital, Milan, IT

A complex and widely distributed neural system, with functionally distinct but integrated components, orchestrates sleep. In normal conditions, the interaction of these integrated components allow an unambiguous separation between the state of wakefulness and sleep, from both a behavioral and a neurophysiological perspective. However, recent experimental evidence in animals and humans demonstrated that the transition from the wake to the sleep state might work with different timing for different brain areas, partially redefining the classical distinction between wake and sleep as separate, incompatible states. In particular a recent study, conducted with intracerebral recordings in drug-resistant epileptic patients, has shown that extensive cortical territories can maintain an activated pattern for several minutes after the thalamic deactivation. In keeping with these observations, our data, obtained from Stereo-EEG recordings in drug-resistant epileptic patients, show that several minutes before sleep onset (detected on scalp EEG by the emergence of the first spindle or K-complex), spindles appeared in the hippocampus with the typical 4 s periodicity. The appearance of localized simultaneous sleeplike and wake-like activity during NREM sleep may explain paradoxical sleep phenomena such as sleepwalking and confusional arousal, which have been attributed to a breakdown of the boundaries between wakefulness and NREM sleep. Indeed, we have recently shown that NREM arousal para-

somnias, such as confusional arousals, can be characterized by the persistence of local sleep-like state (in the frontal, parietal associative and hippocampal cortices) in contrast to the presence of a wake-like state in other cortical structures (the motor, cingulate, insular, amygdalar and temporopolar cortices). However, the presence of wake-like and sleep-like electrophysiological states is not only a features on NREM parasomnias. Indeed, we have confirmed that the appearance of local dissociated states is an intrinsic feature of NREM sleep. In conclusion intracerebral EEG studies show that the boundaries between sleep and wakefulness are less clearly defined than expected. These findings add a new dimension to the concept of local sleep regulation and opens new perspectives in the interpretation of the substrates underlying behavioral states of vigilance.

S83

Sleep EEG topography in humans as a fingerprint

P. ACHERMANN

University of Zurich, Zurich, CH

Sleep homeostasis refers to the increase of sleep propensity during waking and the decrease of sleep intensity during sleep. EEG slow-wave activity (SWA; EEG power in the 0.75–4.5 Hz range) is a marker of non-REM sleep intensity and shows a frontal predominance that increases most prominently after sleep deprivation.

Slow waves represent a salient EEG feature of non-REM sleep. We investigated the activation of brain structures during slow wave sleep under normal conditions and after sleep deprivation. We analyzed the EEG of baseline and recovery sleep after 40 h of sustained wakefulness (8 healthy young men, 27 EEG channels). Power maps were computed for the first non-REM sleep episode (where sleep pressure is highest) of both nights (0.5–2 Hz). A frontal predominance of all frequencies between 0.5 and 2 Hz was observed. An additional occipital focus of activity was present below 1 Hz. Power maps at 1 Hz and below were not affected by sleep deprivation, whereas an increase in power was present in the maps above 1 Hz. Based on the response to sleep deprivation, low- and mid-delta activity (0.5–1 Hz; 1.25–2 Hz) were dissociated. Within a subject we observed a high similarity of power maps in both nights. Within-subject similarity between maps was assessed by hierarchical cluster analysis. The normalized maps of baseline and recovery sleep clustered in both frequency bands, pointing to fingerprint-like features of the maps. Electrical sources within the cortex of low- and mid-delta activity were estimated. Source localization highlighted a predominantly frontal distribution of activity for both low- and mid-delta activity. Sleep deprivation resulted in an increase in source strength for mid-delta activity only, mainly in parietal and frontal regions. Fingerprint-like features were observed also at the level of electrical sources.

Given the trait-like features of maps and electrical sources the question arises whether the dynamics of the homeostatic Process S also show regional specificity. We quantified inter-individual variation in the parameters of the homeostatic Process S and investigated their spatial distribution. Distinct individual patterns were observed. The decrease and build-up of Process S was slowest in fronto-central areas and the fastest dynamics were observed in parieto-occipital (decrease) and frontal (buildup) areas.

Our data support the notion of local aspects of sleep regulation. Sleep EEG topography can serve as a trait marker.

Symposium – New Approaches to the Study of Sleep and Dreams: tACS and tDCS

S84

A closer look onto the impact of oscillatory transcranial electric currents on memory consolidation in sleep

L. MARSHALL, K. BOUMGHAR and D. AUMANN
University of Luebeck, Luebeck, DE

Objective: In humans, slowly oscillating transcranial direct current electric stimulation when applied during Non-rapid eye movement (NREM) sleep stage 2 or deeper oscillating at the frequency of the sleep slow oscillation (SO, ~ 0.75 Hz) increased endogenous slow oscillatory and spindle activity as well as improved declarative memory consolidation. The present studies aim to refine these findings by testing the differential effects of anodal and cathodal so-tDCS on declarative and non-declarative sleep-associated memory consolidation.

Methods: After an adaptation night in two experimental sessions separated by at least 1 week subjects receive either stimulation or sham-stimulation. Anodal or cathodal so-tDCS is applied after the first 4 min of stable stage 2 sleep following sleep onset for five 5 min blocks, each separated by a 1 min stimulation-free interval. Two studies are conducted each using a different set of memory tasks. Declarative and non-declarative tasks are presented for learning before nocturnal sleep, with recall performance tested the next morning. Psychometric control measures are similarly collected at these time points. Analyses are conducted for total sleep time, for the 1-min stimulation free intervals, and for performance on the memory and psychometric tests. Spectral EEG power in particular in the slow oscillatory and spindle frequency bands is analyzed.

Results and conclusion: Preliminary results indicate the relevance of the oscillatory mode of stimulation regarding effects on endogenous EEG activity. Results furthermore lend support for the notion that effects of so-tDCS on memory can be extended to the sleep-associated consolidation of non-declarative memory.

Supported by the DFG and BMBF/Bernstein Network.

S85

Can transcranial direct current stimulation over sensorimotor cortex alter dream content?

K. J. VALLI, V. NOREIKA and T. KONTTO
University of Turku, Turku, FI

Objectives: With transcranial direct current stimulation (tDCS), which uses small excitatory and inhibitory electric currents to modulate cortical excitability, we may be able to directly affect the brain activity likely to underlie dream experiences, without interrupting or disturbing sleep. The aim of the study was to investigate the role of the primary sensorimotor cortex in bringing about subjectively experienced bodily sensations and movement in rapid eye movement (REM) sleep dreams.

Methods: In a placebo controlled, single-blind, within subjects experiment, tDCS (1 mA electric current) was applied bilaterally on the scalp surface over the hand representations of the primary sensorimotor cortex during REM sleep. The stimulation sites were verified individually for each of the ten subjects with magnetic resonance imaging (MRI) -based anatomical brain images and transcranial magnetic stimulation (TMS). The tDCS electrode over the right sensorimotor area was always the anode, and the electrode over the left sensorimotor area was the cathode. Polysomnography was recorded to score sleep stages. During two nights, after 10 min of tDC stimulation or placebo during REM sleep, the subjects were awakened and questioned about their dream experiences. The intensity and frequency of bodily experiences and movement in dreams was evaluated with the Dream Body Questionnaire, and the free-worded dream reports were also content analyzed with scales corresponding to the questionnaire.

Results: Compared with the control condition, a significant decrease in the subjective estimate of the amount of movement in the dreams was found after 10 min of tDC stimulation. Other bodily sensations (vestibular, tactile and somatosensory experiences, movement or body scheme alterations) were not affected. In contrast to self-reports, no differences between the tDCS and placebo dreams were found in an observer-rated content analysis.

Conclusions: Our main result, self-reported decrease in the amount of movement in tDCS condition, might be related to the lateralization of motor functions of right handed participants to the dominant left hemisphere which was inhibited by cathodal tDC stimulation. However, the self-reports and content analysis yield different results as to the effects of tDCS stimulation on dream content. The study opens novel possibilities for experimental dream research with tDCS.

S86

Effects of transcranial alternating current stimulation (tACS) on sleep and dreaming

U. VOSS[1], R. HOLZMANN[2], M. NITSCHE[3] and W. PAULUS[3]
[1]Frankfurt University, Frankfurt, DE, [2]Helmholtz Centre for Heavy Ion Research, Darmstadt, DE, [3]Goettingen University, Goettingen, DE

Objectives: The current experiment was carried out to test a possible causal relationship between activity in the 40 Hz frequency band and secondary, i.e. higher order consciousness in dreams. Specifically, we investigated whether it is possible to change the brain's state of consciousness from normal REM-sleep dreaming to lucid dreaming through low voltage 40 Hz stimulation at fronto-temporal sites of the scalp. This incorporates two important steps: a demonstration that an externally applied low voltage electrical current is effective in changing the ongoing EEG and evidence that the dream content is altered as a function of the applied current.

Methods: We tested 13 subjects during three consecutive nights in the Goettingen sleep laboratory. Transcranial alternating current stimulation (tACS) was performed only after 3 am and only during REM phases. In nights 1 and 3, subjects were stimulated with 40 Hz or 2 Hz currents, counterbalanced for time of night. In night 2, participants received sham stimulations. Stimulations were carried out in double-blind fashion.

Results: Our analyses show that the external application of a weak electrical current changes the ongoing cortical activity as evidenced by EEG recordings. This effect was traceable for the 40 Hz but not for the 2 Hz condition which is most likely due to the high delta power that is naturally present during REM sleep. Regarding subjective correlates of induced EEG changes during REM sleep, we observed increased dissociative thought specific to 40 Hz stimulation. Dissociative thought has been shown to be typical for lucid dreaming, especially in young children.

Conclusion: We interpret this finding as strong support for the 40 Hz band hypothesis stating that frequencies around 40 Hz are somehow involved in higher order or secondary consciousness. Moreover, results suggest a causal relationship between lucid dreaming and 40 Hz activity in fronto-temporal areas of the brain. Although the method itself has been shown to influence cognitive performance by other laboratories, this is the first demonstration of an effect on the ongoing EEG. We consider our results a proof-of-principle, and trust that it will encourage further research into the possibilities and boundaries of low current electrical stimulation of the brain during sleep.

S87

Cerebral stimulation in psychotic disorders: increasing cognitive control?

A. D'AGOSTINO
University of Milan, Milan, IT

Objectives: The pharmacological revolution that began in the 1950s progressively diminished interest in cerebral stimulation techniques for psychiatric patients. However, available psychotropic compounds fail to target several dimensions of complex disorders such as schizophrenia. Current stagnation in the development of effective drugs with truly novel mechanisms of action contributed to a renewed interest towards non-invasive and inexpensive means of directly stimulating the brain of psychotic patients who fail to completely remit from their debilitating symptoms. Available trials and putative mechanisms of response to direct brain stimulation will be discussed.

Methods: Differences between transcranial Direct and Alternating Current Stimulation (tDCS – tACS) and their current application in the treatment of schizophrenic patients with persistent psychotic symptoms will be reviewed.

Results: Significant improvement in positive symptoms has been reported with tDCS, although further studies will need to clarify optimal stimulation parameters and treatment duration. This experimental therapeutic procedure appears to directly modulate cortical synaptic plasticity in stimulated areas. Indeed, aberrant synaptic plasticity has been extensively related to the pathophysiology of schizophrenia. In particular, stimulation of frontal cortices seems to contribute to improvement in psychotic symptoms and possibly also typically deficient neurocognitive domains. More work is needed to also determine which type of environmental input should be associated to the stimulation.

Conclusion: Restoriation of synaptic plasticity in frontal cortices through direct cerebral stimulation seems to contribute to clinical improvement in psychotic patients. Activation of neurodevelopmentally impaired cortical networks related to self-reflective awareness, abstract thinking and metacognition could play a crucial role in the observed therapeutic effect. This hypothesis will be discussed in relationship to current understanding of neurofunctional organization of sleep-dependent states of the brain/mind characterized by hypofrontality.

Symposium – Circadian and Homeostatic Regulation of Sleep and Wakefulness: an Integrative Approach

S88

Interaction between clock genes and sleep homeostasis

T. CURIE and P. FRANKEN
Center for Integrative Genomics, Lausanne, CH

Objectives: Besides the well-established role of clock genes in generating circadian rhythms, work on mice carrying targeted deletions of core clock genes, together with our findings that brain mRNA levels of the clock gene Period2 (Per2) increase with time-spent-awake, indicates they also play a role in the homeostatic aspect of sleep regulation. Here we determine the effects of sleep loss on PER2 protein. Moreover, the interaction between time-of-day and sleep deprivation (SD) on Per2 mRNA in the brain was determined.

Results: Using Per2: Luciferase mice we demonstrate that also PER2 protein increases with SD, not only in the brain but also in kidney and liver. Within the brain, SD affected PER2 in the cerebral cortex the most, while sparing the suprachiasmatic nucleus (SCN), the master circadian pacemaker. Next we determined whether the SD effects depended on time-of-day. qPCR data were obtained for SDs starting at ZT0 (= light onset), -6, -12, or -18. The SD-induced changes in Per2 mRNA expression importantly depended on the ongoing changes such that Per2 could even decrease when SD occurred during the falling limb of its baseline change. These unexpected dynamics were reliably predicted assuming that Per2 behaves according to a harmonic oscillator with wakefulness and corticosterone as driving forces.

Conclusion: Per2 mRNA levels are widely used as a state variable of the circadian clock. Our findings confirm a considerable cross-talk between these circadian and homeostatic process at the molecular level. As Per2 in the cerebral cortex responds to both sleep loss and time-of-day, this molecule is well positioned to keep track and anticipate homeostatic sleep need.

Funding: This work was supported by the Marie Curie Intra-European program (IEF-FP7-Project Number: 221254), the Novartis Foundation, the Swiss National Science Foundation (31003A-111974, -130825, and -108478), EUMODIC (Contract no.: 037188), and the University of Lausanne.

S89

Circadian and homeostatic regulation of sleep and electroencephalogram patterns in the rat

T. DE BOER
LUMC S-05-P, Leiden, NL

Objective: Sleep is regulated by circadian and homeostatic processes. The sleep homeostat keeps track of the duration of prior sleep and waking and determines the intensity of sleep. In mammals the homeostatic process is reflected by slow-wave activity (SWA; ~1–4 Hz) in the non-rapid eye-movement (NREM) sleep electroencephalogram (EEG). The circadian process is controlled by a pacemaker located in the suprachiasmatic nucleus of the hypothalamus and provides the sleep homeostat with a circadian framework. Many different experimental manipulations and sleep deprivation protocols have been applied in humans to investigate the interaction between the two processes. They show that in humans the period of consolidated waking during the light period of the day is a consequence of the interaction between an increasing homeostatic sleep drive and a circadian signal, which promotes waking during the day and sleep during the night. In particular, in humans a clear increase in REM sleep was found in the early morning, and a short period of increased waking was observed in the evening, shortly before habitual bedtime.

Results: In the rat we have shown that under constant homeostatic sleep pressure (constant SWA levels), in a nap protocol in constant dark conditions, still a small circadian modulation of the amount of NREM sleep and waking is observed. This modulation was the result of a circadian modulation of waking and NREM sleep episode duration. However, a significant circadian modulation in REM sleep was absent. Also a short period of increased waking was not found in the rat. Spectral analysis of EEG frequency activity showed clear frequency dependent circadian and homeostatic changes in the different vigilance states.

Conclusion: The data show that circadian and homeostatic changes in EEG frequencies, particular in NREM sleep, are similar between rats and humans. In contrast, the influence of the circadian clock on sleep-wake distribution is small in the rat, compared to humans. In the rat, the sleep homeostatic modulation, in phase with the circadian clock, seems to amplify the relatively weak clock induced circadian changes in NREM sleep and waking, and is probably the main cause of a circadian modulation in REM sleep in the rat.

This research was supported by the Netherlands Organization for Scientific Research (NWO) grant 818.02.016.

S90

Circadian and homeostatic modulation of cognition-related cerebral activity in humans

C. SCHMIDT[1], M. MAIRE[1], C. F. REICHERT[1], K. SCHEFFLER[2], M. KLARHOEFER[2], W. STROBEL[3], J. KREBS[1], P. BERTHOMIER[4], C. BERTHOMIER[4] and C. CAJOCHEN[1]
[1]Center for Chronobiology, Basel, CH, [2]Radiological Physics, Basel, CH, [3]Respiratory Medicine, Basel, CH, [4]Physip, Paris, FR

Brain mechanisms involved in the maintenance of wakefulness and associated cognitive processes are affected by inter-individual differences in sleep-wake regulation. For instance, different time-of-day and sleep-wake related modulations in cognition-associated cerebral activity are chronotype and PERIOD3 genotype dependent. However, the respective contributions of circadian and homeostatic processes on neurobehavioral performance and their cerebral correlates throughout the 24-h cycle remain largely unexplored. In a current project, we further investigate the impact of these processes on the cerebral correlates underlying human cognition in a 40-h multiple nap (NP) and sleep deprivation (SD) protocol.

Results: In this ongoing study we have observed that the circadian and sleep-wake homeostatic modulation in subjective sleepiness and objective vigilance undergoes considerable inter-individual differences. Electrophysiological data report the classical slow wave sleep rebound or decrease observed during the recovery night after the SD and NP conditions respectively. A preliminary analysis of the fMRI data, comparing task-related BOLD activity while performing the psychomotor vigilance task during the biological night (3 h before

scheduled wake up time) in the first 11 participants indicated that differential homeostatic sleep pressure levels (SD versus NP) exert an effect on task-related BOLD activity. Globally, cortical responses (e.g. inferior frontal, middle temporal, insula) are higher while performing intermediate reaction time levels on the PVT when sleep pressure is kept low by multiple naps. When looking at BOLD activity underlying optimal PVT performance, at the end of the biological night, the preliminary results indicate that hypothalamic responses as well as several cortical areas (e.g. bilateral insula) are more active under NP as compared to SD conditions. Whether the above mentioned inter-individual variations in neurobehavioral performance are paralleled by differences in cognition-related BOLD activity is currently being analysed.

Conclusion: Time of day and disproportional homeostatic sleep pressure affect neurobehavioral performance modulation, which is mirrored at the cerebral level. The existence of large inter-individual variability in the vulnerability to circadian and/or homeostatic related detrimental effects on neurobehavioral performance should be taken into account in future analyses.

This work was supported by the Swiss National Science Foundation # 310030_130689 to CC.

S91

Effects of time of day and sleep pressure on cortical excitability in bipolar depression as measured by TMS/EEG

S. CASAROTTO[1], P. CANALI[2], M. ROSANOVA[1], A. PIGORINI[1], A. G. CASALI[1], M. MARIOTTI[1], F. BENEDETTI[2] and M. MASSIMINI[1]
[1]University of Milan, Milan, IT, [2]Scientific Institute and University Vita-Salute San Raffaele, Milan, IT

Objectives: This study explores the relationship between sleep homeostasis and cortical excitability in bipolar depressed patients (BPD). Specifically, we test whether the increase of cortical excitability observed in control (CTR) subjects during wakefulness and after total sleep deprivation (TSD) could also be detected in BPD patients.

Methods: Six CTR subjects and 13 BPD patients were involved in this study. Each participant underwent a cycle of TSD, ancompassing about 40 h of continuous wakefulness, starting at 7:00 am and ending at 11:00 pm of the following day. Electroencephalographic (EEG) responses to transcranial magnetic stimulation (TMS) of the frontal cortex were recorded in all participants twice a day, at 9:00 am and 9:00 pm. Cortical excitability was measured as the amplitude of the early neuronal response of the stimulated cortical area and was compared among sessions using non-parametric statistical analysis.

Results: In CTR subjects cortical excitability progressively increased during the prolonged wakefulness period. BPD patients failed to show a significant increase of cortical excitability during the first day as well as at the end of the whole TSD period.

Conclusion: This study confirms the progressive increase of cortical excitability with time awake in CTR subjects and suggests the possibility that the relationship between sleep pressure and cortical excitability might be altered in BPD patients.

This work was supported by the Università degli Studi di Milano co-financed by Regione Lombardia within the project 'Dote Ricerca: FSE (Fondo Sociale Europeo)' (to S. Casarotto).

Symposium – Sleep and Cognition in Aging

S92

Impact of light on non-visual responses in young and older subjects

J. CARRIER[1], G. VANDEWALLE[1], V. DANEAUL[1], M. HÉBERT[2], J. DOYON[1], C. GRONFIER[3], H. M. COOPER[3] and M. DUMONT[4]
[1]University of Montreal, Montreal, CA,[2]Institut universitaire en santé mental de Québec, Québec, CA, [3]Stem Cell and Brain Research Institute, INSERM U846, Bron, FR, [4]Sacré-Cœur Hospital, Montreal, CA

Objective: Light, and especially blue light, has direct effects on circadian rhythms, vigilance levels, and many other non-visual functions. Many changes in the retina, circadian rhythms and sleep-wake regulation occur with aging and could be associated with age-related modifications in the effect of light on non-visual functions. We investigated the acute effect of blue monochromatic light exposure (480 nm), presented at low (7×10^{12} ph/cm^2/s), medium (3×10^{13} ph/cm^2/s), and high (10^{14} ph/cm^2/s) irradiance levels, on steady-state pupil light reflex (PLR) and non-visual cognitive brain activity as a function of age.

Methodology: Thirty subjects (16 young: 23 year; 14 older: 61 year) completed separate PLR and fMRI measures with undilated pupils. During fMRI acquisitions, subjects performed an auditory working memory 2-back task while alternatively exposed to darkness or short (45 s) monochromatic blue light pulses.

Results: Young subjects had larger pupils than older subjects, both in darkness ($P = 0.01$) and during light exposure ($P = 0.02$). Normalized steady-state PLR, however, revealed greater relative constriction with higher irradiances of blue light ($P < 0.01$), but without any significant effect of age. fMRI analyses revealed that blue light exposure induced higher brain activation in the amygdala, thalamus and cerebellum in young than in older subjects ($P_{corrected} < 0.05$). In addition, compared to older subjects, young subjects showed enhanced brain responses to increasing light irradiance in the prefrontal cortex, occipital cortex, and cerebellum ($P_{corrected} < 0.05$).

Conclusion: Despite a smaller pupil size, relative PLR does not seem to be affected by aging, while, in contrast, the impact of light on subcortical and cortical brain areas involved in the ongoing cognitive process differs between young and older individuals. These results support the notion that aging differentially affects distinct non-visual responses to light and, as suggested by animal studies, light sensitivity may differ between non-image forming functions.

Funding support: IRSC, CRSNG, FRSQ, Fonds France-Canada pour la recherche, Fonds échanges FRSQ/INSERM Rhône-Alpes Cluster HVN, Unadev, Retina France.

S93

Age and brain developmental factors that moderate the effect of sleep on cognition

E. VAN SOMEREN, R. ASTILL, J. BENJAMINS, F. MIGLIORATI, S. MOENS and K. DEKKER
Netherlands Institute for Neuroscience, Amsterdam, NL

Objectives: Many reports indicate that sleep supports cognitive performance. Error bars indicate that there are always some that profit most, and others that do not profit. An important question is what determines the extent to which someone's cognitive performance improves with sleep, or suffers from sleep deprivation. What are the characteristics of those that do, and do not, profit from sleep for example for overnight memory consolidation?

Methods: Does sensitivity to sleep restriction change across lifespan? A developmental approach may help to unravel brain mechanisms involved in individual differences.

Results: A recently published meta-analysis (Astill et al, Psychol Bull 2012, 138:doi: 10.1037/a0028204) on the association between sleep duration and cognitive performance in children shows marked differences as compared to studies on adults. In children, sleep duration shows no significant association with sustained attention and memory, allegedly the cognitive domains that are most sensitive to sleep restriction in adult.

Conclusion: The findings will be discussed from the perspective that certain brain networks need to be functional in order to be able to profit from sleep. The presentation will conclude with a demonstration of a novel approach to assess data on factors that modulate the importance of sleep for cognitive functioning by means of the internet survey and task assessment platform 'The Sleep Registry'. This approach allows for larger samples and thus a more powerful approach to determinants of individual differences in sensitivity to sleep restriction, including aging and comorbidity.

S94

The somatotrophic axis in older adults; growth hormones, cognition and sleep

M. V. VITIELLO
University of Washington, Seattle, US

Many of the body's systems that function to maintain optimal health and well being decline with advancing age. Aerobic capacity, muscle mass and strength all progressively diminish. Significant sleep disturbances increase and are associated with increases in morbidity and mortality. Cognition declines, impacting an older individual's ability to function independently. Interventions that could possibly improve, or at least stabilize, functional capacity, sleep quality and cognitive function have the theoretical potential to prolong an older individual's ability to live independently. One such intervention may be stimulation of the 'somatotrophic' axis via growth hormone-releasing hormone (GHRH). We review the evidence for such somatotrophic interventions including our ongoing work examining GHRH treatment on the somatotrophic hormones, body composition, functional status, sleep and cognitive function of healthy older men and women as well as those suffering from mild cognitive impairment.

S95

Pre-sleep cognitive training improves sleep stability, continuity and organization in healthy elderly subjects

G. FICCA, G. CAROBBI, F. CONTE and B. M. ERRICO
University of Naples II, Caserta, IT

Several studies have consistently shown that pre-sleep learning is associated to changes of sleep structure. Whereas previous research has mainly focused on sleep states, namely REM and NREM amount, very little attention has been paid to the hypothesis that pre-sleep learning might improve sleep continuity, stability and cyclic organization, which are often impaired in aging.

Objective: The aim of this research was to assess, in a sample of 18 healthy elderly subjects, whether a memory task administered at

bedtime would determine changes in any sleep parameter, with special regard to sleep continuity, stability and organization.

Methods: Baseline sleep (BL), i.e. a normal sleep with 9-h Time in Bed (TIB), was compared to a Post-Training sleep (TR), with the same TIB but preceded by an intensive training session. For the latter, a verbal declarative task was used, consisting in learning paired-word lists, rehearsed and recalled for three times in a row. To control for individual learning abilities, subjects were administered several sets of lists with increasing difficulty, until they reached an error rate ≥20% at third recall.

Results: Relative to BL, TR shows a significant reduction in the frequency of brief awakenings, arousals, state transitions, 'functional uncertainty' (FU) periods, and in the percentage of time in FU over Total Sleep Time (TST). A significant increase in the number of complete cycles, total cycle time (TCT), and TCT/TST proportion was also found. All these changes are evenly distributed over the sleep episode. No sleep stage measure display significant changes, apart from a slight reduction in the percentage of Stage 1. Scores at retest are negatively correlated with both the frequency of arousals and of state transitions.

Conclusion: Our data suggest that pre-sleep learning can yield a beneficial re-organizing effect on elderlies' sleep quality. The inverse correlation between recall scores and the measures of sleep continuity and stability provides further support to the role of these features in memory processes.

Keynote Lecture

S96

About time and brain

P. MAQUET

C. H. U. Sart Tilman, Liège, BE

Translational neuroscience has always been considered as the difficult task that tries to integrate mechanisms across different levels of description. In particular for sleep, a behavior deemed conserved across species, it is perceived that its comprehensive understanding should ultimately imply a thorough knowledge of brain mechanisms at each and every spatial scale, from molecular mechanisms to first-person sleep perception or even public health issues. It appears that an equally daunting task consists in integrating knowledge of brain functions across time scales ranging from milliseconds to several months (seasons) or years (ageing). Several examples in which basic temporal organization of brain function is still fragmentary will be given in the context of sleep/wake regulation and memory consolidation during sleep.

Oral Session 1 – Epidemiology of Sleep and Sleep Disorders

O97

Sleep disorders in Australia: a nation-wide survey

L. LACK[1] and D. HILLMAN[2]
[1]*Flinders University, Adelaide, AU,* [2]*Sir Charles Gairdner Hospital, Perth, AU*

Objectives: Poor sleep has significant personal consequences as well as high societal and economic impact. It is important to have accurate estimates of these disorders in order to make appropriate health policy decisions. The present study is the first comprehensive survey of sleep habits, disorders, and daytime impairments conducted on a representative sample of the Australian population.

Methods: A professionally conducted nation wide telephone survey in 2010 used representative sampling from all states, gender and ages 14–70+ years. A total of 1512 responses was obtained. Frequency of sleeping and daytime problems were judged on a four point scale from 'rarely or never' to 'almost every night (day)' and was the same or similar rating scale to surveys in other Western countries.

Results: Frequent (at least a few times/week or more) sleep difficulties (initiating, maintaining and inadequate sleep) and daytime fatigue, sleepiness, and irritability were highly prevalent (20–35%) and generally more so in women. Older age groups (50+) reported more difficulty maintaining sleep, pauses in breathing during sleep, restless legs, and prescribed sleep medication. However, the older age groups also reported less difficulty initiating sleep, more refreshing sleep, less inadequate sleep, and fewer daytime impairments. More sleep was reported for weekends (7.37 h) than week nights (7.16 h) except in the 18–24 and the 65 + age groups. Total sleep declined with age to the 35–49 age group after which it showed a small increase.

Conclusions: Sleeping difficulties and daytime impairments in Australia are highly prevalent and at least comparable to that in European and North American countries. In this study it is the young to middle aged groups (18–50 years) that suffer the most from inadequate sleep. Although night time awakening is more common in the older age groups, they have more reported adequate sleep and better daytime functioning and, therefore, seem more likely to achieve their sleep need than the young to middle aged groups.

O98

Family situation and sleep in a representative sample of 400 women – a field study of polysomnography

T. ÅKERSTEDT[1], J. F. A. SCHWARZ[1], E. LINDBERG[2], G. KECKLUND[1] and J. THEORELL-HAGLOW[2]
[1]*Stockholm University, Stockholm, SE,* [2]*Uppsala University, Uppsala, SE*

Objectives: Being single, having children, working full time, sharing bedroom, having a snoring bedpartner is frequently assumed to impair sleep, but we know rather little about polysomnography in relation to these variables. The present study was focused on a representative sample of 400 women (with oversampling of snorers) having sleep recordings made at home in the midst of their day-to-day living.

Methods: Traditional PSG recordings were carried out in the home (Embla) and the participants were asked to maintain normal sleep behavior. The results for all standard PSG variables were analyzed using an ancova design, controlling for age and BMI (which were strong predictors of sleep impairment).

Results: The results showed that marriage status had a significant relation to wake after sleep onset (WASO) (for married/cohabiting, 79 min for singles and 79 min for divorced). Also sleep efficiency (SE) (86.5, 82.3, 82.0%) and number of full body position changes (35, 42, 46) had significant links. In particular, being married/cohabiting had more positive values.

Having children was associated less WASO than not having children (64 versus 80 min) in those who were married/cohabited or were divorced. Only a few children were seen among the singles. Too few small children were present and could not be analyzed.

Not sharing bedroom among those married or cohabiting was unusual (23% versus 27%) but significant differences were seen for total sleep time (TST) (355 min versus 394 min), SE (82.5 versus 86.7%), stage1% (13.6 versus 9.1). Complaining of a snoring husband (among those who shared bedroom) showed longer TST (405 versus 376 min) without complaints.

Labor market status (full time, parttime, student, retired) was related to better sleep for full time employed. WASO was higher in that group compared to parttime workers (59 versus 72 min) and for number of REM episodes (4.6 vs4.0). Sleep latency, SE, Stage1% and REM% also differed between groups: However, much of this was due to poorer values of the retired participants (but controlled for age and BMI).

Discussion and conclusions: The results were obtained from one home sleep recording and must be interpreted with caution. However, the impression is that having a partner is associated with better sleep than not having one, as is sharing bedroom, possibly having children and having fulltime work. Surprisingly, a snoring husband was only modestly reflected in PSG measures.

O99

Trajectories of sleep complaints from early mid-life to old age: longitudinal modelling study

P. SALO[1], J. VAHTERA[2], J. E. FERRIE[3], T. AKBARALY[3], M. GOLDBERG[4], M. ZINS[4], J. PENTTI[1], M. VIRTANEN[5], M. J. SHIPLEY[3], A. SINGH-MANOUX[3], Y. DAUVILLIERS[6] and M. KIVIMÄKI[3]
[1]*Finnish Institute of Occupational Health, Turku, FI,* [2]*University of Turku, Turku, FI,* [3]*University College London, London, UK,* [4]*French National Institute of Health and Medical Research, Paris, FR,* [5]*Finnish Institute of Occupational Health, Helsinki, FI,* [6]*French National Institute of Health and Medical Research, Montpellier, FR*

Objectives: To estimate trajectories of sleep lost over worry as a function of age, using longitudinal modeling, and compare these trajectories with those for insomnia symptoms.

Methods: We used data from two prospective, occupational cohorts (the Whitehall II and Finnish Public Sector studies) comprising 84 384 observations from 4–8 repeat measurements in 1985–2010. Participants included 16 408 men and women aged 34–79. Age-related trajectories of sleep lost over worry and insomnia symptoms (sleep initiation or maintenance problems, non-refreshing sleep) were estimated using repeated-measures log-binomial regression analysis

and generalized estimating equations. These analyses were adjusted for year of birth and time of measurement to minimize confounding by cohort or period effects.

Results: The prevalence ratio for insomnia symptoms for every 10-year increase in age was 1.48 (95% confidence interval 1.42–1.55) in men and 1.37 (1.33–1.40) in women. In contrast, the age-related trajectory of sleep lost over worry included two phases: a period of high prevalence of sleep complaints at ages 34–55 followed by a declining trajectory at older ages. Compared to participants aged 34–55, prevalence ratios for sleep lost over worry were 0.82 (0.76–0.89) and 0.59 (0.49–0.70) in the Whitehall II study participants aged 56–60 and 71–79 years. Corresponding figures were 0.96 (0.90–1.02) and 0.49 (0.37–0.66) in the Finnish Public Sector study.

Conclusion: Our study shows a general age-related decrease in sleep lost over worry between late mid-life and old-age, a pattern strikingly different from the monotonic age-related increase in insomnia symptoms.

O100

Association between short total sleep time and hypertension – the Skara Sleep Cohort

D. ZOU[1], D. N. EDER[1], D. ESKANDARI[1], L. GROTE[1], K. BENGTSSON-BOSTRÖM[2], U. LINDBLAD[3] and J. HEDNER[1]
[1]Sahlgrenska University Hospital, Gothenburg, SE, [2]R&D Center Skaraborg Primary Care, Skövde, SE, [3]Skaraborg Institute, Skövde, SE

Objectives: Apnea hypopnea index (AHI) is used to study the association between obstructive sleep apnea (OSA) and hypertension, but the independent contributions of total sleep time (TST) and apnea/hypopnea event count to hypertension have not been previously investigated. We studied the relationship between polysomnographically assessed TST and hypertension in a gender-balanced community-dwelling cohort of hypertensive patients and normotensive controls (Skara Sleep Cohort).

Methods: Participants (n = 344, males 173, age 61.2 ± 6.5 years, body mass index 28.6 ± 4.8 kg/m^2) underwent ambulatory home polysomnography. Hypertension was defined according to contemporary Swedish national guidelines. A multivariate logistic regression model was used to predict hypertension status from TST and apnea/hypopnea count (total events/night) adjusting for gender, age and body mass index.

Results: OSA was highly prevalent in this population (AHI 26 ± 24 events/h). Hypertension patients had shorter TST compared with normotensives (353 ± 81 versus 389 ± 65 min, $P \leq 0.001$) while total apnea/hypopnea count did not differ (167 ± 138 versus 146 ± 148 events/night, $P = 0.2$). Multivariate logistic regression analysis revealed that TST and apnea/hypopnea count were independently associated with hypertension status [TST odds ratio 2.0 (1.2–3.3), 331 min versus 426 min (25 percentile versus 75 percentile), $P = 0.0015$; apnea/hypopnea count odds ratio 2.6 (1.2–5.8), 218 events versus 47 events (75 percentile versus 25 percentile), $P = 0.04$]. The type of antihypertensive treatment was not found to significantly influence TST.

Conclusion: Short sleep time assessed by polysomnography was associated with hypertension in this community-dwelling population. Short sleep and presence of sleep apnea appear to independently link to hypertension.

O101

Pulse wave amplitude drops during sleep are associated with increased glucose level and higher blood pressure in the general population

J. MEYRAT DIAKHATE[1], J. HABA-RUBIO[1], D. ANDRIES[1], N. TOBBACK[1], M. TAFTI[1], J.-W. FITTING[2] and R. HEINZER[1]
[1]Center fo investigation and research in sleep, Lausanne, CH, [2]Pulmonary Department, Lausanne, CH

Objectives: Pulse wave amplitude (PWA) variations derived from the digital pulse oximetry signal have been shown to reflect sympathetic activations during sleep. We assessed the relationship between nocturnal PWA drops during sleep, blood pressure (BP), glucose and insulin levels.

Methods: One thousand two hundred and ninety-three subjects (48.1% women, 51.6 ± 7.6 years old, BMI 25.3 ± 4.2 kg/m^2) participating in an ongoing population-based sleep cohort study (HypnoLaus, Lausanne, Switzerland) underwent complete polysomnographic recordings at home. The PWA drops index (PDI), defined as the number of PWA drops per hour of sleep, and the PWA drops duration (PDD) were determined using Somnologica software. All subjects had an extensive clinical workup including blood pressure measurements, as well as fasting glucose and insulin level measurements. Type 2 diabetes was defined as a fasting glucose level ≥7.0 mM or the use of an antidiabetic treatment.

Results: Mean (±SD) PDD was 14.5 ± 2.8 s. Mean PDI was 41.0 ± 16.0/h. Mean apnea hypopnea index (AHI) was 7.1 ± 11.2. Mean fasting glucose level was 5.7 ± 08 mM. PDD was significantly correlated with systolic blood pressure (r = 0.21, $P = 0.0001$), diastolic blood pressure (r = 0.18, $P < 0.0001$), fasting glucose level (r = 0.18, $P < 0.0001$), and insulin level (r = 0.15, $P < 0.0001$). PDI was significantly correlated with sleep disruption indexes such as AHI (r = 0.29, $P < 0.0001$), arousal index (r = 0.26, $P < 0.0001$), low sleep efficiency (r = -0.25, $P < 0.0001$) and the% of wake time after sleep onset (r = 0.23, $P < 0.001$). Subjects who had a PDD >14.5 s had a higher systolic (difference = 5.6 mmHg, $P < 0.0001$) and diastolic (difference = 3.4 mmHg, $P < 0.0001$) blood pressure levels, a higher insulin level (difference 0.9 U/l, $P = 0.007$) and a higher type 2 diabetes prevalence (4.4% versus 2.1%, $P = 0.03$).

Conclusion: In HypnoLaus population-based study, PDD is associated with a higher glucose, insuline and blood pressure levels, whereas PDI is associated with sleep disruption indexes such as AHI, arousal index and sleep efficiency.

O102

Cardiovascular risk prediction by assessment of autonomic state during sleep – a multicentre evaluation

D. SOMMERMEYER, D. ZOU, D. N. EDER, J. HEDNER, J. FICKER, W. RANDERATH, T. PENZEL, B. SANNER and L. GROTE on behalf of the ASIC study group

Introduction: A combined analysis of continuous physiological signals measured by pulse oximetry during sleep has been proposed as a novel method to assess cardiovascular (CV) risk. The autonomic state indicator (ASI) algorithm which extracts information from a photoplethysmographic pulse wave signal for computation of a CV risk index has been extended and evaluated.

Methods: Subjects (n = 520, 346 male, age 55.0 ± 13.4 years, BMI 29.9 ± 6.1 kg/m^2) referred to five different sleep centers for a sleep diagnostic test were studied. The occurrence of CV risk factors was assessed and subjects were classified using the ESC/ESH risk matrix into five separate risk classes. Peripheral pulse wave was

measured by overnight digital photoplethysmography. The ASI algorithm extracted patterns of the peripheral pulse wave and SpO2 signal by amplitude and time/frequency analysis. The previously developed ASI algorithm was extended and optimized by adding four new parameters (irregular pulse, reduced chronotropic reaction to desaturations, duration of periodic symmetric desaturations and time below 90% SpO2) for the determination of the final ASI score (range 0–1).

Results: On the validation data set (n = 390) the developed algorithm detected high risk patients, defined as ESC/ESH risk classes 4 and 5, with a positive predictive value (PPV) of 81% and a negative predictive value (NPV) of 68%. Positive likelihood ratio (LR) was 2.9, negative LR of 0.3, respectively.

Univariate logistic regression showed significant effects for each derived pulse wave parameter. Multiple logistic regression analysis provided a reduced model of four parameters (pulse index, time below 90% SpO2, SpO2 index and pulse propagation time) which showed a C-index predictive accuracy of 0.81 with 4 degrees of freedom.

Conclusions: The ASI technique appears to provide a possibility to recognize subjects with increased CV risk based on recording of physiological signals. Interestingly, the sleep period appears to be a particularly useful window for assessment. This technique – based on a modified pulse oximeter – may be useful in both sleep and cardiovascular medicine.

The study was supported by Weinmann GMBH, the Swedish Heart and Lung Foundation and the University of Gothenburg.

O103

Obstructive sleep apnoea – prevalence, co-morbitities and familiarity – a nation-wide epidemiological survey – The Icelandic Sleep Apnea Cohort

T. GISLASON[1], H. HELGADOTTIR[2], K. KRISTJANSSON[1], B. BENEDIKTSDOTTIR[1], I. JONSDOTTIR[2] and A. PACK[3]
[1]Landspitali, Reykjavik, IS, [2]DeCODE, Reykjavik, IS, [3]Center for Sleep, Philadelphia, US

Objectives: Obstructive sleep apnea (OSA) has been widely recognized during the last three decades, and is reported to affect a substantial number of the middle-aged population often accompanied by systemic hypertension, cardiovascular diseases and diabetes. We are able to report nationwide data on prevalence, comorbitities and familiarity of OSA among Icelanders.

Material and methods: Among all Icelanders (total population 320 000) ever diagnosed with clinically significant OSA from 1987 until December 2011 there where altogether 7788 patients; 5551 males and 2237 females. In December 2011 6677 were alive and 2790 currently CPAP treated. Data has been systematically reviewed among 3621 OSA patients who participated in a genetic study from 2003 to 2009.

Results: In December 2011, alive OSA patients (N = 6677) constituted 6.2% of the middle- aged (40–70 years) male population and 2.6% of the female population. In this age group 3.0% of males and 1.0% of all Icelandic females were current CPAP users. OSA severity data was available for 3206 OSA patients who had signed an informed consent. Of them, 59% had systemic hypertension and were on anti-hypertensive medications and 14.4% had type two diabetes. 36.1% had a history of myocardial infarction and/or a heart failure, 10.8% had a history of CVL or TIA and11.6% atrial fibrillation the different comorbitities often coexist and altogether 70% of the OSA population suffers from at least one of the above mentioned comorbitities.

Relatedness was estimated among the OSA group using a computerized genealogy database. The estimated risk ratios for relatedness among first degree relatives of patients with OSA was 1.89 (1.74–1.93, 95% confidence interval) and 1.38 (1.27–1.39) for second-degree relatives. The relative risk was higher for obese OSA patients and those with comorbitities, but is still significantly increased for non-obese OSA patients and those with and without comorbitities.

Conclusions: Nationwide Icelandic data show that clinically significant OSA is even more prevalent than previously reported. Comorbitities are common and very often coexists. There is an increased relatedness among OSA patients that is not only contributed by obesity and co morbidity.

O104

U-shape associations of sleep hours with physical and mental functioning of Japanese civil servants: roles of work, family and behavioural characteristics

M. SEKINE and T. TATSUSE
University of Toyama, Toyama, JP

Objectives: In general, there are U-shape associations of sleep hours with physical and mental health. However, little is known about the underlying mechanisms for the U-shape associations. This study aims to evaluate (i) whether work, family, and behavioural characteristics differ among those with different sleep hours and (ii) whether work, family and behavioural characteristics contribute to the commonly observed U-shape associations of sleep with health.

Methods: The subjects were 3510 employees (2371 men and 1139 women), aged 20–65, working in local government in Japan. Participants completed a self-administered questionnaire that asked about work (e.g. grades of employment, job strain and work hours), family (e.g. family structure and work-family conflicts), and behavioural characteristics. Poor sleep quality and physical and mental functioning was evaluated using the Pittsburgh Sleep Quality Index (PSQI) and the physical and mental component summary (the PCS and the MCS) scale of Short-Form 36 (SF-36).

Results: Known risk factors for poor health such as low employment grade, high demand, long work hours, and high work-family conflict tended to be accumulated among short sleepers. Long sleepers also had some problems such as low support and longstanding illness. The lowest prevalence of poor sleep and physical and mental functioning was observed for those taking around 8 h of sleep. While short sleepers had poor sleep quality due to poor subjective sleep quality and daytime dysfunction, long sleepers had poor sleep due to long sleep latency, poor sleep efficiency and sleep disturbances. The U-shape associations of sleep hours with poor health reduced considerably by making adjustment for various factors, and work and family factors have contributed more to the reduction than lifestyle factors and longstanding illness.

Conclusion: The generally observed U-shape associations of sleep hours with health may be, in part, explained by U-shape associations of sleep hours with disadvantaged work, family, and behavioural characteristics.

O105

Clinical and polysomnographic predictors of the natural history of excessive daytime sleepiness in the general population

J. FERNANDEZ-MENDOZA, A. VGONTZAS, I. KRITIKOU, S. CALHOUN, S. PEJOVIC, D. LIAO and E. BIXLER
Penn State College of Medicine, Hershey, US

Objective: To examine the clinical and polysomnographic risk factors associated with the incidence, persistence, and remission of excessive daytime sleepiness (EDS).

Methods: From a random, general population sample of 1741 adults of the Penn State Cohort, 1395 were followed-up after 7.5 years. All subjects underwent polysomnography at baseline and sleep apnea was defined as an apnea/hypopnea index ≥15. Self-reported EDS was defined as moderate-to-severe daytime drowsiness/sleepiness and/or irresistible sleep attacks.

Results: The incidence rate of EDS was 8.2%. Multivariate regression models showed that the most significant risk factors for incident EDS were depression (OR = 3.51; $P = 0.0001$), age <40 (OR = 2.47; $P = 0.001$), non-Caucasian race (OR = 2.42; $P = 0.009$), male gender (OR = 2.14; $P = 0.001$), obesity (OR = 1.90; $P = 0.009$), and age >60 (OR = 1.60; $P = 0.082$). In a backward stepwise model that included hypertension and sleep apnea, obesity (OR = 1.85; $P = 0.006$) and diabetes (OR = 1.60; $P = 0.083$) were the strongest cardiometabolic risk factors for incident EDS. Neither subjective nor objective short sleep duration predicted incident EDS; in fact, the longer the objective sleep duration the higher the risk of incident EDS (OR = 1.3; $P = 0.014$), even after controlling for confounders. Persistence and remission rates of EDS were 38% and 62%, respectively. A multivariate regression model showed that weight gain (OR = 1.2 for each 1-unit increase in BMI; $P = 0.008$) was the main risk factor for the persistence EDS. Incident and persistent EDS cases gained significantly more weight (2.5 BMI units) as compared to those who did not develop EDS (1.3 BMI units) and those who remitted from EDS (0.4 BMI units). In fact, 21.2% of remitted EDS cases and only 9.5% of persistent EDS cases lost weight over time (i.e., ≤ -1 BMI-units).

Conclusions: This study shows for the first time that depression, obesity, and weight gain are the strongest risk factors for incident EDS. Furthermore, this study shows that weight gain is also a predictor of the persistence of EDS and that weight loss is associated with its remission. These results suggest that the 'epidemic' of sleepiness parallels the 'epidemic' of obesity and that weight loss should be our priority in terms of early intervention.

O106

Sleep complaints and cognitive decline in community-dwelling elderly: an 8-year prospective study

I. JAUSSENT[1], J. BOUYER[2], M. ANCELIN[1], C. BERR[1], A. FOUBERT-SAMIER[3], K. RITCHIE[1], M. OHAYON[4], A. BESSET[1] and Y. DAUVILLIERS[1]
[1]INSERM, Montpellier, FR, [2]INSERM, Villejuif, FR, [3]INSERM, Bordeaux, FR, [4]Stanford University, Stanford, US

Objectives: To examine the association of insomnia complaints, excessive daytime sleepiness (EDS) and medication reported at baseline with cognitive decline during 8-year follow-up in a community-based sample of subjects aged 65 years and over.

Methods: Analyses were carried out on 4894 non-demented subjects recruited from 3 French cities and having a Mini Mental Status Examination (MMSE) score ≥24 points at baseline. Subjects were defined as cognitive decliners if they had a 4-point reduction in MMSE score during follow-up at 2, 4 and 8-years. Insomnia symptoms (poor sleep quality, difficulty in initiating sleep, difficulty in maintaining sleep, and early morning awakening) and EDS were self-rated at baseline and detailed information on medication use was also gathered. Logistic regression models were adjusted for sociodemographic, behavioural, physical and mental health variables, and APOE genotype.

Results: EDS independently increased the risk of cognitive decline (OR = 1.26, 95% CI = 1.02–1.56), especially for decliners having developed dementia during the follow-up (OR = 1.39 95% CI = 1.00–1.97). The number of insomnia complaints and difficulty in maintaining sleep were negatively associated with MMSE cognitive decline (OR = 0.77 95% CI = 0.60–0.98 for 3–4 complaints, OR = 0.81 95% CI = 0.68–0.96, respectively). The three others components of insomnia were not significantly associated with MMSE cognitive decline.

Conclusion: Our results suggest that EDS is associated independently with the risk of cognitive decline in the elderly population. Such results could have important public health implications since EDS may be an early marker and potentially reversible risk factor of cognitive decline and onset of dementia.

Oral Session 2 – Psychiatric and Behavioural Aspects of Sleep and Sleep Disorders

O119

Sleep changes under condition of chronic stress

I. RUSAKOVA[1], S. I. POSOHOV[2], S. S. POSOHOV[2] and G. KOVROV[2]

[1]Severtsov Institute Ecology/Evolution Russian Academy of Sciences, Moscow, RU, [2]Sechenov First Moscow Medical State University, Moscow, RU

Objectives: Stress is a factor, which should be taking into account as cause of sleep disturbances and insomnia. So far, there are only a few experimental data about sleep quality under chronic stress.

Methods: This experiment is a part of the project 'Mars-105'. Six healthy males were isolated in the model of spaceship for 105 days. Their sleep was studied by questionnaires (sleep dairy every 6 days) and standard polysomnography. Two consecutive nights sleep recordings were performed before, 2 weeks and 3 months after onset of the experiment. Then they were scored according to standard criteria of the American Association of Sleep Medicine. Fisher's combined probability test was used to analyze time evolution of sleep changes.

Results: Sleep diary shows that the 'astronauts' went to bed late (in average 1:15 a.m.), had prolonged subjective sleep latency (≥20 min) and long night awakenings (≥30 min). They had daytime sleepiness (more than a half of cases) and naps 2–3 times a week. Polysomnographic recordings confirm problems to fall asleep (sleep latency ≥20 min in 20% of all recordings) and long night awakenings (≥30 min in 24%).

Analysis of time progress of these insomnia-like changes by subjective and objective data was performed. Amount of the 'pathologic' recordings was statistically significant increased at the end of third month of isolation in comparison with background data ($P < 0.05$) and polysomnographies during second week of isolation ($P < 0.05$). In opposite, subjective quality of sleep elevated from onset to end of the experiment.

Conclusions: Longterm isolation led to insomnia-like changes in healthy men. This confirms that chronic stress may be a cause of sleep disorders. In contrary to insomniac patients, who usually overestimate their sleep problems, our 'astronauts' showed less progress of subjective complains compare with polysomnographic data. This may be possible mechanism prevented development of insomnia in healthy persons.

This study was supported by the Russian Humanities Scientific Foundation (Project 11-06-01052a).

O120

Gender differences in sleep and activity in patients with schizophrenia and healthy controls

A. WICHNIAK[1], A. WIERZBICKA[1], K. S. JANKOWSKI[2], E. WALINIOWSKA[1], K. CZASAK[1], I. MUSINSKA[1], A. SEK[1], T. JAKUBCZYK[1], W. JERNAJCZYK[1] and M. JAREMA[1]

[1]Institute of Psychiatry and Neurology, Warsaw, PL, [2]University of Warsaw, Warsaw, PL

Objectives: Low daily activity and sleep disturbances are frequent clinical problems in patients with schizophrenia. The aim of the present study was to assess sleep, activity and daytime sleepiness in patients with schizophrenia taking into regard sex and the kind of antipsychotic treatment.

Methods: Ninety seven patients with paranoid schizophrenia (54 males, mean age 27.3 ± 6.9) and 40 healthy controls (HC) (20 males, mean age 28.6 ± 7.4) were assessed during seven consecutive days with the use of wrist actigraphy (Cambridge Neurotechnology AW4), sleep diaries, Epworth Sleepiness Scale (ESS) and Athens Insomnia Scale (AIS). Patients were treated (monotherapy) with the following antipsychotics: aripiprazole (ARI) $N = 20$, olanzapine (OLA) $N = 40$, risperidone (RIS) $N = 20$, sertindole (SER) $N = 17$. Two-way ANOVA was used to test differences between patients with various treatments and HC, and between sexes.

Results: Patients, as compared to HC, had longer time in bed (TIB), sleep period and total sleep time ($P < 0.001$). Moreover, sleep period and total sleep time were longer in OLA and RIS groups as compared to ARI group ($P < 0.05$) and sleep time was longer in RIS group than in SER group ($P < 0.01$).Females exhibited greater 24 h-Acitivity than males, but only in HC group ($P < 0.001$). Among patients no sex differences appeared according to 24 h-Acitivity. Female HC exhibited greater 24 h-Acitivity than patients from each treatment group ($P < 0.001$), while males' 24 h-Acitivity was greater in HC than in RIS and SER groups. Patients with various treatments did not differ in 24 h-activity, both in females and males. Patients treated with ARI had lower total score in ESS than patients treated with other antipsychotics and HC ($P < 0.05$) and females obtained greater ESS scores than males ($P < 0.05$).

Conclusion: Patients with schizophrenia had longer rest periods and lower 24 h-activity than healthy controls. The low activity of schizophrenia patients was not related to their gender. It was also not strongly influenced by the kind of antipsychotic treatment e.g. its sedative effects.

O121

Sleep-wake patterns as reported by parents in children with ADHD compared to matched controls

A. ALLEN GOMES[1], C. PARCHÃO[1], A. ALMEIDA[1], V. CLEMENTE[2] and M. H. AZEVEDO[3]

[1]University of Aveiro, Aveiro, PT, [2]Coimbra Hospital Centre, Coimbra, PT, [3]University of Coimbra, Coimbra, PT

Objective: This study aimed to compare sleep, as reported by parents, (i) in ADHD versus in community children, and (ii) in medicated versus non medicated ADHD children.

Methods: Parents filled out a previously validated questionnaire about sleep-wake patterns (adapt. from Clemente et al., 1997, published by Bos et al., 2009). Thirty children (83.3% male), 5–13 years old, with a diagnosis of ADHD according to their pedopsychiatrists, took part of the study. This clinical sample was obtained at the Department of Children and Adolescents Mental Health, Magalhães Lemos Hospital, Oporto Hospital Centre, Portugal. A group of 30 children matched for sex, age and school year, were selected from a large community sample.

Results: Several statistically significant differences ($P < 0.05$) emerged between the clinical sample and the community matched sample: ADHD children showed later bedtimes, stronger bedtime resistance, and longer sleep latency; they fell asleep into parents

bed, and needed something special to fall asleep, more often; obtained shorter sleep on school nights (1 h less per night, in median); had more frequent symptoms of nightmares, sleep talking, fear from darkness, and, most notably, loud snoring, 26.7% (as defined by Ferreira et al., 2000); and showed higher daytime somnolence. Comparing ADHD children taking metilphenidate ($n = 13$) versus not taking medication ($n = 17$), the former tended to present later bedtimes ($P \sim 0.05$) and higher bedtime resistance ($P < 0.05$), tended to show more nightmares ($P < 0.10$), but appeared to return to sleep autonomously more easily.

Conclusion: Our results are in line with previous findings in children with a diagnosis of ADHD, and indicate that these children may have more sleep problems than typical development children. Alternatively, these results may reflect misdiagnose situations, thus, special attention should be directed to the differential diagnosis between sleep disturbances and ADHD. These results have important implications for ADHD diagnose and therapeutics in children.

O122

The relationship of sleep duration with suicide idea in depressed individuals

Y. J. LEE[1], W. J. LIM[2] and S. J. KIM[3]

[1]Gachon Medical School Gil Hospital, Incheon, KR, [2]Ewha Woman's University Hospital, Seoul, KR [3]Seoul National University College of Medicine, Seoul, KR

Introduction: There has been an increasing interest in the relationship between sleep and suicidality in depression. In addition, suicidal patients habitually report problems with their sleep. Although sleep-related complaints and electroencephalographic changes are generally encountered in psychiatric disorders, sleep complaints, such as insomnia, hypersomnia and nightmares, are more common in suicidal patients. In current study, we aimed at investigating the relationship between sleep duration and suicidality in depressed subjects.

Methods: One thousand general population (male: 500, female: 500, mean 39.6 ± 11.6 years, ranged 20–77 years) completed CES-D (Center for Epidemiologic Study-Depression), BSI (Beck Suicide Intent scale), STAIX (Spielberger State-Trait Anger Expression Inventory), BIS (Barratt Impulsiveness Scale and brief questionnaire of sleep habits.

Results: After controlling for age and gender, there was no significant association between sleep duration and the score of CES-D on partial correlation analysis. Score of BSI showed no significant correlation with sleep duration either. However, regression analysis (dependent variable: BSI score, independent variable: age, gender, sleep duration, STAIX and BIS) revealed that short (<5 h) or long (>10 h) sleep duration and score of STAIX were related to higher score of BSI significantly in depressed subjects with 16 or higher score of CES-D ($P < 0.001$ and $P = 0.002$ respectively).

Conclusion: Current result suggested that short sleep (<5 h) or long sleep (>10 h) might be related to suicidality in depressed people.

O123

Sleep and sleep-wake patterns of adolescents with bipolar disorder, borderline personality disorder and without mental disorder: an actigraphy study

C. HUYNH, J. GUILÉ, J. J. BRETON and R. GODBOUT

Hôpital Rivière-des-Prairies, Montréal, CA

Sleep-wake cycle disruptions are frequently reported by adults with Bipolar Disorder (BD) during euthymia. In many cases, changes in the sleep duration precede a manic episode. Studies in adults with Borderline Personality Disorder (BPD) also report disturbances in sleep duration and architecture. Fewer studies have investigated the sleep-wake cycle in BD or BPD adolescents, and the clinical picture is made more complex by the fact that typical adolescence is marked by a phase delay of the sleep-wake cycle influenced by chronobiological as well as environmental factors. To better understand what belongs to this age period and what is associated with psychopathology we explored the sleep-wake cycle of adolescents with BD or BPD using actigraphy during periods with and without entrainment by school/work schedules.

Method: Adolescents (12–17 years old) were classified in three groups: euthymic BPD (15 girls, three boys), euthymic BD (four girls, two boys), and no mental health problems (seven girls, one boy). One boy from the healthy group was excluded because of aberrant data. Sleep-wake patterns were assessed using wrist actigraphy during at least nine consecutive days, including two weekends. A sleep diary helped determining the sleep-wake schedule. Kruskal-Willis ANOVA tests were used to compare the three groups, followed by *post-hoc* Mann–Whitney *U* tests on significant variables. The significance level was fixed at 0.05.

Results: During school/work days, compared to the BD group and the healthy controls, BPD adolescents spent more time awake (BPD: 21.3 ± 6.0% versus BD: 17.3 ± 6.6% versus controls: 15.6 ± 3.4%, $P = 0.03$) and slept less (BPD: 78.7 ± 5.9% versus BD: 82.9 ± 6.6% versus controls: 84.4 ± 3.4, $P = 0.03$) when they were in bed. On schedule-free days, euthymic BD adolescents had longer sleep latencies than healthy controls (23.3 ± 7.3 min versus 12.6 ± 7.2 min, $P = 0.02$) and BPD youths spent less time immobile in bed (76.4 ± 7.4% versus 81.0 ± 4.8%, $P = 0.02$) than healthy controls.

Conclusion: These results suggest that BPD adolescents present more sleep disturbances than euthymic BD youths: the sleep of BPD adolescents would be more specifically characterised by sleep maintenance problems regardless of entrainment schedules whereas BD adolescents would show a phase delay on schedule-free nights. These observations lead to treatment strategies adapted specifically to each clinical group. More studies on sleep in adolescents with BD and BPD are needed to assess the impact of poor sleep on clinical measures.

Supported by Fonds de la recherche en santé du Québec, Fondation Enfants Soleil, Fondation Dédé Fortin and Fondation Les petits trésors de l'Hôpital Rivière-des-Prairies.

O124

Sleep in the post-partum period in women at high and low risk for depression

R. ARMITAGE[1], H. BERTRAM[1], L. SWANSON[1], D. VAZQUEZ[1], S. MARCUS[1] and H. FLYNN[2]

[1]University of Michigan, Ann Arbor, MI, US, [2]Florida State University, Tallahassee, US

Introduction: Pregnancy and the post-partum period mark a significant increase in both sleep disturbance and risk for major depressive disorders (MDD). Women with a prior history of MDD are particularly vulnerable to developing post-partum depression. Recent studies have shown insomnia and fragmented sleep are strongly associated with maternal depression. The purpose of the present study was to evaluate actigraphy measures of sleep in the post-partum period in two groups of women: those at high and low risk of developing post-partum MDD, expecting that women at high risk for MDD would show more disturbed sleep throughout the first 6–8 months post-partum.

Methods: Twenty-three women participated in study, 8 with no history of depression and defined as low risk, and 15 in the high-risk category: eight women with a past history of MDD and seven women with current symptoms. Sleep was measured from light and motion-sensing actigraphs (AW2) and sleep diary for 1 week every month starting at 2 weeks post partum, and continuing until 30 weeks post partum. Depression symptoms were assessed by self-report using Beck II depression inventory (BDI-II).

Results: No sleep differences were evident between the groups with a past and current MDD and thus, the 15 women were combined into a single high-risk group. At 2 weeks post-partum, high-risk women showed longer sleep latency and higher sleep fragmentation than the low-risk women ($P < 0.02$) with differences persisting at 30 weeks ($P < 0.05$). At 2 weeks post-partum, high-risk women showed better sleep efficiency than low-risk women, an effect that reversed by 30 weeks ($P < 0.004$). Total sleep time did not differ between risk groups and did not show a significant change across the post-partum period. Sleep measures predicted BDI-II scores with the most disturbed sleep among those with the worst depression ($F = 3.1$; $R^2 = 0.41$; $P < 0.04$). Sleep latency was the best predictor of depression symptoms overall (P 0.007),accounting for more than 30% of the variance. Finally, those women with the highest BDI-II scores at Week 30 had the longest sleep latency and the shortest total sleep time ($P < 0.008$).

Conclusions: The results of this study indicate that women at high risk for post-partum depression have poor sleep throughout the post-partum period, compared to low-risk women. These findings identify the need for management strategies to reduce the sleep-related risks of post-partum period depression.

Research supported by: R21-MH65062, the Jack L. and Barbara A. Berman Depression Center Fund and the Cohen Family Fund.

O125

Sleep and the HPA axis; the effect on sleep of two doses of hydrocortisone administered as a bolus during the day in healthy volunteers

C. F. DURANT, S. J. WILSON, S. LIGHTMAN, D. J. NUTT, L. M. PATERSON, A. S. RICH and A. L. MALIZIA
University of Bristol, Bristol, UK

Manipulation of the hypothalamic-pituitary-adrenal (HPA) axis has significant effects on objective sleep measures; timing, dose and specific compounds can all alter the effect on sleep. There is evidence that targeting the HPA axis in depression may alter sleep and be of clinical benefit; bolus dosing with high dose steroids, have been investigated in patients with refractory depression and may allow these patients to respond to conventional antidepressants. Studies in healthy volunteers have focused on nocturnal manipulation of the HPA axis and its effects on sleep. This study was designed to investigate the effects of high dose hydrocortisone, given as a bolus during the day (as in clinical practice), on sleep in healthy volunteers, to help interpret a sleep study of patients with refractory depression.

Twelve healthy male volunteers completed a double blind, randomised three-way crossover study, receiving placebo (P) (saline), 0.7 mg/kg hydrocortisone (Low-L) and 7 mg/kg hydrocortisone (High-H) at approximately 3 pm on each study day, with an interval of at least 1 week. Home polysomnography was used to assess sleep that night. Subjective sleep ratings and saliva cortisol samples were also collected. Sleep analysis was performed blind to drug condition according to R&K criteria.

Significant dose-dependent reductions in total REM sleep (REM P: 113 min, L: 97 min, H: 61 min) and increases in REM onset latency (P: 77 min, L: 111 min, H: 132 min) were observed. A significant increase in slow wave sleep (SWS) was found after the high dose (P: 112 min, H: 131 min). After the low dose there was a significant increase in latency to persistent sleep and subjective reports of poor sleep. Salivary cortisol was significantly raised at bedtime after the high but not the low dose compared with placebo.

Suppression of REM sleep and increased SWS has been described in previous studies altering cortisol levels during the nocturnal period; we have shown a dose-related effect. We also found that effects on sleep can be observed after a time interval of 8–12 h after hydrocortisone injection. The increase in SWS may be secondary to effects on corticotropin releasing hormone (CRH) but may also reflect direct effects on sleep pathways. The mechanism of REM suppression though previously described is unclear. Our finding that the lower dose alone resulted in a longer sleep onset and reduced sleep quality is new and of interest in the consideration of feedback mechanisms.

O126

The relationship between sleep and memory in post-traumatic stress disorder

M. LIPINSKA[1], K. G. F. THOMAS[1], D. KAMINER[1], R. TIMOL[1] and M. GOUNDER[2]
[1]University of Cape Town, Cape Town, ZA, [2]Vincent Pallotti Hospital, Cape Town, ZA

Objectives: Previous research has shown that in healthy individuals sleep is critical to memory formation. Successful memory consolidation during sleep is contingent on slow-wave sleep (SWS), REM sleep and the successful transition of stages across the night. In posttraumatic stress disorder (PTSD), both sleep and memory processes are disrupted, but no previous study has examined whether these two variables are inter-related. This study aimed to determine whether disrupted sleep is a mechanism underlying declarative memory deficits in PTSD – investigating whether memory consolidation during sleep is disrupted in PTSD diagnosed individuals in comparison with controls.

Methods: Participants were recruited to one of four groups – PTSD ($n = 16$), trauma-exposed non-PTSD ($n = 15$), depression ($n = 15$) and healthy controls ($n = 14$). After screening, participants attended the Vincent Pallotti Hospital sleep laboratory for one night. Participants completed declarative and procedural memory tasks before and after an 8 h sleep period. Declarative memory performance was assessed using a story recall task. Procedural memory performance was measured using a computerised finger tapping task. Sleep variables such as total sleep time, sleep latency, number of awakenings, and REM and SWS percentage were measured using sleep adapted EEG.

Results: Results were analysed using one-way ANOVA, for sleep and memory variables, and regression analysis. PTSD participants retained significantly less information on a declarative memory task than healthy controls after sleep. Furthermore, disruptions in SWS predicted poor memory performance in at least one domain of declarative memory.

Conclusion: Overall results show some support for the disruption of declarative memory consolidation during sleep in PTSD, suggesting that disrupted sleep may have broader implications than just the inability to maintain and fall asleep.

O127

Sleepiness and driving performance in adults with attention deficit hyperactivity disorder

S. BIOULAC[1], A. CAPELLI[2], A. CLARET[2], M. GAUDUCHEAU[2], P. SAGASPE[2], J. TAILLARD[2], J.-P. RENERIC[1], M. BOUVARD[1] and P. PHILIP[2]

[1]CHS Charles Perrens, Bordeaux, FR, [2]USR CNRS 3413 SANPSY, Bordeaux, FR

Introduction: Attention Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder characterized by a triad of symptoms involving hyperactivity, impulsivity and inattention. Several studies in children with attention deficit hyperactivity disorder (ADHD) showed a high prevalence of excessive daytime sleepiness. To our knowledge, no study has objectively assessed sleepiness in adults with ADHD. Moreover, it has been shown that adults with ADHD were at risk for driving accidents. The objectives of this study are to quantify objective sleepiness and its impact on driving performance in adult with ADHD.

Methods: Twenty-four subjects with ADHD (age (mean ± SE) = 35.8 ± 1.9) and 10 control subjects [age (mean ± SE) = 32.6 ± 1.4] were included. Nocturnal polysomnography was performed to identify potential sleep disorder. The next day patients were submitted to a Maintenance Wakefulness Test (MWT) at 10H, 12H, 14H, 16H to examine their level of daytime sleepiness. After a training of 15 min, a driving test of 1 h was carried out at 17H on a simulator (Oktal) to evaluate driving performance.

Results: They were divided into three groups according to their level of sleepiness at the MWT: the 'sleepy' group consisted of fourteen subjects (mean sleep latency (SL) = 23.1 ± 1.4 min) and the 'alert' group included ten subjects (LE = 36.9 ± 1.3 min). The two patients groups differ significantly at the MWT ($F(1, 22) = 66.1$, $P < 0.001$). The 'control' group exhibited less inappropriate line crossings (20.8 ± 3.8) than the 'alert' group (48.2 ± 8.7) and the 'sleepy' group (51.2 ± 6.9) ($F(2, 40) = 5.16$, $P < 0.01$). Moreover, driving performance degrades over time for ADHD participants when it improves for control subjects ($F_{4,80} = 13.51$, $P = 0.0001$).

Conclusion: In our sample, half of the patients suffer of excessive daytime sleepiness, which deteriorates significantly their driving performance.

O128

Acute effects of agomelatine on sleep and awakening in major depression: controlled polysomnographic and psychometric studies

B. SALETU, P. ANDERER, M. SALETU, S. ROSALES-RODRIGUEZ and G. SALETU-ZYHLARZ

Medical University of Vienna, Vienna, AT

While most research efforts on agomelatine (Valdoxan®) (AGO) have concentrated on chronic antidepressant and sleep-promoting effects evaluated by subjective methods, the acute effect of the drug has not yet been studied in sleep laboratories. In this investigator-initiated trial, clinical, polysomnographic (PSG) and psychometric differences between 10 depressed patients and healthy controls and the acute effect of AGO 25 mg as compared with placebo were studied.

Methods: In a single-blind, placebo-controlled study 10 drug-free patients (41 ± 10 a) with nonorganic insomnia (ICD-10 F51.0, DSM IV-TR 307.42) associated with major depressive disorder spent three nights in the sleep laboratory (one adaptation and twi randomized treatment nights with placebo and AGO 25 mg, 1 h before lights-off). They were compared with 10 age- and sex-matched controls (42 ± 11 a). Evaluations included clinical, PSG and psychometric variables (Wilcoxon and *U*-Tests).

Results: Patients demonstrated a CGI of 4.7 ± 1.3, HAMD of 27.1 ± 4.7, SDS of 48.9 ± 11.0, SAS of 39.7 ± 10.4; PSQI of 15 ± 3.0, SSA of 46.8 ± 13.6, ESS of 4.6 ± 3.9 and QOL of 5.9 ± 1.3. PSG showed a significantly ($P < 0.05$) decreased sleep efficiency (73.1 versus 92.9% TIB), total sleep period (TSP) and total sleep time (TST), an increased frequency of awakenings, stage shifts/h TST and WASO, shortened S2 min and an increased number of PLM/TIB. Psychometry revealed deteriorated subjective sleep and awakening quality, morning well-being, drive and attention. As compared with placebo, AGO 25 mg significantly improved ($P < 0.05$) sleep efficiency (88.8 versus 73.1%TIB), TSP, TST, sleep latency and latency to 10 min of continuous sleep, lengthened S2 min and decreased the number of PLM /TIB, specifically the number of PLM during wake. However, the changes in psychometric measures did not reach the level of statistical significance.

Conclusion: This study again demonstrated a deterioration of objective and subjective sleep and awakening in patients with major depression, which was counteracted by single doses of 25 mg AGO, which improved objective sleep initiation, maintenance, sleep architecture and PLM in the sense of a key-lock principle. The fact that the acute efficacy of AGO could only be proved by objective PSG suggests the importance of drug evaluations on both an objective and a subjective level, with the objective therapeutic success being of great importance for drug acceptance and prognosis in the individual patient.

Bernd Saletu has received research support from Abiogen Pharma, Actelion, Astra Zeneca, Cephalon, GlaxoSmithKline, Sanofi Aventis, Schwarz Pharma, Servier and Takeda; has received honoraria (not exceeding US$ 10 000/year) for serving on scientific advisory boards for Nycomed, Servier, Takeda, UCB and Sanofi Aventis, for being a consultant for Merck and Xenoport and a speaker for Astra Zeneca, Cephalon, Ixico, Janssen and Lundbeck. He is a shareholder of The Siesta Group Schlafanalyse GmbH, Austria.

Oral Session 3 – Sleep restriction

O129

Sleep deprivation disrupts cognitive control: top-down but not bottom-up sequential effects in the Stroop task

W. GEVERS[1], G. DELIENS[1], S. HOFFMANN[1], W. NOTEBAERT[2] and P. PEIGNEUX[1]

[1]Université Libre de Bruxelles, Brussels, BE, [2]Ghent University, Ghent, BE

Objectives: Sleep deprivation [SD] markedly impacts prefrontal cortex, a brain area known as an essential component in executive functions [EF] and cognitive control. In the EF paradigmatic Stroop task, participants must name the ink colour of written colour words, eventually leading to interference [i.e. slowed response time (RT)] when meaning and ink colour are discrepant (e.g. 'green' printed in red as compared to 'green' printed in green). However, beside overall increased RT, prior studies failed to show SD-related changes in Stroop interference (e.g. Cain et al., 2011 Brain & Cognition). Here, we investigated this issue taking sequence effects into account. Indeed, it is known that congruency effects are weaker after incongruent than after congruent trials, a sequential modulation effect explained by top-down, increased cognitive control after the detection of conflict. Alternatively, bottom-up repetition effects of stimulus and response features have been proposed. Notebaert et al. (2006 Psychonomic Bulletin & Review) demonstrated that both bottom-up and top-down modulations operate in parallel but that top-down control needs time and cognitive resources to build up. We used this paradigm to investigate the influence the influence of SD on bottom-up and top-down processes in the Stroop task.

Methods: Thirteen healthy young volunteers (four males, mean age = 20.1 ± 1.8 years) were tested in a within-subject counterbalanced design after regular sleep (RS) or SD. The computerized Stroop task adapted from Notebaert et al. comprised congruent (C) and incongruent (I) stimuli, sequentially displayed in pseudo-random order in such a way that 33% of words and 33% of ink colours were the repetition of the previous stimulus.

Results: All analyses disclosed main Sleep (RTs SD>RS) and Stroop (RTs I>C) effects (all $P < 0.001$). However, analyses computed on complete and partial repetition trials (bottom-up) showed no Stroop effect at trials following incongruent items similarly in RS and SD conditions (interaction effect $P > 0.18$), whereas for complete alternation trials (top-down) the Stroop effect at trials following incongruent items decreased after RS but persisted after SD (interaction $P < 0.04$).

Conclusions: We demonstrate that SD impacts on top-down but not bottom-up modulations of congruency effects in the Stroop task, hence reflecting the inability of sleep-deprived subjects to raise cognitive resources needed for increased cognitive control after conflict detection.

GD is supported by FRS-FNRS, Belgium.

O130

Changes in sleep patterns and highway driving: comparative study between 1996 and 2011

M. A. QUERA SALVA[1], S. HARTLEY[1], F. BARBOT[1], V. LONDE[1], J. TAILLART[2] and P. PHILIP[2]

[1]APHP Hospital Raymond Poincaré, Garches, FR, [2]University of Bordeaux, Bordeaux, FR

Introduction: Sleepiness at the wheel is a major international public heath issue, as hypovigilance is an important factor contributing to the burden of traffic related morbidity and mortality. Studies have shown that night driving and sleep deprivation are key risk factors, and recent French road safety campaigns have focussed on the need for drivers to avoid starting trips at night and to have sufficient sleep.

Methods: This prospective observational study aimed to evaluate changes in sleep hygiene and drivers' behaviour. Data from 2011 was compared with a similar study in 1996. Both studies were performed in identical conditions.

Results: Three thousand five hundred and forty-nine drivers stopped by the highway patrol at motorway toll booths agreed to participate (85% of those stopped). 74.4% were male, mean age 46 ± 13 years. The proportion of drivers starting their trip between midnight and 6 a.m. was near two fold less in 2011 than in 1996. Mean driving distance was 337 ± 230 km in 2011 and 377 ± 294 km in 1996. There was a significant reduction of sleep debt during the 24 h before the travel in 2011 in comparison to 1996 (7 ± 108 min in 2011 versus 22.4 ± 121 min in 1996; t test, $P < 0.0001$). The linear regression analysis showed that duration of driving was not determinant of sleep debt in 2011 but was the most important factor in 1996. Both the 2011 and 1996 study found that one third of the population with a sleep debt superior to 3 h remain unaware that they have an important sleep debt.

Conclusion: The present study shows an improvement of driver's behaviour from 1996 to 2011. However one third of sleep-deprived drivers remain unaware of their sleep debt, implying that there are still drivers who remain resistant to road safety messages.

The authors have no conflicts of interestThe study was funded by a grant from Vinci Foundation. The funder had no role in study design, data collection and analysis, interpretation of data.

O131

Consistent increases of delta sleep in individuals exposed to chronic sleep restriction

J. AXELSSON[1], G. KECKLUND[2], T. ÅKERSTEDT[2] and M. INGRE[2]

[1]Karolinska Institute, Stockholm, SE, [2]Stockholm University, Stockholm, SE

Objective: There is still a debate whether chronic sleep restriction results in an allostatic or homeostatic responses of deep sleep. An animal study showed a striking allostatic response among rodents exposed to chronic sleep restriction (1), although we could later confirm that humans increase their deep sleep in a homeostatic manner (2). A possible explanation for the different findings could be large individual differences in the response to restricted sleep. Thus, we investigated whether the increase of delta sleep (in response to repeated sleep restriction) is consistent across individuals or whether some individuals fail to respond with an increase of delta power.

Methods: Nine healthy males (age range 23–28 years) went though a laboratory protocol including two baseline days (sleep 23–07 h)

and 5 days with sleep restriction (03–07 h). The first 3.8 h of NREM-sleep EEG was analysed with respect to spectral analysis. The first step included observation of raw data. However, since raw data are contaminated by measurement errors a model based approach was also used to produce empirical Bayes estimates of individual response patterns (in the 0.75–32 Hz band) to restricted sleep across 5 days with restricted sleep. A linear mixed effect model was used with (polynomial) fixed effects for days of sleep deprivation and frequency response profiles. The final model included 8 fixed and 8 random effects, the latter accounting for individual differences.

Results: The raw data indicate that sleep restriction resulted in increased delta sleep in 52 out of 54 sleep episodes occurring after restricted sleep. The empirical Bayes estimates suggested that all participants reacted with an increase of the delta band after 2 days of restricted sleep with continued increased delta sleep power until recovery (*P*'s < 0.01 for all fixed effects).

Conclusions: To conclude, the uniform increase of delta sleep amongst individuals supports the notion of a very robust and stable homeostatic response to restricted sleep.

References:

1) Kim et al., (2007) PNAS 104:10697–702.
2) Akerstedt et al., (2009) Sleep Feb 1;32 (2):217–22.

O132

Why sleep matters: individual differences in adolescents with low, medium, and high chronic sleep reduction

A. M. MEIJER, J. F. DEWALD, S. M. BÖGELS and F. J. OORT
University of Amsterdam, Amsterdam, NL

Objectives: This study aims to investigate individual differences concerning sleep and daytime functioning between adolescents with low (*N* = 187), medium (*N* = 577) and high chronic sleep reduction (*N* = 161). We examined sleep characteristics (sleep duration on school nights and weekend nights, daytime sleepiness, sleep quality), sleep disorders (insomnia, circadian rhythm sleep disorder), and daytime functioning, including psychological measures (depression, attention), school functioning (achievement motivation, teacher-child relationship, academic self-concept), and school performance.

Method: Nine hundred and twenty-five adolescents filled in online questionnaires (mean age = 14.68 years; 41.2% boys).

Results: With the exception of weekend sleep duration and school performance, the three groups differed significantly from each other on all outcome variables. Concerning school performance, the high chronic sleep reduction group showed significantly lower grades compared to both the medium and low chronic reduction groups. In the high chronic sleep reduction group prevalence rates of clinical insomnia, circadian rhythm sleep disorder, depression, and attention problems ranged from 14.89% to 73.13%.

Conclusion: This study highlights the impact of individual differences in chronic sleep reduction on adolescents' sleep and daytime functioning. The results demonstrate that psychological problems and sleep problems dramatically grow with an increase in chronic sleep reduction. Furthermore, prevalence rates of individuals scoring above the clinical cut-off were extremely high in the high chronic sleep reduction group, indicating the severity of chronic sleep reduction. Based on these results, programs aimed at reducing chronic sleep reduction in adolescents are highly warranted.

There are no conflicts of interest for each author.

O133

Gradual sleep extension in chronically sleep-reduced adolescents: an experimental study

J. F. DEWALD, F. J. OORT and A. M. MEIJER
University of Amsterdam, Amsterdam, NL

Objectives: To investigate the effects of gradual sleep extension in adolescents with chronic sleep reduction. Outcome variables were objectively measured sleep, sleep related problems (chronic sleep reduction, daytime sleepiness, insomnia, circadian rhythm sleep disorder (CRSD), sleep quality), and daytime functioning (depression, attention problems).

Method: Fifity-five adolescents with chronic sleep reduction (mean age: 15.44 years; 85.5% female) were randomly assigned to either an experimental group (gradual sleep extension) or a control group (no instruction). Sleep was monitored with actigraphy during 3 weeks, the first week was the baseline week, the last 2 weeks were the experimental weeks. Chronic sleep reduction, sleep quality, daytime sleepiness, insomnia, CRSD, depression, and attention problems were assessed during the baseline week (T1) and at the last day of the experiment (T2).

Results: At the end of the experiment adolescents in the experimental group had earlier bedtimes (beta = -0.66, $P \leq 0.001$), earlier sleep onsets (beta = -0.60, $P \leq 0.01$), and spent more time in bed (beta = 0.67, $P \leq 0.01$) than the control group. Furthermore, there was a trend towards longer total sleep times in the experimental group (beta = 0.44, $P = 0.06$). We found a significant decline in chronic sleep reduction (beta = -4.37, $P \leq 0.001$) and depression (beta = -2.22, $P \leq 0.01$), and a trend towards a significant reduction in CRSD symptoms (beta = -0.30, $P = 0.08$) and improved sleep quality (beta = 0.91, $P = 0.06$). However, we did not find changes with regard to daytime sleepiness, insomnia, and attention problems (all $P > 0.05$).

Conclusion: This study is the first experimental study examining the effect of gradual sleep extension on sleep and daytime functioning of adolescents with chronic sleep reduction. Based on the promising results it can be concluded that gradual sleep extension has beneficial effects on adolescents' sleep and daytime functioning. The proposed approach of this study may provide an attractive alternative to adaptation of school start times.

O134

Influence of age, circadian and homeostatic processes on inhibitory motor control: a go/no-go task study

P. SAGASPE[1], J. TAILLARD[1], H. AMIEVA[2], A. BECK[3], O. RASCOL[3], J.-F. DARTIGUES[2], A. CAPELLI[1] and P. PHILIP[1]
[1]CNRS USR 3413 SANPSY, Bordeaux, FR, [2]INSERM U897, Bordeaux, FR, [3]MEDES, Toulouse, FR

Introduction: Lower vulnerability with aging to extended wakefulness appears to be related more on an attenuation of the circadian rather than homeostatic pressure influence on basic reaction time performance. The aim of our study is to determine the respective weight of these two regulatory systems according to age on inhibitory motor control (i.e., ability to suppress a prepotent motor response) and sustained attention.

Methods: Fourteen healthy young males (mean age = 23 ± 2.7; 20–29 years) and 11 healthy elderly males (mean age = 68 ± 1.4; 66–70 years) were recruited. The volunteers were placed for 40 h in 'constant routine'. In the 'Sleep Deprivation SD' condition, the volunteer was kept awake for 40 h in high sleep pressure condition. In the 'NAP' condition, the volunteer adopted a short wake/sleep

cycle (150/75 min) resulting in a low sleep pressure condition to counteract the homeostatic pressure and isolate the circadian process.

Performances were evaluated by a simple reaction time task and a Go/Nogo task repeated every 3H45.

Results: In the SD condition, inhibitory motor control is equally impaired by extended wakefulness in both age groups ($P < 0.01$). Sustained attention decreases under sleep deprivation in the executive task in both groups, even more in young participants ($P < 0.05$). In the SD and NAP conditions, elderly demonstrate reaction time performance less fluctuating across time of day than those of young participants ($P < 0.001$).

Conclusion: Aging would be a protective factor against the effects of extended wakefulness especially on sustained attention failures due to an attenuation of the homeostatic sleep pressure.

O135

Association between variability in amount of night-time sleep and inhibitory control in adolescence

S. REYES[1], C. ALGARIN[1], B. LUNA[2], B. LOZOFF[3] and P. PEIRANO[1]

[1]University of Chile, Santiago, CL, [2]University of Pittsburgh, Pittsburgh, PA, US, [3]University of Michigan, Ann Arbor, US

Objective: To examine the association between variability in the amount of daytime and nighttime sleep and inhibitory control in healthy adolescents.

Methods: The 74 participants were part of an infancy iron deficiency anemia preventive trial and follow-up study: 52% were male, mean age = 15.3 years (15.0–17.6). Motor activity was recorded continuously for a week with actigraphs (Actiwatch-16/64) worn in the nondominant wrist, yielding estimates of the amount of daytime and nighttime sleep. The variability of daytime and nighttime sleep amounts were calculated by dividing the standard deviation of sleep amounts within the week by the square root of the number of data points. Participants also performed the antisaccade task, an oculomotor test of inhibitory control. They were instructed to avoid looking at a visual stimulus appearing on the screen and look in the opposite location, which was considered a correct response.

Results: The mean sleep amount during daytime and nighttime was 0.9 ± 0.8 h and 8.1 ± 1.2 h, respectively. In linear regression analyses, adjusted by gender and the antecedent of iron deficiency anemia in infancy, greater variability in the amount of nighttime sleep was independently associated with a reduced percentage of correct responses in the antisaccade task (beta coefficient = -0.27, $P < 0.05$). Variability in the amount of daytime sleep showed no significant associations.

Conclusion: Our results show an association between nighttime sleep amount variability and inhibitory control, adding support to the hypothesis relating sleep patterns and cognitive control. We speculate that maintaining a regular nighttime sleep amount throughout the whole week may help adolescents improve their performance on tasks that demand inhibition.

Support: Fondecyt 1110513 & NIH HD33487 grants, & (*)CONICYT, PhD program fellowship.

O136

Overnight cardiac autonomic function during sleep disturbance in peri- and postmenopausal women

I. VIRTANEN[1], N. KALLEINEN[2], A. URRILA[3] and P. POLO-KANTOLA[2]

[1]VSSHP TYKS-SAPA, Turku, FI, [2]Turku University Hospital, Turku, FI, [3]University of Helsinki, Helsinki, FI

Objective: To study the effect of partial sleep disturbance on heart rate variability (HRV) during sleep in peri- and postmenopausal women on and off hormone therapy (HT).

Methods: We studied peri- (PER) and postmenopausal (POST) women aged 47.8 (0.4) years ($n = 17$) and 62.8 (0.7) years ($n = 18$) using a prospective case–control protocol. Polysomnography (PSG) was performed over three nights: adaptation, baseline, and sleep disturbance due to frequent blood sampling. The studies were repeated after 6 months during which the patients were randomised to peroral HT and non-HT groups. PSG recordings were scored in 30 s epochs. Time and frequency domain and nonlinear HRV were assessed overnight from baseline and sleep deprived nights. HRV was analysed at baseline and during sleep disturbance, and the effects of sleep disturbance, time and HT were analysed between groups.

Results: At baseline, the POST group had higher power law slopes ($P = 0.035$) and lower spectral entropy ($P = 0.025$) than the PER group. After 6 months, HRV was similar between groups during baseline. No significant HRV differences were seen between the two baseline nights.

During sleep restriction, the POST group had higher maximum heart rate ($P = 0.022$) and lower LF power ($P = 0.035$). After 6 months, the only effect was an increase in minimum heart rate in the POST HT group compared to the POST non-HT group ($P = 0.024$). When the two sleep restriction nights were compared, power law slopes decreased in both PER HT ($P = 0.049$) and PER non-HT ($P = 0.028$) groups over time. No change was seen in the POST non-HT group, but in the POST HT group, total power ($P = 0.046$), VLF power ($P = 0.028$) and power law slope ($P = 0.027$) decreased and spectral entropy increased ($P = 0.028$) over time. There were no group differences in the time-induced changes.

Comparison between baseline and sleep restriction showed no HRV change in the PER group. In the POST group, maximum heart rate ($P = 0.003$) and RMSSD ($P = 0.034$) increased. After 6 months, no sleep restriction effect was seen, nor were there group differences.

Conclusions: Postmenopausal women had an increased vulnerability to tachycardia and rapid HRV changes during partial extrinsic sleep disturbance, while perimenopausal women were practically unaffected. After 6 months, however, this difference was not seen irrespective of HT use. This suggests a high estrogen-independent capability for adaptation in the cardiovascular autonomic system even after menopause.

O137

Investigating testosterone as a modulator of subjective symptoms following sleep restriction

A. C. REYNOLDS[1], J. DORRIAN[1], J. L. PATERSON[2], P. LIU[3], H. P. A VAN DONGEN[4], G. A. WITTERT[5], L. J. HARMER[6] and S. BANKS[1]

[1]University of South Australia, Adelaide, AU, [2]Central Queensland University, Adelaide, AU, [3]University of Sydney, Sydney, AU, [4]Washington State University, Spokane, WA, US, [5]University of Adelaide, Adelaide, AU, [6]Adelaide Institute for Sleep Health, Adelaide, AU

Objectives: Data from our laboratory suggested that endogenous testosterone (Te) modulates individual vulnerability to cognitive impairment after sustained sleep restriction (SR). Both SR and Te have been documented to be associated with impaired mood and increased sleepiness. In this pilot study, we examined whether the same modulatory effect of Te on cognitive impairment was also apparent in subjective symptoms following SR.

Methods: Fourteen healthy men (age range 23–36 year, mean BMI 23.5 ± 2.9 kg/m^2) with normal blood biochemistry participated in a live-in, laboratory-based SR protocol. Subjects underwent 2 baseline nights (B1 & B2; 10 h time in bed (TIB); 10:00–08:00) followed by 5 SR nights (SR1-5; 4 h TIB; 04:00–08:00) and 1 recovery night (10 h TIB; 10:00–08:00). Meal timings and calories were strictly controlled, and only non-vigorous physical activity was allowed. Blood was sampled on B1 and SR5 via an indwelling catheter at 09:00, and then at 2-h intervals from 10:00 until 20:00. Serum samples were assayed for total Te using the Cobas electrochemiluminescence immunoassay (Roche Diagnositcs Ltd., Indianapolis, IN, USA). Mood was assessed using a visual analogue scale (VAS) ranging from 1 (Elated) to 9 (Depressed), and subjective sleepiness was assessed using the Karolinska Sleepiness Scale (KSS). On B1 and SR5, the VAS and KSS were completed at 11:00, 12:30, 16:30 and 19:30. The modulatory effect of Te on the change in mood and sleepiness from B1 to SR5 was assessed using mixed-effects linear regression.

Results: SR adversely degraded mood on the VAS ($F_{1,83} = 15.1$, $P < 0.001$) and increased sleepiness on the KSS ($F_{1,83} = 51.9$, $P < 0.001$). Te levels were not significantly altered by SR ($F_{1,90} = 4.1$, $P = 0.079$). However, higher endogenous Te levels were associated with greater adverse effects of SR on VAS mood ($F_{2,81} = 5.1$, $P = 0.008$) and KSS sleepiness ($F_{2,81} = 12.7$, $P < 0.001$).

Conclusion: Subjects with higher endogenous Te levels experienced greater degradation of mood and elevation of sleepiness following SR, suggesting that Te may modulate individual vulnerability to subjective symptoms due to SR.

Research supported by a University of South Australia Women in Science Grant, and through a collaboration with the Sleep and Performance Research Center of Washington State University, Spokane.

O138

The effect of sleep deprivation on memory, anxiety like-behaviour and serum neurochemicals in rat model

M. TORABI NAMI, M. NASEHI and M. R. ZARRINDAST

Institute for Cognitive Sciences Studies, Tehran, IR

Background/aims: Neuro-cognitive functions and mainly memory is drastically affected by inefficient sleep. The resultant oxidative stress is hypothesized to hasten neurodegenerative processes namely Alzheimer's disease. We evaluated how Total Sleep Deprivation (TSD) and Chronic Partial Sleep Restriction (CPSR) may affect memory, anxiety-related behaviors and alter serum level of neurobiochemical markers like BDNF (Brain Derived Neurotrophic Factor) and cortisol in rat model.

Material and method: Male Wistar rats weighing 220–260 g were used. The disk over water (DOW) apparatus was applied to induce TSD and CPSR. The four study arms were: cage control, DOW control, TSD and CPSR. Elevated Plus Maze (EPM) was used to measure parameters (%OAT,%OAE, locomotor activity) for anxiety on day 1 (T1) and memory on day 2 (T2). Control rats were either placed in cage or off apparatus for 48 h and experimental rats underwent either 48 h of TSD or modeled as CPSR. CPSR rats were in DOW 12 h on and 12 h off intermittently, for seven consecutive days. Post intervention or control condition, T3 was done to assess anxiety level and T4 to examine memory. Blood were drawn from all rats on T4 day at 5 pm to measure serum BDNF and cortisol levels using the ELISA method.

Results: The results showed that TSD ($P < 0.001$) and CPSR ($P < 0.01$) induce memory impairment and meanwhile have anxiolytic-like effect compared to controls. Data showed that CPSR as compared to TSD caused more memory impairment and anxiolytic effect ($P < 0.05$). Serum cortisol level raised dramatically in CPSR rats compared to TSD and controls. The serum BDNF level was lowest is CPSR arm.

Conclusion: Our results suggest the more drastic effect of CPSR rather than TSD in impairing memory and reducing anxiety. Decreased BDNF and peaked cortisol level in TSD and CPSR may be a clue to suggest inflammatory processes involved in possible insults to the brain caused by sleep deprivation.

Oral Session 4 – Narcolepsy and Sleepiness

O139

The effect of intranasal hypocretin-1 on daytime sleep in patients with narcolepsy with cataplexy

S. L. WEINHOLD[1], M. SEECK-HIRSCHNER[1], A. NOWAK[1], M. HALLSCHMID[2], R. GÖDER[1] and P. C. BAIER[1]
[1]Christian-Albrechts-University Kiel, Kiel, DE, [2]University Lübeck, Lübeck, DE

Objectives: Narcolepsy with cataplexy is an intrinsic sleep wake regulation disorder typically caused by a deficiency of hypocretin-1 (hcrt-1), also called orexin A. In a previous study we found that the intranasal administration of hcrt-1 in the evening had a stabilizing effect on nocturnal sleep as indicated by a reduction in wake-REM-sleep-transitions, whereas a slight wake-promoting effect was not statistically significant. The aim of the present study was to investigate the effect of intranasal hcrt-1 administration in the morning on daytime sleepiness and sleep-wake-stability.

Methods: In a double-blind, random-order crossover, placebo-controlled, within-subject design study we administered human recombinant hcrt-1 (435 nmol) intranasally to twelve subjects with narcolepsy with cataplexy (diagnosed according to ICSD-2 criteria) at 7:15 a.m. The administration was preceded by standard diagnostic polysomnography and followed by respective daytime recordings. At 09:00 a.m., 11:00 a.m., 1:00 p.m. and 3:00 p.m. a modified version of the multiple sleep latency test was performed.

Results: There were no differences in sleep quantity and quality as well as wake-REM-sleep transitions in the diagnostic nights preceding substance application ($P > 0.200$). Intranasal hcrt-1 application induced a significant reduction of wake-REM-transitions (mea $n = 0.500$; standard deviatio $n = 0.855$) compared to placebo (mea $n = 1.286$; standard deviatio $n = 1.773$; $P = 0.043$) in the daytime sleep tests. The total number of sleep stage changes did not show any differences. There were neither statistically significant effects of substance administration on sleep latency, nor on the number of sleep onset periods.

Conclusion: Our results support previous findings that intranasal hcrt-1 enters the central nervous system and can restore the wake-REM-sleep instability in patients with narcolepsy with cataplexy. Further studies are necessary to investigate the potential clinical relevance of these observations.

Acknowledgements: This study was supported by the Deutsche Forschungsgemeinschaft (DFG, SFB 654).

O140

Narcolepsy in Norwegian children and adolescents after Pandemrix® vaccination

M. S. HEIER[1], K. GAUTVIK[1], E. WANNAG[1], K. H. BRONDER[1], E. MIDTLYNG[1], Y. KAMALERI[1] and J. STORSÆTHER[2]
[1]Oslo University Hospital, Oslo, NO, [2]National Institute of Public Health, Oslo, NO

Background: During September through November 2009, ca. 470 000 children and adolescents in Norway aged 4–19 were vaccinated with Pandemrix® against influenza AH1N1. Vaccination coverage in this age cohort was about 50%. Alerted by reports of a sudden increase of narcolepsy symptoms in vaccinated children and adolescents in Finland and Sweden, the Norwegian health authorities initiated an investigation of the situation in Norway, through the National Institute of Public Health.

Objectives: The study was undertaken to evaluate the possible association between Pandemrix vaccination and debut of narcolepsy in Norway.

Methods: The four Norwegians health regions were called upon to report children and adolescents with sudden onset of excessive daytime sleepiness (EDS) and cataplexy occurring after the 2009–2010 vaccination period. Further clinical data and results from measurements of mean sleep latency and number of SOREMs in Multiple Sleep Latency Test (MSLT), CSF hypocretin levels and determination of HLA DQB1*0602 tissue type were collected after informed consent from the patients or their parents. Vaccination status was obtained from the national vaccination registry.

Results: Thirty-six vaccinated children and adolescents 4–19 years were diagnosed as new cases of confirmed narcolepsy and included in the study during 2010 and 2011. Median age 11 years. All had EDS, and 31 of 36 had documented cataplexy. Twenty-seven had mean sleep latency <8 min, 22 had ≥2 SOREM periods in MSLT. For two children MSLT was not conclusive, for 7 the test was not performed. HLADQB1*0602 was positve for 28, negative for 0, unknown for 8. Hypocretin levels were low for 27, borderline for 1 and unknown for 8, During the same periode six unvaccinated cases could be included. Median age 15 years, t with documented cataplexy and 3 with low hypocretin values. In the majority of cases symptom debut occurred in 2010, but complete data are not yet available for all. The number of patients recorded is therefore a minimum, and may be higher when complete data are available.

Conclusion: Our preliminary data indicate an increased risk of narcolepsy in children 4–19 years after Pandemrix® vaccination, with a minimum incidence of 3.8/100 000/Y in vaccinated children during 2010–2011, compared to 0.6/100 000/Y in unvaccinated children during the same period.

O141

Impact of stimulants on self-reported impulsivity and decision-making in narcolepsy with cataplexy

S. BAYARD, S. SCHOLZ and Y. DAUVILLIERS
Hôpital Gui-de-Chauliac, Montpellier, FR

Objective: Hypocretin (also known as orexin) system is a critical regulator of dopaminergic activity in reward circuits. Narcolepsy-cataplexy (NC) is caused by a loss of neurons that produce hypocretin. We recently reported in drug-free patients with NC selective changes in reward processing. Traditional stimulant medications used in NC are known to modulate dopaminergic transmission. The aim of this study was to investigate the impact of stimulants on self-reported impulsivity and reward processing in patients with NC.

Methods: The sample included 43 drug-free and 37 treated patients with NC, and 42 matched healthy controls. Impulsivity was assessed by the UPPS Impulsive Behavior Scale and decision-making under ambiguity using the Iowa Gambling task (IGT), and under risk using the Game of Dice task (GDT). All participants underwent a semi-structured face-to-face clinical interview for impulse control and addictive behaviors, and completed the Beck Depression Inventory-II. All patients with NC underwent one night of polysomnography following the next day by a multiple sleep latency test for drug-free patients, and by a maintenance wakefulness test for treated patients. A sub-group of patients ($n = 15$) were evaluated twice at baseline and after stimulant therapy.

Results: When the clinical cut-offs guidelines for BDI-II total score were applied, no group effect was observed. We found no significant difference between patient groups and healthy controls for UPPS subscales. Both drug-free and treated patients with NC demonstrated selective reduced IGT performance and normal performance on the GDT. For each patient groups, no clinical or polysomnographic characteristics were associated with the IGT pattern. More specifically, stimulant intake and daily dose of stimulant were not related to the IGT performances.

Conclusion: Our results add further evidence for a selective reduced performance on decision-making under ambiguity in NC. Furthermore, we demonstrated that stimulants have no effect on decision-making processes and self-reported impulsivity in NC.

O142

Narcolepsy: a disorder of imbalance between sleep-and wakefulness-promoting substance

F. HAN[1], X. S. DONG[1], J. LI[1], Y. SHANG[1], P. AN[1], Y. N. LIU[1], H. YAN[1], X. Z. ZHANG[1], L. LIN[2], E. MIGNOT[2], T. POLLMÄCHER[3], Z. L. HUANG[4], Y. URADE[5] and K. STROHL[6]

[1]Peking University People's Hospital, Beijing, CN, [2]Stanford University, Palo Alto, CA, US, [3]Center for Mental Health Klinikum Ingolstadt, Ingolstadt, DE, [4]Fu Dan University, Shang Hai, CN, [5]Osaka Bioscience Institute, Osaka, JP, [6]Case Western Reserved University, Cleveland, US

Objectives: A common cause of narcolepsy is defective hypocretin/orexin transmission. The wake-active amine, histamine, was also found decreased in cerebrospinal fluid (CSF) of human narcolepsy. The prostaglandin D system produced in the brain by the action of the enzyme PGD synthase (PGDS) is considered as a major sleep promoter. Few studies investigated the possible importance of PGDS in the mediation of daytime sleepiness in human narcolepsy.

Methods: In addition to HLADQ0602 status and MSLT following a nocturnal PSG test, CSF hypocretin-1, and serum and CSF LPGDS levels were measured in 128 patients with narcolepsy (97 as NC with and 31 as NWC without cataplexy) and 52 controls.

Results: A low CSF hypocretin-1 was noticed in 95% of the NC and in 40% of NWC patients. Elevated serum and CSF LPGDS levels were revealed in patients with narcolepsy, and this is independent of cataplexy status and the levels of CSF hypocretin-1 (>110 pg/ml).

Conclusion: The imbalance of wake and sleep promoting factors exsists in narcolepsy.

This work was supported by research grants from NSFC (81070069), The Sino-German Center for Research Promotion (GZ538), and the Beijing Municipal Science & Technology Commission (D1011000050010029) to F. Han.

O143

Clinical profile of patients developing narcolepsy within 1 year of H1N1 vaccination

E. M. PURCELL[1], C. CROWE[1], S. KEANE[1], M. MCGANN[2], D. OROURKE[2] and B. LYNCH[2]

[1]Mater Private Hospital, Dublin, IE, [2]Childrens' University Hospital, Temple St., Dublin, IE

Introduction: An increased incidence of narcolepsy has been reported in Finland and Sweden associated with H1N1 vaccination. Ireland also experienced a surge in cases with a younger age of presentation than is usual. Vaccinations occurred November 2009–February 2010. We present symptoms and findings within the first 2 years of presentation. Clinical experience suggests there is an evolution of symptoms with time and that symptoms are influenced by age of onset. It is now possible to describe the very early symptoms of narcolepsy, while they are evolving and still current in patients'/their parents' memory.

Methods: We retrospectively reviewed a case cohort of 34 patients who presented to a single tertiary referral sleep centre with symptoms suggestive of narcolepsy. Most patients had full polysomnography with MSLT, HLA typing and hypocretin levels.

Results: Thirty-four patients were seen between August 2010 and March 2012. Thirty-two percent (11) were male and 68% (23)were female. Eleven were <10 years. Mean age was 15.5 ranging from 3 to 56. All presented with EDS,disturbed nocturnal sleep and had been vaccinated. Mean latency from vaccination to onset of symptoms was 15 weeks (2–53 weeks).The mean ESS was 17.5. Parasomnias were common in the form of sleep talking and nightmares (68%) 0.44%(15)had hypnogogic hallucinations. Thirty-two percent had sleep paralysis which was commoner in older patients ($P < 0.005$) 0.79% had cataplexy which tended to be more severe in adult patients. Polysomnographic findings include a mean Sleep Latency of 11 min; mean REM Latency of 59 min. Mean AHI was 1 (0–11). Mean PLM Index and leg jerk index was 12 and 9/h. Sleep fragmentation was marked with an awake and arousal index of 4.5 and 17/h. Mean Sleep Latency on MSLT was 2.5 min (0–14 mins). The mean number of SOREM's was 4 in 80% of patients with 17% having 3 and a 4-year-old child having none. Hundred percent of those tested (18) were positive for HLA DQB1*0602. Of 18 CSF samples, all Hypocretin levels were <50 pg/ml (2 pending).

Conclusion: This represents a comprehensive view of a large number of patients seen in 1 centre over a short period of time, following H1N1 vaccination, with recent onset of symptoms. Adult patients had more severe cataplexy. Despite varying clinical presentation relative to age, there was no variation in standard diagnostic test results. Further studies are needed to ascertain if these patients are phenotypically equivalent to other patients with narcolepsy, not associated with vaccination.

O144

Event-related potentials and reaction time results in a reward-based task in patients with narcolepsy, parkinson's disease, and healthy controls

A. MENSEN[1], R. PORYAZOVA[2], N. ZOLLINGER[2], F. BISLIMI[2], G. HUEGLI[1], L. BADEL[1], C. R. BAUMANN[2] and R. KHATAMI[1]

[1]Clinic Barmelweid, Barmelweid, CH, [2]University Hospital Zurich, Zurich, CH

Introduction: Hypocretin (orexin) and dopamine deficiency/dysfunction in narcolepsy–cataplexy (NC) and Parkinson's disease (PD) patients has been linked to disturbed reward processing. We aimed to assess reaction time (RT) and event-related potentials (ERPs), in these patients in a reward-based reaction time task, and to compare outcomes to healthy controls.

Methods: Seventeen NC patients (HLA positive, hypocretin-deficient), 10 PD patients (Hoehn & Yahr stage I-III), and 18 healthy controls performed a reward-based task using different value (high and low) and valence cues (positive and negative). The participants had to press a button as fast as possible while a picture of a landscape was presented on the screen in order to gain or not lose money. Analysis of reaction time was performed using repeated measures ANOVA (with group as a between subject factor, valence – positive versus negative, and value – high versus low cues, as within subject factors and participants' age as a covariant).

EEG was measured using a 125 channel geodesic array. ERPs were segmented 200 ms prior to reward cue onset until 800 ms post event. ERPs were analyzed using a threshold-free cluster enhancement, followed by non-parametric permutation statistics on potential reward size and group.

Results: Behaviourally, NC, PD patients and controls did not show any significant differences. For ERPs, a trend towards a reduced response to higher reward cues in NC patients compared to controls was observed. Interaction effects peaked around 80 ms and again at 200 ms.

Conclusion: NC and PD patients are able to achieve normal behavioral outcome in a reward based tasks, while only NC patients may differ from controls in their EEG response to reward anticipation.

O145

Night-sleep onset stroke: clinical characteristics, radiological features and long-term outcome

J. HABA-RUBIO, M. FAOUZI and P. MICHEL
Centre Hospitalier Uinversitaire Vaudois, Lausanne, CH

Objectives: A significant number of ischemic strokes occur during night sleep, but data about epidemiology, severity and outcome of stroke during sleep (NS) are conflicting. We conducted this prospective hospital-based study in order to better characterize NS in a large cohort of patients with acute ischemic stroke.

Methods: We used data from the Acute STroke Registry and Analysis of Lausanne (ASTRAL), which is the prospective registry of all acute ischemic stroke patients admitted to the CHUV within 24 h after last-well time. ASTRAL includes demographic data, vascular risk factors and comorbidities, metabolic, hematological variables and vital signs on admission, stroke pathophysiology, clinical and radiological findings and outcomes.

Results: A total of 2471 patients with acute ischemic stroke were included in the study. NS was documented in 564 cases (22.8%). Compared with patients with known stroke onset while awake (KO) patients with NS were slightly older (70.3 ± 15.8 versus 68.3 ± 15.2, $P < 0.01$) and more of them were taking antihypertensive (60.4% versus 55.1% $P < 0.05$) and oral antidiabetic drugs (11.2 versus 8.3 $P < 0.05$). No major differences were found in vital signs, hematologic and metabolic variables on admission. The NIH severity score at admission was lower (8.1 ± 7.5 versus 8.8 ± 7.6, $P = 0.05$) and far fewer NS patients were treated with a recanalization procedure (1.2% versus 28.7%, $P < 0.001$). Patients with NS have more lacunar strokes (17.8% versus 13.8%, $P < 0.05$), and clinically presented with less aphasia, dysathria and sensory and visual fields deficits. The acute CT showed in 44.3% lesions related with acute stroke (versus 31.3% in KO, $P < 0.001$) and in 37.5% other vascular lesions (chronic or subacute), not related with present stroke (versus 32% in KO, $P < 0.05$). The CT perfusion sequences showed less acute focal hypoperfussion (37.3% versus 50.8%, $P < 0.01$) and the CT performed during subactute period showed less haemorragic transformations (12.8% versus 17.7% $P < 0.05$). No differences in Rankin at neither 3 nor 12 months, or in mortality at 3 and 12 months, or in stroke recurrence during the following year were found.

Conclusion: Despite multiple similarities there are significant differences between KO and NS strokes, the latter are associated with lacunar pathogenesis and antihypertensive pretreatment. Short and long-term outcome and recurrences are similar. Cerebral hypoperfussion due to excessive nocturnal blood pressure fall during sleep may play a role in the physiopathology NS.

O146

Carotid artery atherosclerosis and sleep-disordered breathing in healthy elderly: the Synapse cohort

M. SAINT MARTIN, E. SFORZA, S. CELLE, V. PICHOT, C. BOISSIER, D. MAUDOUX, J.-C. BARTHÉLÉMY and F. ROCHE
University Hospital, Saint-Etienne, FR

Background: Sleep-related breathing disorder (SRBD) has emerged as an independent risk factor for carotid atherosclerosis and cerebrovascular disease in middle-aged subjects, but its effect in elderly is not yet understood. The aim of this study was to assess the impact of SRBD on carotid atherosclerosis in a cohort of healthy elderly subjects.

Methods: Seven hundred fifty-five participants of a French epidemiological study (PROOF SYNAPSE cohort study) on the association between SRBD and cardiovascular morbidity during a 7-year follow-up, aged 68 year at study entry, underwent carotid ultrasonography. Risk factors for atherosclerosis including smoking, metabolic syndrome and hypertension were determined. Presence of SRBD was assessed by nocturnal polygraphy and a respiratory disturbances index (RDI) >15 was considered as indicator of SRBD.

Results: Presence of carotid lesion was found in 35% of the sample greatly in men and in overweight subjects. The more frequent alteration was arteriosclerosis present in 74% of cases, carotid stenosis >50% found only in 9% of subjects. No significant differences in the prevalence of carotid lesion were found between subjects with and without SRBD. Despite a significant association between RDI and presence of carotid stenosis ($P = 0.006$), male gender, ($P < 0.001$), systolic and diastolic blood pressure ($P < 0.001$), dyslipidemia ($P = 0.003$) and use of hypotensive medications ($P = 0.009$) were the variables independently associated with carotid lesions.

Conclusions: The incidence of carotid atherosclerosis in healthy elderly is more frequent in men and is mediated more by metabolic factors and hypertension than presence of SRBD. Future clinical studies including an extensive evaluation of all atherosclerosis risk factors founded in elderly are needed to elucidate the predisposing role of SRBD for cerebrovascular risk.

O147

Subjective perception of sleepiness in a driving simulator is different from perception in the maintenance of wakefulness test

D. SCHREIER, C. ROTH and J. MATHIS
University Hospital Berne, Berne, CH

Objectives: We have recently described sleep deprived healthy subjects, who did not signal their subjective sleepiness before the first microsleep during the maintenance of wakefulness test (MWT) [1]. Here we tested whether subjects spontaneously signalled sleepiness before their first microsleep in four conditions, the MWT and while steering a driving simulator both, before and after sleep deprivation.

Methods: Twenty-four healthy subjects (20–26 year) were tested before and after one night of sleep deprivation in a MWT and in a 'divided attention steering simulator' (DASS) during 40 and 60 min respectively. Participants were instructed to signal sleepiness as soon as they realized the first symptoms of sleepiness or tiredness in addition to stay awake as long as possible. They were rewarded for optimal performance. Data acquisition consisted of a standard electroencephalography (EEG), electrooculography (EOG), submental electromyography (EMG) and face videography. Microsleep was

defined by a sleep fragment in EEG lasting >3 s and overt sleep >15 s (AASM criteria) respectively while the eyes were closed. For statistical comparisons between conditions and missed sleep perception Chi-squared test was used.

Results: Seven subjects (29%) missed to signal sleepiness before the first microsleep in the MWT after sleep deprivation and one subject did so in the MWT before sleep deprivation ($P < 0.02$). No subject missed to signal sleepiness before the first microsleep in both DASS. After sleep deprivation significantly less subjects missed to signal their sleepiness in the DASS compared to the MWT ($P < 0.004$) whereas no relevant difference between the tests was observed before sleep deprivation.

Conclusion: These results confirm our earlier study in MWT [1], but in addition show, that purely internally driven subjective perception of sleepiness is more accurate during tasks which include a permanent feedback of performance such as driving compared to the passive situation of the MWT. Subjective perception of sleepiness is less accurate after sleep deprivation compared to the rested state suggesting that sleepiness impairs perception of sleepiness itself. However this effect is overweighed by the performance feedback while driving.

References:

1. U. S. Herrmann, C. W. Hess, A. G. Guggisberg, C. Roth, M. Gugger, and J. Mathis. Sleepiness is not always perceived before falling asleep in healthy, sleep-deprived subjects. Sleep Med 11 (8):747–751, 2010.

This was not an industry-supported study. Participants were paid out of a research grant from the Dept. of Neurology, Inselspital, Bern University Hospital, Switzerland.

O148

Barcelona Sleepiness Scale validation to assess sleepiness in obstructive sleep apnoea

M. GUAITA, M. SALAMERO, M. ROMERO-CARDOS, I. VILASECA, J. MOTSERRAT, C. EMBID, A. IRANZO, J. DE PABLO, C. GAIG, C. LEON and J. SANTAMARIA

Hospital Clinic, Barcelona, ES

Background: Excessive daytime sleepiness (EDS) is a common problem with serious health and social consequences. A reliable measure of sleepiness in obstructive sleep apnea (OSA) that correlates well with objective EDS is needed and not available. The Epworth Sleepiness Scale (ESS), the most common method to quantify EDS, is poorly correlated with objective tests (Multiple Sleep Latency Test, MSLT; Maintenance of Wakefulness Test, MWT) in OSA.

Aim: To validate a new sleepiness scale for clinical use in OSA that correlates well with objective measures of sleepiness.

Methods: Generation and depuration of items: 52 consecutive patients with OSA and EDS and their partners were interviewed using focus group techniques. A preliminary list of 224 sleepiness items were generated. Items were specifically created to distinguish between the feeling of sleepiness and to fall asleep and reflected circumstances that modulate sleepiness like time of the day, motivation, duration of activity and body position. In a second step, 30 different patients with OSA were evaluated in order to depurate the 224-item list. Each item was scored according to the severity of sleepiness, frequency of appearance and latency to fall asleep. After the analysis, 16 common situations were the most frequently answered and showed a homogeneous representation of the sleepiness severity. Validation: Fifty-nine new consecutive patients complaining of snoring or apneas with and without EDS were included. All patients were evaluated with the MWT and the MSLT, using 5 naps, every 2 h, and answered the ESS and the new 16-item list. The study was preceded by a nocturnal polysomnography (PSG) and actigraphy and sleep diary that were recorded during the previous week. A composite of MSLT and MWT was calculated as an objective criterion of sleepiness. Exhaustive regression analysis of all the subsets of the list was performed. Mallow's Cp minimization was used to choose the best item combination.

Results: A combination of just two items ('In the morning, when I get relaxed' and 'In the afternoon, while standing in a line') had the best correlation with objective tests and made up the Barcelona Sleepiness Scale (BSS). The correlation between the Composite Score and the BSS in that group was much higher than with the ESS (0.61 versus 0.28; $P = 0.013$).

Conclusion: Our data suggest that the BSS, a simple sleepiness scale of two items, shows the best correlation with objective sleepiness tests.

Oral Session 5 – Light and Circadian Regulation of Sleep

O149

Acute exposure to blue-enriched light impacts on melatonin and sleep in humans

S. CHELLAPPA, R. STEINER, P. OELHAFEN, T. GÖTZ, J. KREBS and C. CAJOCHEN
University of Basel, Basel, CH

Objectives: Light at the short wavelength range (446–483 nm) triggers acute effects on human physiology and behavior, including human sleep-wake cycles, presumably mediated by the circadian and sleep homeostatic processes, via non-image-forming photoreceptors. Nonetheless, how blue-enriched light impacts on human sleep architecture and electroencephalographic (EEG) activity remains fairly unknown.

Methods: Here we investigated sleep structure and EEG activity in 37 healthy young participants (21 men, 16 women; age range: 20–31 years) following evening light exposure to polychromatic light of 40 lux at 6500, 2500 and 3000 K. Furthermore, salivary melatonin and subjective sleepiness were sampled every 40 min throughout the study.

Results: The time-course of salivary melatonin significantly differed across light conditions, with more nocturnal melatonin suppression, particularly after 90 min of light exposure, following only blue-enriched light. Analysis of the time-course of subjective sleepiness did not yield significant differences across the light conditions. Sleep structure across the first three cycles did not reveal significant differences following light exposure. All-night NREM sleep EEG power density revealed that exposure to light at 6500 K resulted in a tendency for less frontal NREM EEG power density in the range of 1.75–3.25 Hz, in comparison to light at 2500 and 3000 K. All-night REM sleep EEG power density did not significantly differ across the three light conditions. The dynamics of NREM EEG slow-wave activity (SWA: 2.50–4.0 Hz), a functional index of homeostatic sleep pressure, indicated that SWA was significantly reduced during the first NREM-REM sleep cycle, particularly in the frontal derivation, after exposure to light at 6500 K, in comparison to light at 2500 and at 3000 K.

Conclusion: Our data indicates that exposure to blue-enriched polychromatic light may have elicited a more prominent alerting effect that persisted onto the initial part of subsequent sleep. These effects may be driven by the interplay of the circadian and homeostatic processes.

O150

Beneficial effect of light exposure during sleep deprivation in young and older volunteers

V. GABEL, M. MAIRE, C. F. REICHERT, C. SCHMIDT, C. CAJOCHEN and A. VIOLA
University of Basel, Basel, CH

Objectives: Light exposure elicits numerous effects on human physiology and behaviour. However, it remains inconclusive whether light exposure has beneficial effects on cognitive performance and circadian physiology during sleep deprivation (SD) and even less whether light affects young and older people in the same way. Here we investigated the role of light exposure as a countermeasure for impaired cognitive performance and sleepiness during SD.

Methods: Currently, 16 participants (11 young (23.4 ± 0.5) and 5 old (65.6 ± 2.4)) have completed the in-lab part of the study, which consists of a balanced cross-over design with light exposure during 40 h of sleep deprivation. Participants underwent two sessions where they were subject to either a moderate light (ML: 250 lux) exposure or a dim light (DL: 8 lux) exposure. Cognitive tests were performed every 2.5 h and questionnaires were administered hourly to assess subjective sleepiness. Salivary melatonin was collected at regular intervals.

Results: Analysis of cognitive performance yielded a significant main effect of 'light condition' ($P < 0.0001$) in both age groups. Cognitive performance remained stable across time but with a significantly higher level in ML compared to DL. Analysis of subjective sleepiness revealed no significant differences in the older. However, a main effect of 'time' ($P < 0.0001$) and 'light' ($P < 0.0001$) condition was observed in the young, such that bright light exposure led to lower sleepiness levels until the end of the biological night. On the second day, these differences did not further reveal significances between ML and DL. Concerning the melatonin, no significant differences were observed in the older, whereas in the young, we observed a significant main effect of the condition 'light' ($P = 0.0006$), 'time' ($P < 0.0001$) and the interaction between this 2 conditions ($P = 0.0038$). Bright light exposure led to a phase delay of melatonin onset.

Conclusion: Our preliminary data indicate that light exposure during a sleep deprivation protocol improves subjective sleepiness and affects circadian phase markers in young participants. However, these differences are not emerging in the older people. These results should be confirmed with largest effectives. On the other side, ML improves cognitive performance in both age groups. In a broader context, these light conditions may provide an effective rationale for enhancing performance and sleepiness in individuals who experience prolonged wakefulness.

O151

Prevention of depression in elderly with memory-problems by activation of the biological clock with light

E. I. S. MØST[1], P. SCHELTENS[2] and E. J. W. VAN SOMEREN[1]
[1]Netherlands Institute for Neuroscience, Amsterdam, NL, [2]VU University Medical Center, Amsterdam, NL

Elderly people with memory complaints related to Alzheimer's Disease (AD) show more depressive symptoms than elderly who are cognitively intact. AD patients are also more likely to have hypothalamic-pituitary-adrenal (HPA) axis hyperactivity. The HPA axis is under control of the suprachiasmatic nucleus (SCN), which dysfunctions in both depression and AD. Long-term daily stimulation of the SCN by means of bright light attenuates depressive symptoms in moderate to severely demented institutionalized elderly people. It is unknown whether long-term daily bright light exposure similarly improves mood and HPA axis function in community-dwelling elderly with early, moderate and prodromal stages of AD.

Objective: To determine the effect of long-term daily bright light exposure on mood and HPA axis function in community-dwelling elderly participants diagnosed with either early or moderate stage AD or being at an increased risk to develop it, being diagnosed with Mild Cognitive Impairment or subjective memory complaints.

Method: A double blind, placebo controlled, randomized, practical clinical trial in 73 patients with memory complaints, between 50 and 80 years of age, assessed at baseline and up to 2 years in treatment,

followed-up at 6 months intervals. At each assessment the Geriatric Depression Scale (GDS) and diurnal saliva cortisol levels were obtained. Light treatment was given at home, and, consisting of either bright (10 000 lux) or normal indoor (300 lux) light exposure. Participants exposed themselves for 30 min twice a day, at fixed times in the morning and evening.

Result: As compared to the placebo condition, daily bright light exposure attenuated GDS ratings by -1.17 points per year ($P = 0.009$). While evening cortisol increased over the years in the placebo condition (1.61 nM/year, $P < 0.02$), levels did not change in the bright light condition (0.01 nM/year, $P = 0.96$), yielding a significant time by treatment interaction effect (one-sided $P < 0.006$).

Conclusion: Long term light treatment applying a fixed skeleton photoperiod daily for 2 years is effective in attenuating subclinical depressive symptoms and elevated evening cortisol levels in community-dwelling elderly people with early, moderate or prodromal stages of AD.

O152

Non-visual photoresponses in the aged: time course of spectral sensitivity

R. P. NAJJAR[1], P. TEIKARI[1], P.-L. CORNUT[2], B. CLAUSTRAT[1], P. DENIS[3], H. M. COOPER[1] and C. GRONFIER[1]

[1]INSERM U846, Stem Cell and Brain Research Institute, Lyon, FR, [2]Hôpital Edouard Herriot, Lyon, FR, [3]Hôpital de la Croix-Rousse, Lyon, FR

Objectives: Sleep and circadian rhythm disturbances are prevalent in the elderly. These alterations have been proposed to result from an inappropriate photic entrainment of the circadian clock. The aim of our study is to investigate the effects of ageing on non-visual sensitivity over the visible light spectrum, and to test if these alterations are related to an increased ocular lens density.

Methods: Eight aged (55–63 years old) and five young (24–27 years old) participants underwent ten experimental sessions. Nine sessions included a 60-min monochromatic light exposure (LE) from 00:30 to 01:30 (wavelengths from 420 to 620 nm, at equal photon density: 3.16E13 photons/cm^2/s). Plasma melatonin suppression was calculated for each light session and used to derive individual sensitivity spectra. Lens density was assessed using a validated psychophysical heterochromatic flicker photometry technique.

Results: Lens density measurements (18 young, 15 old) show a decreased transmittance of the ocular lens in the elderly, mainly for short wavelength lights (<500 nm). Non-visual sensitivity to light remained similar in the short wavelength region of the spectrum (<500 nm) but was greater in the long, 530–560 nm region, resulting in a shift of peak sensitivity to longer wavelengths (484–494 nm). In addition, the dynamics of melatonin suppression during the LE follow a different (delayed) pattern in the aged. In young subjects, peak sensitivity of melatonin suppression was ~490 nm after 15 min of LE, and ~480 nm after 30–60 min. In the aged, the peak sensitivity was ~510 nm after 15–30 min of LE and required 45 min to shift to a stable peak value of 494 nm. After 30 min of LE, the amplitude of melatonin suppression at the peak value was 20% less in the aged compared to young. Suppression became similar by 45 min.

Conclusion: Overall our results do not support the hypothesis that increased lens filtering is related to a decrease in non-visual sensitivity to light. Changes in non-visual light sensitivity in the aged subject may involve compensatory or adaptive mechanisms. Alterations in melatonin suppression dynamics could be due to a modified photoreceptor contribution and/or input to the central clock with ageing.

R.N. is funded by 'Ministère de l'Enseignement Supérieur et de la Recherche Français' and 'Fédération des Aveugles et Handicapés Visuels de France'

This work was supported by grants from FP6-EUCLOCK, ANR, Rhône-Alpes Cluster HVN, and Retina France.

O153

Narrowband lights can modulate biomarkers associate with hunger in sleep-deprived individuals

M. FIGUEIRO and M. REA

Rensselaer Polytechnic Institute, Troy, US

Objectives: Acute and chronic sleep restrictions cause a reduction in serum concentrations of leptin and an increase in serum concentrations of ghrelin, both biomarkers that are associated with hunger. Given that light/dark patterns are so closely associated with sleep/wake patterns, it is not unreasonable to hypothesize that light can also acutely impact these biomarkers. In the present study, we investigated if different light spectra could counteract the impact of sleep restriction on biomarkers associated with hunger by increasing leptin and decreasing ghrelin levels.

Methods: Eleven participants were recruited for a 9-week study. During the first week, participants were asked to maintain a regular, 8-h sleep opportunity schedule (baseline week), after which they alternated between 5-h and 8-h sleep schedules for additional 8 weeks. At the end of the baseline week and at the end of the weeks when they had 5-h sleep opportunities, participants slept in the laboratory. Upon awakening, participants remained in dim red light (630 nm, <0.5 lux at the eye) after the baseline week and after the first 5-h sleep opportunity week. For the remaining 3 weeks in which they were on the restricted sleep schedule, participants were exposed to 60 lux (0.325 W/m^2) of 633 nm (red), 60 lux (0.105 W/m^2) of 532 nm (green), or 60 lux (0.585 W/m^2) of 475 nm (blue) light for 2 h upon awakening; these conditions were counterbalanced across all participants.

Results: One sample two-tailed t tests revealed that sleep restriction significantly reduced leptin levels compared to the baseline week ($t_{1,32} = 2.9$; $P = 0.007$). Compared to the 5-h/dim light condition, exposure to red, green and blue lights significantly increased leptin levels ($t_{1,32} = 5.7$; $P < 0.0001$, $t_{1,32} = 3.6$; $P = 0.001$, $t_{1,32} = 3.0$; $P = 0.005$, respectively). Eight-hour sleep opportunity increased leptin levels by nearly 20% while light increased leptin levels by over 50% to the levels obtained in the 5-h/dim light condition. The one-sample *t*-tests also revealed a significant decrease in ghrelin levels after exposure to red light ($t_{1,32} = 3.3$; $P < 0.003$) and green light ($t_{1,32} = 2.2$; $P = 0.04$), but not to blue light ($t_{1,32} = 1.0$; $P = 0.3$).

Conclusions: This study is the first to demonstrate that narrowband light sources can modulate leptin and ghrelin levels, suggesting that light can potentially impact obesity by reducing hunger that accompanies sleep deprivation.

O154

A novel diurnal rodent model, *Arvicanthis ansorgei*: validation and characterisation of sleep regulatory mechanisms

J. HUBBARD, E. RUPPERT, C. ALLEMANN, L. CHOTEAU, C.-M. GROPP, L. CALVEL, E. CHALLET and P. BOURGIN

Strasbourg University Hospital, Strasbourg, FR

Objectives: Sleep regulation involves two principle mechanisms: a circadian and a homeostatic process. Additionally, mounting

evidence has indicated that a third mechanism, based on the non-circadian direct effect of light also contributes significantly to sleep/wake regulation. These mechanisms have been extensively studied and analyzed in nocturnal rodent species. However, studies in diurnal rodents, which can serve as a translational model to human research to examine these regulatory processes, does not currently exist. Our goal was to phenotype the *Arvicanthis ansorgei*, a diurnal rodent, to observe whether the circadian process and non-circadian direct effects of light are inverted from mice, as well as whether the homeostatic process is conserved.

Methods: Fourteen Male *Arvicanthis ansorgei* were implanted with EEG, EMG, EOG, and in a subset of animals recorded with video, to examine sleep and waking states. Animals underwent a 48-h baseline assessment of their circadian cycle, as well as 24-h period of continuous darkness. Non-circadian conditions were used to observe the direct effects of light; a 1-h light pulse (LP) at ZT15 during the dark period, a 1-h dark pulse (DP) at ZT3 during the light period, and an ultradian 1hLP:1hDP cycle over 24 h. Finally, a 6-h sleep deprivation starting at dark onset (ZT12), when sleep pressure is high in diurnal animals, was performed to study the homeostatic process. Specific EEG rhythms and associated vigilance states were characterized (theta, delta) and scored accordingly.

Results: Vigilance states (wake, NREM, and REM) were easily identifiable with recordings, and were similar to nocturnal rodents. Under 12hL:12hD arvicanthis had an inverted sleep-wake cycle compared to mice, though with large amounts of crepuscular activity at light and dark onset. Analysis of slow wave activity (EEG delta power) during NREM across the sleep deprivation experiment showed the conservation of the homeostatic process. Under the 1hL:1hD cycle, light exerted a wake promoting effect in arvicanthis, as opposed to the dark-induced effect in mice. The distribution of sleep and waking under constant darkness confirmed the presence of a rhythm, thus the conservation of the circadian process.

Conclusion: Our preliminary results show that *Arvicanthis ansorgei* is a valid model for studying sleep regulatory mechanisms and suggests that the non-circadian effects of light are inverted when compared to nocturnal rodents.

O155

Empirical evidence for circadian and homeostatic trends in electroencephalogram-derived vigilance parameters

G. KOENIG[1], G. DORFFNER[2], S. HANKE[1], G. KLOESCH[2], E. LORETZ[3], W. MAYR[2] and J. ZEITLHOFER[2]

[1]AIT Austrian Institute of Technology GmbH, Vienna, AT, [2]Medical University of Vienna, Vienna, AT, [3]The Siesta Group Schlafanalyse GmbH, Vienna, AT

Objectives: The two process model of sleep regulation was introduced by Borbély in 1982. The homeostatic and circadian processes can be modularly combined to form a predictor for daytime sleepiness and vigilance.

Our aim is to objectively describe daytime vigilance and sleepiness on a long-term all-day basis, based on Electroencephalogram (EEG)-derived parameters. We provide empirical evidence for the model's processes based on robust and objective parameters.

Methods: We conducted an exploratory study under real-world conditions, including 26 healthy female and male subjects. For two 24 h periods we recorded EEG channels using a mobile system, along with hourly subjective sleepiness ratings and reaction times. The sessions consisted of a night and a day under a sleep-deprived and a normal-sleep condition. The two sessions were embedded in 14 days of recording actigraphy and sleep quality ratings.

We derived 62 features from the acquired data, e.g. frequency band powers, band ratios, complexity and entropy measures, and EEG events such as alpha events or diurnal sleep spindles. We also used EEG artefacts as features.

Using statistical means such as correlation coefficients and likelihood-ratio tests we analyzed the features' homeostatic and circadian trends and compared them to the two-process model.

The actigraphy data was used to estimate the individual circadian rhythm. For the analysis of circadian trends we scaled the data relative to the individual circadian phase, for the homeostatic analysis relative to the time of wake up.

Results: In our analysis we discovered several features that show behaviour significantly correlated to the predictions of the two-process model. Especially the daytime-trends of EEG-artefacts provide an interesting insight, as those artefacts are usually not seen as being useful, e.g. the EOG artefacts, which correlate strongly negative with the homeostatic timescale (Kendall tau -0.92, $P < 0.000$). The standard deviation of the theta band and the relative gamma band power are examples of features with a strong circadian behaviour.

Conclusion: We were able to provide significant empirical evidence for the circadian and homeostatic behaviour.

Our exploratory work is an important step towards objectively describing and predicting daytime vigilance and sleepiness. The choice of EEG-based features enables the quantification in an unbiased way. Our positive results encourage us to investigate the topic on a larger scale.

Our work was funded by the Austrian Research Promotion Agency FFG (827600), the government of Lower Austria, and the European Commission (EFRD WST3-T-81/015-2008).

Georg Dorffner is the CEO of The Siesta Group GmbH and a part-time employee of Philips-Respironics.

O156

'Trait-like' susceptibility to sleep loss varies with circadian phase and the task used to index vulnerable-resilient sleep-deprived performance

J. A. GROEGER[1], J. C. LO[2], N. SANTHI[2], E. L. ARBON[2], A. LAZAR[2], S. HASAN[2], M. VON SCHANTZ[2], S. N. ARCHER[2] and D. J. DIJK[2]

[1]University College Cork, Cork, IE, [2]University of Surrey, Guilford, UK

Objective: It has been suggested that trait-like variability can be quantified by calculating the intraclass correlation coefficient (ICC) across individuals exposed to the same stressor on different occasions. The size of the ICC will reflect both stable individual differences and the differences between the circumstances prior to the stressor's application. Using this approach we attempted to identify trait-like susceptibility to the effects of sleep loss by contrasting rested and sleep-deprived performance of a number of cognitive tasks.

Methods: Thirty-six adults were exposed to two episodes of 36 h of total sleep deprivation (TSD), following a week where nightly sleep restricted (6 h per night) or where they had 10 h sleep opportunity per night. Across both TSD episodes, at two hourly intervals, individuals performed a battery of cognitive tasks. Separate baselines were derived from rested or restricted baseline performance on entering TSD.

Results: Effect sizes (Cohen's d) of changes from restricted or rested baselines varied in relation to homeostatic and circadian pressures. Effects of trait-like variability were substantial by common metrics, but varied across time awake and task. Separately for each time point and task, individuals were classified according to whether they performed above or below the group median on a particular task. Individuals were classified as 'vulnerable', 'resilient', where they had performed consistently above or below the session median in both TSD episodes. Effects of sleep loss were reliably different between 'vulnerable' and 'resilient' participants. For individual tasks, those classified as 'vulnerable' after 24 h sleep loss we reliably classified as 'vulnerable' after 36 h sleep loss. Resilience was similarly stable across accumulating sleep loss. However, classification of vulnerability or resilience was highly task dependent, in that classification of vulnerability or resilience on one task did not predict vulnerability or resilience with respect to other tasks.

Conclusion: Our results show that individuals exhibit a stable trait-like response to sleep loss. This trait-like response is consistent across increasing amounts of sleep loss, but this stable vulnerability or resilience is specific to particular aspects of cognitive functioning. Vulnerability of performance to sleep loss depends who, when and what is being performed.

This research was supported by grants from the AFOSR (FA-9550-08-1-0080) and the BBSRC (BB/F022883/1).

O157

At-sea trial of 24-h based submarine watchstanding schedules: implications for circadian rhythm management

M. KELLER[1], K. MARVIN[2], C. STEELE[3], M. FIGUEIRO[4] and M. REA[4]

[1]Naval Medical Center San Diego, San Diego, CA, US, [2]Naval Submarine Medical Research Laboratory, Groton, CT, US, [3]Uniformed Services University of the Health Sciences, Bethesda, MD, US, [4]Rennselaer Polytechnic Institute, Troy, US

Background: The environment aboard a US Navy submarine requires living on a non-24-h daily schedule without exposure to the circadian-regulating effects of natural sunlight. These living conditions combined with standing rotating 6-h watch shifts leads to a unique state of circadian regulation.

Methods: The experimental period ran for 6 weeks aboard a US Navy submarine and involved 34 subjects. The underway operational study compared 18-h versus 24-h based watchstanding schedules. The 24-h schedules consisted of both a 3-section sequential 8-h rotating schedule and a variant 8-h watch rotation that staggered sleep periods to facilitate crew administrative tasks. These schedules were compared to a traditional 18-h submarine watchstanding schedule. Individuals were also phase-advanced between four and 8 h during trials of the 24-h schedules to study circadian phase-shifting. Throughout the study, the subjects underwent cognitive and hormonal testing to include actigraphy, salivary hormone sampling (melatonin, cortisol, alpha-amylase), handheld cognitive tests, light dosimetry, written surveys, and sleep logs.

Results: The data shows that individuals sleep longer and more efficiently and have better circadian entrainment on the 24-h based schedules. Subjects slept nearly an hour more per sleep episode on the 24-h based schedules than on the 6/12 schedule [24-h avg. 6 h 30 ± 16 min; 18-h avg. 5 h 41 min ± 12 min ($P = 0.033$)]. There were no observed performance decrements on cognitive testing. Raw salivary hormone data were subjected to two cosinor fits, one with a period of 24-h and the other with a period of 18-h. The Residual Sum of Squares (RSS), a measurement of the deviation of the cosinor fit to the original data, revealed a significantly lower RSS value for the two 24 h schedules ($t_{58} = -2.3$, $P = 0.01$ and $t_{58} = 1.67$, $P = 0.01$), versus the 18-h schedule ($t_{58} = -2.19$, $P = 0.02$) indicating that the 24 h schedule better aligned circadian markers to sleep-wake cycles. The 24-h based watch schedules were preferred by a two-thirds ratio.

Conclusions: The results demonstrate both the operational viability and sleep efficiency enhancing effects of the 24-h based watch schedules. The ability of the crew to phase-shift their circadian rhythms despite low ambient light exposure may indicate a long-term circadian adaptation to lower light thresholds.

O158

The development of circadian rhythms in human infants: cortisol the switch; melatonin the messenger and clock genes

D. V. JOSEPH[1], N. CHONG[2], N. A. TAUB[2], E. ROSATO[2], M. SHANKS[3], S. A PETERSEN[2] and M. P. WAILOO[2]

[1]University of Nottingham, Nottingham, UK, [2]University of Leicester, Leicester, UK, [3]University of Oxford, Oxford, UK

Introduction: Circadian diurnal rhythms in human infants are not fully present at birth and develop over the first postnatal months with full maturity being achieved at around 3 months of age. Deep body temperature during night time sleep is used as marker of physiological maturity. The pattern and order of the maturation of different outputs of the central clock have not been fully elucidated in human infants.

We report on the longitudinal changes in physiological development with age in 35 human infants, related to core body temperature, night time sleep patterns, melatonin, and cortisol, in conjunction peripheral circadian gene expression.

Methods: Infants were recruited at the age of 6 weeks till 18 weeks for inclusion in the study. Home based monitoring of deep body temperature was undertaken concurrently with actigraphy to record infant sleep. Urine was collected for estimation of cortisol and melatonin. Buccal swabs were taken for circadian gene expression.

Results: Physiological maturation as evidenced by an 'adult' pattern of biorhythm development occurred just prior to 3 months. An initial cortisol early morning peak preceded the surge in night time melatonin. The appearance of a mature core body temperature rhythm coincided with evidence of sleep consolidation in human infants, culminating in a robust pattern of circadian gene expression.

Conclusion: There was evidence of a sequential, ordered temporal pattern of physiological development in human infants. The measurement of sleep and associated developmental stage in terms of physiology may be used as a marker of illness and vulnerability. Cortisol has a key role a There was evidence of a sequential, ordered temporal pattern of physiological development in human infants along with the messenger of the clock melatonin.

Oral Session 6 – Molecular Sleep

O159

Sleepy metabolites: sleep-related changes in the human metabolome

R. DALLMANN[1], C. SCHMIDT[2], L. TAROKH[1], A. VIOLA[2], C. F. REICHERT[2], M. MAIRE[2], C. CAJOCHEN[2] and S. BROWN[1]
[1]Insitute of Pharmacology and Toxicology, Zurich, CH, [2]Psychiatric Hospital of the University of Basel, Basel, CH

Objectives: Recently, we described the human circadian metabolome in saliva and plasma using liquid and gas chromatography coupled with mass spectroscopy (LC/GC-MS) (Dallmann et al. PNAS, 2012). In a constant routine (CR) study, strictly controlled for sleep and wake, body posture and food intake, about 15% of all identified metabolite levels varied in a circadian fashion. Interestingly, some of the identified metabolites showed a monotonic increase or decrease throughout the 40 h of sleep deprivation (SD) during the CR study. In order to investigate the effect of sleep pressure on metabolism, we conducted a second experiment in which we compare the effects of SD with a frequent Nap protocol that keeps sleep pressure at a low level throughout the 40-h CR study.

Methods: Four healthy male volunteers participated in this study. Two weeks prior to the CR, habitual sleep time was determined and healthy sleep habits were established for all participants. In a balanced cross-over design, volunteers underwent both a 40-h CR and a 40-h CR with naps (NAP, alternating cycle of 160 min of wakefulness and 80 min of sleep). Saliva samples were taken before and after each nap or at corresponding times during the SD protocol (a total of 20 timepoints). Samples of individuals were pooled according to timepoints and conditions. Then 20 pools each for SD and nap were analyzed by LC/GC-MS to quantify all identifiable metabolites in the saliva. We used a permutation algorithm to identify rhythmic compounds.

Results: In total, we identified 260 metabolites in the saliva samples in the SD and Nap pools. As in the previous study, we identified about 15–20% oscillating metabolites in the circadian range and, in addition, found some in the ultradian (8 h) range. Interestingly, there were about twice as many circadian metabolites in the SD compared to the Nap group. Conversely, there was roughly twice the number of ultradian metabolites in the Nap group.

Conclusion: We confirmed the previously published circadian variation of metabolite levels in human saliva. Moreover, we found multiple metabolites that were influenced by frequent naps and showed ultradian patterns. This novel and puzzling finding suggest that sleep is interacting with the circadian control of metabolism to an under-appreciated degree.

O160

Response to sleep deprivation and recovery sleep: human blood biomarkers

E. S. ARNARDOTTIR[1], E. V. NIKONOVA[2], K. R. SHOCKLEY[3], R. C. ANAFI[4], A. A. PODTELEZHNIKOV[4], K. TANIS[4], D. J. STONE[4], G. MAISLIN[4], T. GISLASON[1], J. RENGER[2], C. WINROW[2] and A. I. PACK[4]
[1]Landspitali University Hospital, Reykjavik, IS, [2]Merck Research Laboratories, West Point, NY, US, [3]National Institute of Environmental Health Science, Research Triangle Park, NC, US, [4]Center for Sleep and Circadian Neurobiology, Philadelphia, US

Introduction: The aim of this study was to measure changes in gene expression in human blood in response to sleep deprivation and recovery sleep and the role of inter-individual differences in sleepiness.

Methods: Fourteen healthy subjects that were relatively resistant to sleep deprivation (low responders) and markedly impaired (high responders), based on performance in a psychomotor vigilance task (PVT), were chosen for the study. Blood mRNA expression was measured every 4 h using microarrays in a normal sleep-wake cycle, 24 h of sleep deprivation and 8 h of recovery sleep (total of 19 time points). Significance of differences in gene expression was assessed by multivariate ANOVA model. Selected candidate genes were confirmed by qRT-PCR. Biological pathway enrichment analyses were performed using Target and Gene Identification system (TGI) with correction for multiple comparisons.

Results: Seven thousand nine hundred and seventy-six gene transcripts had a diurnal rhythm in normal sleep-wake cycle (false discovery rate, FDR <5%). Only two genes changed expression significantly during sleep deprivation (FDR <5%), SREBF1 and CPT1A, both significantly involved in lipid metabolism. Twenty-eight known genes were suggestive at a less stringent threshold ($P < 0.001$). Again, these genes were involved significantly in lipid metabolism. Thirty-one known genes could separate high and low responders in sleep deprivation ($P < 0.001$). The suggestive genes were involved in inflammation, oxidative stress, endoplasmic reticulum (ER) stress and biosynthesis. Further suggestive differences were observed in recovery sleep. One hundred and thirty-one genes differed significantly between normal sleep and recovery sleep in high responders and two genes in low responders. These genes were significantly related to immune function.

Discussion: This is the first study to explore genome wide changes in expression in peripheral tissues as a function of behavioural state. Despite profound circadian signature observed in normal sleep-wake, only a small number of genes in blood change expression in response to sleep deprivation and recovery sleep. Individuals resistant to sleep deprivation have some suggestive differences in molecular signatures compared to those markedly impaired; both during sleep deprivation and recovery sleep. These findings may help further blood biomarker development to successfully monitor healthy or diseased sleep homeostasis.

O161

Altered dynamics in the circadian oscillation of clock genes in dermal fibroblasts of patients suffering from idiopathic hypersomnia

J. P. LIPPERT, H. HALFTER, A. HEIDBREDER, D. ROEHR, B. GESS, N. OSADA and P. YOUNG
University of Münster, Münster, DE

Objectives: From single cell forms to the most complex life forms, the 24-h circadian rhythm is of utmost importance for numerous aspects of physiology. Daily periodic fluctuations in the sleep-wake cycles and body temperature are the most obvious examples. These physiological aspects underlie an ubiquitous molecular clock mechanism driven by an interlocked network of transcriptional feedback loops of circadian clock genes (CCG). In analogy to the central pacemaker, peripheral tissues such as fibroblasts harbour the circadian clock mechanism. It is cell-autonomous and equally self-sustaining in an isolated primary cell-culture. Previous studies prove that CCG in fibroblasts display the intraindividual length of circadian rhythm as well as the dynamic in transcriptional regulation (Brown et al, PNAS Feb.2008).

In order to choose a new molecular genetic approach for a better understanding of the pathophysiology of clinical symptoms indicating an endogenous disturbed wake sleep rhythm, the following study aims to investigate the dynamic of CCG in dermal fibroblasts of idiopathic hypersomiacs (IH) in comparison to healthy controls (HC).

Methods: The IH were recruited out of the department of sleep medicine and polysomnographically screened. They were tested for Multiple Sleep Latency. Pre-existing illnesses such as RLS or OSAS were excluded. The transcriptional expression of circadian clock genes in dermal fibroblasts obtained via punch biopsy were investigated. After synchronisation with dexamethasone the totalRNA of the confluent fibroblasts was isolated over 72 h at 14 different time points. Quantitative qRT-PCR proofs a periodic oscillation of expression of the core CCG Bmal, Per1/2, Cry1/2 and allows a direct comparison of the dynamic in the oscillation and total gene expression between IH and HC.

Results: The amplitude of the rhythmically expressed CCG Bmal, Cry1/2, and Per1 is significantly dampened by 54% in dermal fibroblasts of IH compared to HC over two periods whereas the overall expression of only the key transcriptional factor Bmal is significantly reduced. This leads to a clearly diminished dynamic in circadian gene expression in IH.

Conclusion: Currently an evidence of a molecular genetic altered circadian clock in IH is still lacking, this study hints an evidently dampened oscillation in CCG expression suggesting a dynamic genetic impact on the pathophysiology which could explain some features of this idiopathic sleep disorder syndrome.

O162

Effect of total sleep deprivation on clock gene expression and melatonin rhythms in human peripheral blood cells

K. ACKERMANN[1], O. LAO[1], V. L. REVELL[2], R. PLOMP[1], B. MIDDLETON[2], D. J. SKENE[2] and M. KAYSER[1]
[1]Erasmus MC University Medical Centre, Rotterdam, NL, [2]University of Surrey, Guildford, UK

Objectives: Studies of the effect of sleep deprivation on clock gene expression in human peripheral blood cells and melatonin rhythmicity are sparse, especially those in a normal setting rather than under constant routine conditions. The aim of this study was to provide a comprehensive in-depth analysis of clock gene expression and hormone levels in humans under normal sleep-wake conditions and to assess the effect of a night of total sleep deprivation on any observed rhythmicity.

Methods: Healthy young males (n = 12, 23 ± 5 years) participated in the study, consisting of a baseline-at-home period before entering the laboratory, where subjects were kept under highly controlled conditions (light levels (day 100 lux, sleep 0 lux; sleep deprivation <5 lux), posture, meals). The laboratory protocol included two normal sleep-wake cycles (adaptation and baseline night) followed by 29 h of continuous wakefulness. Frequent blood samples were taken across a 48 h period. Relative expression of 12 genes (11 clock genes and a heat shock gene) was assessed using RT-qPCRHormone levels were determined by radioimmunoassay. Diurnal rhythmicity was assessed using single and multiple cosinor analysis, and the effect of sleep deprivation on rhythmicity was determined.

Results: Melatonin and cortisol profiles showed statistically significant rhythmicity for each subject, independent of condition (sleep/sleep deprivation). While cortisol levels were unaffected by sleep deprivation, melatonin acrophase was significantly later during the sleep deprivation night, and both melatonin amplitude and area-under-the-curve were significantly increased. Notably, dim light melatonin onset (DLMO) was not significantly different between the two conditions. The most robust diurnal rhythms in gene expression levels were detected for PER3 and REV-ERBalpha, followed by BMAL1 and PER1. The PER1, PER3, and REV-ERBalpha rhythms were unaffected by sleep deprivation in contrast to the BMAL1 and HSPA1B rhythms which were severely distorted (both timing and amplitude) by sleep deprivation.

Conclusion: One night of sleep deprivation affected the expression of a heat shock gene and some, but not all, clock genes. The increased melatonin production during sleep deprivation might be interpreted as an effect related to its ancient role as a radical scavenger, while the delayed melatonin peak might be a result of the small differences in the lighting conditions (0 lux during sleep; <5 lux during sleep deprivation).

This work was supported by the Netherlands Forensic Institute (NFI), and received additional support from the 6th Framework project EUCLOCK (018741) and a grant from the Netherlands Genomics Initiative (NGI) / Netherlands Organization for Scientific Research (NWO) within the framework of the Forensic Genomics Consortium Netherlands (FGCN). Drs. Skene and Revell have received research support from Philips Lighting.

O163

USF1 regulates sleep and circadian traits in humans

H. M. OLLILA[1], H. LITTOW[2], J. TURUNEN[3], K. SILANDER[3], M. PEROLA[3], V. SALOMAA[3], J. MIETTUNEN[2], M. HÄRMÄ[4], S. PUTTONEN[4], J. VEIJOLA[2], V. KIVINIEMI[2], T. PORKKA-HEISKANEN[1] and T. PAUNIO[3]
[1]University of Helsinki, Helsinki, FI, [2]University of Oulu, Oulu, FI, [3]National Institute for Health and Welfare, Helsinki, FI, [4]Finnish Institute of Occupational Health, Helsinki, FI

Objectives: Epidemiological studies show association between sleep duration and lipid metabolism. Our aim was to characterize gene variants that regulate both metabolism and sleep. One such candidate is USF1 that regulates the expression of several lipid genes and has a similar structure as canonical circadian transcription factors. We studied the polymorphisms in USF1 gene region with sleep duration and coping with circadian stress in Finnish population based samples combined with gene expression and MRI analysis.

Materials and methods: The known USF1 variants that had previously been associated with lipid traits were studied with sleep and coping with circadian stress. The analyses were performed in a Finnish population based sample with no sleep problems (N = 1085) and Finnair workers (N = 1415). RNA expression from mononuclear leucocytes was measured in additional 584 individuals. Finally the variants were studied in resting state fMRI data from 176 healthy individuals.
Results: The genetic analysis identified that the USF1 polymorphisms associated with sleep duration in the healthy individuals. The same variant associated with coping with circadian stress in Finnair workers. Gene expression analysis showed that those individuals carrying minor allele had higher USF1 expression. Finally, fMRI analysis identified activity in distinct brain regions that correlated with the USF1 genotypes.
Conclusions: Our results show that the allelic variants of USF1 associate with sleep duration and coping with circadian stress. The finding may reflect the shared roots of sleep and metabolism. The shared genetic background and the effect of USF1 in functional connectivity of neuronal networks may at least partially explain the mechanism behind the well-established connection between diseases with disrupted metabolism and sleep.

O164

New narcolepsy susceptibility loci identified through dense genotyping of immune-related loci

J. FARACO, L. LIN, E. MIGNOT and the International Immunochip Consortium

Objective: Narcolepsy/ hypocretin deficiency results from a highly specific destruction of approximately 70 000 hypocretin-producing cells in the hypothalamus, through a likely autoimmune mediated process. The onset of symptoms (exessive sleepiness, disturbed nocturnal sleep, and cataplexy) occurs most frequently during childhood or adolescence, and once cell loss has occured, the disorder is life-long. Over 98% of cases (all ethnic groups) carry the human leukocyte antigen (HLA) susceptibility haplotype DQA1*01:02, DQB1*06:02. Specific T cell receptor alpha variants are also significantly associated with disease risk across racial groups, as are variants at additional immunomodulatory genes (P2RY11 purinergic receptor/ DNMT1 region). Together with the International Immunochip Consortium, we genotyped and analyzed ~2000 narcolepsy samples and ~11 000 controls to identify additional immune-related susceptiblity loci missed in previous genome wide association studies, and to fit the genetic architecture of narcolepsy into a broader context of other known autoimmune diseases.
Methods: Samples were typed on the Illumina Immunochip, containing ~200 000 markers selected for high-density coverage of immune related genes. Narcolepsy cases had clear-cut cataplexy and were DQB1*0602 positive, or had documented hypocretin deficiency (CSF hcrt-1 levels), and came from the USA, Canada and Europe. Control genotypes were provided by consortia members and were from individuals with known single European country of origin, or were of mixed European ancestry from North America. Data analysis was performed using Plink, Golden Helix SVS and EMMAX.
Results: Preliminary association results provide strong replication of T Cell Receptor alpha polymorphism rs1154155 (P < 10–27) as has been seen in previous studies. Additional loci showed association with narcolepsy at genome-wide significant levels, and are being tested for replication in additional narcolepsy samples.
Conclusions: The genetic architecture of narcolepsy indicates important roles for a variety of immune-related genes conferring susceptibility to the disease.

O165

Search for microRNAs in cerebrospinal fluid and plasma as diagnostic biomarkers in narcolepsy

A. HOLM[1], C. BANG-BERTHELSEN[1], S. KNUDSEN[2], S. GAMMELTOFT[1] and P. JENNUM[2]
[1]Clinical Biochemistry, Glostrup, DK, [2]Danish Centre for Sleep Medicine, Glostrup, DK

Objectives: MicroRNAs (miRNA) are small non-coding RNAs that serve as important regulators of gene expression at transcriptional or post transcriptional level. MicroRNAs have been shown to play important roles in many human diseases including various types of neurological disorders. We aimed to identify miRNAs found in the CSF and plasma that are dysregulated in patients with narcolepsy.
Methods: Isolation of miRNAs was performed using spin columns from Macherey Nagel for plasma and CSF purification. Comprehensive libraries of several hundred synthetic miRNAs will be used to screen miRNAs in CSF and plasma from patients with narcolepsy with cataplexy (NC), narcolepsy without cataplexy (NwC), ideopathic hypersomnia (IH) and healthy controls (HC).
Results: Using a high-throughput approach, we were able to identify 198 and 286 miRNAs in CFS and plasma, respectively. We identified 25 and 55 miRNAs that are significantly dysregulated with a two-fold change in patients with sleep disorders compared to HC. Selected miRNAs was validated by qRT-PCR. MiR-455-3p is significantly up-regulated in plasma from patients with NC compared to HC. MiR-455-3p, a potential biomarker for NC, will be validated in a larger cohort.
Conclusion: In plasma samples from patients with narcolepsy, cataplexy and with low csf-hcrt-1 miR-455-3p were up-regulated compared to HC. No differences in expression level of miR-455-3p were identified in NwC, IH or HC. Noteworthy, miR-455-3p has also been shown to be up-regulated in glioblastoma and astrocytomas, as well as having an effect on cell death. This could very well turn out to be an important finding concerning the loss of hypocretin cells in NC.

O166

Site-specific effects of orexin gene transfer in narcoleptic mice

P. SHIROMANI, M. LIU, C. BLANCO-CENTURION, R. KONADHODE and D. PELLURU
Medical University of South Carolina, Charleston, US

Narcolepsy is now considered a neurodegenerative sleep disorder characterized by a massive loss of neurons containing the neuropeptide, orexin, also known as hypocretin. Since the orexin neurons have degenerated it is necessary to identify surrogate neurons that can release orexin and thereby ameliorate symptoms of narcolepsy. Can these surrogate orexin neurons be located anywhere in the brain or is there site-specificity? To answer this question the gene for orexin was delivered into the brains of the orexin-ataxin-3 transgenic or the orexin knockout mice model of human narcolepsy. Three weeks after recombinant adeno-associated virus (rAAV)-mediated orexin gene transfer sleep-wake behavior was assessed. rAAV-orexin gene delivery into neurons of the zona incerta (ZI) (n = 8), the lateral hypothalamus (LH) (n = 11) or the dorsolateral pons (n = 5) blocked cataplexy. Orexin gene transfer into the striatum (n = 9) or in the melanin concentrating hormone (MCH) neurons in the ZI or LH (n = 16) had no such effect indicating site-specificity. Lack of an

effect after orexin gene transfer in MCH neurons is particularly interesting as it indicates that even though these neurons project to the same targets as the orexin neurons, the MCH neurons are not active during the cataplexy attacks and are thus not able to release orexin and block cataplexy. Thus, both connectivity and neuronal firing is relevant for behavioral effects. Wake maintenance was partially improved with orexin gene transfer in the pons, but not in other groups. In transgenic mice lacking orexin but given rAAV-orexin, detectable levels of orexin-A were evident in the cerebrospinal fluid indicating release of the peptide from the surrogate neurons. Retrograde tracer studies showed that the amygdala innervates the ZI and the pons consistent with evidence that strong emotions trigger cataplexy. These studies identify a pathway involving the amygdala, ZI and the pons that stabilizes motor tone. Research will be presented to show the effects of optogenetic stimulation of this pathway in controlling cataplexy. Supported by the NIH and the Veterans Administration

O167

Chronic mild stress abolishes a relationship between sleep architecture and translational control

J. GRONLI, G. DAGESTAD, A. M. MILDE, R. MURISON and C. BRAMHAM

University of Bergen, Bergen, NO

Stress and restricted or disrupted sleep trigger adaptive responses in the brain at the level of gene transcription. Here, we investigated a possible relationship between sleep and two key translation factors, eukaryotic initiation factor 4E (eIF4E) and elongation factor 2 (eEF2) important for cognitive function and synaptic plasticity in healthy, chronically stressed and sleep deprived rats.

Thirty six adult male rats were implanted with EEG/EMG electrodes. After postoperative recovery the animals were randomly separated into one CMS (4 weeks of daily exposure to mild stressors) group and one control group. Further, they were subdivided into one group of 8 h sleep deprivation (gentle handling) or non-sleep deprivation. Sleep was recorded before and after termination CMS/control condition. Decapitation was performed directly after sleep deprivation or sleep recording, and prefrontal cortex analysed for post-transcriptional effects.

Exposure to CMS reduced both sleep quality (i.e. depth of sleep) and quantity (i.e. fragmentation of sleep, time in wakefulness). Sleep parameters were correlated with expression of phosphorylated eIF4E and eEF2, normalized to respective total protein. Control rats showed a positive correlation between the phosphorylation state of eEF2 and sleep quality; total time spent in slow wave sleep ($r = 0.97$, $P < 0.01$), and negatively correlated with poor sleep quantity; number of waking episodes ($r = -0.87$, $P = 0.05$). Phosphorylated eIF4E correlated positively with number of REM sleep episodes ($r = 0.92$, $P < 0.05$) and SWS-1 episodes ($r = 0.89$, $P < 0.05$).

There was no association with sleep quality or quantity and translation factor activity for rats exposed to CMS.

Sleep quality prior to acute sleep deprivation with subsequent changes in translation factor activity was also assessed. Phosphorylated eIF4E was positively associated with time spent in wakefulness ($r = 0.88$, $P < 0.01$) and negatively with time in SWS ($r = -0.87$, $P < 0.01$). The phosphorylation of eEF2 tended to show similar pattern, and was significantly negatively correlated with REM sleep ($r = -0.83$, $P < 0.05$).

Again, in CMS treated rats combined with sleep deprivation, there was no association with sleep parameters and changes in translational factor activity.

Thus, measures of both sleep quality and sleep quantity in healthy animals are predictive of changes in eIF4E and eEF2 phosphorylation in the prefrontal cortex. Prior exposure to CMS, which degrades sleep architecture, abolishes such relationship.

O168

Effects of circadian phase and prior partial sleep deprivation on executive functions during total sleep deprivation are modulated by PER3 polymorphism

J. C. LO[1], J. A. GROEGER[2], N. SANTHI[1], E. L. ARBON[1], A. S. LAZAR[1], S. HASAN[1], M. VON SCHANTZ[1], S. N. ARCHER[1] and D.J. DIJK[1]

[1]University of Surrey, Guildford, UK, [2]University College Cork, Cork, IE

Objective: A variable-number tandem-repeat polymorphism (rs57875989) in the clock gene, PER3, predicts individual vulnerability in executive functions during total sleep deprivation (TSD), particularly in the early morning hours. However, PER3 appears not to affect cognition during partial sleep deprivation (PSD). Here, we directly compared the effects of PER3 during both PSD and TSD, and examined the effect of prior PSD on executive functions across the circadian cycle during TSD.

Methods: This study adopted a balanced, cross-over design and consisted of two 12-day laboratory sessions. After two nights of 8 h Time In Bed (TIB), the sleep opportunity of the participants (12 PER34/4s, 10 PER34/5s, and 14 PER35/5s; 18 males; mean ± SD of age = 27.6 ± 4.0 years) in the following seven nights was either 10 h (Control condition) or 6 h (Sleep Restriction condition; SR). This was followed by a ~40 h TSD period and a recovery sleep episode (TIB = 12 h). Working memory/executive function was assessed with verbal 1-, 2-, and 3-back tasks throughout the protocol.

Results: We found that in all n-back tasks, the effect size of the interaction between genotype and both PSD and TSD was small (Cohen's $f2 = 0.002–0.05$). However, during TSD, we found a strong circadian modulation of the differential responses of the PER3 genotypes to prior PSD in the verbal 3-back task, i.e. the working memory task with the highest load on executive functions. Specifically, at 4 h after the nocturnal rise of melatonin secretion, i.e. 02:00–06:00, the genotypes responded differentially to the sleep history manipulation. In the PER34/4 homozygotes, executive functions deteriorated during the TSD period independent of the duration of the sleep opportunities in the previous week. By contrast, in the PER34/5 and the PER35/5 individuals, the deterioration of 3-back performance during TSD was greater following SR than in the Control condition.

Conclusion: Our results show that executive function during TSD is determined by the time of day of the assessment, the chronic sleep debt carried by the individual, and the individual vulnerability conferred by the PER3 polymorphism. The prominent circadian modulation observed suggests that the effect of PER3 genotype is strongest during early morning hours, i.e. the time when performance is typically not assessed in PSD protocols.

This research was supported by grants from the AFOSR (FA-9550–08–1–0080) and the BBSRC (BB/F022883/1).

Symposium – Deconstructing the Sleep-Deprived Brain in Decision-Making

S173

Cognitive components of degraded decision-making when sleep-deprived

H. P. A. VAN DONGEN
Washington State University, Spokane, US

While sleep deprivation has been shown to impair the ability to sustain attention and degrade overall task performance in most individuals, some aspects of performance may be intact or even improved after sleep loss. There is no consensus on whether and how sleep deprivation affects complex tasks such as decision-making, which typically involve the integration of higher level aspects of cognition with emotional signals of risk and reward. Inconsistent findings have been reported in the literature as different paradigms place different demands on cognitive and emotional processing, which can influence decision-making in varying, even opposing directions. For example, sleep loss diminishes affective responses involved in limiting risk-taking, and thus might be expected to increase risk-taking behaviors. On the other hand, sleep loss appears to diminish working memory capacity, which may be expected to decrease risk-taking. We have found sleep-deprived subjects to take selectively longer to make risky decisions, suggesting that in our controlled laboratory environment the sleepy brain may be more deliberate and cautious. Carefully disentangling the sleep deprivation effects on the components of cognitive and emotional processing is beginning to shed light on the effects of sleep loss on decision-making, which will ultimately help to mitigate these effects in the real world.

S174

Sleep deprivation and decision-making with uncertainty and risk

A. M. TUCKER[1], H. P. A. VAN DONGEN[1] and G. KERKHOF[2]
[1]Washington State University, Spokane, US, [2]University of Amsterdam, Amsterdam, NL

Sleep deprivation degrades cognitive performance in general and, as suggested by physiological and neuroimaging findings, may interfere with decision-making in particular. Still, the effects of sleep loss on decision-making are surprisingly difficult to demonstrate consistently in the laboratory. In part this is due to the use of neuropsychological tests developed for brain injury patients. These tests are not optimally designed for examining the effects of sleep deprivation, which have long been demonstrated not to be lesion-like, but rather involve increased performance variability that is difficult to capture reliably in the context of decision-making. Also, laboratory decision-making tests suffer from task impurity, that is, they include a range of cognitive processes that could be affected by sleep deprivation, not just decision-making. We developed cognitive task batteries to examine distinct aspects of decision-making performance, including attention, stimulus encoding, working memory, information throughput, affective influences, and feedback processing. We investigated the effects of sleep loss on these aspects separately and combined at baseline, after sleep deprivation, and post recovery, in healthy young adult subjects studied in a controlled laboratory setting. We observed cognitive deficits in a range of cognitive performance tasks, but found that these deficits are not necessarily due to impaired decision-making per se. Findings from statistical analyses on separate components of performance and from cognitive modeling implied a significant role for impairments in stimulus encoding and other non-decision components of decision-making performance. These impairments had a profound adverse effect on performance in decision-making tasks involving uncertainty (through ambiguous information in stimuli) and risk (where outcomes involved gains or losses). Investigation of deficits in distinct cognitive processes is crucial for understanding the nature of impaired decision-making under conditions of sleep deprivation. Our results point to degraded information processing, rather than decision errors per se, as an underlying cause for deficits in decision outcomes in sleep-deprived individuals. This has important implications for emergency responders and other individuals who, often under time pressure, depend heavily on accumulation and integration of potentially ambiguous information for making critical, risky decisions.

S175

Functional imaging of decision-making in sleep deprived persons

M. W. L. CHEE
Duke-NUS Graduate Medical School, Singapore, SG

Sleep deprivation (SD) is known to affect performance in tasks requiring sustained attention. However, less is known about affective aspects of behavior such as decision-making. Risky decision-making involves weighing the subjective value associated with reward against values associated with losses, taking into account outcome probability. In some tasks, a night of total sleep deprivation increases the propensity to select gain-maximizing choices rather than to reduce the likelihood of loss. State related signal changes occurring in the ventral striatum, ventromedial prefrontal cortex (vmPFC) and insula predict gain chasing and aversion to losses. The valuation of social and monetary rewards appears to shift in heterogeneous manner across individuals exposed to SD. This is tracked by shifts in vmPFC activation. Interestingly, changes in economic decision-making following SD are uncorrelated with alterations in vigilance. We investigated increased impulsivity as a potential cause for alterations in risky decision-making but did not find significant changes in delay discounting. Contrastingly, sleep deprived persons show greater discounting for effort. Effort discounting recruits areas in the anterior prefrontal cortex that we expect to be impaired following SD. We illustrate the varied ways in which functional magnetic resonance imaging (fMRI) can be used to investigate alterations in decision making in sleep deprived persons.

S176

Impaired decision-making in sleep disorders

E. DE VALCK[1] and R. CLUYDTS[2]
[1]University of Brussels, Brussels, BE, [2]University Hospital Antwerp, Antwerp, BE

Objectives: Sleep deprivation in healthy subjects has negative effects on decision-making tasks. We asked whether similar effects are found in sleep disorder patients suffering from chronic sleep insufficiency, or whether tolerance to this phenomemon may develop.

Sleep disorder patients commonly complain about problems concentrating, forgetting, and making 'stupid'' errors and wrong decisions resulting in extreme cases to decidophobia. Can these subjective experiences be objectified, and are these simply the result of a general cognitive decline due to increased sleepiness?

Methods: A systematic literature search was conducted to review results from studies applying decision-making test procedures in sleep disorder patients.

Results: Studies have been mainly conducted in following sleep disorders: sleep apnea, narcolepsy and REM sleep behavior disorder. Neuropsychological tests used include the Iowa Gambling Task, the Balloon Analogue Risk Task, the Multiple Errands Test and the Game of Dice Test. These tasks purport to assess executive performance in a naturalistic environment, but most were developed for brain injury patients and may need adaptation given floor/ceiling effects. The most common finding is that sleep disorder patients show performance decreases and even deficits in reward/emotion dependent decision-making.

Conclusion: If valid procedures to assess decision-making in a clinical context (under time limitation) can be developed, such procedures may become standard diagnostic tools for sleep disorders as well as significant outcome measures in therapeutic interventions. Narcolepsy and REM sleep behavior disorder, having clear neuroanatomical and neuropharmacological correlates, may elucidate the role of hypocretines and dopamine in the neurobiological underpinnings of decision-making. Special interest also goes to sleep apnea patients, since comorbidity in this condition is prevalent and causal relations need to be formulated cautiously. Further, children and adolescents with sleep-related respiratory disturbances need more attention, as brain and behavioral development is critical in this age group.

Symposium – REM Sleep Behavior Disorder: from Neurotoxic and Transgenic Animal Models to Neurodegeneration and Neuroprotection in Humans

S177

Lesion animal models of REM sleep behavior disorder

P.-H. LUPPI, S. VALENCIA GARCIA, O. CLÉMENT and P. FORT
UMR 5292 CNRS/U1028 INSERM, Lyon, FR

Rapid eye movement sleep behavior disorder (RBD) is a parasomnia characterized by the loss of muscle atonia during paradoxical (REM) sleep (PS). The neuronal dysfunctions responsible for RBD are not known. In my talk, I will present an updated integrated model of the mechanisms responsible for PS and explore different hypotheses explaining RBD. We propose that RBD is due to a specific degeneration of PS-on glutamatergic neurons localized in the caudal pontine sublaterodorsal tegmental nucleus (SLD) or the glycinergic/GABAergic premotoneurons localized in the medullary ventral gigantocellular reticular nucleus. In normal condition, the PS-on glutamatergic neurons of the SLD excite the GABA/glycinergic premotoneurons which in turn hyperpolarizes somatic cranial and spinal motoneurons. In RBD patients, one of these two systems would be destroyed. During PS, cortex motor neurons would be activated during vivid dreaming and excite motoneurons and generate movements. I will review experimental evidence supporting the two hypotheses and our more recent results on the effect of the inactivation of the pontine and medullary neurons on the muscle atonia of paradoxical sleep.

S179

Is there any evidence that REM sleep behavior disorder represents neurodegeneration in humans?

B. FRAUSCHER
Innsbruck Medical University, Innsbruck, AT

REM sleep behavior disorder (RBD) is a parasomnia characterized by recurrent episodes of dream enactment which polysomnographic hallmark is REM sleep without atonia. RBD is not only a potentially injurious disorder which can be well treated in most cases with low dosages of clonazepam, but also a very robust early premotor symptom of alpha-synuclein-related neurodegenerative disorders.

Evidence of the latter is based on three longterm natural history studies of RBD patient cohorts. In 1996 Schenck et al. demonstrated that 38% of their patients which were initially diagnosed with idiopathic RBD developed a parkinsonian disorder 4 years after RBD diagnosis. After a further 7-year follow-up period, this frequency increased to 65%. Two other large longterm observational studies could replicate these findings with frequences up to 45% after a 5-year follow-up period. Furthermore, assessment of clinical and imaging risk factors of alpha-synuclein-related neurodegenerative disorders revealed the presence of these markers even in the idiopathic form of RBD. Olfactory dysfunction was found in up to 60% of idiopathic RBD patients compared to 15% of healthy controls and >80% of patients with Parkinson's disease. In line with this finding, disturbed colour vision, neuropsychological deficits, autonomic dysfunction, as well as structural and functional imaging markers such as transcranial ultrasound and dopamine transporter imaging were demonstrated to be at an intermediate level between healthy controls and patients with full-blown synucleinopathies. Apart from this association, recent studies in idiopathic RBD patients have demonstrated that olfaction, color vision, severity of REM atonia loss, transcranial substantia nigra sonography, and dopaminergic neuroimaging can predict development of neurodegenerative disease. Olfaction and disturbed colour vision remain comparatively stable overtime, whereas severity of REM atonia loss, neuropsychological testing as well as results of dopamine transporter imaging and cardial 123I MIBG scintigraphy increase and hence are not only risk markers but also progression markers of evolving neurodegeneration in idiopathic RBD.

There is clear evidence that RBD is a very early non-motor manifestation of alpha-synuclein-related neurodegenerative disorders in a substantial proportion of RBD cases.

S180

Neuroprotection in human REM sleep behavior disorder: is it possible?

A. IRANZO
Hospital Clinic, Barcelona, ES

There are several lines of evidence that indicates that REM sleep behaviour disorder (RBD) is a feature of the prodromal phase of the Lewy body disorders (LBD) Parkinson disease (PD) and dementia with Lewy bodies (DLB). Patients with the idiopathic form of RBD (IRBD) have subclinical features that are typical of LBD including impaired olfaction and reduced DAT imaging. Follow-up of IRBD cohorts shows development of PD and DLB in up to 65% of the cases. It has been shown that IRBD patients with olfactory and colour vision loss and loss and decreased striatal DAT uptake have a high short-term risk to develop PD and DLB. Longitudinal studies in IRBD have shown, though, that olfaction and colour vision impairment do not worsen over time while striatal DAT tracer uptake decreases over a 3 year period before the appearance of parkinsonism.

The LBD have a prodromal phase where progressive cell loss and non-motor symptoms such as RBD occur before the clinical appearance of Parkinsonism and cognitive decline. An early disease-modifying therapy that slows or halts progressive neurodegeneration is an urgent need in the management of the LBD. Identifying individuals during this prodromal phase is a research priority where disease-modifying therapies might be more likely to be effective. The primary end point of these trials in IRBD would be to demonstrate a reduction of the phenoconversion of a LBD in subjects with IRBD. A secondary endpoint would be slowing the reduction of striatal DAT uptake over time, particularly in the putamen. This talk would concentrate on the design of a new trial with a potential neuroprotective drug in subjects with IRBD aimed to stop or slow the appearance of Parkinsonism and dementia.

Symposium – Endocrinological Aspects of Sleep and Sleep Disturbances in Children

S182

Endocrine aspects of pharmacotherapy in narcolepsy

C. E. H. M. DONJACOUR[1], G. J. LAMMERS[1] and M. LECENDREUX[2]

[1]Leiden University Medical Center, Leiden, NL, [2]Hospital Robert Debré, Paris, FR

Objectives: There are no randomized controlled trials or consensus on the treatment of narcolepsy with cataplexy in children, therefore robust data on childhood narcolepsy are lacking. In contrast there have been done several studies on endocrine function in narcolepsy and the effect of treatment in adults.

Methods: Here we review the effect of stimulants, (mainly derived from pediatric ADHD research) anti depressants and sodium oxybate on endocrine function. We present new data showing the effects of sodium oxybate in narcoleptic adults and children as well as the most recent data of stimulants based on the literature.

Results: Stimulants may increase growth hormone secretion, decrease testosterone and total and free T4. Stimulants do seem to have an effect on growth in children. Sodium oxybate increases growth hormone and prolactin secretion and may change insulin sensitivity in adults. In addition it may have a profound effect on weight. Antidepressants used to treat cataplexy may affect insulin sensitivity.

Conclusion: Endocrine function is affected by drugs used to treat narcolepsy with cataplexy. How this affects children especially on the long term is not known. Randomized controlled trials are needed to establish safety and efficacy of treatment of narcolepsy in children. In addition there is a need for a registry in which a standardized assessment of an extensive amount of parameters is noted, depending on the patient's stage of development.

Some of the studies mentioned here have been supported by UCB Pharma.

S183

Pharmacotherapy and growth in ADHD

M. LECENDREUX

Robert Debré Hospital, Paris, FR

Studies providing longitudinal data suggest that treating children with ADHD with stimulant medication generally results in a reduction in both height and weight gain. On average, the reduction in height amounts to approximately 1 cm/year during the first 1–3 years of treatment and the reduction in weight gain about 3 kg less than predicted.

Current data indicate that the initial effect of stimulants on growth appears to attenuate over time. It is possible that the effects of stimulants on growth are dose-dependent. Significant effects on weight and height may require average doses of methylphenidate exceeding 1.5 mg/kg/day which are given continuously.

Preschool children may be particularly vulnerable to growth effects. The National Institute of Mental Health Preschool ADHD Treatment Study reported that children between 3 and 5 years of age treated with methylphenidate had annual growth rates 20.3% less than expected for height (1.38 cm/year) and 55.2% for weight (-1.32 kg/year).

Reduced caloric intake and suboptimal nutrition due to appetite suppression are likely causes of growth suppression. Hypothetically, dysregulation of receptors in the growth system could also be responsible. Adaptation of receptors could contribute to tolerance to growth inhibition over time and to catch-up growth after the medication has been discontinued. Acute effects on growth hormone and prolactin have been observed, but do not yet explain persisting growth deficits.

A hypothesis that ADHD itself is associated with dysregulated growth, either decreased or increased has been put forward, but current evidence is contradictory.

The hypothesis that ADHD was associated with growth dysregulation using an epidemiologic study of ADHD children in France. Our findings suggest that medication-naïve ADHD was associated with being taller and heavier for young children. In contrast, for older children medication-naïve ADHD was associated with being shorter and lighter.

Further research is needed into the causal mechanisms and the long term implications of continuous treatment from childhood to adulthood for ultimate height. The role of stimulants on sleep shoud also be considered, knowing that GH release is closely linked to the sleep–wake cycle and feeding state. Understanding orexin/hypocretin physiology could open new therapeutic possibilities in the treatment of sleep and GH-related pathologies in children with ADHD children and/or neurodevelopmental disorders.

S184

Childhood narcolepsy with cataplexy is associated with precocious puberty and obesity

G. PLAZZI

University of Bologna, Bologna, IT

Objectives: The clinical manifestations of childhood NC can be variable, leading to diagnostic delay and frequent misdiagnosis. NC children also appear to suffer from overweight and/or obesity, and an association with precocious puberty was anecdotally reported suggesting wider metabolic/hormonal derangement.

Materials/Methods: We systematically examined the potential metabolic and endocrine abnormalities in 43 children or adolescents (23 boys, mean age 11.78 ± 3.64 years). Brain magnetic resonance imaging (MRI) was carried out to exclude secondary causes of NC. One boy with secondary NC was excluded. Physical examination included height and body weight measurements and pubertal development staging. Pubertal status was assessed by the visual Tanner score scale. If precocious puberty was clinically suspected, patients underwent pubertal endocrine assessment including: luteinizing hormone releasing hormone (LHRH) stimulation curve, 30 X-ray of the non-dominant wrist for bone/chronological age ratio, pelvic ultrasound (girls), and brain MRI study of the hypothalamic-pituitary region. Height and weight were measured, body mass index (BMI) was calculated, and BMI percentile was determined in comparison with Italian growth percentile scales for boys and girls. Obesity was defined as BMI >97th percentile, overweight as between 85th and 97th percentile, and normal weight as <85th percentile. Additionally, family history of metabolic/internal diseases was collected.

Results: NC children showed a dramatically higher prevalence of precocious puberty (17%) and overweight/obesity (74%) than the general pediatric population (0.015% and 36% respectively). Beyond precocious puberty, isolated signs of accelerated pubertal development (thelarche, pubic hair, advanced bone age) were also present (41%). Overweight/obese NC children displayed lower levels of high density lipoprotein cholesterol and higher levels of C-reactive protein when compared to normal weight NC children. NC symptoms, pubertal signs appearance, and body weight gain started in close temporal sequence.

Conclusions: When NC occurs in prepubertal age, it may be associated with precocious puberty and overweight/obesity, suggesting a wider hypothalamic dysfunction. The severity of these co-morbidities and the potential related risks require a multi-specialist diagnosis and a tailored therapeutic management.

Dr. G. Plazzi declares partial funding with nEUroped (PHEA) grant 2007122 from EU. He received grant honoraria for attending UCB and Jazz advisory board.

Symposium – Pharmacology of Sleep and Sleep-Like States in Man, Mice and Flies

S186

The relationship between natural sleep and general anaesthesia

N. FRANKS, S. BRICKLEY and W. WISDEN
Imperial College, London, UK

Putting a patient to sleep with general anaesthetics has been used as a metaphor ever since their first clinical use. Only relatively recently, however, has the possibility that general anaesthetics may act, at least in part, by affecting some of the natural pathways of sleep and arousal been investigated in detail. I will review the evidence that sleep and anaesthesia may affect common neuronal pathways, and then go on the describe experiments that test a specific hypothesis – namely that the inhibition of histaminergic neurons in the tuberomammillary nucleus (TMN) of the hypothalamus plays an important role in the sedative actions of anaesthetics. We tested the hypothesis in mice by genetically removing ionotropic GABA-A or metabotropic GABA-B receptors from histidine decarboxylase (HDC)-expressing neurons. At the cellular level, we measured the excitability of histaminergic neurons deficient in synaptic GABA-A and their sensitivity to the anesthetic propofol. At the behavioral level, we recorded the EEG in non-tethered mice over 24 h. The results of these experiments will be described.

S187

Wakefulness and its disorders, histaminergic control via H3-receptors

J.-S. LIN
Claude Bernard University, Lyon, FR

The histamine (HA) system fulfills a major role in maintaining the brain awake. HA neurons are located exclusively in the posterior hypothalamus from where they project to virtually all brain areas. The HA H3 receptors (H3R) are firstly autoreceptors damping the release and synthesis of HA and the firing of HA neurons. This action also extends to heteroreceptors on most other neurotransmitter systems, allowing a powerful control over multiple homeostatic functions.

Since the demonstration that sleep and waking (W) can be modulated by activation/inactivation of H3R in the cat in 1900, it has been hypothesised that H3R may constitute a brain target for sleep disorder therapy. Later on, the effects of H3R ligands on the mouse EEG and sleep-W were assessed in comparison to classical psychostimulants and modafinil. Data show that the H3R antagonists/inverse agonists, thioperamide and ciproxifan increase W and cortical fast rhythms and, like modafinil, but unlike amphetamine and caffeine, their waking effects are not accompanied by sleep rebound. Studies using knockout (KO) mice further confirm the essential role of H3R and HA transmission in the wake properties of H3R antagonists. Thus ciproxifan does not enhance W in KO mice lacking either HA synthesis or H1R or H3R whereas its waking effect is maintained in H2R KO-mice. These data validate the hypothesis that H3R antagonists, through disinhibition of H3 autoreceptors, enhance synaptic HA, that in turn activates postsynaptic H1R promoting W. Interestingly amphetamine and modafinil, despite their potent arousal effects, appear unlikely to depend on HArgic mechanism as their effects still occur in HA deficient mice.

Recently, a number of potent, selective and safer H3R antagonists were assessed in preclinical/clinical models of sleep disorders. In orexin KO mice, modafinil improves W but allows the narcoleptic episodes to persist, while pitolisant, a clinically suitable H3R antagonist, improves W and suppresses narcoleptic episodes as well. Moreover, pitolisant improves excessive daytime sleepiness in both adult and teenager narcoleptic patients whilst its possible anti-cataleptic effect is now under clinical trials. Pitolisant also has been shown to improve somnolence in parkinsonian patients.

These data together with the properties of H3R provide quite favourable attributes to make this a most promising target for pharmacological interventions of sleep disorders associated with narcolepsy, Parkinson's disease, and other neuropsychiatric indications.

Research supported by Inserm U628 and Claude Bernard University.

S188

Pharmacology of sleep- and wake-promoting compounds in humans: novel trials

J. BOYLE and D.-J. DIJK
University of Surrey, Guildford, UK

Sleep and wake are under fine neurochemical control with and a large number of neurotransmitters and their multiple associated receptors involved in orchestrating sleep/wake behaviour.

Wake is associated with cortical activation and a variety of neurotransmitter systems have been implicated in wake regulation including: histamine; 5 hydroxytryptamine (5-HT); glutamate; noradrenaline; dopamine and orexins/hypocretins (OX). Sleep is modulated by neurochemicals and hormones involved in its homeostatic and circadian regulation. GABA is accepted to play a central role in promoting sleep, primarily via inhibition of wake-promoting neurones, while the circadian hormone melatonin facilitates sleep initiation and maintenance.

The heterogeneous nature of neurochemical receptors has meant that many of the neuronal systems involved in sleep-wake regulation have become pharmacological targets. In particular, facilitation of histaminergic and glutaminergic transmission, through H3 antagonism, or positive modulation of AMPA receptors is thought to enhance alertness. In contrast, inhibition of histaminergic, serotoninergic and orexinergic effects through antagonism of H1, 5-HT2A/2C, OX1 and OX2 receptor subtypes, or enhancement of GABAergic transmission through GABAA receptor agonists is known to promote sleep. Through novel human clinical trials using models of impairment of wakefulness, cognition and sleep, recent developments in the field will be reviewed. This will include the development of wake-promoting compounds such as the H3-inverse agonist MK-0249, and the AMPAKINE, CX717. Studies will examine the compound's ability to counteract the detrimental effects of sleep deprivation on waking performance and the residual effects on subsequent recovery sleep. Developments in the sedative-hypnotic field will be reviewed with a focus on hypnotic and residual effects of the GABAA modulators eszopiclone, EVT201 and the extrasynaptic GABAA agonist, gaboxadol. Novel sleep promoting mechanisms will be explored including modulation of the wake-promoting orexin system by the dual OX1/OX2 receptor antagonist, SB-649868.

Modulation of sleep-wake behaviour not only provides solutions to sleep disorders such as insomnia but also offers the potential to enhance cognition, both in the healthy adult and compromised patient. Modulation of sleep-wake behaviour may play a vital role in optimising health and counteracting the debilitating effects of psychiatric and neurological disorders.

Dr Boyle has received clinical trial funding from Cortex Pharmaceuticals Inc, Evotec UK Ltd, GlaxoSmithKline, H. Lundbeck A/S and Merck Inc.

Round Table Discussion – Telemedicine and Sleep disorders

202

Management of obstructive sleep apnoea in Europe

I. FIETZE and T. PENZEL
Charité University Hospitals, Berlin, DE

Objectives: In Europe, the management of obstructive sleep apnoea (OSA) varies from country to country. Therefore the current status of diagnostic pathways and therapeutic approaches applied in the treatment of OSA and OSA associated with hypertension in Europe, qualification requirements of physicians involved in diagnosis and treatment of OSA, and reimbursement of these services were investigated.

Methods: Two special questionnaires were sent to 39 physicians in 22 countries in Europe. All participating countries were members of a European project within the European Cooperation in Science and Technology (COST) B26 action. Furthermore an European expert group including the COST B26 consortium created a position paper on the management of OSA patients and hypertension.

Results: Sleep centers from 21 countries (38 physicians) participated. A consistency among countries with respect to pathways included referral to sleep physicians/sleep laboratories, necessity for objective diagnosis by polysomnography, use of ambulatory monitoring, visual analysis of PSG, indications for positive airway pressure (PAP) therapy, application of standard continuous PAP (CPAP) therapy, and the need (90.5%) and management of follow-up was found. Differences were apparent in reimbursement of the diagnostic procedures and follow-up, in the procedures for PAP titration from home APAP titration with polygraphic monitoring (38.1%) up to hospital monitoring with PSG and APAP (85.7%), and in the qualification requirements of sleep physicians.

Conclusions: Management of OSA in different European countries is similar except for reimbursement rules, qualification of sleep specialists and procedures for titration of the CPAP treatment. European networks like the COST action, the ESADA group or the co-operation between different scientific societies could be helpful for implementing these findings into health-service research in order to standardize management of OSA in a cost effective perspective.

203

Cost-Effectiveness of the teletransmission of home respiratory polygraphy for the diagnosis of sleep apnoea and hypopnoea syndrome

J. F. MASA[1], J. CORRAL[1], R. PEREIRA[1], J. DURÁN-CANTOLLA[2], M. CABELLO[3], L. HERNÁNDEZ-BLASCO[4], C. MONASTERIO[5], A. ALONSO-FERNÁNDEZ[6], E. CHINER[7], E. GARCÍA-LEDESMA[1], M. RUBIO[1], L. CANCELO[2], R. CARPIZO[3], L. SACRISTAN[4], N. SALORD[5], M. CARRERA[6], J. N. SANCHO-CHUST[7], C. EMBID[8], F. J. VÁZQUEZ-POLO[9], M. A. NEGRÍN[9] and J. M. MONTSERRAT[10]
[1]San Pedro de Alcantara Hospital, Cáceres, ES, [2]Txagoritxu Hospital, Vitoria, ES, [3]Valdecilla Hospital, Santander, ES, [4]General Universitario Hospital, Alicante, ES, [5]Bellvitge Hospital, Barcelona, ES, [6]Son Espases Hospital, Palma de Mallorca, ES, [7]San Juan Hospital, Alicante, ES, [8]Clinic Hospital, Barcelona, ES, [9]Las Palmas de Gran Canaria University, Las Palmas, ES, [10]Clinic Hospital, Barcelona, ES

Introduction: Home respiratory polygraphy (HRP) a type 3 of AASM portable monitor may be a cost-effective alternative to polysomnography for the diagnosis of sleep apnea-hypopnea syndrome (SAHS), but the studies performed up to day have many differences in design, devices, definitions of hypopneas and criteria for SAHS diagnosis. In addition, only three studies included cost assessment being favorable to HRP but other cost studies based on simulated models of hypothetical patient cohorts showed unfavorable cost-effectiveness. In these circumstances, a big cost-effectiveness study, including real patients, is needed. Normally, patients transport HRP equipment from the hospital to home and back, which may create difficulties for some patients specially those who live far from hospital and patients with reduced mobility.

Objectives: We determine both the diagnostic efficacy and cost of HRP (with and without a transportation service, moving the device and telematic transmission of data) in a large sample, compared with in-hospital polysomnography.

Methods: Patients with an intermediate or high SAHS suspicion were included in a multicenter study (eight sleep centers). They were assigned to home and hospital protocols in random order. We constructed Receiver Operating Characteristic (ROC) curves for manual respiratory polygraphy scoring protocol and different polysomnographic cut-off points. Diagnostic efficacy for several polysomnographic cut-off points was explored and costs for two equally effective alternatives were calculated.

Results: Of 366 randomized patients, 348 completed the protocol. The best ROC curve was obtained with a polysomnographic cut-off of AHI $\geq$5. The sensitive HRP AHI cut-off point (<5) had a sensitivity of 96%, a specificity of 57% and a negative likelihood (LR) of 0.07; the specific cut-off (>10) had a sensitivity of 87%, a specificity of 86% and a positive LR of 6.25. We carried out the cost analysis for the worse ROC curve expressing the worse diagnostic agreement between HRP and PSG. Even in this case, the cost of HRP was half that of polysomnography. Telematic transmission costs were similar if the patients' costs were taken into account.

Conclusion: HRP is a diagnostic alternative to PSG in patients with an intermediate or high SAHS suspicion and telematic procedures may help patients with limited mobility and who live far from the sleep center.

204

E-health solutions for automated sleep classification

P. ANDERER
Medical University of Vienna, Vienna, AT

Objectives: To evaluate advantages and limitations of scoring sleep and associated events by means of e-health solutions.

Methods: In 2005, we published the automated sleep classification system Somnolyzer 24 $\times$ 7, which is embedded in an e-health solution. By means of a client software, sleep data are selected, encrypted and uploaded to the processing unit. After automated classification the processed sleep data are either reviewed by a human expert and subsequently uploaded to the sleep lab, or directly uploaded and the structured expert review process is performed by an expert at the sleep lab. In both cases, in addition to the scorings the expert receives traces depicting information on sleep/wake-related events and on data quality. In 2010, Somnolyzer 24 $\times$ 7 was adapted and validated for scoring sleep, arousals, respiratory events

and leg movements according to the criteria of the American Academy of Sleep Medicine (AASM) published in 2007.

Results: An epoch by epoch analysis of 72 PSG studies of 56 normal healthy subjects and 16 patients with insomnia, neurological or periodic leg movement disorders (38 females, 34 males, aged 21–86 years) demonstrated a reliability between two Somnolyzer-assisted AASM scorings of 99% (Cohen's kappa: 0.99). Only 4.8% and 3.7% of the automatically assigned epochs were corrected by the two expert reviewers, respectively. The reliability between two independent manual scorings of the same recordings was 82% (0.76). The agreement between the two Somnolyzer-assisted and the two visual scorings was between 81% (0.75) and 82% (0.76). In a validation study including 15 patients with mild to severe obstructive sleep apnea syndrome (eight females, seven males, aged 28–56 years), the apnea + hypopnea index (AHI) was 26.4 ± 35.2 for the automated Somnolyzer scoring and ranged from 20.7 ± 28.4 to 29.0 ± 36.2 with a mean of 23.9 ± 33.0 for seven independent manual scorings. The correlation between the mean manual and the automated AHIs was 0.96.

Conclusion: Somnolyzer-assisted scoring of sleep and respiratory events achieved a reliability close to 1 and a validity comparable to that of manual scorings. Thus, e-health solutions help to achieve unbiased and reproducible sleep scoring results anywhere in the world and at any point in time. Finally, the structured expert review guarantees valid results for each individual study and reduces the variability in sleep classification due to the 'human factor' to a minimum.

The author is part-time employee of Philips Austria.

205

Respiradom: a telemedicine system for the follow-up of patients with Sleep Apnea Syndrome

P. ESCOURROU, I. DURAND-ZALESKI, N. CHARRIER, H. AGOSTINI, D. ALFANDARY, E. ORVOEN-FRIJA, F. MARTIN, M.-P. DORTHO, J. C. MEURICE, A. BRION, P. LEFEVRE and S. ROYANT-PAROLA on behalf of Respiradom

The prevalence of SAS is 3–5% in adults and increases with the incidenceof obesity (around 400 000 people are treated by CPAP in France). The mortality and morbidity of SAS is reduced by the use of continuous positive airways pressure (CPAP), but for significant réductions in risk, treatment needs to be used for a minimum of 4 h per night. Increased CPAP use leads to increased reductions in mortality and morbidity. CPAP treatment is demanding and patients are frequently non-compliant with treatment. Optimising CPAP use reduces morbimortailty and is cost beneficial for health systems.

The objectives of the project are the following: 1. Develop an interoperable telemedicine system for the follow-up of patients with sleep apnea syndrome.

2. Collect data from CPAP devices by GPRS transmission, coupled with the physical status of the patient and feed this information into the e-health sleep record.

3. Develop technical and clinical alerts on collected data to trigger technical or medical interventions (e.g. machine service or a clinic visit).

4. Foster patient compliance by interactive training using a serious game application to improve patient education and an informational support, by creating a dedicated website, including a forum, patient community, and advices from a doctor or a psychologist specialized in sleep health.

5. Study the health economic impacts of telemonitored CPAP devices and of the telemonitoring services with the aim of developing a robust financing model.

Methods: The medico-economics protocol will use the MAST (Methodology for Assesment of Telemedicine) criteria and will start in september 2012. Two hundred patients will be randomized into two arms (telemedicine with GPRS transmission of CPAP data from patients' home and classical follow-up) during the three first months of the follow-up. The main end-point is CPAP compliance with the aim of detecting a mean increase of at least 1 h in the use of CPAP. The consortium includes: Réseau Morphée (Sleep Health Network), Assistance Publique-Hôpitaux de Paris, CPAP manufacturers (Resmed, Philips – Respironics), Home care providers (Orkyn'), Information technology providers (Santéos subsidiary of ATOS Origin), Web 2.0 and media specialists (Adverbia) and project management (Acsentis). Associate members include government agencies (DGCIS – Ministry of Industry, and the ARS Agence Régionale de Santé, Professional associations (SFRMS société de Recherche sur le Sommeil and SMSV Syndicat de la Médecine du Sommeil et de la Vigilance) and patient groups (FFAIR, Sommeil et Santé).

Case Discussion – Central Hypersomnias

208

Secondary narcolepsy – case presentation and evaluation

P. JENNUM, S. FRAHM-FALKENBERG and S. KNUDSEN
Glostrup Hospital, Copenhagen, DK

Secondary narcolepsy is rare but may occur when structural lesions, most often involving the hypothalamic hypocretin producing neurons, cause unstable sleep/wake and tonus control. We present a young girl who, secondary to a large craniopharyngeoma and removal of same, developed narcolepsy with cataplexy and hypocretin deficiency. She had no brain stem lesions on MRI. Extensive polysomnographic data proved severely disruptured sleep/wake architecture and extremely short sleep latency but extraordinarily failed to show any REM-sleep! Intact melatonin secretion profile indicate preserved circadian rhythm. REM sleep regulation is traditionally believed to be under brain stem control and absence of REM-sleep has only been described in rare cases with brain stem lesions. The findings suggest additional hypothalamic involvement of REM sleep regulation. This is further discussed in accordance to the sleep-wake physiology, motor control and NREM-REM regulation.

209

Idiopathic Hypersomnia with daytime sleepiness: A case report

R. DEL RÍO-VILLEGAS[1] and R. PERAITA-ADRADOS[2]
[1]University Hospital "La Paz", Madrid, ES, [2]University Hospital Gregorio Marañón, Madrid, ES

Objective: Patients suffering from idiopathic hipersomnia (IH) almost never feel fully awake despite long nocturnal sleep. The information regarding the sleep structure trough the 24 h-period is scarce.

Patient and Method: A 37 years old untreated women reported prolonged difficulty on awakening, confusion, 'sleep drunkenness', slow speech and thinking, automatic acts and hypnagogic hallucinations. Daytime naps were long and non-restorative.

We performed an all night VPSG followed by a Multiple Sleep Latency Test (MSLT) in the Sleep Unit to confirm the diagnosis of IH and eliminate other sleep pathologies. The patient was instructed to follow a regular sleep-wake schedule with 8 h in bed during 3 weeks prior to a 4-days ambulatory-EEG-polygraphic recording followed by a VPSG.

An actigraphy evaluation over 7 days followed by a VPSG and MSLT was made after being treated with 400 mg of Modafinil. One year later, a re-evaluation with 4-days ambulatory-EEG followed by a VPSG was performed. The patient was treated with fluoxetine, topiramate and methylphenidate.

Results: No significant differences were observed between sleep latencies on VPSG nights. Mean sleep latency in all MSLTs was $\leq$ 4.5 min with no SOREMPs. Ambulatory-EEG showed one or two naps a day; a normal sleep structure and a mean TST of 8.5 h. The medication did not modify daytime sleepiness but surprisingly an increase of the TST and arousal index was observed.

Conclusion: The polysymptomatic form of IH may be resistant to stimulant drugs that could change the sleep-wake pattern by increasing the total sleep time and arousal index.

Keynote Lecture

S210

Chronic insomnia: burden of illness and new trends in treatment development and dissemination

C. MORIN

University Laval, Québec, CA

Chronic insomnia is a prevalent health complaint that carries significant burden for the individual and society. It has been associated with reduced quality of life, increased risks for depression, higher disability and absenteeism from work, and increased health care costs. Even with its high prevalence and public health burden, insomnia is for the most part untreated and, when therapy is initiated, it is usually limited to medications. There is now solid research-based evidence that cognitive behavioral therapy (CBT) is effective for chronic insomnia (primary or comorbid), produces durable sleep improvements, and it is generally well accepted by patients. Notwithstanding this strong evidence-based support and endorsement by the scientific and professional community, CBT is still not widely available as first-line therapy and remains under utilized by health care practitioners. Several innovative and cost-effective treatment delivery models (e.g., Internet-based therapy, use of non sleep specialists) have yielded promising results, but this has not yet solved the imbalance between supply and needs. A significant challenge for the future will be to disseminate more efficiently practice guidelines and evidenced-based therapies, convince government agencies of their cost-benefits, and develop incentives to foster their use by practitioners in various clinical settings.

Symposium – The Metabolic Cost of Sleep Loss: From Mechanisms to Metabolic Disorders

S211

Impact of sleep loss and circadian misalignment on diabetes risk

R. LEPROULT
Université libre, Brussels, BE

Chronic lack of sleep due to voluntary bedtime curtailment is increasingly common. Over the past few decades, the prevalence of diabetes has dramatically increased in the US, interestingly together with the trend for shorter sleep duration. While sleep per se modulates glucose metabolism, whether recurrent sleep restriction represents a risk factor for type II diabetes has only recently been investigated. This presentation therefore summarizes the current evidence that supports a role for short sleep duration as an independent risk factor for the development of diabetes.

Laboratory studies have evidenced that behavioral sleep restriction is associated with an increased risk for diabetes. Indeed, healthy young lean men submitted to sleep restriction for several days present marked alterations in glucose metabolism. Whether some adaptation might occur if sleep restriction continues over an extended period of time (months or years), remains an important open question. However, when sleep loss becomes more chronic, adaptation seems to occur as glucose tolerance subside and insulin resistance develops. Consistent with these findings, a growing body of epidemiological evidence supports an association between short sleep duration and the risk for diabetes.

What about circadian misalignment? Shift workers, who are chronically sleep deprived, have an increased risk to develop type II diabetes. It is not known whether the circadian misalignment per se (occasional shift of the sleep period to daytime) has intrinsic effects on insulin sensitivity that exceed those of sleep loss alone. Two laboratory studies, using a forced desynchrony protocol, exhibit higher glucose levels after standardized meals. Another laboratory study using two protocols of similar sleep restriction, one without and one with circadian disruption, demonstrates that insulin sensitivity decreases with sleep loss and that the effect of sleep loss on insulin sensitivity is exacerbated when volunteers experience a circadian misalignment.

In conclusion, sleep loss appears to be an important risk factor for the development of type II diabetes. The alterations in glucose metabolism due to sleep loss seem to be enhanced with circadian misalignment.

S212

Short and long-term adaptation of metabolism to sleep loss

J. AXELSSON
Karolinska Institute, Stockholm, SE

Objective and background: It is well known that sleep deprivation is the threat to our organism and in the long-term may increase the risk to develop a wide range of metabolic disorders. Although acute sleep deprivation is rather well studied, it is less known of how our systems react to these acute effects in the long-term. The objective is to show how metabolism is affected both acutely in the long-term.

Methods: The presentation will go through the literature with respect to both the acute and long-term effects of sleep deprivation.

Results: The presentation will highlight that the effects of acute and long-term effects of sleep deprivation on metabolic hormones such as Thyroid stimulating hormone (TSH), leptin, and others are very different.

Conclusion: The literature suggests that the effects seen after acute sleep deprivation are followed by dynamic downstream effects. It is suggested that the real allostatic cost of sleep deprivation are related to these downstream effects rather than the effects seen in response to acute sleep deprivation.

S213

Sleep loss and appetite regulation: implications for obesity

K. SPIEGEL
Lyon Neuroscience Research Center, Lyon, FR

Chronic sleep loss due to voluntary bedtime restriction has become increasingly common in modern societies. This behavior has developed over the same time period as the recent epidemic of obesity. Interestingly, an ever-increasing number of cross-sectional and prospective epidemiologic studies have provided evidence for an association between short sleep (generally <6 h per night in adults) and the prevalence or incidence of obesity, after controlling for various confounders. Two meta-analyses including more than 600 000 adults and 30 000 children worldwide confirmed that short sleep duration increases the odds of being obese. One pathway that may link short sleep to excess weight is increased caloric intake in short sleepers. In lean subjects, experimental sleep restriction under conditions of similar caloric intake and physical activity down-regulates the satiety hormone leptin, up-regulates the orexigenic hormone ghrelin, and increases hunger and appetite. Subsequent sleep restriction studies yielded inconsistent leptin and ghrelin results that may be partly attributed to differences in severity of sleep restriction, feeding (uncontrolled versus controlled), body composition and prevalence of obstructive sleep apnea. Nevertheless, six of the seven studies that allowed *ad libitum* access to food reported that sleep curtailment increased overall food consumption or food consumption from snacks with poor nutritional value. The adverse impact of sleep deprivation on appetite regulation is likely to be driven by increased activity of orexinergic neurons that promote both waking and feeding. In summary, the current epidemiological and experimental evidence supports a role for reduced sleep duration in the epidemic of obesity through an up-regulation of appetite. Bedtime extension in short sleepers should be explored as a novel behavioral intervention that may prevent weight gain or facilitate weight loss.

S214

Behavioural and physiological mechanisms linking sleep loss to weight gain and obesity

K. WRIGHT
University of Colorado, Boulder, US

Chronic sleep loss affects millions of people worldwide. Findings from epidemiological research show that short sleep schedules are associated with increased risk of weight gain and obesity, yet the behavioral and physiological mechanisms underlying this risk remain to be elucidated. Recently published and unpublished findings from

laboratory based energy metabolism studies will be presented to describe changes in energy expenditure using doubly labeled water and whole room calorimetry, macronutrient intake, and energy balance during sleep loss. Sex differences in overeating responses will be described. An integrated model of how and why sleep loss may contribute to weight gain and risk of obesity in humans will be discussed.

Research supported by NIH HL085705, HL109706, NIH/NCATS TR000154, Sleep Research Society Foundation.

Symposium – Genetics of Obstructive Sleep Apnea – Time for International Collaboration

S215

Phenotyping of intermediate traits for OSA – craniofacial and soft tissue structure

C. BEARN, A. PACK and R. SCHWAB
University of Pennsylvania, Philadelphia, US

Objectives: The primary goal of our study was to objectively and reproducibly measure anatomical differences between apnecis and controls using digital morphometrics and a laser ruler. We hypothesized that the upper airway would be smaller and the tongue, uvula and lateral pharyngeal walls would be larger in the apneic group compared to the control group. Furthermore we hypothesized that there would be decreased visibility of the airway in apneics compared to controls and within apneics the visibility of the airway would be associated with a decrease in apnea hypopnea index (AHI) severity.

Methods: Subjects were sequentially recruited from the University of Pennsylvania Center for Sleep. Recruitment was limited to Caucasian male adults over the age of 18 years. All subjects underwent overnight polysomnography at Penn Center for Sleep Disorders. Digital photographs were obtained using an intraoral laser ruler and digital camera.

Results: Data from reproducibility tests conducted as part of the validation protocol showed that measurements taken with digital morphometics are reliable and reproducible over time and across distances within the range of 35–50 cm. We found that the airway was more frequently visible in controls (57.1%) compared to apneics (42.9%; $P = 0.0007$). Within the apneic population, subjects with a visible airway had a significantly lower mean AHI ($P = 0.0055$) and BMI ($P = 0.0005$) than those with obscured airways. When the airway was visualized using a tongue depressor, controls had a significantly wider airway width ($P = 0.0048$). The area of the extended tongue, and modified Mallampati score were found to be significantly larger in apneics compared to controls ($P = 0.0065$, $P = 0.0060$, $P = 0.007$). The ratio of the uvula width to the airway width (exposed with the tongue depressor) was significantly larger in apneics ($P = 0.0002$) and maintained significance after adjusting for age and BMI ($P = 0.0324$).

Conclusions: This study has shown that the digital morphometrics technique is an accurate, inexpensive, and non-invasive tool that can identify anatomical differences in upper airway soft tissue anatomy between controls and apneics. Digital morphometrics allows for a quantitative assessment of the pharynx and could be used in future population and epidemiologic studies of patients with sleep apnea. Digital morphometrics can also be used in different populations as a method of phenotyping for genetics studies.

S216

Phenotyping of intermediate traits for OSA – craniofacial structure

P. A. CISTULLI
Royal North Shore Hospital, Sydney, AU

Objectives: The aetiology of obstructive sleep apnea (OSA) is multifactorial, consisting of a complex interaction between anatomic and neuromuscular factors and an underlying genetic predisposition toward this common disorder. Although obesity is considered the major anatomical risk factor for OSA, craniofacial morphology is increasingly acknowledged as an important interacting factor. As such craniofacial morphology is an important intermediate phenotype in the investigation of genetic susceptibility to OSA.

Methods: Craniofacial morphology has been evaluated most extensively using various imaging modalities including Cephalometric x-rays, CT and MRI scans. Each modality has unique strengths and limitations in their ability to assess craniofacial anatomy. However, a key to large scale genetic studies is the need for simple, cost-effective, high throughput methods for quantifying the craniofacial phenotype. Novel quantitative photogrammetry methods have recently been reported, and hold promise as a phenotyping tool.

Results: Craniofacial characteristics associated with OSA include aspects of skeletal morphology, as well as soft tissue morphology. Skeletal abnormalities include shorter maxilla and mandibular length, retroposition of the maxilla and mandible, maxillary constriction, inferior displacement of the hyoid bone, longer anterior face, steep mandibular plane, and overjet/overbite. Soft tissue abnormalities include enlargement of the tongue and soft palate, elongated uvula, adenotonsillar hypertrophy, enlargement of the lateral pharyngeal walls and parapharyngeal fat pads. It is the interaction between skeletal and soft tissues that determines the impact on upper airway size and function. The influences of growth, gender, and ethnicity on craniofacial morphology are also gaining recognition.

Conclusion: Craniofacial morphology is an important intermediate phenotype in the pathway to OSA, and therefore is an essential element for the study of OSA genetics. Novel high throughput photographic methods to quantify craniofacial and intraoral characteristics have the potential to facilitate large scale genetic studies in OSA.

References:

1. Lee, RWW, Sutherland K, Cistulli PA. Craniofacial morphology in Obstructive Sleep Apnea: A Review. Clin Pulm Med, 2010; 17: 189–195.
2. Lee RWW, Chan AS, Grunstein RR, Cistulli PA. Craniofacial Phenotyping in Obstructive Sleep Apnea – A Novel Quantitative Photographic Approach. Sleep, 2009;32 (1):37–45.

S217

Cardiovascular phenotyping in genetic studies of OSA

T. PENZEL
Charité University Hospitals, Berlin, DE

Objectives: Sleep apnea is recognized as a cardiovascular risk factor with many cardiovascular implications. Cardiovascular functions recorded during sleep do change with the respiratory events of apnea and hypopnea and in addition they do change with sleep stages. Cardiovascular functions are controlled by the autonomous nervous system.

Methods: For cardiovascular phenotyping of patients with obstructive sleep apnea we record different aspects of the autonomous nervous system. These are ECG/heart rate and pulse wave/pulse wave velocity. In order to derive phenotypes these functions are analyzed for heart rate variability, pulse properties, endothelial function, respiratory variability, and for cardiorespiratory interaction. Variability can be analyzed with methods of time domain analysis (mean value, statistical moments) and frequency domain analysis

(High frequency, low frequency, very low frequency component, and sympathovagal balance). In addition to these analysis methods new statistical approaches can be applied to quantify non-linear signal properties such as short and long time correlation behavior within a time series. Especially the coupling between cardiac and respiratory functions appears to be a good predictor for alterations.

Results/Conclusion: The quantification of additional non-linear properties for a description of sleep apnea subjects for phenotyping sleep disordered breathing in addition to conventional parameters such as apnea/hypopnea index and oxygen desaturation index. Results on limited study sizes in patients with sleep apnea are shown for cardiorespiratory interaction. The coupling between the heart beat and the respiration does change with sleep stages and does reveal different regulations with the occurrence of sleep apnea. We assume that a close coupling between heart rate and respiration presents a better metabolic state which preserves energy during sleep. Altered or disturbed coupling can be interpreted as signs of an increased risk for cardiovascular disorders or at least for lower restoration capacity during sleep.

Reference:

1. Bartsch RP, Schumann AY, Kantelhardt JW, Penzel T, Ivanov PC. Phase transitions in physiologic coupling. PNAS (2012) June 12, 2012, doi: 10.1073/pnas.1204568109.
2. I have shares in Advanced Sleep Research, Somnico, The Siestagroup. Our institution has received research and travel grants from Actelion, Apnex, Breas, Cephalon, Hoffrichter, Itamar, MSD, Philips, Respironics, Resmed, UCB, Weinmann.

S218

The sleep apnea genetics international consortium

A. C. FEDSON

University of Pennsylvania, Philadelphia, US

Objectives: The Sleep Apnea Genetics International Consortium (SAGIC) was initiated to further enable research into the genetics and genomics of obstructive sleep apnea (OSA) (http://www.med.upenn.edu/sleepctr/SAGIC). Primary aims include investigation of the genetic risk factors for OSA and genetic determinants of differential susceptibility to different consequences. SAGIC will bring together experts in sleep disorders research; initiate various phenotypic and genetic projects of international significance; and facilitate SAGIC members to apply to their grant bodies for utilizing the available data.

Methods: The nine international SAGIC sites include: Berlin, Grenoble, Ohio, Perth, Philadelphia, Reykjavik, Sao Paulo, Sydney and Taoyuan. The structure includes a Governance Group; Strategy Group; Working Groups; and Regular Members, and is governed by a governance strategy and data access policy. Meetings include monthly teleconferences, meetings at major sleep conferences, and an Annual Workshop.

Results: Various phenotypic projects have commenced. (i) Development of a standardized sleep questionnaire: we have published a review investigating wording of sleep questionnaires used in epidemiological and genetics studies, and are finalizing a standardized sleep questionnaire for large-scale sleep phenotype collection. (ii) Inter-reliability of sleep scoring: a study has been conducted across sites investigating inter-reliability of polysomnography scoring, using AASM definitions in 15 previously recorded sleep studies. The manuscript is under review. (iii) Craniofacial and intra-oral phenotyping: sites will commence a craniofacial and intra-oral pilot study focused on investigating inter-ethnic comparisons of craniofacial morphology in OSA. (iv) Cardiovascular interactions: we are conducting a review investigating methods of assessing the pulse (i.e.pulse wave velocity), and will conduct a heart rate variability validation study. (v) Neurobehavioral assessment in sleep: collection of objective measures of sleepiness and neurobehavioral function at sites using the PVT (behavioral alertness) and OSLER (behavioral tendency to fall asleep), and to determine whether a single OSLER measure is viable alternative to the standard multiple measures.

Conclusions: Further work will include genome-wide association study, candidate gene and sequencing studies, and determining family-based rare genetic variants focusing on extreme phenotypes. A more comprehensive understanding of the genetic factors associated with OSA will help to better manage, treat and prevent the disorder.

Joint Symposium ESRS - JSSR - WFSRSMS

S219

Relationship between psychiatric state and sleep problems

P. LÉVY[1] and M. HONDA[2]

[1]Joseph Fourier University, Grenoble, FR, [2]Tokyo Metropolitan Institute of Medical Sciences, Tokyo, JP

Compared to the remarkable advance in studies on the relationship between sleep problems (especially sleep related breathing disorders and insufficient sleep) and various lifestyle-related physical diseases, psychiatric symptoms remain to be investigated from the perspective of sleep wake dysregulation. There could be three models regarding the relationship between sleep problems and psychiatric symptoms. (i) Sleep problems are handled as one associated symptom in psychiatric disorders. (ii) Sleep problems and psychiatric symptoms are independent conditions but influencing bi-directionally. (iii) Sleep problems and psychiatric symptoms are intermingled and have the common pathophysiological mechanism. To explore the third model it would be useful to revisit the detailed clinical studies on 'diencephalon-related psycho-neuro-endocrine disorders' by late Dr. Yutaka Honda, describing the simultaneous occurrence of psychic symptoms and hypothalamus-related vital somatic symptoms (including sleep) in parallel fluctuating fashion. Narcolepsy is a typical example. Development of narcolepsy and psychiatric symptoms (psychotic state, narcoleptoid personality) seems to have common underlying mechanism, which needs to be understood in the context of current knowledge of sleep medicine.

In addition, it would be important to evaluate the contribution of various associated factors along with detailed clinical courses (from onset to long-term prognosis) to get a whole picture of multifactorial sleep disorders. It is an excellent example that Dr. Plazzi identified atypical motor and psychiatric symptoms in the onset of childhood narcolepsy and showed the contribution of streptococcal infection to the motor symptoms in subjects with predisposition HLA genes.

S220

Sleep medicine training and certification

T. PENZEL[1] and C. KUSHIDA[2]

[1]Charité University Hospitals, Berlin, DE, [2]Stanford Sleep Medicine Center, Redwood City, US

Introduction: Sleep medicine is regarded as an interdisciplinary medical subspeciality which can be added to a number of main specialities such as pneumology, neurology, psychiatry, pediatrics, ENT medicine, and cardiology. To be trained and certified in a medical subspeciality requires 12–18 months of training. Sleep medicine is a chamber of physician recognized subspeciality in only very few European countries, such as Germany. Several European countries offer different ways for training in sleep medicine. Some universities in offer already university courses and even master programs on sleep.

Methods: The European Sleep Research Society (ESRS) moves towards a European wide recognition of sleep medicine as a subspeciality. In order to promote this process sleep medicine training is supported and organized by the ESRS. A catalogue of knowledge and skills for theoretical knowledge and practical skills had been compiled. Courses with a 5 week schedule are arranged and will educate participants on the subjects listed. The ESRS also organized a certification process for sleep experts. The certification can be obtained by physicians, psychologists, scientists, and technicians. eligibility criteria for the disciplines had been set.

Results: The sleep medicine courses are in place and started as summer schools. They will continue as regular courses given by sleep medicine teaching sites with an approval from the ESRS. The certification started with a grandfather/grandmother process with more than 40 examinees. The examination is a multiple-choice questions exam. A second round of grandfather/grandmother examination will take next year. For these two rounds only people with more than 10 years experience in sleep medicine were eligible. These people will be responsible for the continuation of the examinations. The regular examinations will follow thereafter.

Discussion: The specific contents of the sleep medicine education and certification have to be aligned with related efforts organized by medical societies which also cover some aspects of sleep medicine, such as pneumology, neurology, psychiatry, pediatrics, ENT medicine, and cardiology. The common parts need to be identified and the add-on which is specific to a sleep medicine subspeciality needs to be clearly defined. Negotiations on the specific contents of these layers are ongoing.

Symposium – The Complex Interaction of Sleep and Brain Disorders: Clinical and Experimental Insights

S223

Sleep phenomena in human Parkinson's disease

J. SANTAMARIA
Hospital Clinic, Barcelona, ES

Problems with sleep are common in patients with PD but have only been the focus of special attention in the last few years. PD is one of the few diseases in which the whole spectrum of sleep disorders – insomnia, hypersomnia and parasomnia- may appear. The available evidence suggests that sleep disturbances are 1.5–3.5 times more common in PD than in healthy controls or than in patients with other chronic disorders. Sleep disturbances, with the exception of REM sleep behavior disorder (RBD), do not occur early in the course of the disease. Only when the disease advances sleep disturbances become more common.

Insomnia, particularly sleep maintenance insomnia is one of the most common sleep problems in PD. Patients may go to bed and fall asleep without much difficulty but wake up one to 2 h later and have important difficulties to fall asleep again. In early PD stages, treatment with selegiline or amantadine, particularly when used in the evening may produce insomnia since they have stimulant properties. Excessive dopaminergic treatment may also have alerting effects during the night. Patients with PD may have sleep apnea, with similar symptoms and signs than in non-PD patientsand restless legs syndrome (RLS), despite the treatment with dopaminergic agents. In advanced PD stages poor sleep at night may be due to lack of efficacy of dopaminergic agents with reappearance of tremor, difficulties in turning over in bed, cramps or pain that awake the subject and prevent him to fall asleep again.

Parasomnias.- RBD consists of recurrent episodes of sudden, abnormally vigorous body, head or limb movements during REM sleep, usually associated with dreams in which the patient defends against a threat or aggression. At least 30% of the cases of PD had RBD clinically or PSG detected findings in one study. The presence of RBD in patients with PD may represent a risk factor for the development of cognitive deterioration and possibly dementia. RBD has been found to occur less often in the tremor-predominant subtype of PD.

Excessive daytime sleepiness (EDS). EDS has long been under recognized in PD and although initially considered a side effect of non-ergot D2-D3 agonists, it is not restricted to a specific class of dopaminomimetic agents. Sleepiness occurs either as a constant feeling that the patient is aware of or as episodes of 'sudden, irresistible, overwhelming sleepiness without awareness of falling asleep' (sleep 'attacks'). Sleep attacks usually occur in a background of relaxed wakefulness and mostly while doing sedentary activities. The frequency of EDS in PD depends upon the studies, but ranges between 15–71% of the patients or between 1.5 to 15 times that found in healthy controls, less frequent in untreated PD. The cause of EDS in PD is probably complex with several factors playing a role.

S224

Sleep and memory in Alzheimer's disease

G. RAUCHS, F. BERTRAN, P. CLOCHON, F. DOIDY,
B. DESGRANGES and F. EUSTACHE
Inserm-EPHE-UCBN U1077, Caen, FR

Alzheimer's disease (AD) is the first cause of dementia representing, due to the ageing population, a major public health issue. Neuropathological hallmarks of AD are neurofibrillary tangles, aggregates of Tau protein, and beta-amyloid deposits. On a cognitive stand point, AD patients exhibit early and severe episodic memory impairment. These deficits may be subserved by structural and functional alterations; the most typical being the atrophy of the hippocampal formation and the hypometabolism of the posterior cingulate cortex. AD patients frequently report sleep disturbances, worsening with the severity of dementia. As in normal aging, impaired sleep patterns consist in sleep fragmentation, decrease in slow-wave sleep and slow oscillations. Sleep spindles are also poorly formed, shorter in duration and much less numerous. Later in the course of the disease, REM sleep is also reduced. These sleep disturbances are evident years before diagnosis of AD, in patients with Mild Cognitive Impairment (MCI), the prodromal stage of AD, and more noticeable in Apoϵ4 carriers [1]. As sleep favours consolidation of recently acquired information into long term memory, several studies investigated the relationships between sleep changes and memory impairment. Thus, Westerberg et al. [2] failed to reveal any significant different in sleep patterns in MCI patients and healthy controls, but reported that inadequate memory consolidation in patients was related to decline in subjective sleep indices. In addition, high across-night variability in sleep quality was associated with poor memory performance. In our laboratory, we showed that episodic memory performance in mild AD patients was significantly correlated with changes in theta rhythm [3] and with mean intensity of fast sleep spindles [4]. Finally, pioneering evidence in rodents suggest that sleep troubles may not only contribute to memory deficits but also exacerbate the neuropathological processes leading to the beta-amyloid accumulation [5].

1. Hita-Yañez et al. (2012). Curr Alzh Res 9: 290–7.
2. Westerberg et al. (2010). Alzheimer Dis Assoc Disord, advance online publication.
3. Hot et al. (2011). Biol Psychol 87: 334–9.
4. Rauchs & Schabus, et al. (2008). NeuroReport 19: 1159–62.
5. Kang et al. (2009). Science 326: 1005–7.

S225

Sleep and wakefulness after rodent and human stroke

C. BASSETTI
University of Berne, Berne, CH

A relationship between sleep and stroke was suggested already in the late 19th and early 20th centuries. However, only few studies assessed characteristics, mechanisms and significance of this link. Recent clinical and animal data give support to the idea that this research area may be of clinical and neurobiological interest.

Sleep-wake disorders as independent risk factors for stroke. Sleep disordered breathing (SDB) was shown to represent an independent risk factor for stroke[1]. Recent data raise the possibility that also other

sleep disorders (such as restless legs syndrome (RLS)/periodic limb disorder in sleep, and insomnia) may increase the cerebrovascular risk[1–2].

Sleep-wake disorders as modulators of stroke outcome. Clinical data support the hypothesis that SDB (and its treatment) may affect the short-term and long-term outcome after stroke[1,3,4]. Furthermore, experimental and clinical data suggest that pharmacological and non pharmacological sleep manipulations affect the recovery after stroke. In addition, sleep deprivation preceding stroke may be protective.

Sleep-wake disturbances (SWD) as a direct consequence of stroke. Hypersomnia, insomnia, RLS, REM sleep behaviour disorder, and anoneira (loss of dreaming) can arise in humans with stroke[1]. The analysis of SWD after stroke offers unique insights into the mechanisms of sleep-wake control[1].

Sleep-wake EEG changes as markers of neuroplasticity and stroke recovery. Recovery from stroke is accompanied by specific changes of sleep-wake EEG microstructure in both humans and animals. These changes can be used as markers of neuroplasticity processes involved in functional brain recovery[5–8].

References:

1) Bassetti CL and Hermann D, Handbook of Neurology 2011.
2) Walter AS and Rye DB, Sleep 2009.
3) Ryan CM et al., Stroke 2011.
4) Parra et al., AJRCCM 2011.
5) Siengsukon CF and Boyd L, Neurosci Lett 2009.
6) van Meer MP et al., J Neurosci 2010.
7) Gao B et al., Sleep 2010.
8) Zunzunegui C et al., Sleep 2011.

S226

Posttraumatic sleep-wake disturbances in rats and men

C. R. BAUMANN[1], P. O. VALKO[1], D. NOAIN[1], L. L. IMBACH[1], S. R. SCHREGLMANN[1], T. E. SCAMMELL[2] and C. L. BASSETTI[3]

[1]University Hospital Zurich, Zurich, CH, [2]Beth Israel Deaconess Medical Center, Boston, MA, US, [3]University Hospital Berne, Berne, CH

Background: Traumatic brain injury (TBI) belongs among the most prevalent problems encountered in hospitals and in outpatient clinical practice. Many TBI patients suffer from chronic neurological impairment following TBI, including neuropsychological and psychiatric symptoms, as well as sleep-wake disturbances (SWD). Most common SWD following TBI include excessive daytime sleepiness and hypersomnia, but the frequency of posttraumatic insomnia remains subject of debate. In many TBI patients, the development of TBI is related to the trauma itself. In this regard, a first study of human brains which have been collected after fatal TBI revealed a significant loss of wake-promoting hypocretin neurons in the hypothalamus, which suggests that dysfunctional signaling of this neuronal population might contribute to posttraumatic sleepiness and hypersomnia.

Methods: These findings are being validated and expanded in a larger sample of postmortem TBI brains. Furthermore, we developed a novel rodent TBI model to study sleep-wake characteristics, motor and non-motor behavior, and histological outcomes.

Results: These ongoing studies in larger human post-TBI brains reveal that multiple neuronal systems are likely to be involved in the generation of posttraumatic SWD. In our rodent model of different severities of closed TBI, we found enhanced sleep pressure and a variety of behavioral abnormalities.

Conclusion: Our findings suggest that human TBI impairs signaling of different wake-promoting neuronal systems. Furthermore, a rodent model of TBI helps understanding the associations between TBI, sleep, behavior, and histological outcome in a more standardized setting than in humans.

Symposium – Light as an Alerting and Phase Shifting Agent: Impact of Sleep-Loss, Inter-Individual Differences and Brain Mechanisms

S227

The effect of sleep deprivation on circadian phase shifts to light

H. BURGESS
Rush University Medical Center, Chicago, US

Objectives: Short sleep episodes are increasingly prevalent in modern society. Short sleep episodes are typically associated with increased exposure to evening ambient light, but also partial sleep deprivation. While studies in mice and hamsters suggest that sleep deprivation can reduce phase shifts to light, this has not been previously investigated in humans. Therefore, the objective of this presentation is to describe the effects of partial sleep deprivation on phase shifts to light in humans, while controlling for evening light exposure.

Methods: Thirteen young healthy subjects participated in a within-subjects counterbalanced design. In both conditions subjects followed their habitual sleep schedule at home for six nights before a phase assessment in the laboratory to determine their dim light melatonin onset (DLMO). Subjects returned to sleeping at home for a week before a 4-day laboratory session. During the 4-day laboratory session, subjects underwent a 3-day advancing protocol (3.5 h of bright light each morning, starting 8 h after the DLMO), followed by another phase assessment. In one condition (no sleep deprivation) subjects had an 8 h sleep opportunity during each day of the advancing protocol. In the other condition (partial sleep deprivation) subjects were kept awake for 4 h in darkness, and then had a 4 h sleep opportunity during each day of the advancing protocol.

Results: Ten of thirteen subjects showed reduced phase advances when they were sleep deprived compared to when they were not sleep deprived. The reduction in phase advance ranged from 0.2 to 1.2 h (mea $n = 0.6$ h, paired t-test $P < 0.05$).

Conclusion: These results reveal that partial sleep deprivation, even when controlling for evening light exposure, can reduce circadian responsiveness to morning light. These results also provide further evidence of the complex interaction between the sleep and circadian systems. This finding will be discussed in the broader context of examining the effect of the increasing societal preference for short sleep episodes on the functioning of the human circadian system.

Support: NHLBI R01 HL083971 to HJB.

S228

Light effect on sleep homeostasis, cognitive performance and mood

A. VIOLA[1], V. GABEL[1], M. MAIRE[1], C. F. REICHERT[1], C. SCHMIDT[1], V. HOMMES[2] and C. CAJOCHEN[1]
[1]Universitäre Psychiatrische Kliniken, Basel, CH, [2]IT VitaLight I&D PC Drachten Philips Consumer Lifestyle, Netherlands, NL

Introduction: Light exposure elicits numerous effects on human physiology and behaviour. However, it remains inconclusive whether morning light exposure has beneficial effects on cognitive performance, mood and circadian physiology following sleep restriction (SR). Here we investigated the role of morning light exposure as a countermeasure for impaired cognitive performance and mood during SR.

Methods: Seventeen participants were studied during 42 h in the laboratory in a balanced cross-over design where three different light settings were administered each morning after SR (6 h): blue light (BL) (20 min exposure 2 h after wake-up; 200 lux of light at 470 nm), dawn simulating light (DsL) (blue-enriched polychromatic light gradually increasing from 0 to 250 lux during 30 min before wake-up time, with light around 250 lux for 20 min after wake-up time) and Dim light (DL) (<8 lux). Cognitive tests were performed every 2 h during the wake episode and questionnaires were hourly completed to assess subjective mood and well-being. Salivary melatonin and cortisol were collected during wake episode in regular intervals.

Results: Analysis of cognitive performance yielded a significant main effect of 'light condition' ($P < 0.01$), such that during the first day following SR, performance was significantly deteriorated during DL, while it maintained stable during BL and significantly improved with DsL. After the second SR night, these differences on cognitive performance did not further reveal significances between DsL and DL. Analysis of well-being revealed a significant main effect of 'light condition', such that morning DsL improves levels of well-being, and even more after the second SR night, as compared to DL and BL ($P < 0.001$). Exposure to morning DsL did not significantly affect circadian melatonin phase, while, after morning BL, melatonin onset was significantly earlier as compared to DsL and DL. Furthermore, after DsL, salivary cortisol levels were significantly higher at wake-time as compared to BL and DL.

Conclusion: Our data indicate that exposure to morning light after the first and second day of SR alleviate decrements in cognitive performance under conditions of mild SR. This effect was more pronounced after dawn simulation, since the DsL was able to maintain higher well-being levels and did not affect circadian melatonin phase, whereas morning blue-light induced a phase advance of melatonin, and therefore impacted on the circadian system.

S229

Individual differences in sensitivity to light

N. SANTHI
University of Surrey, Guildford, UK

Objectives: The potent effect light on our circadian system, sleep and cognition, is mediated by a multi-component photoreceptive system consisting of rods, cones and melanopsin-expressing intrinsically-photosensitive retinal ganglion cells (ipRGC), with unique intensity and spectral characteristics. For most of us, our daily light exposure includes outdoor natural and indoor artificial light, with the latter being predominant. This is cause for concern, given the growing evidence for the effects of light on brain function and the health consequences of disruption of circadian rhythmicity and associated sleep deprivation through exposure to artificial light. The talk will present findings from laboratory studies (Santhi et al, 2012, J Pineal Res) investigating the non-visual effects of artificial light and discuss their implications.

Methods: First, the 24-h light exposure at home was characterized. Then, the acute effects of polychromatic light on the (i) dissipation of morning sleep inertia in alertness and cognition and (ii) nocturnal melatonin rhythm, sleep onset, evening sleepiness, were examined in the laboratory. The polychromatic light mixtures were similar in intensity to the artificial light at home but different with respect to spectral composition; they had either, reduced, intermediate or enhanced blue content. The effects of these light conditions were compared to a near-darkness and bright blue-enhanced conditions.
Results: First, sleep inertia in alertness and cognition lasted over an hour. Critically, light condition had a differential effect on the dissipation of sleep inertia in working memory but not on cognitive throughput or alertness. In the evening, light condition had a differential effect on the nocturnal rise in melatonin, subjective sleepiness, Latency to sleep onset, Slow Wave Sleep and Rapid Eye Movement sleep ($P < 0.01$ for trend in all cases). Modelling of these effects showed that they were mediated largely by the melanopsin system. Notably, there was individual variability in the effect of light on melatonin, which was robust against experimental manipulations (ICC: 0.44).
Conclusions: The artificial light at home affects biological rhythms, sleep and cognition, although there are individual differences. With the available biological knowledge we can engineer light mixtures to minimize its disruptive effect and optimize its beneficial effect and thereby design light environments that promote well being and efficiency.
Funding for this research was provided by Philips Lighting, The Netherlands.

S230

Light impact on cognitive brain function depends on circadian phase, sleep pressure and PER3 polymorphism

G. VANDEWALLE
University of Liège, Liège, BE

Objectives: Light stimulates human performance, alertness, and cognition. These effects are likely to be mediated through outputs from photosensitive melanopsin-expressing retinal ganglion cells which are maximally sensitive to shorter-wavelength (blue) light. The brain mechanisms involved are starting to be elucidated, but how they are affected by changes in circadian phase and sleep pressure is not known. In addition, markers of inter-individual differences in the impact of light are largely unknown.
Methods: We used fMRI to assess brain responses to an auditory working memory task, in the morning, right after sleep and during sleep-loss, and in the evening, in two populations stratified according to a genetic marker (PERIOD3 polymorphism) for inter-individual differences in the build-up of sleep pressure and in performance vulnerability to sleep-loss (PER35/5 – $N = 12$ – and PER34/4 – $N = 15$), while participants were exposed to alternating 60 s blue (473 nm – 10^{13} photons/cm^2/s) and green (527 nm – 10^{13} photons/cm^2/s) light.
Results: Results show that, compared with green light, blue light exposure increased brain responses in higher-order frontal and parietal cortical areas and in the pulvinar. These effects were only observed in the sleep-loss-vulnerable genotype (PER35/5) during sleep-loss, and in the less-vulnerable genotype (PER34/4) right after sleep, while no effect were observed in either genotypes in the evening wake-maintenance zone. Connectivity analyses suggest that light acts through a thalamo-fronto-parietal network to affect the ongoing cognitive process.
Conclusion: These data demonstrate that the impact of light on non-visual brain responses vary with circadian phase and sleep pressure in key areas for cognition and arousal regulation. They also establish a polymorphism in PERIOD3 as markers of inter-individual differences in the impact of light on non-visual cognitive brain functions.
Funding: FNRS, FMER, ULg, PAI/IAP, IRSC, FRSQ.

Oral Session 7 – Sleep Disordered Breathing: Other Medical Disorders Epidemiology and Comorbidities

O231

Wake-up stroke and TIA due to paradoxical embolism during long obstructive sleep apnoeas

P. PROSERPIO[1], A. CICCONE[1], D. V. ROCCATAGLIATA[1], M. NICHELATTI[1], G. L. GIGLI[2], C. LOMBARDI[3], G. PARATI[3], F. PIZZA[4], F. CIRIGNOTTA[4], I. M. SANTILLI[1], V. SILANI[3], R. STERZI[1] and L. NOBILI[1]

[1]Niguarda Hospital, Milan, IT, [2]Neurological Clinic and Sleep Center, Udine, IT, [3]Istituto Auxologico Italiano, Milan, IT, [4]S. Orsola-Malpighi Hospital, Bologna, IT

Objectives: A right-to-left blood shunt (RLSh) is considered a potential cause of paradoxical brain embolism and is mostly associated with a patent foramen ovale (PFO). Although PFO is very common, the condition triggering a RLSh just before the stroke is frequently missed. However, in the presence of a PFO, obstructive sleep apnea may cause a RLSh if the respiratory event lasts long enough (>17 s; Beelke et al., Sleep 2002).

We investigated whether the combination of long obstructive sleep apnea (LOSA) and RLSh is associated with ischemic stroke or transient ischemic attack (TIA) on awakening (wake-up stroke.

Methods: We prospectively considered patients aged over 18 years, admitted to 13 stroke units for acute ischemic stroke or TIA. Patients had to be able give consent, to specify whether the event occurred on awakening, and to cooperate sufficiently to undergo contrast transcranial Doppler examination and cardiorespiratory sleep study within 10 days of the onset of symptoms. Single LOSA events, lasting 20 s or more, were considered a possible harbinger of RLSh.

Results: Between April 2008 and March 2010, 335 patients (109 women; 61 TIA, mean age 64 years) were enrolled. Apnea-Hypopnea Index (AHI) was more than 5 in 60% of cases; 202 (60%) patients had at least one LOSA and 37 of these (18%) had an AHI <5. A RLSh was detected in 116 (35%) patients; 69 (21%) had a RLSh and at least one LOSA event. There were significantly more wake-up strokes/TIA in subjects with RLSh plus LOSA than those without this association (27/69 versus 70/266; OR 1.91, controlled for age, sex, hypertension, diabetes, atrial fibrillation, antithrombotic therapy, 95% confidence interval 1.08–3.38; $P = 0.03$). No other risk factor was associated with an increase in the incidence of events on awakening.

Conclusions: This is the first 'epidemiological' study suggesting that the combination of LOSA and RLSh could be a new major, potentially treatable risk factor for ischemic cerebrovascular events occurring on awakening. Previous studies have already shown that obstructive sleep apnea represents an independent risk factor for stroke but our results indicate that the association of RLSh with LOSA could act as a precipitating, acute, factor favoring a cerebrovascular ischemic event through a cardio-embolic mechanism. Should this hypothesis be confirmed in future studies, it would have important implications for a different approach to the treatment of patients with both LOSA and PFO.

O232

Frequent nocturnal sweating – a symptom of obstructive sleep Apnoea: The Icelandic Sleep Apnea Cohort study

E. S. ARNARDOTTIR[1], C. JANSSON[2], B. BENEDIKTSDOTTIR[1], E. BJORNSDOTTIR[1], S. JULIUSSON[1], A. I. PACK[3] and T. GISLASON[1]

[1]Landspitali University Hospital, Reykjavik, IS, [2]Uppsala Universitet, Uppsala, SE, [3]University of Pennsylvania School of Medicine, Philadelphia, US

Objectives: To estimate the prevalence of reported nocturnal sweating in subjects with obstructive sleep apnea (OSA) compared to the general population and changes with continuous positive airway pressure (CPAP) treatment. Also to evaluate what characterizes those who report nocturnal sweating, both OSA patients and subjects in the general population.

Methods: The Icelandic Sleep Apnea Cohort (ISAC) consisted of 822 newly diagnosed subjects with OSA, referred for treatment with CPAP. Of those, 741 subjects returned for a 2 year follow-up visit (90.1%), thereof $n = 475$ CPAP users and $n = 266$ nonusers. Of those, $n = 369$ were full CPAP users as defined by ≥4 h average use and ≥5 nights a week in the last month or subjective report of the same. The control group consisted of 757 randomly selected subjects from the general population (www.boldcopd.org). The severity of OSA was measured in a sleep study (for ISAC participants only).

Results: The ISAC cohort (81.0% males) was on average (±SD) 54.5 ± 10.6 years of age, and had a mean BMI of 33.5 ± 5.7 kg/m^2. The general population subjects (52.9% males) was 3 years older on average (57.0 ± 11.8 years) and less obese (27.9 ± 4.9 kg/m^2). Frequent nocturnal sweating (≥3× a week) was reported in 30.6% of male OSA subjects and 33.3% of female OSA subjects compared to 9.3% and 12.4% in the male and female control groups ($P < 0.001$). In the general population cohort, a significant relationship was found between nocturnal sweating and a higher BMI, not found in the ISAC subjects (adjusted for confounders). Subjects reporting nocturnal sweating were characterized by having diagnosed OSA, lower age, smoking history, hypertension and lower mental and physical quality of life. They were also more likely to have sleep-related and respiratory complaints. In the OSA group, nocturnal sweating was associated with a longer hypoxia time (minutes with SaO_2 <90%) but not with the apnea-hypopnea index or oxygen desaturation index. A decrease was found in the prevalence of nocturnal sweating with full CPAP treatment (from 33.2% to 11.5%, $P < 0.003$ compared to nonusers). No significant change in sweating was found for partial CPAP users compared to nonusers.

Conclusion: Frequent nocturnal sweating is a distinct clinical symptom of OSA, affecting a subgroup of OSA patients. This symptom is responsive to treatment in a majority of patients.

O233

In sleep apnoea patients, nonalcoholic fatty liver disease is associated with the severity of intermittent hypoxia and more severe endothelial dysfunction

C. MINVILLE[1], M.-N. HILLERET[2], R. TAMISIER[3], P. LÉVY[3], J.P. ZARSKI[2] and J.-L. PÉPIN[3]

[1]Institut universitaire de cardiologie et de pneumologie de Québec, Québec, CA, [2]University Hospital of Grenoble, Grenoble, FR, [3]Joseph Fourier University, Grenoble, FR

Introduction: Nonalcoholic fatty liver disease (NAFLD) begins with the accumulation of triglycerides in the liver and elicits an inflammatory response that can progress to cardiovascular complications, cirrhosis and liver cancer. Intermittent hypoxia is a potential contributing factor but NAFLD has not been investigated in an unselected obstructive sleep apnea (OSA) population. Beyond liver biopsy, there are non invasive validated tools allowing a screening of NAFLD in large populations.

Aims: (i) To use non-invasive blood tests (Steatotest®, NASHtest® and Fibrotest®) to evaluate steatosis, Nonalcoholic Steato hepatitis (NASH) and fibrosis in a large cohort of OSA (II) To assess endothelial function by peripheral arterial tone (PAT).

Patients: Two hundred and twenty-six subjects referred for suspicion of OSA were included (men: 55%, median age: 56 years, mean BMI: 34 kg/m^2).

Results: 61.5% of OSA patients exhibited advanced steatosis. By multivariate analysis, triglycerides ($P < 0.0001$), insulin resistance ($P = 0.0004$) and nocturnal cumulative time spent <90% of SaO2 (CT90) ($P = 0.01$) were independent factors for liver steatosis. Thirty-eight percent of OSA displayed NASH (N1 or N2 with NASHtest®). CT90 was significantly associated with NASH ($P = 0.035$) but this became non significant in multivariate analysis. Endothelial function was more impaired in OSA patients with advanced steatosis ($P = 0.04$) and NASH ($P = 0.013$).

Discussion/Conclusion: In a large unselected population of OSA, the severity of intermittent hypoxia was independently associated with steatosis. Endothelial dysfunction was more severely impaired in OSA patients demonstrating NAFLD.

O234

Effect of bed rest and hypoxia on sleep macrostructure and respiration during sleep

L. DOLENC GROŠELJ[1], B. ROJC[1], J. JERAN[1], A. PANGERC[1], S. A. MORRISON[2], O. EIKEN[3] and I. B. MEKJAVIC[2]

[1]Institute of Clinical Neurophysiology, Ljubljana, SI, [2]Jozef Stefan Institute, Ljubljana, SI, [3]Royal Institute of Technology, Stockholm, SE

Introduction: High altitude (>3000 m) sojourns can cause poor-quality sleep, which can result in a risk of pronounced hypoxemia and nocturnal breathing disturbances, including central apnea, and impaired daytime performance. It is anticipated that the ambient conditions in future lunar habitats will be hypoxic. Thus, the aim of the present study was to assess the separate and combined effects of bed rest and hypoxia on objective sleep parameters and the incidence(s) of periodic breathing during sleep.

Methods: Eleven subjects participated in a repeated measures cross-over design study, comprising three experimental campaigns: normobaric hypoxic ambulatory confinement (4000 m), normobaric hypoxic bedrest (4000 m), and normoxic bedrest (990 m). Sleep PSG was derived on seven occasions: (i) BL-baseline night (altitude of 900 m), (ii) 1NB-1st night of normoxia bedrest (altitude: 900 m), (iii) 2NB-10th night of normoxia bedrest (altitude: 900 m), (iv) 1HB-1st night of hypoxia bedrest (simulated altitude: 3000 m), (v) 2HB-10th night hypoxia bedrest (simulated altitude: 4000 m), (vi) 1HW-1st night of hypoxia walking (simulated altitude: 3000 m), (vii) 2HW-10th night of hypoxia walking (simulated altitude: 4000 m). All recordings were performed and visually scored on the basis of the AASM guidelines (American Association of Sleep medicine, 2007).

Results: Objective PSG measurements showed no statistical differences in sleep macrostructure (WASO sleep stage 1, 2, deep sleep (stage 3), REM sleep) in the normoxic compared to the hypoxic trials. However, on the 10th night of hypoxia (4000 m, equivalent) there was a significant increase in the incidence of periodic breathing. Indeed, when comparing the sleep architecture at only the points of periodic breathing occurrence, there were profound differences observed in sleep architecture. Bed rest had no further influence on respiration pattern during sleep.

Conclusions: These data suggest that periodic breathing occurs at a simulated elevation of 4000 m, even after 10 days of acclimatization, and that unloading/inactivity had no further influence on sleep macrostructure. The data also suggest that the episodes of periodic breathing do have an impact on overall sleep architecture.

Acknowledgements: The study was supported, by the European Space Agency (ESA) Programme for European Cooperating States (ESTEC/Contract No. 40001043721/11/NL/KML: Planetary Habitat Simulation), and by the Slovene Research Agency (Contract No. L3-3654 and No. P3-0338).

O235

The effects of morphine on chemoreflexes and breathing in obstructive sleep apnoea

D. WANG[1], A. SOMOGYI[2], B. YEE[1], K. WONG[1], J. KAUR[1], P. WRIGLEY[3] and R. GRUNSTEIN[1]

[1]Royal Prince Alfred Hospital, Camperdown, AU, [2]University of Adelaide, Adelaide, AU, [3]Pain Management Research Institute, North Sydney, AU

Objectives: The effect of morphine on breathing and ventilatory chemoreflexes in obstructive sleep apnea (OSA) is unknown. As part of a proof-of-concept study examining the potential of the glial inhibitor, minocycline to reverse opioid induced respiratory depression, we examined the relationship between breathing during sleep, awake ventilatory control and plasma morphine concentrations in OSA patients, a group potentially at risk of respiratory depression.

Methods: Following baseline polysomnography (PSG) and ventilatory chemoreflex tests, 10 mild-moderate OSA patients underwent a second night PSG 4 h after taking a 30 mg oral controlled-release morphine tablet. Awake ventilatory chemoreflexes were tested and blood samples were collected just prior to the beginning of the sleep study.

Results: Compared to baseline, the administration of 30 mg slow release morphine alone did not cause statistically significant respiratory depression in any key PSG and ventilatory chemoreflex parameter. However, there was a significant positive correlation between a higher plasma morphine concentration in the morphine arm and the increase of the CO_2 recruitment threshold from baseline ($r = 0.86$, $P = 0.006$), as well as with an improvement in the sleep time with $SpO_2 < 90\%$ (T90) from baseline ($r = -0.87$, $P = 0.005$). In addition, the increase of CO_2 recruitment threshold significantly correlated with reduction in T90 ($r = -0.79$, $P = 0.02$). Furthermore, a higher plasma morphine concentration tended to correlate with an improvement in hypopnoea index compared to the baseline ($r = -0.66$, $P = 0.07$).

Conclusion: OSA subjects with a higher plasma morphine concentration after a single dose of oral controlled-release morphine had paradoxically depressed ventilatory chemoreflex and improved sleep apnea. This result is in keeping with new advances in the phenotyping of OSA indicating that patients with milder forms of OSA can have increased chemosensitivity (loop gain). Consequently reduction in loop gain using centrally-acting drugs may actually improve breathing during sleep. Our data question the assumption that small doses of opioids are harmful to patients with OSA, and may have important implications for OSA pharmacological treatment.

O236

Sleep quality in cataract patients before and after surgery: a comparison of intra-ocular lens types

K. WULFF[1], F. CUTHBERTSON[1], G. RATNAJARAN[2], I. ALEXANDER[1], S. PEIRSON[1], S. DOWNES[3] and R. G. FOSTER[1]

[1]University of Oxford, Oxford, UK, [2]King Edward VII Hospital, Windsor, UK, [3]Oxford Eye Hospital, Oxford, UK

Objectives: To compare the impact of different intra-ocular lens (IOL) types [ultra-violet blocking (UVB) and blue-filtering (BF)] on subjective sleep quality before and after cataract surgery.

Methods: Patients listed for cataract surgery at the Oxford Eye Hospital (UVB type: Alcon Acrysof SA60AT) and King Edwards VII Hospital in Windsor (BF type: Alcon AcrySof IQ SN60AT) completed the 19-item self-rated Pittsburgh Sleep Quality Index (PSQI) prior to surgery and at 1, 6 (UVB only) and 12 months following surgery. Five components on sleep (quality, latency, duration, efficiency, level of disturbance) were scored as well as day-time dysfunction and sleep medication on a 0–3 point scale (3 being worse). The sum provided the index for global sleep quality (range 0–21), whereby a score >5 indicates poor sleep. In addition, the patients' age, sex, best-corrected visual acuity (VA) for each eye and any existing ocular co-morbidity were noted. VA was classified as good if VA = 6/7.5 and better, and poor if VA = 6/9 and worse. To date, the pre-operative and 1, 6 and 12 months post-operative PSQI scores are completed for UVB lens data and pre- and 1-month postoperative PSQI scores for BF lens data.

Results: A total of 520 patients with fully completed pre-op information and PSQI were included in the UVB IOL group and 271 in the BF IOL group. The mean pre-op sleep score for the UVB IOL group was 6.31 and post-op 5.85 ($P = 0.001$, Wilcoxon Signed Rank Test). For the BF IOL group the pre-op and post-op sleep scores were the same, 6.20 ($P = 0.870$). Sub-group analysis based on VA pre-op for the UVB IOL group showed an improvement in sleep scores from 5.94 to 5.49 ($P = 0.028$) in the good VA group and from 6.79 to 6.28 ($P = 0.009$) in the poor VA group. In the BF IOL group, sleep scores did not change significantly either in the good VA group (6.53–6.72, $P = 0.893$) or the poor VA group (6.14–6.10, $P = 0.841$). In the UVB IOL group only, the improvement in global PSQI was sustained at 6 months ($Z = -2.008$, $P = 0.045$), and this was for patients with poor VA and first eye operation ($Z = -2.232$, $P = 0.026$).

Conclusions: This is the first study showing that intra-ocular lens type has a differential effect on subjective sleep quality. If lens type is shown to have a significant effect on sleep, then individuals with poorly lit environments such as nursing homes may benefit more from clear, non-blue filtering lens implantation.

FC has received funding from Novartis and Allergan to attend meetings.

O237

Impact of obstructive sleep apnoea on quantitative sleep electroencephalogram analysis: sex differences

L. L. MORSELLI[1], K. TEMPLE[1], B. MOKHLESI[1], H. R. WHITMORE[1], K. SPIEGEL[2], R. LEPROULT[1], D. A. EHRMANN[1] and E. VAN CAUTER[1]

[1]University of Chicago, Chicago, US, [2]INSERM U1028 – CNRS UMR 5292, Lyon, FR

There are sex differences in sleep architecture and in the risk of obstructive sleep apnea (OSA). The prevalence of OSA in women has sharply increased in the past decade, because of the obesity epidemic. Previous studies, mainly in men, have shown that OSA is associated with decreased slow-wave activity.

Objectives: To identify sex differences in the impact of OSA on the microarchitecture of sleep by quantitative EEG analysis.

Methods: Overnight polysomnography was performed in 104 obese subjects (43 M, 61 F, age 34 ± 1 years, BMI 37 ± 1 kg/m^2). Recordings were visually scored in stages wake, N1, N2, N3 and REM using standardized criteria. The presence of OSA was defined by an apnea-hypopnea index (AHI) >5 events/h. Spectral analysis on the central EEG lead was performed after elimination of muscular, ocular and movement artifacts. Delta, theta, and alpha activities were calculated as absolute spectral power in the 0.75–4 Hz, 4.5–8 Hz, and 8.5–12 Hz bands, respectively. Mean power per 30-s epoch was calculated for each band. Sex comparisons were performed on log-transformed values after adjusting for age, BMI and ethnicity. Results are reported as mean ± SEM.

Results: Obstructive sleep apnea was present in 74% of men and in 44% of women. No difference was observed between men and women with OSA for total AHI (M 25 ± 5, F 18 ± 4; $P = 0.53$), NREM AHI (M 22 ± 5, F 16 ± 4; $P = 0.80$) and REM AHI (M 30 ± 4, F 25 ± 5; $P = 0.92$). The presence of OSA had a minimal impact on mean delta activity in the first 3 h of NREM sleep in women (-9.7%; 575 ± 17 versus 637 ± 17 mcV^2; $P = 0.09$). In contrast, the presence of OSA in men was associated with a robust decrease in delta activity (-23%; OSA- 481 ± 24 mcV^2; OSA+ 369 ± 21 mcV^2; $P = 0.0012$). This sex difference in the impact of OSA on delta activity was confirmed by a significant sex*log AHI interaction in a general linear model ($P = 0.0007$). Mean theta activity in the first 3 h of NREM sleep was higher in women than in men, irrespective of the presence or absence of OSA (F 53 ± 1 mcV^2, M 37 ± 1 mcV^2, $P < 0.0001$), while OSA was associated with lower alpha activity in both women and men (women: OSA- 22.6 ± 0.2 mcV^2, OSA+ 24.7 ± 0.3 mcV^2; men: OSA- 17.8 ± 0.7 mcV^2, OSA+ 20.5 ± 0.3 mcV^2, $P < 0.0001$).

Conclusion: Contrary to what is observed in men, OSA does not appear to significantly decrease delta activity levels in women. Delta activity has been linked to glucose homeostasis. A sex-specific impact of OSA on glucose metabolism could thus be expected.

This work was supported by the National Heart, Lung and Blood Institute (NHLBI) grant, R01HL75025, by the National Institute of Diabetes, Digestive and Kidney Disease (NIDDK) grant P60DK-020595, by the National Institute on Aging (NIA) grant PO1-AG11412 and by the National Institute of Health grants MO1-RR-00055 and P50 HD057796.

O238

Adverse impact of obstructive sleep apnoea on glucose tolerance: sex-specific mechanisms

K. TEMPLE[1], R. LEPROULT[2], L. MORSELLI[1], H. WHITMORE[1], J. SYKES[1], D. A. EHRMANN[1], E. VAN CAUTER[1] and B. MOKHLESI[1]
[1]University of Chicago, Chicago, US, [2]Université Libre, Brussels, BE

Objectives: Obstructive sleep apnea (OSA) is an independent risk factor for the metabolic syndrome, and is more prevalent in men than women. The objective of this study was to determine if there are sex differences in the impact of OSA on glucose tolerance, insulin sensitivity, beta-cell response and diabetes risk.

Methods: Subjects were 143 overweight/obese men and women who underwent an overnight polysomnogram followed by a 2-h 75-g oral glucose tolerance test (OGTT). Samples were assayed for glucose, insulin, and C-peptide. Severity of OSA was assessed by the apnea-hypopnea index (AHI). Fasting insulin resistance was estimated by the HOMA-IR index. Insulin resistance during the OGTT was assessed by the area under the curve of HOMA-IR, and insulin sensitivity was assessed by the Matsuda index. Beta-cell response was assessed by the insulinogenic index and C-peptide levels. Diabetes risk was estimated by the oral disposition index (Matsuda index × insulinogenic index). All comparisons were adjusted for age, BMI, and race risk.

Results: Forty men and 37 women had OSA (73% versus 42%; $P < 0.001$). Prediabetes (impaired fasting glucose/impaired glucose tolerance) was present in 27% of women but 45% of men ($P < 0.05$) with OSA. The presence of OSA was associated with higher fasting glucose levels in women, but not in men ($P < 0.001$). During the OGTT, glucose tolerance was lower in the presence of OSA, without significant sex difference. During fasting conditions, the adverse impact of OSA on insulin resistance was similar in both sexes. In contrast, during the OGTT, increased severity of OSA tended to be associated with a larger decrease in insulin sensitivity ($P < 0.09$) and a greater increase in insulin resistance ($P < 0.05$) in men than women. With increasing AHI, men had an increase in insulinogenic index ($r^2 = 0.2$; $P = 0.003$), while women had a decrease in insulinogenic index ($r^2 = 0.2$; $P = 0.006$). Increasing AHI was associated with a greater decrease in oral disposition index in women than in men (women: $r^2 = 0.43$; $P < 0.0001$, men:$r^2 = 0.17$; $P < 0.002$).

Conclusion: OSA is associated with decreased glucose tolerance in both men and women, but the cause differs by sex. OSA is associated with greater reductions in insulin sensitivity in men than women. However, the adverse impact of OSA on beta-cell responsiveness is larger in women than in men, resulting in an overall greater risk of diabetes in women.

Supported by NIH grants MO1-RR-00055, P50-HD057796, R01-HL75025, PO1-AG-11412, P60-DK020595.

O239

Sleep complaints and stress predict the incidence of obesity

J. FERNANDEZ-MENDOZA, A. VGONTZAS, M. SHAFFER, I. KRITIKOU, S. CALHOUN, M. BASTA, D. LIAO and E. BIXLER
Penn State College of Medicine, Hershey, US

Objective: Several epidemiologic, longitudinal studies have focused on the role of short sleep duration as a risk factor for the incidence of obesity. However, the vast majority of these studies used self-reported measures of sleep duration and did not examine the potential role of other factors such as objective sleep duration, subjective sleep disturbances, or emotional stress.

Methods: We studied a random sample of 1111 non-obese adults from the Penn State Cohort in the sleep laboratory for one night using polysomnography (PSG) and followed them up for a mean of 7.5 years. Subjective and objective (PSG) measures of sleep were obtained at baseline. Emotional stress was assessed using the MMPI-2 at baseline. Obesity was defined as a body mass index (BMI) ≥30 kg/m^2.

Results: The incidence of obesity was 15%. Individuals who developed obesity reported shorter sleep duration (7.0 ± 1.2 versus 6.6 ± 1.2; $P < 0.05$), more subjective sleep disturbances (13.3% versus 22.9%; $P < 0.01$), and higher emotional stress (0.6 ± 1.2 versus 1.2 ± 1.8; $P < 0.01$) at baseline when compared to non-obese individuals. There was a synergistic effect between these variables as individuals with subjective sleep disturbances reported shorter sleep duration (7.0 ± 1.1 versus 6.6 ± 1.4; $P < 0.01$) and scored higher for emotional stress (0.6 ± 1.1 versus 1.2 ± 1.9; $P < 0.01$). There was no association between objective short sleep duration and incident obesity (6.0 ± 1.2 versus 6.1 ± 1.1). Subjective sleep disturbances and emotional stress were significant predictors of incident obesity after controlling for gender, age, depression, sleep apnea, and BMI. Self-reported short sleep duration did not predict incident obesity after controlling for confounding factors, including emotional stress.

Conclusion: Emotional stress, subjective sleep complaints, and self-reported short sleep duration, which appears to be a surrogate marker of stress and complaints of poor sleep, are associated with incident obesity. Objective short sleep duration per se does not predict the development of obesity. The detection and treatment of sleep disturbances and emotional stress should be the focus of our preventive strategies against obesity.

O240

Continuous positive airway pressure improves hyposomatotropism in men

C. HOYOS[1], R. KILLICK[1], D. KEENAN[2], J. VELDIUS[3] and P. LIU[1]
[1]Woolcock Institute of Medical Research, Sydney, AU, [2]University of Virginia, Charlottesville, US, [3]Mayo Clinic College of Medicine, Rochester, US

Background: OSA is a common condition that is characterised by intermittent hypoxia, which disrupts sleep and is associated with reduced growth hormone (GH) secretion. Hyposomatotropism contributes to metabolic ill-health in men with OSA, but the only randomised sham-controlled trial reported no change morning IGF-1 after 4 weeks of Continuous Positive Airway Pressure (CPAP).

Methods: Sixty-five CPAP naive men with moderate to severe OSA [age = 49 ± 12 year, apnea hypopnea index (AHI) = 40 ± 18 events/h, BMI = 31 ± 5 kg/m^2, IGF-1 = 20.4 ± 6.3 nM] were randomised in a 12-week double blind sham-controlled parallel group study, to receive either active ($n = 34$) or sham ($n = 31$) CPAP. OSA was measured by polysomnography at week 0 and 12 and fasting morning glucose, insulin, C-peptide and IGF-1 blood levels at 0, 6 and 12 weeks in all men. GH was also measured in a subgroup of 18 men (active $n = 11$, sham $n = 7$) every 10-min from 10 PM until 6 AM (49 samples) at week 12 while sleep architecture (960 epochs) was simultaneously assessed. GH secretion was determined by mathematical deconvolution. Data are mean SD.

Results: AHI, BMI and IGF-1 (all $P > 0.16$) were not different at baseline between groups. As expected 12 weeks of active, compared to sham, CPAP reversed OSA by 33 events/h ($P < 0.0001$) and increased slow wave sleep by 7% ($P = 0.05$). Mixed model analyses showed that active, compared with sham, CPAP increased IGF-1 by 2.94 nM ($P = 0.006$) at 12 weeks, but not at 6 weeks

(0.83 nM, $P = 0.4$). Changes in fasting glucose, insulin, C-peptide/glucose and HOMA insulin sensitivity were not different between groups at 6 or 12 weeks (all $P > 0.15$). In the subgroup of 18 men that underwent overnight blood sampling at 12 weeks, total (35.0 ± 28.0 versus 8.5 ± 7.3 ng/ml/8 h, $P = 0.001$) and pulsatile (32.3 ± 27.7 versus 6.8 ± 6.8 ng/ml/8 h, $P = 0.002$) GH secretion, mean GH concentration (1.2 ± 1.0 versus 0.3 ± 0.3 ng/ml, $P = 0.002$) and mass of GH secreted per pulse (8.7 ± 9.0 versus 2.2 ± 2.3 ng/ml, $P = 0.01$) were all significantly higher in active compared with sham CPAP users, respectively. The pulse frequency ($P = 0.11$), interpulse regularity ($P = 0.6$) and GH regularity ($P = 0.78$) were not different between groups.

Conclusions: Twelve weeks of CPAP increases total and pulsatile GH secretion, secretory burst mass and pulse frequency. Six weeks of CPAP may be insufficient, whereas 3 months is sufficient, to increase IGF-1 but not alter insulin action. Persistence with CPAP is required to improve abnormalities in GH secretion and consequent metabolic effects associated with OSA.

Oral Session 8 – Paediatrics and Developmental Aspects of Sleep

O241

The maturation of specific skills is predicted by the topographical distribution of sleep slow wave activity

S. KURTH[1], M. RINGLI[2], A. GEIGER[2], A. BUCHMANN[3], O. JENNI[2], M. LEBOURGEOIS[1] and R. HUBER[2]

[1]University of Colorado, Boulder, US, [2]University Children's Hospital Zurich, Zurich, CH, [3]University of Wisconsin, Madison, US

Objectives: Sleep slow wave activity (SWA, 1–4.5 Hz) reflecting the depth of sleep, has been suggested to play a crucial role in synaptic plasticity. SWA topography exhibits major changes across maturation which parallel morphological changes of cortical gray matter. However, how the maturation of SWA, gray matter changes and behavioral skills are related, has not been addressed.

Methods: Sleep SWA was measured using all-night high-density (hd)-EEG (128 electrodes) in subjects between 2 and 26 years ($n = 63$, 38 males). A maturation index (SWAMI) indicated the maturational stage of SWA topography based on the region exhibiting maximal SWA (initial 60 min N2-3). Behavioral tasks were performed to assess behavioral skills in subgroups of individuals (4–26 year, $n = 21$–56, e.g. Zurich Neuromotor Assessment for motor skills). We estimated gray matter thickness based on magnetic resonance images (MRI, T1) in a subgroup of subjects (8–26 year, $n = 44$). Electrodes were digitized and co-registered with the subjects MRI to identify Brodmann areas (BAs) underlying the electrodes. Based on BAs, regions of interest were defined, e.g. 'complex motor': BA 1-4,6 representing somatosensory and motor areas.

Results: SWAMI and skill performance showed a positive correlation ($R = 0.31$ $P = 0.02$ for complex motor; $R = 0.41$, $P < 0.002$ for pooled skills). Thus, individuals with a more mature SWA topography also had better skills. A comparison of the time course of SWAMI (double exponential fit, $R = 0.59$ $P < 0.0001$) and skills ($R = 0.82$, $P < 0.0001$) across age revealed that the maturation of SWA topography preceded the maturation of skills by about 3.7 years. Gray matter matured last.

Conclusion: We found that SWA topography matured before skills and gray matter. An explanation for this finding might be that the three variables (SWA topography, skills, gray matter) reflect different aspects of maturation. Our results also show that mapping of cortical maturation by sleep SWA topography might represent a promising tool to study developmental disorders.

O242

Changes of sleep slow wave characteristics during infancy – a longitudinal study

S. FATTINGER[1], O. JENNI[1], B. SCHMITT[1], P. ACHERMANN[2] and R. HUBER[1]

[1]University Children's Hospital Zurich, Zurich, CH, [2]University of Zurich, Zurich, CH

Objectives: Sleep slow waves (SW, 1–4.5 Hz) are the most prominent electrophysiological sign of non-rapid-eye-movement (NREM) sleep. It has been shown that the slope of these SW directly reflects changes in cortical synchronisation and therefore represents a reliable indicator of synaptic strength. The synaptic homeostasis hypothesis claims that increasing synaptic strength during the day is rebalanced (i.e. downscaled) during subsequent sleep. This synaptic downscaling is reflected in a decrease of the slope of slow waves in the course of sleep. The early postnatal period of cortical development is characterised by vast formation of synapses. Hence, we asked the question whether these changes in cortical connectivity are reflected in slope changes of sleep SW.

Methods: We reanalyzed previously published data of a longitudinal study carried out in 11 healthy full-termed infants (5 m, 6 f; Jenni et al., 2004). All night sleep EEG (F3A2, C3A2, P3A2, O1A2) were recorded at 2, 4, 6, and 9 months after birth using the 10–20 system. After visual scoring of sleep stages and semiautomatic artefact removal we calculated the slope of SW at a fixed amplitude of 75 μV for the first and last hour of NREM sleep.

Results: The slope of slow waves during the first and last hour of NREM sleep increased with age (e.g. first hour: 349.59 μV/s at 2 months to 493.12 μV/s at 9 months, $P < 0.001$). This increase was most prominent over occipital areas. Furthermore, when looking at overnight changes, the slope of SW decreased from the first to the last hour of NREM sleep at all ages ($P < 0.001$). This overnight decrease was also most prominent over occipital areas ($P > 0.001$) and increased with age (e. g. 23.91 μV/s at 2 months to 69.59 μV/s at 9 months, $P < 0.001$).

Conclusion: Our results suggest an age dependent increase in synchronization of cortical activity during infancy. This increased synchronization could be due to the increase in cortical connectivity. Synaptogenesis increases first over the occipital cortex, which might explain why the most prominent slope changes were found for the occipital derivation. Finally, our results show that the downscaling of synaptic strength during sleep is present already during infancy.

This work was supported by Swiss National Science Foundation grant PP00P3-135438 (R.H.) and a research grant from the Zurich Centre for Integrative Human Physiology (R.H., O.G.J., P.A.).

O243

Spectral acoustic analysis of nocturnal breathing sounds in snoring children: prediction of obstructive sleep apnoea and neurocognitive impairments

M. URSCHITZ[1], P. BROCKMANN[2], M. CAVUSOGLU[3] and C. POETS[1]

[1]University Children's Hospital Tuebingen, Tuebingen, DE, [2]Pontificia Universidad Catolica de Chile, Santiago de Chile, CL, [3]Swiss Federal Institute of Technology, Zurich, CH

Objectives: The diagnosis of obstructive sleep apnoea (OSA) is based on the apnoea hypopnoea index (AHI) obtained with polysomnography (PSG). However, PSG is not widely available and the AHI is only weakly correlated to OSA-associated neurocognitive impairments (NCI). We aimed to estimate the diagnostic test accuracy (DTA) of spectral acoustic analysis (SAA) of nocturnal breathing sounds in predicting OSA and to investigate its association with OSA-associated NCI.

Methods: Prospective DTA study including 50 habitually snoring children (median age 9.7 years; 28 boys), who underwent sleep lab-based full overnight PSG according to AASM standard including digital video and high-end audio recording. The latter was analyzed using an adapted SAA classification algorithm to discriminate between snore and non-snore sound episodes and to qualify and

quantify the snoring. Children were also tested for NCI (e.g., inattention, low intelligence, daytime sleepiness) using questionnaires, the Continuous Performance Test (CPT), the Hamburg Wechsler's Intelligence Test (HAWIK), and the Pupillographic Sleepiness Test (PST). Diagnosis of OSA was based on AHI >1 per hour of sleep. Classical measures of DTA [e.g., area under the receiver operating characteristic curve (AUC)] and correlation coefficients between PSG, SAA and NCI variables were calculated.

Results: Forty-four of 50 audio recordings could be successfully analyzed; 10 patients were classified as having OSA. There were moderate correlations between SAA variables and the AHI: r = 0.48 for snoring number, 0.47 for snoring length, and 0.53 for snoring loudness. SAA variables showed good DTA in predicting OSA on PSG: AUC = 0.782 for snoring number, 0.762 for snoring length, and 0.759 for snoring loudness. Neither a PSG nor a SAA variable correlated significantly with CPT or HAWIK variables. However, SAA variables correlated better than the AHI (r = 0.27; $P > 0.05$) with PST results (r = 0.32 and 0.34; $P < 0.05$).

Conclusion: SAA of nocturnal breathing sounds is a feasible and objective method to identify, qualify and quantify snoring in children. SAA variables are predictors of OSA and OSA-related NCI and may be used to discriminate habitually snoring children who may benefit from therapy.

This study was supported by a research grant of the University Hospital Tuebingen (AKF program, grant application number 240-0-0).

O244

Clinical and polysomnographic characteristics in 117 children with narcolepsy

C. O. INOCENTE[1], S. LAVAULT[2], Y. DAUVILLIERS[3], M. LECENDREUX[4], R. REIMÃO[5], J.-S. LIN[1], I. ARNULF[6] and P. FRANCO[1]

[1]University of Lyon, Lyon, FR, [2]CNRS UMR7225 – Inserm, U975, Paris, FR, [3]CHU Montpellier, Montpellier, FR, [4]Hôpital Robert Debré & CNR narcolepsie-hypersomnie, Paris, FR, [5]University of São Paulo, São Paulo, BR, [6]CNRS UMR7225 – Inserm, U975, Paris, FR

Objective: To report the clinical and polysomnographic characteristics in a consecutive cohort of narcoleptic children and adolescents evaluated in the National French Multicentric Research program on narcolepsy.

Methods: The children received the diagnosis of narcolepsy after a complete evaluation including questionnaires [Epworth, Children's Depression Inventory (CDI)], Quality of Life (QOL), a nocturnal polysomnography followed by a multiple sleep latency test (MSLT) and HLA typing, with CSF hypocretin-1 assessed in 31 cases. Wilcoxon non-matched pairs signed-ranks test and Spearman test were used.

Results: The cohort included 117 children (65 boys) with a mean age of 11.6 ± 3.1 years at diagnosis (41.8% <10 years). The first symptom at onset was excessive daytime sleepiness (9.25 ± 3.8 years). Other symptoms were cataplexy (80%), hypnagogic hallucinations (40%), sleep paralysis (24.7%), insomnia (16.2%), parasomnia (74.3%) and night eating (12.8%). 91.3% were DQB1*0602 positive. CSF hypocretin-1 level was 31 ± 46 pg/ml. Mean BMI was 23.2 ± 5.2 kg/m^2, 59.8% were obese, Z-score was 2.92 ± 2.63. Eight out of 31 girls (26%) had precocious puberty (62.5% obese). Thirty patients (11.1%) received H1N1 vaccination prior the onset of the symptoms, 6.8% had a familial narcolepsy. Twenty-one percent had signs of depression on the CDI score. There was a positive correlation between CDI and Epworth (r = 0.40, $P = 0.001$) but not Z-score. 36.7% of the children had school difficulties, 23.6% repeated a year and 26.5% had absenteeism. The QOL for children, adolescents, parents were correlated to CDI score (r = -0.48 $P = 0.008$, r = -0.78 $P < 0.001$, r = -0.57 $P < 0.001$) but not to Epworth or Z-score. The mean total sleep time was 471.4 ± 85 min, sleep efficiency 81.8 ± 16.1%, % N3 27.6 ± 11.2, %REM 19.8 ± 7, AHI 2.2 ± 3.6/h, arousal index 7.6 ± 7.5/h. The sleep latency was 16.8 ± 24.6 min and the REM latency on PSG was at 88.5 ± 86.2 min. The sleep latency on MSLT was 5.5 ± 4.6 min with 3.3 ± 1.3 SOREM. No correlation was found between sleep onset latency on MSLT and sleep efficiency, apnea-hypopnea index, respiratory related arousals, CDI and QOL.

In this large cohort study, narcolepsy in children was associated with obesity and precocious puberty in respectively 60% and 25% of the patients. This disease had a severe impact on mood and school performances. Depression worsened the sleepiness score and the quality of life of these children.

O245

Influence of prenatal factors on sleep patterns: data from AUBE prospective study

P. FRANCO[1], E. MONTEMITRO[2], S. FLORI[3], V. PORCHER-GUINET[1], C. O. INOCENTE[1], J.-S. LIN[1], J. ADRIEN[4], F. BAT-PITAULT[5] and H. PATURAL[3]

[1]University of Lyon, Lyon, FR, [2]Ospedale Bambino Gesù di Roma, Rome, IT, [3]University Jean Monet, Saint-Etienne, FR, [4]Hospital Pitié-Salpêtrière, Paris, FR, [5]University of Aix-Marseille II, Marseille, FR

Objective: To evaluate the links between prenatal environmental factors on sleep patterns during the first 18 months of life.

The Autonomic Baby Evaluation and Sleep development (AuBe) study is a prospective study on the maturation of sleep and autonomic nervous system during the first 2 years of life. The newborns were enrolled at birth and were followed every 6 months with questionnaires, polysomnographic (birth-6 months) and holter ECG recordings (12–18–24 months) and neuropsychological evaluation (WPPSI-III) at 30 months. Only the questionnaires data until 18 months were reported here.

Results: Two hundred and ninety-six newborns (56% boys) were involved in this study. Nineteen babies were small for gestational age. There were 31 preterm infants (10.4%) with a gestational age of 35.92 ± 0.73 weeks. Forty-three mothers were overweight (14.5%) and 23 were obese (7.7%). There was no alcohol consumption during pregnancy but 74 mothers smoked (25%), 14 smoked more than 10 cigarettes per day. Twenty-two mothers were depressed on the HAD and Mini evaluation but only 2 were on SSRI treatment. There was a decrease in daytime sleep duration from 6 to 18 months ($P < 0.001$) but only a decrease in night sleep time between 6 and 12 months ($P = 0.025$). A negative correlation was found between total sleep duration and weight ($P = 0.035$), especially at 18 months ($P = 0.048$).

Sleep problems (sleep onset problems or disruptive night waking) were found in 51.8% of 6-month-olds, 33.6% of 12-month-olds and 34.4% of 18-month-olds. No statistical changes for sleep disorders were found with maturation. Sleep onset problems (10.1%), night waking (37.8%), short sleep duration (11.6%) and sleep problems (42.4%) were reported by parents. 9.1% parents were present at time of sleep onset and 6.6% parents bed shared with their children. We did not find a relation between sleep problems and the parental presence or bedsharing. Breastfeeding decreased total sleep time ($P = 0.003$). Maternal depression during pregnancy increased the

risk of night waking at 6 months ($P = 0.009$). At 18 months, there was a relation between gestational age and sleep onset problems ($P = 0.001$), night waking ($P < 0.001$), sleep problems ($P = 0.013$) and noisy breathing ($P = 0.017$). SGA was correlated with sleep onset difficulties ($P = 0.017$). No effects of maternal obesity, gestational HTA ($n = 12$) or diabetes ($n = 14$), pre or postnatal exposure to tobacco were found.

Some prenatal factors (birth weight, gestational age, maternal depression) could influence sleep patterns in children.

O246

Sleep variability and cardiac arrhythmia in adolescents – Penn State Child Cohort Study

D. LIAO, A. BERG, W. FREEMAN, M. SHAFFER, A. VGONTZAS, S. CALHOUN and E. BIXLER

Penn State University, Hershey, US

Objectives: To associate actigraphy-based 7-night sleep and sleep variability and cardiac electrophysiological patterns in the Penn State Child Cohort (PSCC) adolescents.

Methods: We used available data from the first 169 adolescents who have completed the follow up examinations in the population-based PSCC study. Actigraphy was used to record total sleep time on a nightly basis for seven consecutive nights. First night data were excluded. Using a mixed-effect model, we calculated the (i) average within-subject sleep time, (ii) within-subject variability of sleep time, (iii) average within-subject sleep efficiency, and (iv) within-subject variability of sleep efficiency. Arrhythmia, predominantly premature ventricular complex (PVC), was assessed using a 39-h high resolution Holter system. The PVC data were analyzed number of PVC per hour on a hourly basis (39 hourly repeated measures). Negative binomial regression models were used to assess the sleep and PVC relationship. Cardiac autonomic modulation (CAM) was assessed by heart rate variability (HRV) analysis of normal R-R intervals from the Holter ECG. The HRV indices in frequency domain [high frequency power (HF), low frequency power (LF), and LF/HF ratio] and time domain [standard deviation of normal RR intervals (SDNN), and the square root of the mean squared difference of successive normal RR intervals (RMSSD), and heart rate (HR)] were calculated on a 30-min basis (78 repeated measures). HRV indices and sleep were analyzed using mixed-effects models.

Results: The mean age was 17 years (SD = 2.0), with 56% male and 75% white. The average PVC was 0.43/Hr (ranging 0–133). After adjusting for covariables, individuals with higher within-subject variability of sleep time have a 4-fold increase in the PVC frequency as compared to individuals with lower within-subject variability (RR = 3.95, 95% CI (1.17, 8.34), $P = 0.01$). Also, individuals with higher within-subject variability of sleep efficiency have lower HRV indices and higher HR, indicative of lower parasympathetic and higher sympathetic modulation (all $P < 0.05$).

Conclusion: There is a significant adverse association between night-to-night sleep variability and cardiac electrophysiological parameters in healthy adolescents.

Support: NIH: R01 HL603772, R01 HL97165, UL1 RR033184, C06 RR16499.

O247

Periodic limb movements in sleep in children with nocturnal enuresis and/or nocturnal polyuria: a retrospective case–control study

K. DHONDT, E. BAERT, C. VAN HERZEELE, A. RAES and J. VANDE WALLE

Ghent University Hospital, Ghent, BE

Purpose: The relation between sleep and nocturnal enuresis has been an area of interest for many years. Children with enuresis are generally believed to be deep sleepers with decreased arousability. A previous pilot study in which a group of 29 children with desmopressin dependent/resistant nocturnal enuresis and nocturnal polyuria received a polysomnographic study, showed the opposite (1). A significant increased PLMS-index was found in these children. In this study we want to examine these preliminary data further in a retrospective case–control study design.

Material and Methods: Fifty boys and 17 girls between 6 and 16 years old (mean age ± SD: 11.04 ± 2.86) diagnosed with desmopressin resistant (50), desmopressin dependent enuresis (17) and/or nocturnal polyuria (50, Hjalmas formula) executed a standardized investigation protocol including one night polysomnography (PSG). The same protocol was applied to a control group of 67 children. Forty-eight boys and 19 girls between 6 and 16 years old (mean age ± SD: 11.09 ± 2.76) were indicated to have a PSG because of a possible sleep disorder, but selected for this study only on sex and age match. Children with enuresis were excluded from the control group. All patients were drug free during PSG.

Results: Periodic limb movements per hour of sleep (PLMS-index) were increased in the study population to 13.9 ± 7.1. The amount of cortical arousals per hour of sleep (A-index) and Arousel-Awakening-index (AA-index) was 7.3 ± 4.0 resp. 9.3 ± 4.2. Differences were calculated by Mann–Whitney *U*-test. Compared to the control group differences were significant for PLMS-index: 8.6 ± 5.3 ($P < 0.001$) and 5.2 ± 3.4 resp. 7.6 ± 4.0 ($P = 0.002$, $P = 0.007$) for A-index and AA-index. Further analysis showed no significant difference in amount of slow wave sleep (SWS) in both study and control group.

Conclusions: This new data confirm the high incidence of increased PLMS-index in children with desmopressin dependent or resistant nocturnal enuresis and/or polyuria. To elaborate the relation between PLMS and nocturnal enuresis and/or polyuria, further research needs to be done.

Reference:

1. Dhondt K. et al. Evidence for abnormal sleep architecture in refractory nocturnal enuresis: a pilot study. J. Urol. 2009 oct;182 (4 Suppl):1961–5.

O248

Sleep-disordered breathing and cognitive development, early learning and behavioural adjustment in children at age 3 and 4

A. GILL, E. SCHAUGHENCY, C. LOBB and B. GALLAND

University of Otago, Dunedin, NZ

Objectives: To investigate unique population variances attributed to sleep disordered breathing (SDB) in respect of cognitive development, early learning, and behavioural adjustment in children aged 3 and 4.

Methods: Participants were 170 children aged 3.2–4.0 years identified at study commencement as at high ($n = 85$ M/F = 1.4:1) or low ($n = 85$ M/F = 1.4:1) risk for significant SDB (parent-rated using a system where scores for individual questions were rated more or less

heavy depending on their association with SDB). Each year for 2 years participants completed assessments designed to measure IQ, memory, executive functioning, early numeracy, and early literacy. While over the same period, parents completed sleep questionnaires, and parents and early childhood educators completed behavioural adjustment questionnaires.

Results: After controlling for potential confounders, SDB accounted for moderate but statistically significant unique population variance within many measures, particularly in behavioural adjustment. At age 3, SDB accounted for 19% and 13% of the unique variance of internalising and externalising behaviours respectively (as reported by parents) and 8% of the early childhood educator's functional communication ratings. Correlations between behavioural adjustment measures and SDB remained largely stable from ages 3 to 4. SDB accounted for unique variance within all 4 domains of cognitive and language assessment (verbal, performance, full and general language) at age 3, but only performance and general language measures at age 4. SDB explained small but significant unique variance in oral counting fluency at age 3, and number concept, visual discrimination and quantity comparison in children at age 4.

Conclusions: The results showed that some of the diversity in cognitive development, early learning, and behavioural adjustment of 3 and 4-year old children can be explained by the SDB status of the children. Furthermore the data suggest that history of SDB at age 3 relates to learning outcomes at age 4, moderating children's response to instructional experiences in early childhood. This finding has implications for potentially critical timing of early interventions to treat SDB to allow children to develop to their full potential. SDB severity was associated with significant decrements in many, but not all measures assessed as part of this study.

O249

Paediatric OSA, myo-facial re-education and facial growth

C. GUILLEMINAULT[1], Y. S. HUANG[2], C. LIN[2] and P.-J. MONTEYROL[3]

[1]Stanford University, Redwood City, US, [2]Chang Gung University, Taipei, TW, [3]Clinique du Tondu, Bordeaux, FR

Pediatric OSA involves facial growth impairment, and orthodontic techniques have been used to treat sleep-disordered-breathing. But as shown in the infant monkey model of nasal obstruction, abnormal oro-facial growth is related to abnormaltongue and facial muscles contractions This retrospective study look at the effect of myo-facial reeducation on the control of pediatric OSA.

Subjects: Twenty-four children- mean age 5 years-diagnosed with OSA and treated with adenotonsillectomy and orthodontic treatment with complete resolution of abnormal polysomnographic findings, but presence of oral breathing during sleep were recommended to undergo myo-facial reeducation and follow-up for 36 months.

Myo-facial reeducation methods: Standard myo-facial reeducation techniques performed about 10 times daily were performed with trained specialists for following 3 years beginning at end of maxillary distraction.

Results: Ten children did not either started or finish treatment program but 19 did. Follow-up with polysomnography was performed a mean of 5 years post-orthodontic treatment. All children without myo-facial reeducation presented relapse of OSA, while those with treatment had normal oro-facial growth andpolysomnograms

Conclusion: Pediatric OSA is related to abnormal oro-facial growth and appropriatetreatment is needed to avoiddevelopment of adult OSA.

O250

Sleep-dependent motor skill consolidation in adolescents with iron deficiency anaemia in infancy

C. ALGARIN[1], S. REYES[1], P. PEIGNEUX[2], B. LOZOFF[3] and P. PEIRANO[1]

[1]University of Chile, Santiago, CL, [2]Université Libre, Brussels, BE, [3]University of Michigan, Ann Arbor, US

Objective: Scientific evidence indicates that sleep may participate in the consolidation of procedural memory. Besides, dopamine appears to be strongly involved in the brain circuits underlying this function. Since iron deficiency anemia (IDA) in infancy is associated with long-lasting effects upon the dopaminergic neurotransmission system and in several neurofunctional domains, we investigated whether sleep contributes in motor skill learning in former IDA (FIDA) adolescents.

Methods: As part of a longitudinal study, 93 adolescents (mean age 15.2 years, 62% boys, 56% FIDA) who were part of a cohort followed since infancy at the Institute of Nutrition and Food Technology, U of Chile, were assessed at 15 years. Procedural memory was assessed using the finger sequence-tapping task (FTT), which entails repeatedly tapping a given sequence of buttons on a key board. FTT was performed in the sleep laboratory before an overnight sleep study and consisted of three successive sessions: session A (learning; 12 blocks) in the evening, session B (motor boost) 30 min later, and session C (sleep effect) the next morning after awakening. The performance (i.e. the number of sequences correctly performed during each 30-s block) was entered in ANOVAs with within-subject factors of session (A versus B, B versus C) and blocks (repetition effects) and between-subject factors of group (FIDA versus Controls) and gender.

Results: Both groups showed learning on session A, but the number of correct sequences was lower in FIDA subjects (8.2 + 0.6 versus 10.0 + 0.7, $P < 0.02$). Although a difference between groups was also apparent on sessions B (12.1 + 0.8 versus 14.5 + 0.8, $P < 0.01$) and C (13.1 + 0.7 versus 14.1 + 0.8, $P < 0.02$), only FIDA subjects showed a significant improvement between B and C sessions ($P < 0.01$).

Conclusions: Our results indicate differences in motor skill learning abilities between controls and FIDA adolescents, further supporting evidence of lasting cognitive effects of iron deficiency anemia in infancy. Further, given that FIDA subjects showed an improvement in motor memory consolidation after nighttime sleep, the results also help emphasize the relationship between sleep and cognition and, in particular, the role of sleep in adolescents with alterations in the cognitive domain.

Support: NIH 33487 and Fondecyt 1110513 grants.

Oral Session 9 – Learning, Dreaming and Emotions

O251

Sleep and memory consolidation in memory champions

M. DRESLER, B. KONRAD, L. HALIMSETIAWAN, L. GENZEL, V. SPOORMAKER, M. CZISCH and A. STEIGER
Max Planck Institute of Psychiatry, Munich, DE

Objectives: Increasing evidence suggests a supportive role of sleep in memory consolidation. However, the details of the sleep-memory relation are still under debate. While there is a wide consensus on a general beneficial effect of sleep on memory consolidation, in contrast the effects of intense memorizing periods on sleep are much less clear. In addition, little is known about the influence of individual differences (e.g. cognitive capabilities) on the sleep–memory relationship.

Methods: We addressed these points in a study including 14 world-class memory athletes out of the top-50 of the memory championships world ranking list. As a control group served 14 subjects matched for age, gender and intelligence. All subjects underwent three nights of polysomnography and a battery of declarative learning tasks. In a crossover-designed manner, subjects spent a night in the sleep lab either after an intense learning session of four consecutive hours, memorizing circa 1000 declarative information chunks, or after a day without active memorizing activity.

Results: Surprisingly, despite huge differences in memory performance (e.g. 192 ± 49 versus 16 ± 9 playing cards remembered after 20 min of memorization), we did not find any significant differences in sleep data between the groups: Both in the control and study nights memory champions and control subjects spent similar time in each sleep stage. Also for sleep spindles, REM density, and spectral data we did not find any significant differences between memory champions and control subjects. Even more surprisingly, also inside the two study groups no differences between the high and low memory load condition was found: Memory champions spent 213 ± 32 versus 208 ± 46 min in S2, 80 ± 35 versus 84 ± 33 min in SWS, 96 ± 25 versus 80 ± 19 min in REM in the control and study night, respectively, while control subjects spent 238 ± 29 versus 224 ± 32 min in S2, 82 ± 34 versus 80 ± 34 min in SWS, 96 ± 14 versus 97 ± 18 min in REM in the control and study night, respectively. Again, also for sleep spindles, REM density, and spectral data we did not find any significant differences between the two study conditions, neither for memory champions nor for control subjects.

Conclusion: In conclusion, our data are in line with several recent studies suggesting that the sleep-memory relationship is less straightforward than previously thought.

O252

The intelligence quotient and spindle activity

R. S. NADER[1], C. T. SMITH[1] and M. SABBAGH[2]
[1]Trent University, Peterborough, CA, [2]Queens University, Kingston, CA

Introduction: This study was designed to examine the relationship between intelligence quotient (IQ) scores and spindle density in all stages of sleep, including SWS, Stage 2 and REM. Slow (11–13.5 Hz), fast (13.51–16 Hz) and super-fast (16.01–18.5 Hz) spindles were examined separately in each stage of sleep.

Method: Participants were 32 healthy adolescents (17 female) aged 12–19 years (M = 15.36 years). In home recordings of EEG (C3/C4/FZ/PZ), EOG, and EMG were obtained using Suzanne™ (Tyco-Healthcare Group LP, Mansfield, MA, USA) portable polysomnographic systems.

Sleep spindles were automatically counted using PRANA® (Phi-Tools, Strasbourg, France). Peak amplitudes of 30 spindles in Stage 2 sleep were identified. Values were used to calculate the mean and standard deviation of peak amplitude for each subject. The minimal amplitude criterion was determined by subtracting 1.96 SD units from each mean. Minimum spindle duration was 0.5 s; spindles were counted separately in 11–13.5, 13.51–16, 16.01–18.5 Hz bins.

The WISC-IV-R was administered to each participant by a qualified administrator 1 week after the sleep portion of the study.

Results: Full scale IQ was not well correlated with spindle density in any sleep stage or with any spindle type. However, the sub-scale of Perceptual reasoning was related to slow spindle density in REM (C3: $r_{30} = 0.35$, $P = 0.049$); C4: $r_{30} = 0.31$, $P = 0.085$) and super spindle density in SWS (C3: $r_{29} = 0.48$, $P = 0.007$; C4: $r_{30} = 0.41$, $P = 0.019$; PZ: $r_{29} = 0.38$, $P = 0.033$). The sub-scale of Processing speed was positively related to slow spindle density in REM (C3: $r_{30} = 0.38$, $P = 0.03$), fast spindle density in REM (C3: $r_{29} = 0.45$, $P = 0.012$; C4: $r_{30} = 0.40$, $P = 0.024$; FZ: $r_{30} = 0.55$, $P = 0.001$), super spindle density in REM (FZ: $r_{30} = 0.42$, $P = 0.017$) and super spindle density in SWS (C3: $r_{29} = 0.36$, $P = 0.044$; PZ: $r_{29} = 0.45$, $P = 0.011$).

Conclusions: Full scale IQ was not found to be significantly related to spindle density in adolescents. However, both perceptual reasoning and processing speed subscales were significantly, positively related to spindle density in REM and SWS. Interestingly, spindle activity in Stage 2 sleep, was not found to be correlated with these intellectual skills. Assessments of learning potential would appear to be more accurately predicted from spindle activity in SWS and REM sleep in young adolescents.

O253

The impact of sleep spindles on cognitive performance and emotional abilities in school aged children

K. HOEDLMOSER[1], J. ROELL[1], P. PEIGNEUX[2], A. SADEH[3] and M. SCHABUS[1]
[1]University of Salzburg, Salzburg, AT, [2]University of Brussels, Brussels, BE, [3]University of Tel Aviv, Tel Aviv, IL

Objective: There is a growing body of evidence supporting the role of sleep for memory and learning processes. However, studies concerning sleep and cognition in children are still very rare. Therefore the aim of our study was to investigate the impact of sleep spindles in school aged children on declarative memory performance, general intelligence as well as emotional abilities.

Methods: Sixty-three (28 girls, 35 boys) healthy, pre-pubertal, school aged children (8–11 years, M = 9.56; SD = 0.76 years) participated in the presented study. In an entrance examination both general intelligence (Wechsler intelligence scale, WISC-IV) and emotional abilities (Strengths and difficulties questionnaire, SDQ) were examined. Sleep was recorded ambulatory during two nights: (A) adaptation-night, (B) learning-night. Polysomnographic recordings started between 7:30–8:30 PM. Subjects had to perform a declarative memory task (50 paired-associate word list) before (6:30 PM, encoding, cued recall) and after (7:00 AM, cued recall only) the learning-night. Additionally a follow-up test session (7:00 AM, cued recall only) 2 weeks after the learning-night evalu-

ated the stability of the learned information. Sleep was scored visually according to AASM criteria. Sleep spindles were detected automatically (Somnolyzer The Siesta Group©). Frontal slow (11–13 Hz) and central fast (13–15 Hz) spindles were differentiated.

Results: (i) Children with good declarative memory performance show higher N2 spindle intensity (13–15 Hz) during the learning-night, (ii) more intelligent children generally have higher N2 spindle intensity (11–13 Hz), and (iii) emotional ability is positively related to sleep spindle activity (12–15 Hz) during adaptation night.

Conclusion: Like in adults we found a positive relationship between N2 sleep spindle activity and declarative memory consolidation in children. Those subjects who had higher N2 sleep spindle intensity (13–15 Hz) during the learning-night were able to recall more word-pairs after 2 weeks. Additionally more intelligent children generally (adaptation- and learning-night) showed higher sleep spindle intensity (most pronounced for 11–13 Hz). For the first time we could observe that emotional ability affects N2 sleep spindles during adaptation-night indicating that sleep spindles could be a biological marker for the first night effect.

O254

Novelty of newly encoded semantic memories is associated with increased sleep spindle and slow oscillation activity

J. TAMMINEN[1], M. LAMBON RALPH[2] and P. LEWIS[2]

[1]Royal Holloway, University of London, Egham, UK, [2]University of Manchester, Manchester, UK

Objectives: Sleep plays an active role in consolidation of new memories. However, consolidation acts preferentially on some memories relative to others. Recent research has begun to map the properties of memories that are given priority in consolidation, including emotionality, expected reward, expected testing, and encoding difficulty. We test the hypothesis that information which is novel with respect to what is already stored in semantic memory also triggers enhanced consolidation during sleep.

Methods: Twenty-six subjects were trained on 64 fictitious words referring to fictitious concepts, (e.g. 'fecton is a saddle used on reindeer') in the evening followed by a polysomnographically monitored night of sleep. We used free association norms to determine semantic neighbourhood density for each concept, i.e. how much semantically associated information people already have about a given concept. This allowed comparison of two types of trained concept: for high-novelty concepts (e.g. 'saddle') people know little associated information, for low-novelty concepts (e.g. 'rabbit') they know more associated information. Concepts were matched in other relevant variables, e.g. frequency of occurrence and imageability. Tests known to be sensitive to semantic processing were administered immediately after training, after sleep, and 1 week later.

Results: Our primary interest was in seeing how stimulus novelty impacts aspects of sleep architecture known to mediate consolidation. T-tests showed that subjects exhibited more sleep spindles ($P = 0.002$) and slow oscillation activity ($P = 0.02$ in left hemisphere) after learning the high-novelty items compared to low-novelty items. Behavioural tests showed facilitated access to high-novelty concepts relative to low-novelty concepts immediately after training in one task (synonym judgement, $P = 0.04$) and after consolidation in two other tasks (animacy judgement, $P = 0.02$, and naming speed, $P = 0.003$).

Conclusion: Recent work in rats has shown increased reactivation in sleep of neurons associated with new experiences after exploration of a novel maze compared to a familiar maze. Ours is the first similar finding in humans, suggesting that sleep-associated consolidation operates preferentially on memories for which there is little related information already in existence in semantic memory. This may occur through increased spindle and slow oscillation activity which likely reflects preferential reactivation of the highly novel memory traces.

O255

The effect of sleep deprivation on emotional processing following exposure to an analogue depressing event

K. PORCHERET, E. HOLMES, G. GOODWIN, C. KENNARD, R. G. FOSTER and K. WULFF

University of Oxford, Oxford, UK

Objectives: To explore the relationship between sleep, affect and spontaneous emotional memory using the combination of an analogue emotionally distressing event (a series of film clips) and a sleep deprivation paradigm in healthy young subjects.

Methods: Forty one University students, aged 18–25 years, with no personal history of any psychiatric condition underwent a 2-week assessment of their mood, personality, circadian profile (actigraphy and 48-h melatonin), and sleep using polysomnography. The subjects were then exposed to an analogue depressing event (film footage) in the evening and either sleep deprived (DSL) or allowed to sleep normally (NSL). The subjects' affect, sleep and emotional processing were assessed by questionnaires, visual analogue scales (VAS) and polysomnographic recordings before and after the event and self-report of intrusive memories for the following 6 days after sleep manipulation.

Results: Both groups, DSL, $n = 19$ and NSL, $n = 22$), were similar in age, sex, daily caffeine and weekly alcohol consumption, trait mood and personality, and good circadian/sleep profiles (time in bed: 7.9 h SD = 0.03).

The immediate response to the film was a decrease in positive affect ($z = -2.54$, $P = 0.01$) and an increase in negative affect ($z = 2.67$, $P = 0.01$) in both groups.

In the first 12 h after the film, DSL subjects spend more time doing visual-spatial activities than NSL subjects ($z = -10.54$, $P < 0.0001$), who spend more time doing verbal activities ($z = 4.804$, $P < 0.0001$).

The morning following the manipulation, the DSL group reported being less distressed on the Impact of Event Scale (DSL: mea $n = 8.133$, SD = 5.306, NSL: mea $n = 11.52$, SD = 6.64, $z = 3.24$, $P = 0.0012$), with the intrusion subscale as main contributor ($z = 4.44$, $P < 0.001$).

The majority of intrusive memories over 6 days following the experimental manipulation were reported in the first 2 days and gradually decreased thereafter, with the DSL group reporting fewer intrusions on day 1 ($z = 2.19$, $P = 0.028$) and after the recovery night on day 2 ($z = 2.09$, $P = 0.037$) than the NSL group.

Conclusion: Sleep deprivation immediately after an analogue depressive event, as compared to sleep as normal, resulted in fewer negative intrusions, which was sustained after a night of recovery sleep. A number of possibilities could be responsible for this difference such as types of activities during sleep deprivation disrupting information processing or disruption of specific memory consolidation processes.

O256

The effects of sleep restriction on attractiveness and social desirability

T. SUNDELIN[1], M. LEKANDER[2] and J. AXELSSON[3]
[1]Stockholm University, Stockholm, SE; [2]Stress Research Institute, Stockholm, SE, [3]Karolinska Institute, Stockholm, SE

Objectives: Sleep deprivation inflicts a wide range of behavioural changes in the affected individual. Less is known of whether sleep deprived people are treated differently by others, a notion indicated by the earlier finding that sleep deprivation negatively affects attractiveness (Axelsson 2010). The aim of the present study was to investigate whether we are less willing to spend time with someone who has been exposed to 2 days of restricted sleep. A secondary aim was to validate the recent findings that total sleep deprivation affects attractiveness, using a more ecologically valid sleep restriction protocol.

Method: Twenty-five participants with a reported sleep need of 7–8 h came into our lab to be photographed on two separate occasions: after two nights of normal sleep (8 h in bed/night), and after two nights of sleep restriction (4 h in bed/night). The conditions were in a balanced order and the photographs taken in a controlled setting. Two facial photographs of each participant – one from each condition – were then shown to 40 naïve raters, rating the faces on 7-point Likert scales of attractiveness as well as how much they would like to socialize with that person.

Results: Participants were rated as less attractive when photos had been taken during sleep restriction, as compared to after two nights of normal sleep ($P < 0.05$). The raters were less willing to socialize with sleep restricted participants ($P < 0.05$); this effect seemed, at least partially, driven by the effect of sleep restriction on attractiveness ($P = 0.24$ when controlling for attractiveness).

Conclusion: Decreasing sleep to 4 h/night for two nights affects our appearance in the same way total sleep deprivation does, leaving us less attractive to others. Furthermore, in missing out on our beauty sleep, our peers are less likely to want to socialize with us. The fact that the amount of sleep we get may affect how others behave towards us is a phenomena requiring further attention. For example, are people with poor or disturbed sleep differently treated in work settings or other social situations: when we are in need of social support or when trying to get a date?

References:

1. Axelsson, J., Sundelin, T., Ingre, M., Van Someren, E., Olsson, A., & Lekander, M. (2010) Beauty sleep: An experimental study on the perceived health and attractiveness of sleep deprived individuals. BMJ 341:c6614

O257

Emotions in dreams relate to emotional brain reactivity during wakefulness

S. SCHWARTZ and V. STERPENICH
University of Geneva, Geneva, CH

Objectives: Dream research has brought support to the traditional belief that dreams are highly emotional. On the one hand, elevated emotionality in dreams plausibly relates to amygdala activation during REM sleep and may contribute to the consolidation of emotional memories. On the other hand, sleep and possibly dreaming may foster emotion regulation processes, which could be mediated by the persistence of activity in mPFC cortex during REM sleep, a region (particularly its ventral part) that is known to send inhibitory feedbacks to the amygdala. Here we tested whether emotions experienced in dreams relate to emotional brain functions during wakefulness.

Methods: Data were collected across four different functional MRI (fMRI) studies on a total of 128 healthy volunteers. In each fMRI study, the participants were exposed to both aversive and neutral stimuli, thus allowing an assessment of brain responses to emotional signals. All participants also kept a dream diary, including specific questions about emotions experienced in their dreams, over the 2 weeks prior to the fMRI session. Experienced emotions in dreams were subjected to a principal component analysis (PCA), resulting in two main factors: (i) emotional valence, (ii) primary (basic) versus secondary (social) emotions. Whole-brain regression analyses were performed between fMRI responses to aversive (versus neutral) stimuli and dreamed emotions (from the PCA).

Results: Our preliminary results suggest that individuals with a more negative balance of emotions in their dreams showed decreased activity in the insula bilaterally, and in the cingulate gyrus. Individuals with more basic, arousing emotions in their dreams showed increased mPFC activity together with decreased amygdala activity in response to aversive stimuli.

Conclusions: The present study demonstrates a link between the types of negative emotions experienced during dreaming and brain responses to aversive stimuli during wakefulness. Together with previous evidence showing that sleep deprivation can disrupt the normal inhibitory influence of the mPFC on the amygdala, our findings suggest that emotions in dreams may contribute to the observed influence of sleep on emotional reactivity during wakefulness.

Acknowledgments: this work is supported by grants from the Swiss National Science Foundation, Mercier Foundation, Boninchi Foundation.

O258

Non-rapid eye movement sleep dreaming in relation to the cyclic alternating pattern

D. S. WAINSTEIN, S. MALCOLM-SMITH and M. SOLMS
University of Cape Town, Cape Town, ZA

Objectives: Non-rapid eye movement (NREM)sleep dreaming has been studied extensively in relation to tonic cortical arousal during sleep; however, no research to date has systematically studied NREM dreaming in relation to phasic arousal activity occurring naturally throughout sleep. This study aimed to explore the relationship between NREM dream recall and phasic arousal activity, by drawing on the cyclic alternating pattern (CAP) as a framework in which to predict the occurrence of dreaming during NREM sleep. We hypothesised that there would be a positive relationship between NREM dream recall and the presence of CAP sequences in the minutes preceding awakening, throughout all NREM sleep stages.

Methods: Eleven healthy university students (aged 18–25 years) were recruited to spend 3 inconsecutive nights each in a sleep laboratory. The first night served as an adaptation night. On the second and third (experimental) nights, each participant was awakened six times and a dream report was obtained. The awakenings followed specific electrophysiological criteria: (i) CAP sequences in light and deep NREM sleep; (ii) non-CAP (NCAP) sequences in light and deep NREM sleep; (iii) REM sleep. A dream was defined as any experience that could be remembered and described. Dream reports were digitally recorded and a Likert scale questionnaire was used to rate a number of subjective qualitative elements for each dream.

Results: Preliminary results indicated that NREM dream recall was significantly more frequent following CAP awakenings in deep NREM sleep only; in particular, around 70% of the awakenings following CAP sequences resulted in dream recall, compared with only 30% recall following NCAP conditions. While no difference in dream recall was apparent following NCAP and CAP awakenings in light NREM sleep, there was a trend towards more intense dreaming following CAP. Ongoing studies will either confirm or disconfirm these preliminary trends.

Conclusion: Should a relationship between dream recall and CAP in deep NREM sleep be established, dreaming during these sleep stages will finally be more predictable, enabling it to be more reliably studied. Such a relationship could also go a long way toward explaining the intra-stage variation in NREM dream recall often reported across dream studies. Additionally, the relationship between dreaming and CAP appears to differ according to NREM sleep stage; the possible significance of this inconsistency is discussed as well.

This research was funded by the National Research Foundation (Grant Number: 73898_Solms).

O259

The role of cortisol in mediating the relationship between sleep architecture and the memory-content of dreams in individuals with asthma

R. TIMOL[1], K. G. F THOMAS[1], E. GOUNDER[2] and J. TOP[3]

[1]University of Cape Town, Cape Town, ZA, [2]Sleep Disorder Centre Life Vincent Pallotti Hospital, Cape Town, ZA, [3]Panorama Medi-Clinic Sleep Laboratory, Cape Town, ZA

Objectives: Episodic memory consolidation is thought to be most efficient during the first half of sleep, proportional to the richness of slow wave sleep (SWS) contained during that period. Cortisol is at its nadir during the first half of sleep, rises as the night progresses, until it reaches its peak upon awakening and this balance has been implicated in maintaining normal sleep architecture. Elevating cortisol during early sleep disrupts both SWS and episodic memory consolidation. Coinciding with this trend, awakening studies reveal that early dreams contain more autobiographical elements than later dreams which tend to be more creative, bizarre and incongruous with recent waking preoccupations. The aim of this study was to investigate the impact of chronically elevated cortisol on sleep architecture and subsequently on dreaming, in a population known to suffer from abnormal cortisol patterns such as asthmatics.

Methods: Participants ($N = 65$), aged between 18 and 40 (M = 21.32, SD = 4.31) years, were recruited to one of five groups: (i) Mild Asthma ($n = 14$), (ii) Moderate-to-Severe Asthma ($n = 12$), (iii) Untreated Asthma ($n = 14$), (iv) Eczema Control ($n = 13$) and (v) Healthy Control ($n = 12$). Sleep was recorded polysomnographically. Salivary cortisol and dream reports were collected during the first 2 REM periods and after spontaneous morning awakening. A dream was defined as any experience that could be remembered and described. Dream reports were digitally recorded and a Likert-scale questionnaire was used to rate a number of subjective qualitative elements for each dream.

Results: All of the three asthma groups as well as the eczema group showed significantly higher cortisol levels than the healthy control group at REM1 and REM2, lower percentages of SWS ($P = 0.032$) and REM ($P = 0.003$) with less REM intensification and almost evenly distributed SWS between the two halves of the night for the non- healthy groups. Although no between group differences in dream patterns were demonstrated, analyses revealed significant, inverse relationships between (i) cortisol level and the presence of episodic content in dreams, and (ii) percentage SWS and episodic content in dreams.

Conclusion: Chronically elevated cortisol during sleep is associated with changes in sleep architecture and the memory content of dreams. Abnormal cortisol patterns in asthma may interfere with the cognitive and restorative functions of sleep, with implications yet to be explored.

O260

Cuing neural replay with sounds during slow-wave sleep has dissociative effects upon emotionally negative and neutral memories

S. A. CAIRNEY[1], S. J. DURRANT[2], J. HULLEMAN[1] and P. A. LEWIS[1]

[1]University of Manchester, Manchester, UK, [2]University of Lincoln, Lincoln, UK

Objectives: Recent work has suggested that neural replay can be augmented by re-presenting auditory cues during SWS, leading to superior memory performance. While compelling, the precise mechanism underpinning this effect is unclear. One possibility is that cued replay strengthens associative memories directly, whilst another indirect view is that auditory cues serve to 'prime' memories for a targeted consolidation process which occurs throughout subsequent SWS. Moreover, since previous work has focused upon the reactivation of neutral memories alone, it is unclear whether the same effects occur for emotional memories. Here, we investigated how presenting learning-associated sound cues during SWS impacted upon the consolidation of emotionally negative and neutral picture-location memories.

Methods: Fifteen participants (10 male) encoded 72 picture-location associations. Pictures were taken from the international affective picture system (IAPS), where half were rated as negative and the other half as neutral. Importantly, each image was paired with a semantically related sound taken from the international affective digitized sounds (IADS) battery. Participants then took a 90 min nap (2 pm), during which they were re-exposed to half (18 negative, 18 neutral) of the learning-associated sounds during SWS. Shortly after waking, memory for picture locations was tested. The impact of cued replay was assessed using memory performance and response times (RT) for correctly recalled items.

Results: A 2 (Replay: cued/not cued) by 2 (Valence: negative/neutral) repeated measures ANCOVA (SWS duration (mins) covariate) assessed whether the impact of cued replay was dependent on time spent in SWS. While no significant effects were found for memory performance, a three-way interaction between Replay, Valence and SWS was revealed for RT ($F_{1,13} = 9.40$; $P = 0.01$). Subsequent analyses showed that SWS duration predicted faster RT for negative cued (versus neutral cued) items ($r = 0.66$; $P = 0.008$), but slower RT for neutral cued (versus neutral non-cued) items ($r = -0.60$; $P = 0.018$).

Conclusions: These findings not only indicate that the mnemonic influences of cued replay are indirect in nature, but also suggest that SWS mediates a targeted enhancement and suppression of respective negative and neutral cued memory traces. Thus, in order to preserve information that is most valuable for the future, SWS may exert qualitatively diverse effects upon cued memories with different emotional valences.

Oral Session 10 – Neurological Disorders and Sleep

O261

A longitudinal study of restless legs syndrome in Parkinson's disease

L. F. SCHOOLDERMAN[1], D. VERBAAN[2], S. M. VAN ROODEN[3], J. J. VAN HILTEN[3] and R. M. RIJSMAN[1]

[1]MCH Westeinde, The Hague, NL, [2]Academic Medical Center, Amsterdam, NL, [3]Leiden University Medical Center, Leiden, NL

Objectives: In this study the prevalence, incidence and clinical profile of RLS is evaluated in a large cohort of patients with Parkinson's disease (PD).

Methods: In this follow-up study, 236 non-demented Caucasian PD patients, received two consecutive assessments with an 1 year interval. To diagnose RLS, the four international criteria of the IRLSSG were administered by a personal interview taken by a RLS trained researcher. Furthermore, in all patients (non)motor PD symptoms were assessed and dopaminergic medication was recorded.

Results: In 236 PD patients (62% male), 11% had definite RLS during the first assessment, of which 77% persisted to have RLS in the second assessment and in 33% RLS complaints disappeared. The prevalence of RLS in the second assessment was 14.8%; newly diagnosed RLS (incident RLS) was 6.4% and 8.5% had persistent RLS. Vulnerable RLS (RLS in at least 1 of the 2 assessments) was seen in 17.4% and were more often female ($P = 0.001$) compared to group without RLS in both assessments ('absence of RLS').

All patients who had RLS in the second assessment were more often female compared to patients without RLS (63% versus 33%, $P = 0.001$). All other demographic and clinical variables were not significantly different between these two groups.

Incident RLS compared to group 'absence of RLS' were of the same age but had a younger age of PD onset ($P < 0.001$). Furthermore, incident RLS had a larger decrease of total levodopa equivalent (difference between first and second assessment; $P = 0.003$) and a larger decrease of total levodopa (difference between first and second assessment; $P = 0.022$) compared to 'absence of RLS'. Also, less autonomic symptoms (difference between first and second assessment; $P = 0.019$) persisted in the incident RLS compared to group 'absence of RLS'.

Conclusion: The incidence rate of RLS is high, while the persistence of RLS over 1 year is rather low, suggesting that RLS symptoms vary considerably in this PD cohort. The higher incidence rate among women is consistent with previous prevalence data.

Incident RLS had a younger onset of PD. Incident RLS in this PD population may be explained by unveiling of RLS symptoms after relatively lower dose of dopaminergic medication in the year that RLS debuted compared to the first assessment year.

O262

REM sleep behaviour disorder in drug-naive newly diagnosed patients with Parkinson's disease

L. PLOMHAUSE, K. DUJARDIN, L. DEFEBVRE, P. DERAMBURE and C. MONACA-CHARLEY

Lille University Medical Center, Lille, FR

Introduction: REM sleep behavior disorder (RBD) associated with Parkinson's disease (PD) is considered as a risk of developing dementia.

Objective: The aims of the present study was (i) to evaluate the frequency of RBD in a sample of drug naive newly diagnosed PD patients, (ii) to compare PD patients with and without RBD in terms of sleep characterisitics and cognition.

Methods: Fifty-seven newly diagnosed PD patients were consecutively recruited at the Lille University Medical Center (35 men; average age: 61 ± 11 years; average disease duration: 14 ± 10 months; education: 11 ± 4 years; severity of motor symptoms: 15 ± 7 at the part 3 of the Unified Parkinson's Disease Rating Scale). All patients underwent two overnight polysomnographic recordings with continuous audiovisual monitoring. RBD was diagnosed according to the International Classification of Sleep Disorders-II criteria. Daytime sleepiness was measured by multiple sleep latency test (MSLT). Cutoff for excessive daytime sleepiness was set at 8 min. Overall cognitive efficiency was assessed with the Mattis Dementia Rating Scale (MDRS).

Results: Seventeen PD patients met PSG criteria for RBD (30%). The patients with and without RBD (N-RBD) did not differ in terms of age, disease duration and severity of motor symptoms. Nine (53%) RBD patients and 13 (33%) N-RBD patients were women. The average percentage of REM sleep was 15 ± 9 in RBD patients and 19 ± 5 in N-RBD patients. Severe sleep apnea was detected in 3 (18%) RBD patients and in 5 (13%) N-RBD patients. Excessive daytime sleepiness was found in 1 RBD patient (6%) and in 5 N-RBD patients (12%). All these variables did not differ between RBD and non-RBD patients. The presence of RBD was no associated with poorer MDRS performances levels.

Conclusion: A high proportion of RBD were found in our sample of 57 PD patients. At the early stage of PD, RBD was not associated with other sleep disorders or cognitive decline. A follow-up is needed to address the issue of the risk of developing dementia in PD patients with RBD.

O263

Relation between periodic limb movements in sleep and the mean blood pressure

M. SIEMINSKI[1] and M. PARTINEN[2]

[1]Medical University of Gdansk, Gdansk, PL, [2]Vitalmed Helsinki Sleep Clinic, Helsinki, FI

Objectives: It is hypothesized that restless legs syndrome and periodic limb movements in sleep (PLMS) have an impact on the circulatory system and cardiovascular diseases. The aim of our study was to analyze the relation between periodic limb movements and the values of mean blood pressure.

Methods: Patients from a tertiary sleep clinic who underwent full polysomnography were included to the study. Subject with sleep disordered breathing (with apnoea/hypopnea index >5) were excluded from the study. The examined group consisted of subjects with periodic limb movements in sleep index (PLMS-I) higher than 5. The control group consisted of subjects with PLMS-I equal 5 or less. During the polysomnography a holter recording of beat-to-beat blood pressure was performed during the daytime and the nighttime. The mean values of systolic and diastolic blood pressure during sleep, wake, night and day were compared.

Results: There were 53 subjects (24 men, mean age 46.8 years) in the examined group and 53 subjects (25 men, mean age 41.2 years) in the control group. There was no statistically significant difference between the groups regarding age and sex. All the mean values of blood pressure (systolic and diastolic during sleep, wake, nighttime

and daytime) were higher in the examined group. The difference was statistically significant for systolic blood pressure in sleep (119.74 versus 112.74; $P = 0.041$), diastolic blood pressure in wake (77.53 versus 71.94; $P = 0.015$) and diastolic blood pressure in nighttime (75.49 versus 70.87; $P = 0.049$).

Conclusion: Our study shows that presence of periodic limb movements in sleep may alter the values of blood pressure. PLMS influence not only the values of blood pressure during the sleep or nighttime but also in the wake. Our results suggest that there is a link between the presence of PLMS and blood pressure that may have a therapeutic consequences.

O264

Mirtazapine provokes periodic leg movements during sleep in young healthy men

S. FULDA[1], S. KLOIBER[2], T. DOSE[2], S. LUCAE[2], F. HOLSBOER[2], L. SCHAAF[2] and J. HENNINGS[2]

[1]Neurocenter of Southern Switzerland, Lugano, CH, [2]Max Planck Institute of Psychiatry, Munich, DE

Objectives: Recent evidence suggests that certain antidepressants are associated with an increase in sleep-related movements, especially periodic leg movements (PLMS) that may disturb sleep. So far, this has been shown in patients clinically treated for depression and in cross-sectional studies for various substances, but not mirtazapine. It is unclear whether antidepressants induce the new onset of PLMS or only increase pre-existing PLMS and whether this is a general property of the antidepressant or only seen in depressed patients. We report here the effect of mirtazapine on PLMS in young healthy men.

Methods: Twelve healthy young (20–25 years) men participated in an open-labeled clinical trial (NCT00878540), which included a 3 week preparatory phase with standardized food, physical activity, and sleep-wake behavior and a 10 day experimental inpatient phase with two baseline days and 7 days of nightly (22:00) intake of 30 mg mirtazapine. Sleep was recorded on two drug-free baseline nights, the first two drug nights, and the last two drug nights.

Results: Eight of the twelve subjects showed increased PLMS after the first dose of mirtazapine (PLMS indices 28–98). Frequency of PLMS was highest on the first drug night and attenuated over the course of the next 6 days. There were no baseline differences in any sleep or other parameter between participants with mirtazapine-induced PLMS compared to those without.

Conclusions: Mirtazapine provoked PLMS in a substantial portion of young healthy males. The effect was most pronounced in the first days. Histaminergic and serotonergic mechanisms may be implicated mirtazapine-induced PLMS.

O265

Pharmacological dissociation of periodic leg movements from cortical arousals in restless legs syndrome

M. MANCONI[1], R. FERRI[2], M. ZUCCONI[3], C. BASSETTI[1], S. FULDA[1], D. ARICÒ[2] and L. FERINI-STRAMBI[3]

[1]Civic Hospital, Lugano, CH, [2]Oasi Institute, Troina, IT, [3]Institute and Ospedale San Raffaele, Milan, IT

The purpose of this study was to characterize the nature of the relationship between periodic leg movements during sleep (PLMS) and cortical arousals in order to address the question of the clinical significance and treatment necessity of PLMS. The specific aim was to explore whether drug treatment can dissociate PLMS from cortical arousals by analyzing the differential effects of clonazepam or pramipexole on sleep, arousals, and PLMS in patients with restless legs syndrome (RLS). Addressing this question might be relevant to extract preliminary clues on their possible joint use for RLS.

A prospective, placebo-controlled, single-blind, parallel group study was carried out including 46 drug naive patients with idiopathic RLS. Each patient underwent two consecutive full night polysomnographic studies. The first night was the baseline night. Prior to the second night, one group received a single oral dose of 0.25 mg pramipexole while a second group received a single oral dose of 0.5 mg clonazepam, and the remaining patients received placebo. Sleep stages, Cyclic Alternating Pattern (CAP), and leg movement activity were scored following standard criteria; symptoms of RLS were also assessed. Pramipexole suppressed PLMS without affecting EEG instability (CAP) and arousals (corresponding to CAP A3 and, partially, A2 subtypes), while clonazepam did the opposite, reducing the NREM sleep EEG instability without effects on PLMS. Both drugs were effective on sensitive RLS symptoms. This study demonstrates that a selective pharmacological approach can disconnect PLMS from arousal events, suggesting an indirect mutual relationship between each other, and opens the doors to the possibility of a joint treatment for RLS targeting sensory and motor symptoms, as well as sleep instability.

O266

Effects of pregabalin and pramipexole on sleep and quality of life in patients with restless legs syndrome: results from a long-term, randomised, double-blinded, parallel-group, placebo-controlled, active-comparator trial

D. GARCIA-BORREGUERO[1], C. CHEN[2], R. P. ALLEN[3], J. WINKELMAN[4], O. POLO[5], S. DUBRAVA[2], J. MICELI[2] and L. KNAPP[2]

[1]Sleep Research Institute, Madrid, ES, [2]Pfizer, Groton, US, [3]Johns Hopkins Sleep Disorders Pfizer, Baltimore, US, [4]Brigham and Women's Hospital, Boston, US, [5]Tampere University Hospital, Tampere, FI

Objectives: In the first long-term, active-comparator trial of efficacy and augmentation in restless legs syndrome (RLS), pregabalin (PGB) was shown to improve RLS symptoms (as measured by International RLS Study Group Rating Scale) compared with placebo (PBO) and pramipexole (PPX), with less augmentation than PPX. Here, we aimed to establish whether improvements in RLS symptoms with PGB were accompanied by subjective improvements in sleep and overall quality of life.

Methods: This was a 12-week placebo-controlled, 52-week active-comparator, randomised, double-blinded, multicentre trial. Participants with moderate to severe RLS received PGB 300 mg/day, PPX 0.25 mg/day or PPX 0.5 mg/day for 52 weeks, or PBO for the first 12 weeks followed by randomisation to one of the three active treatments for the remaining 40 weeks. In addition to primary endpoints of efficacy and rate of augmentation, Subjective Sleep Questionnaire (SSQ) and RLS-Quality of Life (QoL) scores were assessed at 2–6 week intervals throughout the study. Secondary endpoints of SSQ and RLS-QoL fell outside the step-down statistical testing procedure of this multiple endpoint study, therefore only descriptive statistics are used.

Results: Seven hundred and nineteen participants received treatment: 182 PGB, 178 PPX 0.25 mg/day, 180 PPX 0.5 mg/day and 179 PBO. Improvements in SSQ measures of sleep maintenance and quality were greater with PGB versus PBO than with PPX versus PBO over the first 12 weeks' treatment: Wake After Sleep Onset (difference in change from baseline versus PBO: PGB, -17.2 min;

PPX 0.25 mg/day, -1.1; 0.5 mg/day, -4.6); Total Sleep Time (PGB, 25.8 min; PPX 0.25 mg/day, 4.8; 0.5 mg/day, 10.8); Number of Awakenings (PGB, -0.6; PPX 0.25 mg/day, 0.04; 0.5 mg/day, 0.02); Quality of Sleep score (PGB, 10.6; PPX 0.25 mg/day, 1.2; 0.5 mg/day, 3.3; scored from 0 to 100). Improvements in SSQ Sleep Latency were lower with PGB versus PBO (-5.5 min) than with PPX versus PBO (0.25 mg/day, -8.2; 0.5 mg/day, -13.1). RLS-QoL (scored from 0 to 100) showed greater improvement with PGB versus PBO (3.8) than with PPX versus PBO (0.25 mg/day, 0.4; 0.5 mg/day, 2.1). Improvements in sleep and quality of life with PGB were maintained for the duration of the study (52 weeks).

Conclusion: PGB improved RLS-associated sleep disturbance (other than latency) and quality of life compared with PBO and PPX. Considered together with previously reported improvements in RLS symptoms and rates of augmentation compared with PPX, these data indicate PGB provides an effective treatment for RLS.

This study was sponsored by Pfizer Inc., who were involved in the design and conduct of the study. CC, SD, JM and LK are employees of Pfizer Inc. RPA, DGB and JW have served as consultants for Pfizer Inc. Medical writing support was provided by Joshua Fink of UBC Scientific Solutions and funded by Pfizer Inc.

O267

Sleep-wake patterns in vegetative state: 24-h polysomnographic findings in 15 subjects

R. MANNI[1], D. ARNALDI[2], M. TERZAGHI[1], R. CREMASCOLI[1], G. MAGGIONI[3], C. PISTARINI[3] and A. MOGLIA[4]

[1]IRCCS C. Mondino Foundation, Pavia, IT, [2]University of Genoa, Genoa, IT, [3]IRCCS S. Maugeri Foundation, Pavia, IT, [4]University of Pavia, Pavia, IT

Objectives: Despite the occurrence of behavioural states suggesting persistence of sleep in patients in a vegetative state (VS), the real existence of sleep patterns and its meaning with respect to the VS evolution are far from being established. This study is aimed at featuring sleep wake patterns in patients in a persistent VS by mean of a 24-h standard Polysomnographic (PSG) monitoring and at correlating the PSG findings with the Vs evolution.

Methods: Patients were 15 adult (mean age 51.5 years, age range 18–79; 10 males) brain injured subjects (anoxic insult in six cases, traumatic in 9 and haemorrhagic in 3).

In all the patients a 24 h PSG was done within a 2–12 month period (mean 5.9) after the insult. At the time of the PSG monitoring the patients state could be defined as in a persistent VS according to standard criteria and their Glasgow scale score was 6.3, SD 2.2. The eventual correlation of PSG findings with the VS evolution within a mean follow up of 18.3 months, SD 9.4, was tested.

Results: Patients who evolved to a Permanent VS (eight patients 3 of whom died): No clear distinct pattern of wakefulness and sleep in two cases. Dissociate patterns of NREM and REM sleep or isolated phasic events of NREM (spindles and k complexes) or REM sleep (Rapid eye movements: REMs) in five cases. Alternating patterns of wakefulness and near normal NREM sleep in one case.

Patients who evolved to a Minimal Consciousness State (MCS) (seven patients): Alternating patterns of wakefulness and near normal sleep in five cases. Dissociated patterns of NREM sleep in two cases.

As a whole REMs, within the context of normal REM sleep, dissociated REM sleep or as isolated elements were scorable in five out of the seven patients who evolved into a MCS and only one out of the eight patients who evolved into a Permanent VS.

There was a significant ($P = 0.039$) correlation between the degree of sleep structure integrity and VS evolution at the maximum likelihood chi-square test.

Conclusions: Our preliminary findings indicate that the persistence of near normal NREM and REM sleep patterns and the persistence of REMs within the context of dissociated patterns of sleep or even as isolated elements are more frequently observed in patients in a VS who evolve into a MCS than in those who evolve into a Permanent VS or die. The data stress the potential useful role of PSG investigation in the assessment and prognosis of patients with VS.

O268

Cholinergic and striatal dopaminergic dysfunction as a risk marker for developing a neurodegenerative disease in patients with idiopathic REM sleep behaviour disorder

J. VALERIO, V. SOSSI, K. DINELLE, J. MCKENZIE, S. MCCORMICK, N. HEFFERNAN, J. FLEMING and J. STOESSL

University of British Columbia, Vancouver, CA

Objectives: Rapid Eye Movement (REM) sleep behaviour disorder (RBD) is characterized by dream enactment during REM sleep. Dopaminergic dysfunction in idiopathic RBD (iRBD) is predictive of developing a synucleinopathy, such as Parkinson's disease (PD). IRBD needs to be distinguished from secondary RBD, often seen in narcolepsy and obstructive Sleep apnea (OSA). We postulate that subjects with iRBD will have a higher level of dopaminergic and cholinergic dysfunction reflective of their higher risk for developing a synucleinopathy compared to healthy controls and patients with secondary RBD.

Methods: In a prospective study, 10 patients with RBD (mean age 60.8 ± 11.1), were recruited by the movement disorders clinic, from 2005 to 2012. Patients were followed serially for 12–84 months to monitor for the development of a neurodegenerative disease. Baseline PET imaging was performed on all 10 subjects, using radiotracers [11C] PMP (acetylcholinesterase) and [11C] dihydrotetrabenazine (DTBZ). PMP k3 was determined based on either striatal input or shape analysis and was judged to be reduced when values were below 2 SD of the corresponding values in healthy controls.

Results: Ten patients were diagnosed with RBD in a sleep lab prior to PET scanning. Three had OSA requiring CPAP, and another had narcolepsy. PMP and DTBZ binding were normal in these four subjects. Of the remaining six subjects (presumed iRBD), 4 had reduced occipital cortical cholinergic innervation and 2 of these subjects also had reduced striatal DBTZ uptake, compared to control data. Two patients have developed parkinsonism and another mild cognitive impairment, 2–4 years after scanning, and all showed significantly reduced occipital PMP compared to controls (0.0212 ± 0.0010 versus 0.0250 ± 0.0011, $P = 0.0028$). IRBD patients also had reduced thalamic cholinergic function compared to secondary RBD (0.0674 ± 0.0107 versus 0.0776 ± 0.0037, $P = 0.0193$).

Conclusions: Decline in DBTZ and PMP in cortical and subcortical structures of patients with iRBD likely reflects dopaminergic and cholinergic dysfunction during the premotor stages of neurodegenerative disease. This is the first time *in vivo* cholinergic dysfunction has been shown in iRBD. Disrupted occipital cholinergic function may predict patients at greater risk of progressing to a synucleinopathy. Monitoring cholinergic dysfunction in an iRBD population may provide further insight into the pathophysiology of RBD and subsequent neurodegeneration.

O269

Microstructural brain stem lesions as neuroanatomic correlate of central sleep apnoea

T. DUNING, A. HEIDBREDER, C. BECHT, M. DEPPE and P. YOUNG

University Hospital of Muenster, Muenster, DE

Objectives: Cheyne-Stokes respiration with central sleep apnea (CSR) is considered as a rather serious form of sleep-disordered breathing. The exact underlying pathomechanism of CSR is still unclear. A dysfunction of respiratory control centers in the brainstem, e.g. the reticular formation, was suggested by some authors. However, conventional MRI fails to identify primary or secondary structural changes of the brainstem in most patients with CSR.

Diffusion Tensor Imaging (DTI) now allows far more subtle assessment of microstructural degenerative cerebral changes. The aim of this study was to investigate, (i) whether and what severity of subtle structural cerebral changes could lead to CSR, and (ii) whether there is a specific pattern of neurodegenerative changes that cause CSR. Therefore, we examined patients with Fabry disease (FD), an inherited, lysosomal storage disease. Marked white matter lesions are early and frequent finding in FD patients. Due to the young age of onset and the resulting significantly lower comorbidity, FD as a rather pure form of cerebral microangiopathy can serve as a 'model disease' of cerebral microangiopathy.

Methods: Twenty-three genetically proven FD-patients as well as 44 healthy volunteers were included. All patients underwent a cardio-respiratory polysomnography, a detailed clinical examination, and a comprehensive neuropyschological testing. We additionally applied different MR-imaging techniques, ranging from semiquantitative measurement of white matter hyperintensities (WMH) and automated calculation of brain parenchyma volumes up to diffusion tensor imaging (DTI) to detect even subtle neural changes.

Results: Voxel-based analysis revealed a widespread decline in DTI analysis in FD patients when compared to the healthy controls, significantly exceeding the WMH on conventional MRI. Polysomnography revealed CSR with Cheyne-Stokes respiration in 5 of 23 Fabry patients (22%). When calculated as a separat group, DTI changes of CSR patients were most pronounced in the brainstem. The voxel-based regression analysis revealed a significant association between the length of Cheyne-Stokes breathing pattern and microstructural DTI changes within the brain stem.

Conclusion: Subtle microstructural changes in the brain stem might be a neuroanatomical correlate of sleep-disordered breathing with central apnea. The severity of the CSR correlates with the severity of microstructural degeneration in circumscribed areas within the upper brainstem.

O270

Sleep-disordered breathing in idiopathic Parkinson's disease

P. O. VALKO, S. HAUSER, M. SOMMERAUER, E. WERTH and C. R. BAUMANN

University Hospital of Zurich, Zurich, CH

Objectives: Sleep-disordered breathing (SDB) is frequent in patients with idiopathic Parkinson's disease (PD). Earlier studies showed that excessive daytime sleepiness is not an appropriate predictor of SDB in PD. We aimed at identifying parameters that should lead to the suspicion of SDB in PD.

Methods: We retrospectively analyzed clinical and polysomnographic data of 119 consecutive, unselected PD patients.

Results: Sleep-disordered breathing was diagnosed in 57 PD patients (48%). Age, sex and disease severity were similar in PD patients with and without SDB. PD patients with SDB had a higher body mass index than those without SDB (26.8 ± 4.5 versus 22.9 ± 3.2, $P < 0.001$). A pathological body mass index (>25) was found in only 19% of PD patients without SDB, while it was common in PD patients with SDB (63%). In addition, the combination of increased body mass index and male sex predicted SDB in almost four of five PD patients (79%). Compared to PD patients with predominantly obstructive SDB ($n = 50$, 88%), PD patients with predominantly central SDB ($n = 7$, 12%) revealed a higher apnea-hypopnea index (39.3 ± 16.7 versus 20.9 ± 16.8, $P = 0.003$). On the other hand, body mass index was lower in central SDB (24.2 ± 2.7 versus 27.2 ± 4.6, $P = 0.03$). All seven PD patients with central SDB (100%) were treated with both L-dopa and dopamine agonists (ropinirole, $n = 4$; pramipexole, $n = 2$; and cabergoline, $n = 1$), whereas only 56% of those with obstructive SDB were on this combined treatment ($P = 0.03$). Disease duration correlated with central apnea indices (rho = 0.31, $P = 0.02$), but not with obstructive apnea indices (rho = 0.11, $P = 0.42$) or the combined apnea-hypopnea index (rho = 0.12, $P = 0.37$).

Conclusions: Our findings indicate that male sex and increased body mass index should be considered as risk factors of SDB in patients with idiopathic PD. Importantly, body mass index is not predictive in PD patients with predominantly central SDB. Conversely, central SDB must be suspected in every PD patient with longer disease duration and, in particular, dopaminergic treatment consisting of both L-Dopa and a dopamine agonist. An association between the use of dopamine agonists and sudden sleep attacks has been reported by several groups, but none of these studies had searched for SDB. Our results suggest that central SDB should be considered as a contributing factor for sleep attacks in PD patients treated with dopamine agonists.

Oral Session 11 – Genetics Sleep

O271

The interaction of homeostatic and circadian regulation of sleepiness depends on a PER3 polymorphism

M. MAIRE[1], C. F. REICHERT[1], V. GABEL[1], A. VALOMON[2], J. KREBS[1], A. VIOLA[1], W. STROBEL[3], V. BACHMANN[2], H.-P. LANDOLT[2], S. C. HOLST[2], C. CAJOCHEN[1] and C. SCHMIDT[1]
[1]Center for Chronobiology, Basel, CH, [2]Institute for Pharmacology and Toxicology, Zurich, CH, [3]Respiratory Medicine, Basel, CH

Objectives: The variable number tandem repeat polymorphism of the human clock gene PER3 is involved in circadian and homeostatic regulation of human sleep and wakefulness. Here we investigated subjective sleepiness and sleep during naps in homozygous PER3 4/4 and PER3 5/5 allele carriers under high and low sleep pressure conditions. The aim of this study was to further unravel associations between inter-individual differences in the homeostatic and circadian impact on sleep and wakefulness related to this polymorphism.

Methods: So far, 22 healthy participants (25.1 ± 3.4 year), thereof 12 PER3-5/5 (5 m, 7 f) and 10 PER3-4/4 (4 m, 6 f), underwent both a 40-h sleep deprivation (SD) and nap (NP; 10 cycles of 160-min wakefulness and 80-min naps) protocol. The groups were matched according to sex, age, BMI, sleep quality and chronotype. Subjective sleepiness was assessed at regular intervals during both protocols along with subjective sleep quality after each nap. Polysomnographic recordings during naps were scored visually according to standard criteria.

Results: Significant effects for genotype × time ($P < 0.05$) and a trend for genotype × sleep pressure ($P = 0.07$) revealed higher sleepiness levels in PER35/5 than in PER34/4 subjects at specific times during SD and NP. PER35/5 carries were sleepier after 9–16.5 h of scheduled wakefulness ($P < 0.05$) during SD, while during NP they differed after six naps and stated less difficulties to fall asleep in the subsequent nap at the rise of the second biological day ($P < 0.05$). Analysis of total sleep time, sleep efficiency, wakefulness and sleep stages over all naps did not reveal a main effect of genotype. Both groups slept least in the naps during biological evenings (wake-maintenance zone, WMZ) and most during the biological night. However, during the WMZ, PER35/5 carriers slept more than PER34/4 individuals, as indexed by a greater amount of NREM sleep ($P < 0.05$).

Conclusion: Our data suggest greater subjective susceptibility of PER35/5 than PER34/4 carriers to increases in homeostatic sleep pressure, emerging already after 9 h awake. In conjunction with the finding of more NREM sleep during the nap in the WMZ in PER35/5, as well as the higher sleepiness in the beginning of the second biological day, the data indicate that the reported differential vulnerability to sleep homeostasis in PER35/5 and PER34/4 carriers might be partially mediated by a difference in the strength of the circadian arousal signal.

O272

Sleep in transgenic mouse models for a polymorphism in the human PER3 gene

S. HASAN, R. WINSKY-SOMMERER, D.-J. DIJK and S. N. ARCHER
University of Surrey, Guildford, UK

Objectives: In humans, a variable number tandem repeat (VNTR) polymorphism in the circadian clock gene PERIOD3 (PER3; 4-repeat and 5-repeat) is associated with diurnal preference, sleep homeostasis, and cognitive decline in response to sleep loss. We generated 'humanised' mice homozygous for each allele of the VNTR polymorphism to further study the effect of the PER3 VNTR polymorphism on sleep at baseline and when sleep was displaced to the circadian night by a 12 h sleep deprivation.

Methods: C57BL/6J knock-in mice homozygous for the 4- (Per34/4) and 5-repeat (Per35/5) VNTR and wild-type (WT) male mice ($n = 8$ per genotype; 11.2 ± 0.5 weeks old) were implanted with telemetry EEG/EMG transmitters and housed on a 12:12 Light-Dark cycle. After recovery from surgery, continuous EEG/EMG recordings were obtained through a 24 h baseline (day 1) and a subsequent 12 h sleep deprivation (day 2) during the light period and recovery sleep starting at the beginning of the next dark period for 36 h. Vigilance states were scored for 4-s epochs. EEG power spectra were computed. Data were analysed using SAS (v9.2) Proc Mixed.

Results: During the 24-h baseline, time spent in the different vigilance states (% of total recording time) did not differ between genotypes. During the first 3 h of recovery, delta power was increased ($P < 0.005$) in all mice. During the first 12 h of recovery, which coincided with the dark period, a decrease in wakefulness ($P < 0.0001$) and an increase of NREM ($P < 0.0001$) and REM ($P < 0.0001$) sleep time were observed in all genotypes, when compared to the 12 h dark baseline. During recovery in day 3, genotype differences were observed for time spent in REM sleep, as well as EEG delta power.

Conclusion: The humanised Per3 mice have normal sleep patterns and respond to sleep loss. The observed differences in delta power during recovery sleep are reminiscent of the differences in delta power observed in human PER3 genotypes. Further analyses will be required to establish whether these differences reflect genotype-dependent differences in sleep homeostasis.

Research was supported by the BBSRC (BB/F022883/1).

O273

Short and long sleepers: a difference in sleep capacity or in the tolerance of sleep pressure?

M. A. MOGRASS, S. H. WIELINGA, S. BADDAM and D. AESCHBACH
Brigham and Women's Hospital/Harvard Medical School, Boston, US

Objectives: Sleep duration varies greatly among individuals. Whether this variation has a biological basis is largely unknown. Here we compared two extreme phenotypic groups, short sleepers and long sleepers. We tested (i) whether there is difference in the maximal sleep capacity between the two groups, or (ii) whether there is a difference in the tolerance of homeostatic sleep pressure as measured on the basis of cognitive performance.

Methods: Healthy young (18–30 year) individuals who based on actigraphy were either short sleepers ($n = 7$, habitual bedrest <6.5 h) or long sleepers ($n = 11$, >9 h) underwent a 28-day inpatient protocol, including 4 days of habitual sleep (HS), 20 days of extended (12 h) sleep opportunities, a 36-h sleep deprivation (SD) period, and 2 days of recovery sleep. Total sleep time (TST) was quantified daily with polysomnography, and performance with the psychomotor vigilance task (PVT) several times every wake episode. Performance variables included number of lapses (reaction times, RT

>500 ms), median speed (1/RT), and interpercentile (IPR) range (difference between 90th and 10th percentile in 1/RT).

Results: In the HS condition, TST was 5.8 h in the short sleepers and 8.9 h in the long sleepers ($P < 0.001$). At the end of the sleep extension protocol (average of last three nights), daily TST was 8.5 h in the short sleepers and 8.8 h in the long sleepers (n.s.). None of the PVT measures differed between the two groups in the HS condition. When given extended sleep opportunities, PVT performance improved in the short sleepers ($P < 0.001$) but not in the long sleepers. Two-hourly PVTs during the SD revealed that short sleepers showed fewer lapses ($P < 0.001$) and a smaller IPR ($P < 0.04$) than the long sleepers, particularly in the latter part of the SD.

Conclusion: The maximal sleep capacity of young healthy adults is approximately 8.9 h. The disparity in habitual sleep duration between short and long sleepers appears to reflect a trait-like difference in the tolerance of homeostatic sleep pressure rather than in the capacity to sleep. Short sleepers seem to possess a 'cognitive reserve' that becomes apparent at very low and very high levels of sleep pressure.

O274

Influence of a genetic variation of adenosine deaminase on individual susceptibility to variations in sleep pressure

C. F. REICHERT[1], M. MAIRE[1], V. GABEL[1], J. KREBS[2], A. VALOMON[3], W. STROBEL[4], A. VIOLA[1], V. BACHMANN[3], H.-P. LANDOLT[3], C. CAJOCHEN[1] and C. SCHMIDT[1]

[1]Center for Chronobiology, Basel, CH, [2]University Basel, Basel, CH, [3]University of Zürich, Zurich, CH, [4]University Hospital Basel, Basel, CH

Objectives: A genetic variation in the adenosine metabolizing enzyme adenosine deaminase (ADA) is associated with inter-individual differences in sleep depth and subjective sleepiness. Here we investigated whether this polymorphism also modulates the response to a sleep homeostatic challenge, achieved by sleep satiation (nap protocol, NP) and deprivation (total sleep deprivation, SD), respectively.

Methods: So far, 8 heterozygous G/A allele carriers (6 f, 2 m) and 10 homozygous G/G allele carriers (7 f, 3 m) underwent a 40-h SD and a 40-h NP (10 alternating cycles of 160 min of wakefulness and 80 min of sleep) protocol under constant posture conditions. The two groups did not differ according to age (25 years+ -3.71), Body Mass Index, sleep quality and chronotype. Subjective sleepiness (Karolinska Sleepiness Symptom Checklist, KSSCL) was assessed regularly throughout wakefulness. In order to analyse the response to variations in sleep pressure, differences in KSSCL-values were calculated between NP and SD. Polysomnographic recordings during the naps were visually scored according to standard criteria.

Results: We observed a significant interaction in subjective sleepiness for the factors genotype, sleep pressure level (i.e. NP versus SD) and time ($P < 0.05$). During the biological night, heterozygous individuals indicated significantly higher subjective sleepiness in the SD compared to homozygous participants. Moreover, differences in subjective sleepiness between SD and NP occurred at nighttime in subjects with the G/A-genotype, while they appeared later and less pronounced in the G/G allele carriers ($P < 0.05$). Furthermore, heterozygous individuals spent more time in wakefulness and stage 1 and had more movement time during the naps in the sleep satiation condition ($P = 0.07$), particularly during the first biological day.

Conclusion: Our data corroborate the implication of ADA in the homeostatic regulation of sleepiness and sleep. Moreover, our results indicate a more sensitive response in subjective sleepiness to challenges in homeostatic sleep pressure (low and high) in individuals with the G/A- compared to G/G-genotype. This susceptibility was also mirrored in the sleep structure under low sleep pressure, as indexed by greater difficulties to initiate and maintain sleep in G/A compared to the G/G allele carriers. The circadian dynamics of the observed heightened sensitivity in subjective and physiological variables remains to be further investigated.

O275

A genetic polymorphism of dopamine transporter modulates EEG markers of sleep homeostasis and effects of caffeine after sleep deprivation

S. C. HOLST, A. BERSAGLIERE, V. BACHMANN, P. ACHERMANN and H.-P. LANDOLT

University of Zurich, Zurich, CH

Objectives: The roles for dopamine in sleep-wake regulation in humans are poorly understood. We investigated the impact of a variable-number-tandem-repeat polymorphism (rs28363170) of the gene encoding dopamine transporter (DAT) on behavioral and EEG markers of sleep homeostasis. Furthermore, we studied whether this polymorphism modulates the effects of caffeine and modafinil after prolonged wakefulness.

Methods: DAT genotype was determined in 57 healthy participants of controlled sleep deprivation studies. The experimental protocol included baseline and recovery sleep recordings after 40 h of prolonged wakefulness. During sleep deprivation, two subgroups of male volunteers were administered 2×200 mg caffeine ($n = 16$) or 2×100 mg modafinil ($n = 22$) in placebo-controlled, double-blind, cross-over fashion. Sleep stages, EEG power spectra, and individual slow half-waves (>37.5 μ V; 0.5–2 Hz) in baseline and recovery sleep, as well as subjective sleepiness and psychomotor vigilance task (PVT) performance during prolonged waking were analyzed. Statistical analyses were based on mixed-model ANOVA with the factors 'genotype' (9-allele carriers, 10/10-homozygotes), 'condition' (baseline, sleep deprivation) and 'treatment' (placebo, caffeine/modafinil).

Results: The evolution of sleepiness and PVT performance during sleep deprivation was similar in 9- ($n = 27$) and 10/10-allele carriers ($n = 30$) of DAT. In the placebo condition, sleep deprivation enhanced slow wave sleep (SWS) and slow-wave activity (SWA), as well as number, amplitude and slope of slow waves in both genotypes. Nevertheless, the rebound in SWS/SWA and in the number of slow waves was significantly larger in 10/10-homozygotes than in 9-allele carriers. Moreover, caffeine improved optimal PVT speed and attenuated the sleep deprivation-induced rebound in amplitude and number of slow waves in 10/10-homozygotes only. By contrast, the effects of modafinil were independent of DAT genotype.

Conclusion: The functional consequences of rs28363170 have not been well established. Our refined sleep EEG analyses indicate a slightly different response to sleep deprivation in 9- and 10/10-allele carriers of DAT. Furthermore, the genotype-dependent effects of caffeine on PVT performance and EEG slow waves in recovery sleep suggest that caffeine interferes with sleep homeostasis in part by modulating dopaminergic neurotransmission.

Research supported by Swiss National Science Foundation grant # 310000-120377.

O276

Genetic polymorphisms of DAT and COMT influence rest-activity profiles and sleep in humans: an actigraphy study

A. VALOMON[1], V. BACHMANN[1], S. C. HOLST[1], A. U. VIOLA[2], C. CAJOCHEN[2] and H.-P. LANDOLT[1]

[1]University of Zürich, Zurich, CH, [2]Universitäre Psychiatrische Kliniken, Basel, CH

Objectives: Dopamine (DA) exhibits a pronounced circadian rhythm and may play a role in sleep-wake regulation. Cerebral DA levels are primarily regulated by DA transporter (DAT) and catechol-*O*-methyltransferase (COMT). We hypothesized that distinct polymorphisms of the genes encoding DAT (3′-UTR VNTR; rs28363170) and COMT (Val158Met; rs4680) affect rest-activity profiles and sleep in healthy humans.

Methods: Daytime sleepiness (ESS), chronotype (MCTQ), rest-activity patterns, light exposure, and sleep timing and quality were obtained in 136 men and women (Actiwatch; Cambridge Neurotechnology Ltd.; age range: 19–35 years). The data were analyzed with mixed-model ANOVA including the factors 'genotype' (10/10-, 9-allele carriers of DAT; Val/Val, Val/Met, Met/Met genotypes of COMT), 'gender' (men, women), 'season' (summer, winter) and 'time' (30-min bins), followed by two-tailed t-tests.

Results: This analysis includes a subgroup of 83 participants (46 men, 37 women), of whom an average of 27 ± 4 day-night recordings per person were available. Sleep timing was earlier and sleep efficiency was higher in women than in men. Chronotype, light exposure and absolute levels of activity did not differ between the genders. Despite higher intensity and duration of light exposure in summer than in winter, the circadian rest-activity patterns were unchanged across the seasons. DAT 9-carriers showed more overall activity than the 10/10 homozygotes ($P = 0.01$), whereas this polymorphism did not affect sleep. By contrast, time in bed (TIB; $P = 0.01$), total sleep time (TST; $P < 0.05$) and sleep latency ($P = 0.03$) showed significant 'gender' × 'genotype' interactions for COMT. TIB and TST were longer in women than in men, except in Val/Met genotype. Sleep latency was lower in women than in men for the Val/Met genotype while there was no gender difference for Val/Val and Met/Met genotypes. Only in men, TIB, TST and sleep latency were longer in Val/Met compared to Met/Met genotype.

Conclusion: DAT regulates DA levels primarily in the striatum, whereas COMT is mostly expressed in PFC. Thus, the differential effects of functional polymorphisms of DAT and COMT on rest-activity patterns and actigraphy-derived sleep characteristics are interesting, and consistent with preclinical (DAT knock-out mice) and clinical data (narcolepsy). Ongoing analyses will include the entire study sample and explore potential interactions between the genetic variants of DAT and COMT.

O277

Altered sleep homeostasis in Rev-erb(alpha) knock-out mice

G. M. MANG[1], Y. EMMENEGGER[1], U. ALBRECHT[2] and P. FRANKEN[1]

[1]University of Lausanne, Lausanne, CH, [2]University of Fribourg, Fribourg, CH

Objectives: Sleep is known to be regulated by the tight interaction between circadian and homeostatic processes. At the molecular level, circadian rhythms are driven by an interaction of transcriptional-translational feedback loops involving clock genes and their protein products. A similar detailed account of the molecular mechanisms underlying the sleep homeostat is lacking. We have previously demonstrated that clock genes also contribute to the homeostatic aspect of sleep regulation. To further document the involvement of the molecular circadian clock in sleep homeostasis, we investigated the role of the clock gene Rev-erb(alpha), by studying sleep and the electroencephalogram/electromyogram (EEG/EMG) in Rev-erb(alpha) knockout (KO) mice.

Methods: Thirteen Rev-erb(alpha) KO and eight wild type (WT) male mice, 11–16 weeks old were used. These KO mice were constructed by Ueli Schibler, University of Geneva. Mice were maintained under standard housing conditions including a 12 h:12 h light/dark cycle and equipped with EEG/EMG electrodes under deep anesthesia. After recovery, EEG/EMG signals were recorded continuously for 48 h of baseline, 6 h of sleep deprivation (SD) starting at light onset, and 18 h of recovery.

Results: In baseline, KO showed an altered sleep/wake distribution compared to WT mice and were significantly more awake at the light/dark transition and spent more time asleep in the subsequent hours of the dark period. Moreover, lack of Rev-erb(alpha) affected the spectral composition of the Rapid Eye Movement sleep (REMS) and wake EEG with higher levels in the 2–6 Hz range and, for REMS, lower activity in theta (6–9 Hz). Of importance, sleep homeostasis was affected, with KO mice showing lower levels of EEG delta power (1–4 Hz) reached at sleep onset in baseline as well as after SD. The reduced increased in EEG delta power after SD was accompanied by a smaller relative increase in Non-REMS (NREMS) consolidation.

Conclusion: Our results add further evidence to the notion that clock genes are involved in the homeostatic regulation of sleep. Because clock genes and Rev-erb(alpha) in particular, are intimately coupled to metabolism this molecular pathway could functionally link recovery sleep to the metabolic challenge imposed at the neuronal level by periods of extended wakefulness.

O278

Sleep pressure and a PER3 polymorphism affect blood pressure in healthy young people

A. VIOLA[1], C. F. REICHERT[1], M. MAIRE[1], V. GABEL[1], A. VALOMON[1], V. BACHMANN[2], H.-P. LANDOLT[2], C. SCHMIDT[1] and C. CAJOCHEN[1]

[1]Universitäre Psychiatrische Kliniken, Basel, CH, [2]Institute of Pharmacology and Toxicology, Zurich, CH

Background: A variable number tandem repeat polymorphism in the coding region of the clock gene PERIOD3 has been shown to affect several markers of sleep homeostasis as well as the autonomic nervous system such as the cardiac control similar to the effect of sleep deprivation. Here we investigated blood pressure levels under high and low sleep pressure conditions in individuals homozygous for the long (PER3-5/5) or short (PER3-4/4) variant of this polymorphism.

Methods: In this on-going project, twenty healthy volunteers (seven men and 13 women; 25.7 ± 0.7 years, BMI 22.35 ± 0.44 kg/m^2) were selected exclusively on the basis of their PER3 genotype. Ten PER3-5/5 (four men and six women) and 10 PER3-4/4 (three men and seven women) participants underwent a 40-h sleep deprivation protocol (SD, high sleep pressure) and a 40-h nap protocol (NAP, low sleep pressure, alternating cycle of 160 min of wakefulness and 80 min of sleep) under constant conditions in a balanced crossover design, starting at habitual wake time. Blood pressure and heart rate were recorded every 2 h after being in a very controlled postural position for 3 min. Comparisons of repeated measures between genotypes were made with a mixed-model approach (SAS version

9.1). Genotypes as well as time were factors in all analyses. Contrasts were assessed with the LSMEANS statement.

Results: Heart rate did not significantly differ between sleep pressure conditions (i.e. SD versus NAP) and between the long and short PER3 variant. However, systolic and diastolic blood pressure increased significantly under SD, particularly during the night ($P < 0.05$). Furthermore, there was a significant interaction between gene and condition during the night period ($F = 6$; $P = 0.01$), such that the PER3-5/5 individuals were more affected by SD (i.e. stronger increase in systolic and diastolic blood pressure) than the PER3-4/4 individuals.

Conclusion: Our data show that a state challenge of the sleep homeostat by total sleep deprivation as well as a trait-like challenge, as induced by the PER3 polymorphism can impact on diastolic and systolic blood pressure. Thus, besides sleep structure, behavioural and neuronal responses to sleep deprivation and autonomic cardiac control, this polymorphism may also account for inter-individual differences in blood pressure modulation.

Funding: This work was supported by the Swiss National Science Foundation # 310030_130689.

O279

The circadian and homeostatic regulation of sleep spindle activity: effect of the PER3 VNTR polymorphism

A. LAZAR, N. SANTHI, J. LO, A. SLAK, S. HASAN, M. VON SCHANTZ, S. ARCHER and D.-J. DIJK

University of Surrey, Guildford, UK

Introduction: Sleep spindles are thought to be closely associated with physiological processes underlying sleep consolidation. We investigated whether allelic variants in a (VNTR) polymorphism (rs57875989) in PERIOD3 (PER3) previously associated with diurnal preference and sleep homeostasis associate with the circadian and homeostatic regulation of sleep spindles as assessed in a forced desynchrony (FD) protocol.

Methods: Thirty-five young (mean age: 25.5 ± 3.4 years; 13 PER34/4, 8 PER34/5, 14 PER35/5) healthy individuals with no reported shift-work, matched in age and gender per genotype, completed a 10-day FD protocol, during which a 28-h sleep-wake cycle was imposed. Sleep EEG was recorded throughout the protocol from multiple electrodes and scored according to standard criteria (R&K). Slow (SSP) and fast (FSP) sleep spindles were detected (NREM 2, 3 and 4) based on a semi-automatic approach accounting for individual-specific spindle frequency and amplitude. Multiple spindle parameters were analyzed. Circadian phase was derived from the assessment of Dim Light Melatonin Onset.

Results: The average mid-frequency (MF) was 13.8 ± 0.5 Hz for FSP and 11.9 ± 0.5 Hz for SSP. The MF of both FSP and SSP showed a marked circadian and a homeostatic variation as well as significant interaction between the two factors ($P < 0.001$). MF, which increased throughout the sleep episode, peaked in the early circadian afternoon whereas the nadir coincided with the wake maintenance zone (WMZ).

The density of FSP showed both a marked circadian and a homeostatic effect ($P < 0.001$) as well as an interaction between the two factors ($P < 0.01$). It increased throughout the sleep episode and peaked during the WMZ. The circadian nadir was located in the early afternoon. SSP density showed a genotype effect ($P < 0.05$) with more SSP in PER34/4 s than in the other genotypes ($P < 0.05$). FSP duration showed a marked circadian variation ($P < 0.005$) while SSP duration exhibited a genotype effect ($P < 0.05$). PER34/5 s had longer SSP than PER35/5 s ($P < 0.01$). FSP amplitude showed both a circadian ($P < 0.05$) and a homeostatic effect ($P < 0.001$) as well as a three way interaction ($P < 0.005$). SSP amplitude was larger in PER34/4 s than in PER34/5 s ($P < 0.05$).

Conclusion: The data showed that FSP and SSP are differentially modulated by circadian and homeostatic processes as well as PER3. How these aspects of sleep spindle regulation relate to the circadian regulation of sleep consolidation, remains to be investigated.

Funding: BBSRC (BB/F022883/1).

O280

Difference in neural correlates of discrimination during sleep deprivation in PER3 homozygous

A. SHAFFII-LE BOURDIEC[1], V. MUTO[1], M. JASPAR[1], C. KUSSÉ[1], A. FORÊT[1], S. N. ARCHER[2], F. LE BOURDIEC[1], G. VANDEWALLE[1], F. COLLETTE[1], D. J. DIJK[2] and P. MAQUET[1]

[1]University of Liège, Liège, BE, [2]University of Surrey, Guildford, UK

Objectives: In young healthy volunteers, a PERIOD3 (PER3) variable number tandem repeat polymorphism has been associated with difference in sleep homeostasis (the buildup of sleep pressure during wakefulness) but not in circadian markers. Here, we tested whether responses to a working memory task would differ during sleep loss between groups of individuals homozygous for either the 4- (PER34/4) or 5-repeat (PER35/5) allele, while maintained in a constant routine.

Methods: We conducted a 42-h constant routine (CR) protocol on 28 healthy subjects (aged 18–25, 14 women). Volunteers (12 PER35/5, 16 PER34/4) were matched for sex, age, and level of education at the group level. Brain activity was assessed by functional magnetic resonance imaging during blocks of auditory 3-back (3B) and 0-back (0B) tasks during four successive sessions distributed during the CR: morning session (MS), evening session (ES), and morning (MSD) and evening (ESD) sessions after sleep loss. We contrasted responses for 3B and 0B tasks at two opposite times of day, [MS-MSD] and [ES-ESD] and assessed whether any change in response covaried with changes in individual performance (discrimination index d').

Results: No differences in accuracy were found between groups across sessions ($P = 0.4$). The 3B d' tended to differ between genotypes across sessions ($P = 0.06$), while the 0B d' did not ($P = 0.2$). Reaction times (RTs) were not significantly different across groups.

Statistical parametric mapping of the imaging data revealed that the changes in executive responses (3B-0B) between morning sessions in left intraparietal sulcus, left orbitofrontal cortex, and hypothalamus significantly correlated with changes in d' in PER35/5 but not in PER34/4. No regression between these areas and RTs could be found. However, we observed significantly increased activations or reduced deactivations in SD with increasing d' scores in PER35/5, while PER34/4 showed no activation underlying d' scores. No correlations with d' were found in either group for evening sessions.

Conclusion: Taken together, our data confirm that brain activity associated with executive function during sleep loss is differently modulated between PER3 homozygous genotypes. We report for the first time changes in regional brain activity that support behavioural performance, especially during the early morning hours during sleep loss.

Symposium – Risk of Narcolepsy Associated with Administration of A/H1N1 Pandemic Influenza Vaccine

S285

Increased incidence of narcolepsy after the A/H1N1 pandemic influenza vaccination campaign in the Nordic countries

M. PARTINEN on behalf of the NARPANord Consortium

Narcolepsy is a rare neurological sleep disorder. In Finland the prevalence is around 26 per 100 000. In Minnesota the incidence of narcolepsy with cataplexy has been 0.74 per 100 000 per year. Among children aged 0–9 the incidence has been 0.4 and in the age group 10–19 around 1.8 per 100 000 per year (Silber et al. 2002). In the Spring 2010 several new incident cases of childhood narcolepsy were diagnosed. Systematic studies were started in August 2010 to understand the link between the H1N1 epidemics, the Pandemrix vaccinations and narcolepsy.

The average annual incidence of narcolepsy between 2002 and 2009 among children younger than 17 had been 0.31 per 100 000, and in 2010, this incidence was about 17 times higher, at 5.3 cases per 100 000. In contrast, the incidence rate for adults over 20 was essentially unchanged over that same time period. The incidence for vaccinated individuals in this age group was 9.0 per 100 000 people, as compared to 0.7 per 100 000 for unvaccinated individuals – 13 times lower. Many children are doing better but some are still severely affected with cataplectic attacks and psychiatric problems (challenging behavior, aggression etc). Altogether more than 200 new patients have been diagnosed with narcolepsy between 2010 and 2011. The final figures from Finland should be available by September 2012. In most cases the onset occurred between December 2009 and July 2010. Most children who have been diagnosed in 2012 were vaccinated in November-December 2009 increasing the odds ratio of the association between vaccination and onset of narcolepsy to more than 20. The awareness of narcolepsy has increased and the interval between onset and diagnosis has shortened. Different pathogenetic studies are going on in Finland and in Sweden. We have received more evidence that the causative factor/s can be are linked to the Pandemrix vaccine and not to an A/H1N1 infection. Can the type or patches of vaccines make some difference? In Finland, Sweden and Norway the AS03 adjuvanted Pandemrix (D-pan from Dresden) was used. In Canada AS03 adjuvanted Arepanrix (Q-pan from Québec) was used. Denmark did not use AS03 adjuvanted A/H1N1 vaccines and there was no increase of narcolepsy. Several immunological hits are probably needed in susceptible people before developing narcolepsy. The Pandemrix vaccination has been one hit. It remains to be seen what is its significance in developing narcolepsy after possible future immunological hits.

M Partinen is a consultant for UCB Pharma, Bioprojet, and Leiras Nycomed. He has received honoraries for lecturing and travel grants from Cephalon, Glaxo Smith Kline, Leiras, MSD, Servier and UCB Pharma. He has been involved in clinical trials on narcolepsy and other sleep disorders relevant to this abstract supported by Actelion, Bioprojet, and MSD. He is Chairman of the Board of the Finnish Narcolepsy Research Centre, Helsinki Sleep Clinic, and member of the Board in the Finnish Sleep Federation and Finnish Sleep Research Society.

S286

The link between H1N1 and narcolepsy

F. HAN

Peking University People's Hospital, Beijing, CN

Cases of narcolepsy with cataplexy have been reported following 2009 H1N1 influenza vaccination or infections. Studies in Finland reported six to nine-fold increased risks of narcolepsy after pandemic H1N1 (pH1N1) flu vaccination in children and adolescents following H1N1 vaccination with Pandemrix, a squalene/a-tocopherol (AS03) adjuvanted H1N1 vaccine. Although the small numbers of children and adolescents with narcolepsy precluded any meaningful conclusions in a population based cohort studies, however, there are evidences suggesting that exposure to H1N1 infections per se may also increase narcolepsy susceptibility in children. The occurrence of childhood cases was found to increase three fold following the winter of 2009–2010, independent of vaccination in China. In this context, it is notable that the great H1N1 pandemic of 1918 was followed by a seasonal encephalitis, "von Economo encephalitis lethargica," led to extreme somnolence and ophthalmoplegia (associated with lesions of the posterior hypothalamus and upper brainstem), insomnia and sleep inversion (associated with lesions of the anterior hypothalamus), psychosis, chorea type movement disorders (reminiscent of Sydenham chorea, with lesions of the basal ganglia). Two mechanisms of H1N1 vaccination or infection trigger narcolepsy could be involved, a specific immune response to H1N1 (and subsequent molecular mimicry) or a generalized stimulation of the immune system mediated by the vaccine, as AS03 adjuvanted vaccines have been shown to induce a somewhat stronger immune response.

Symposium – Recording in- and Outside of the Human Brain: What We Learn About Sleep

S288

Coupling and decoupling of thalamo-cortical activity during sleep in humans

H. BASTUJI[1], M. REY[2], L. GARCIA-LARREA[1] and M. MAGNIN[1]
[1]CRNL Neuropain Team, Bron, FR, [2]Hôpital La Timone, Marseille, FR

Thalamic and cortical activities are assumed to be time-locked throughout all vigilance states. Using simultaneous intracortical and intrathalamic recordings, we demonstrate here the decoupling of thalamic and cortical activities during two periods of the sleep/wake cycle. The first one occurs at sleep onset during which thalamic deactivation most often precedes that of the cortex by several minutes, whereas reactivation of both structures during awakening is synchronized. Delays between thalamus and cortex deactivations can vary from one subject to another when a similar cortical region is considered. In addition, heterogeneity in activity levels throughout the cortical mantle is larger than previously thought during the descent into sleep. Thus, asynchronous thalamocortical deactivation while falling asleep probably explains the production of hypnagogic hallucinations by a still-activated cortex and the common self-overestimation of the time needed to fall asleep.

The second one concerns paradoxical sleep (PS), during which unexpected intermittent delta frequency oscillations, as well as a surprisingly low amount of high-frequency activities are observed, in a posterior region of the thalamus, mainly the medial pulvinar nucleus (PuM). Wakefulness and (PS) are supposed to share a similar electrophysiological trait, namely, a more elevated level of high-frequency activities at both thalamic and cortical levels relative to slow wave sleep. The spatio-temporal binding of these high-frequency activities within thalamo-cortical networks is presumed to generate cognitive experiences during wakefulness. Similarly during PS, this phenomenon could be at the origin of the perceptual experiences forming dreams. However, contents of dreams often present some bizarre features that depart from our cognitive experiences in waking. This suggests some differences in processing and/or integration of brain activities during waking and PS. This discrepancy between activities at the thalamic and cortical levels during PS may compromise the spatio-temporal binding of the high-frequency activities, resulting in altered perceptual experiences during dream periods.

S289

Local sleep oscillations – intracranial EEG and unit recordings in humans

Y. NIR
University of Wisconsin-Madison, Madison, US

Objectives: Increasing evidence suggests that slow waves and sleep spindles, the EEG hallmarks of NREM sleep, may show regional diversity. We set out to better characterize this phenomenon by recording intracranial depth EEG and single-unit activity in multiple brain regions of neurosurgical patients.

Methods: We obtained full night continuous polysomnographic sleep recordings in 13 pharmacologically intractable epilepsy patients implanted with depth electrodes for potential surgical treatment. Polysomnography included electrooculogram (EOG), electromyogram (EMG), scalp EEG, and video monitoring. Depth intracranial electrodes recorded activity in 129 medial brain regions in frontal and parietal cortices, as well as medial temporal lobe regions. We simultaneously recorded scalp EEG, depth EEG, and single-neuron spike activity ($n = 600$). Individual slow waves and sleep spindles were automatically detected for detailed analysis and carefully separated from paroxysmal discharges.

Results: Slow waves are associated with underlying neuronal bistability between active (ON) and inactive (OFF) states. Most slow waves and corresponding ON/OFF states occur locally, where some regions can be active while others are silent, and this is especially evident in late sleep. Slow waves have a tendency to propagate from medial prefrontal cortex to the medial temporal lobe, and mostly from the neocortex to the hippocampus.

Sleep spindles are also mostly spatially restricted to specific brain regions. In addition, spindle frequency is topographically organized with a marked distinction between fast (13–15 Hz) centroparietal spindles often occurring with slow-wave up-states, and slow (9–12 Hz) frontal spindles occurring 200 ms later on average. During individual spindles, frequency decreases within and between regions. Deeper NREM sleep is associated with a reduction in spindle occurrence and spindle frequency. Finally, neuronal firing rates are not consistently modulated during spindles, although some neurons exhibit phase-locked discharges.

Conclusion: Intracranial EEG and unit recordings in humans reveal extensive regional diversity in the occurrence, spectral, and temporal aspects of sleep oscillations, showing that slow waves and sleep spindles are a diverse rather than prototypical phenomenon. The two fundamental brain oscillations of sleep – slow waves and spindles – occur mostly locally, thereby constraining intracerebral communication during sleep.

S290

Mapping cortical plasticity by means of high-density sleep EEG

R. HUBER
University Children's Hospital Zurich, Zurich, CH

Cortical plasticity, i.e. the formation and elimination of synapses, is essential for learning, development and recovery processes. Electroencephalographically (EEG) recorded slow wave activity (SWA, 1–4.5 Hz) during non rapid eye movement sleep is regulated use dependently. A popular hypothesis about the function of sleep suggests that SWA plays a crucial role in synaptic plasticity. Thus, the question arises whether sleep SWA can be used to map cortical plasticity, e.g. as present during cortical maturation. Indeed, mapping of SWA by means of high-density EEG (128 electrodes) revealed that cortical regions undergoing maturational changes (structural and behavioural) during childhood and adolescence show more SWA. Moreover, the topographical distribution of SWA predicted the maturation of specific skills, leading the maturation of performance by about 3 years. Thus, high-density EEG recordings during sleep can be used to map cortical plasticity. Whether sleep SWA plays an active role in shaping our cortex remains an open question. Hinting for an active role are observations in children with an encephalopathy related to electrical status epilepticus during slow wave sleep

(ESES). These children showed on the one hand a disturbance of sleep related synaptic plasticity and on the other hand developmental regressions. Interestingly, these patients also showed reduced sleep dependent memory consolidation. In the future, animal models may help to uncover the mechanisms underlying the close relationship between sleep SWA and cortical plasticity during development.

S291

Electrophysiological behavior of cortical and subcortical structures at sleep onset and during sleep

M. FERRARA

University of L'Aquila, L`Aquila, IT

Intracerebral stereo-EEG (SEEG) sleep recordings have recently provided robust support to the local sleep theory, indicating that different cortical and sub-cortical brain structures may have different and peculiar sleep characteristics.

In humans, the thalamus and the cortical mantle are not strictly coupled during the wake–sleep transition, with thalamic deactivation preceding the cortical one by several minutes. Moreover, our data suggest that hippocampal spindle activity anticipate the occurrence of sleep rhythms in other cortical structures. Studies in the animal model have shown that local 'islands of sleep' can appear during wakefulness. However, also 'local wakefulness' could appear during sleep. We indeed observed that sleep can be characterized by the coexistence of wake-like and sleep-like EEG patterns in different cortical areas.

As far as the characterization of hippocampal sleep is concerned, delta band exhibits, also in the hippocampus, the typical progressive decrease of power across sleep cycles, indicating that a kind of homeostatic regulation of delta activity is present also in this subcortical structure. Hippocampal sleep also showed some very distinctive features during both NREM and REM sleep periods, in particular a lower relative power in the slow oscillation range (<1 Hz) during NREM sleep compared to the scalp EEG and a relatively high power even during REM sleep. Finally, a decrease of power in the beta band was found during REM sleep. Together, these findings indicate that during REM sleep the hippocampus shows a generalized tendency to EEG synchronization. Such a synchronization in the low rhythms during REM sleep seems to be the most peculiar feature of the hippocampal sleep.

In particular, we recently showed the existence of two distinct hippocampal slow rhythms in the spontaneous SEEG also during wakefulness. The first is a low-delta rhythm (0.5–2 Hz), which appears as a transient (phasic) rhythm present during all the vigilance states, but intriguingly synchronous between the hippocampi mainly during the activated states (wake and REM sleep). The second is a high-delta rhythm (2–4 Hz), which instead appears as an oscillatory background rhythm present during all the states, but only weakly in phase between hemispheres. Further studies focusing on task-dependent SEEG activity may shed light on the possible functional differences between slow and fast hippocampal delta rhythms in relation to learning.

This work has been funded in part by a grant from the Compagnia di S. Paolo, Programma Neuroscienze 2008/09 (3896SD/SD, 2008.2130).

Symposium – Neuroimaging Insights into the Pathophysiology of Sleep Disorders

S292

Neuroimaging and cognitive function in obstructive sleep apnea syndrome

L. FERINI-STRAMBI
University Vita-Salute San Raffaele, Milan, IT

Several studies have shown in obstructive sleep apnea syndrome (OSAS) significant daytime cognitive and behavioral dysfunction that seems to extend beyond that associated with simple sleepiness and that persists in some patients after treatment. A still unanswered question is whether cognitive symptoms in OSAS are primarily a consequence of sleep fragmentation and hypoxemia. Structural brain changes in OSAS patients were first described by Macey et al. (AJRCCM 2002) that used voxel-based morphometery (VBM) to detect diffuse reductions in gray matter (GM) across the brain, including the frontal and parietal cortex, temporal lobe, hippocampus. Results of more recent structural studies investigating GM density or volume changes are heterogeneous, although hippocampal involvement is reported frequently. The discrepancies between the studies are most likely due to methodological differences. Recently, Canessa et al (AJRCCM 2011) investigated the cognitive deficits and the corresponding brain morphology changes in OSAS, and the modifications after CPAP treatment. Neuropsychologic results in pretreatment OSAS showed impairments in most cognitive areas. These impairments were associated with focal reductions of GM volume in the left hippocampus, left posterior parietal cortex, and right superior frontal gyrus. After 3-month CPAP, the authors observed significant improvements involving memory, attention, and executive-functioning that paralleled GM volume increases in hippocampal and frontal structures. As regard to the detection of structural white matter (WM) alterations in OSAS, Macey et al (Sleep 2008) used Diffusion Tensor Imaging (DTI) to examine Fractional Anisotropy (FA), a measure of WM integrity, in OSAS patients. Patients showed several areas of abnormal FA when compared to controls, suggesting a bilateral and nearly global WM involvement in OSAS. We recently demonstrated in OSAS impairment in most cognitive areas that was associated with diffuse reduction of WM fibers integrity reflected by diminished FA in multiple brain areas. In our study, after 3-month CPAP only limited changes of DTI metrics were found. However, after 12-month treatment an almost complete reversal of WM abnormalities in all the affected regions was observed, with concomitant improvement of cognitive functioning. These data indicate that adherence to CPAP treatment can lead not only to clinical, but also to brain structural recovery in OSAS.

S293

Brain imaging of insomnia

Y. D. VAN DER WERF[1], D. STOFFERS[1], E. ALTENA[2] and E. J. W. VAN SOMEREN[1]
[1]Netherlands Institute for Neuroscience, Amsterdam, NL, [2]CITA Alzheimer Foundation, San Sebastián, ES

Objectives: Affecting about 10% of the population, insomnia constitutes the most common symptom in general practice. Patients suffering from insomnia complain of daytime consequences of their poor sleep, for instance poor memory and decreased complex problem solving abilities. Often, these complaints cannot be substantiated when tested formally. We here report brain activation differences in insomnia patients as compared to well-sleeping controls, in spite of equal performance.

Methods: We tested 25 patients with primary insomnia, excluding patients with neurological, somatic or psychiatric diseases, compared with 13 matched well-sleeping controls. Patients were divided in two groups, one receiving a 6-week non-medicated sleep therapy before re-testing, the other a wait-list procedure of equal duration. At both test and re-test, all participants underwent functional MRI during memory encoding (visual memory paradigm), semantic memory (verbal fluency task) and complex problem solving (Tower of London task) using parallel versions of each task for the two timepoints.

Results: Patients scored at similar levels as well-sleeping controls on the visual memory task and the Tower of London task, and even higher than control subjects on the verbal fluency task. Yet, in every task, patients showed brain activation differences in the form of reduced task-specific activity: a lower prefrontal activity (memory and fluency tasks) and a lower activity of the left caudate nucleus (Tower of London task). No consistent compensatory activations were noted. Upon sleep therapy but not the wait-list procedure, prefrontal activation recovered only partly, the caudate did not.

Conclusions: Insomnia patients show local and task-dependent reductions in brain activity while performing cognitive tasks; yet their performance levels are never lower than those of well-sleeping controls. The brain underactivation appears to reflect in part the state of poor sleep and in part an underlying trait of insomnia. We propose that the subjective feelings of poor cognitive functioning are real and reflect sub-optimal levels of performance relative to the patients' own standards that may be higher than those of well-sleeping subjects. It remains to be shown whether longer-lasting therapy may induce more robust changes in brain activation. Future endeavours will attempt to investigate subtypes of insomnia, patients' respective cognitive performance, brain activation and response to sleep intervention.

S294

Functional neuroimaging of parasomnias

T. T. DANG-VU
Concordia University, Montreal, CA

Objectives: Parasomnias – particularly sleepwalking and REM sleep behaviour disorder (RBD) – are frequent conditions resulting in injuries and sleep fragmentation. The neural mechanisms of sleepwalking remain poorly understood, with only scarce data suggesting a state of functional dissociation. On the other hand, RBD is a risk factor for the development of neurodegenerative diseases, such as Parkinson's disease, and recent research now focuses on the identification of biomarkers for clinical evolution. Functional neuroimaging using Single Photon Emission Computed Tomography (SPECT) can be used to assess the cerebral correlates of sleepwalking and to characterize the neural patterns predicting the short-term emergence of neurodegenerative disease in RBD patients.

Methods: Ten sleepwalking patients were scanned using SPECT with 99mTc-Ethylene Cysteinate Dimer (ECD) in a resting state. Patients were also scanned during a second session, after a

complete night of sleep deprivation. Twelve healthy control subjects, matched for age and gender, followed the same procedure.

Twenty RBD patients were scanned using SPECT with 99mTc-ECD in a resting state. Patients then had a yearly clinical follow-up (3 years), and were subdivided in two groups: those who developed a neurodegenerative disease within the follow-up period ($n = 10$; RBDEv), and those who remained stable ($n = 10$; RBDSt).

SPECT data analysis was performed using Statistical Parametric Mapping (SPM8) and compared regional cerebral blood flow (rCBF) between groups.

Results: Diiferences in rCBF between sleepwalking patients and controls were mostly observed after sleep deprivation, and mainly located in the inferior temporal cortex.

In RBD patients, rCBF was higher in the hippocampus of RBDEv compared to RBDSt ($P < 0.05$ corrected).

Conclusion: Sleepwalking patients show decreased perfusion in association cortices of the ventral visual stream, possibly in relationship with the visual hallucinatory content frequently associated with sleepwalking episodes. This pattern is already observed during wakefulness, but revealed only after sleep deprivation, in line with the facilitating effect of sleep deprivation in sleepwalking.

SPECT also shows that it is possible to predict the short-term development of neurodegenerative disease in RBD patients: disease progression can be predicted by abnormal perfusion in the hippocampus at baseline.

This work was supported by the Canadian Institutes of Health Research, the Belgian Fonds National de la Recherche Scientifique, the Fonds Léon Frédéricq, and the Belgian College of Neuropsychopharmacology and Biological Psychiatry.

S295

Sleep and emotional brain functions: insights from human narcolepsy

S. SCHWARTZ

University of Geneva, Geneva, CH

Elucidating the neural mechanisms that underlie the interaction between sleep and affect emerges as an important and timely objective for sleep medicine and neuroscience research.

In my presentation, I will review evidence supporting a pivotal role of the hypocretin/orexin system in the regulation of sleep and emotion/reward brain functions in humans. In particular, I will show that recent behavioral and brain imaging studies in human narcolepsy with cataplexy (NC) confirm and extend recent animal data indicating that the hypocretin/orexin system is involved in the expression of motivated behaviors and addiction.

NC is a major sleep disorder related to a deficiency in hypocretin/orexin, which also presents with a striking emotional component: cataplexy (sudden loss of muscle tone) in NC patients is typically triggered by emotional experiences. Using functional magnetic resonance imaging (fMRI) in NC patients, we demonstrated impaired emotional learning in the patients, expressed by the lack of amygdala modulation by aversively-conditioned stimuli. Conversely, we found amplified amygdala response during the experience of rewards and positive emotions, associated with altered responses in mesolimbic reward circuits as well as in medial prefrontal regions involved in emotion regulation functions. Altogether, these findings reveal that the regulation of sleep-wake states recruits neurotransmitters and neural pathways (in particular the mesolimbic dopaminergic reward system) that are also critically involved in the processing of emotional and motivational signals.

Finally, I will suggest that these observations may have implications for our understanding of memory processes operating during sleep, such as the prioritization of information with high emotional or motivational relevance for reprocessing during sleep and dreaming.

This work was supported by the Swiss National Science Foundation.

Symposium – What Causes Delayed Sleep Phase Disorder?

S296

Individual differences in the circadian regulation of sleep

D.-J. DIJK

University of Surrey, Guildford, UK

Objectives: The circadian timing system plays an important role in the regulation of sleep and variation in circadian parameters may explain individual differences in sleep timing, duration as well as susceptibility to unstable entrainment. Circadian parameters of interest include (i) the intrinsic period of the circadian pacemaker driving the sleep propensity rhythm, (ii) the sensitivity to the phase resetting and amplitude altering effects of light, and (iii) interactions between genotype, diurnal preference and the correlates and consequences of habitual sleep patterns. The objective of the experiments was to assess individual differences in these parameters and responses.

Methods: Intrinsic period of the human melatonin rhythm was assessed in a forced desynchrony protocol, and *in vitro*, in fibroblasts in which the firefly luciferase was put under control of the BMAL1 promoter (Hasan et al. 2012). Individual differences in the effects of light were assessed in a re-entrainment protocol through gradual advance of the sleep-wake cycle, with or without bright light Dijk et al. 2012). Interactions between genotype, diurnal preference and sleep patterns were assessed in as survey study (Lazar et al. 2012).

Results: Individual differences in the melatonin rhythm correlated significantly with the timing of habitual sleep relative to the onset of melatonin as well as with diurnal preference (Horne-Ostberg Scale). No significant correlations were observed between *in vitro* period assessments and sleep or diurnal preference parameters.

Individual differences in the phase shifts and in the reduction of circadian amplitude during reentrainment were observed both in the presence and absence of bright light and correlated across multiple physiological and behavioural variables.

Analyses of the interaction between habitual sleep parameters and diurnal preference and PER3 VNTR genotype revealed that consequences of short sleep, e.g. increased body weight, as well as changes in sleep timing during the weekend compared to weekdays, varied across genotypes.

Conclusion: Individual differences in circadian parameters can be observed in a variety of physiological variables and protocols and may help to explain individual differences in sleep timing and in the response to insufficient or mistimed sleep.

Supported by BBSRC, AFOSR, NASA

References:

1. Dijk et al. PLoS. ONE., 2012, 7: e30037.
2. Hasan et al. FASEB J., 2012, 26: 2414–2423.
3. Lazar et al. Chronobiol. Int., 2012, 29: 131–146.

S297

Characterization of circadian rhythmicity and sleep during entrainment and temporal isolation in Delayed Sleep Phase Disorder

S CAMPBELL[1], P. MURPHY[1], M. YOUNG[2] and A. PATKE[2]

[1]Weill Cornell Medical College, White Plains, NY, US, [2]Rockefeller University, New York, US

Objectives: Although Delayed Sleep Phase Disorder (DSPD) is the most commonly diagnosed Circadian Rhythm Sleep Disorder, diagnosis and treatment is hampered by a remarkable paucity of data addressing key aspects of the disorder, including a virtual absence of studies that adequately characterize the sleep disturbance, itself. To better understand the behavioral, physiologic and molecular alterations hypothesized to underlie DSPD, we studied subjects who met criteria for DSPD, as well as controls, under both entrained conditions and in temporal isolation.

Methods: Nineteen subjects (9 DPSD (D); 10 Control (C)) were studied in a 20-day lab protocol. Polysomnography (PSG) and core body temperature (CBT) were recorded continuously for an adaptation night, followed by 4 entrainment (EN) and then 14 free-run (FR) days. Bedtimes (BT) and wake times (WT) were at habitual/preferred times on EN1-2 and at 2300 h–0700 h on EN3-4. Sleep/wake times in FR were self-selected.

Results: On EN1-2, D exhibited a significantly later average CBT phase (0941 h) than did C (0318 h) ($P < 0.0001$). Likewise, there was a significant group difference on average Horne-Ostberg (H-O) scores (D = 31 versus C = 56 $P < 0.001$). There was a strong correlation between H-O and phase for C (-0.89 $P = 0.001$), but this was substantially weaker for D (-0.32 P = ns). In FR, D showed a longer average tau than C (25.4 h + 1.25 versus 24.4 h + 0.28 $P < 0.03$). There was not a significant correlation between H-O score and tau in either D or C alone, but there was for the sample as a whole (-0.65 $P < 0.003$). Similarly, EN phase and tau were correlated for the entire sample (0.65 $P = 0.005$), but for neither D nor C alone. In addition to circadian variables such as those reported above, analyses of continuously recorded EEG sleep/wake variables, during EN and FR, will be reported, as will preliminary findings of molecular mechanisms underlying DSPD.

Conclusions: This examination of individuals with DSPD and control counterparts studied in temporal isolation quantifies and supports some hypotheses regarding physiological and behavioral aspects of the disorder. These data have important implications for accurate and reliable diagnosis of DSPD. They also potentially call into question several important notions that underlie the current diagnosis and treatment of DSPD, particularly with regard to the conceptualization of DSPD as a disorder of sleep timing only, rather than a disorder of both homeostatic and circadian sleep regulation.

Symposium – New Emerging Cellular and Molecular Methods Applied to Sleep-Wake Circuits

S301

The supramammillary nucleus activates cortical structures during paradoxical (REM) sleep

L. RENOUARD, P. FORT, K. OGAWA, O. CLÉMENT, F. BILLWILLER, N. CAMARGO, M. ABDELKARIM, D. GERVASONI, N. GAY, C. SCOTÉ, P.-A. LIBOUREL, P. RAVASSARD, D. SALVERT, C. PEYRON, B. CLAUSTRAT, L. LÉGER, P.-A. SALIN, G. MALLERET and P.-H. LUPPI

UMR 5292 CNRS/U1028 INSERM, Lyon, FR

Cortical activity is classically believed to be fast and intense during rapid eye movement sleep ('REM sleep' also called paradoxical sleep 'PS') and waking in contrast to non-REM sleep. Positron emission tomography in humans further indicates that the limbic cortices are more active during REM sleep than waking. However, the state of the cortex at the cellular and molecular level during PS and the neuronal pathways involved in its activation remain to be defined. Here we show that only a few interconnected limbic cortical areas are activated during PS by a projection from the supramammillary nucleus, a small hypothalamic structure. Combining cDNA microarray, qPCR, '*in situ*' hybridization and immunohistochemistry we find that, during PS hypersomnia, the dentate gyrus, the claustrum, the cortical amygdaloid nucleus, the anterior cingulate, medial entorhinal and retrosplenial cortices are the only cortical structures containing neurons with an increased expression of BDNF, FOS and ARC, known markers of activation and/or synaptic plasticity. Such limited activation contrasts with the near global cortical activation occurring during waking as reflected by FOS staining. Combining FOS staining, retrograde labeling and neurochemical lesion, we further show that the activation of the cortex during PS is induced by a direct or indirect projection by means of the claustrum arising from the lateral part of the supramammillary nucleus. These data contrast with classical views suggesting a widespread cortical activation during PS and an exclusive role of the projections from the basal forebrain and the intralaminar thalamic nuclei. We propose that the activation during PS of the supramammillary-limbic cortical network revealed for the first time in the present study may trigger dreams and contribute to the consolidation of emotional memory known to occur during this state.

S303

Key electrophysiological, molecular and metabolic signatures of sleep and wakefulness revealed in primary cortical cultures

M. TAFTI[1], V. HINARD[1], C. MIKHAIL[1], S. PRADERVAND[1], T. CURIE[1], R. HOUTKOOPER[2], J. AUWERX[2] and P. FRANKEN[1]

[1]University of Lausanne, Lausanne, CH, [2]EPFL, Lausanne, CH

Although sleep is defined as a behavioral state, at the cortical level sleep has local and use-dependent features suggesting that sleep is a property of neuronal assemblies requiring sleep in function of the activation experienced during prior wakefulness. Here we show that mature cortical cultured neurons display synchronized burst-pause firing activity reminiscent of sleep while stimulation induces transient tonic firing reminiscent of wakefulness. Besides electrophysiological similarities, also the transcriptome of stimulated cultures resembles the cortical transcriptome of sleep-deprived animals. We then used our *in vitro* model as well as sleep deprived animals to map the metabolic pathways activated by waking and found evidence for increased lysolipid release, strongly suggesting that sleep plays a major role in re-establishing the neuronal membrane homeostasis. With our *in vitro* model the cellular and molecular consequences of sleep and wakefulness can now be investigated in a dish.

Oral Session 12 – Sleep Disordered Breathing – Treatment

O305

Prevalence of primary sleep disorders in a large sample of patients with presumed chronic fatigue syndrome referred to a tertiary care referral centre

A. MARIMAN[1], L. DELESIE[1], E. TOBBACK[1], I. HANOULLE[1], E. SERMIJN[1], P. VERMEIR[1], D. PEVERNAGIE[2] and D. VOGELAERS[1]
[1]University Hospital Ghent, Ghent, BE, [2]Sleep Medicine Centre, Kempenhaeghe Foundation, Heeze, NL

Objectives: Assessment of different diagnostic categories in patients presenting with unexplained chronic fatigue for more than 6 months referred to a tertiary care referral centre with a presumptive diagnosis of chronic fatigue syndrome CFS.

Methods: Patients referred for chronic unexplained fatigue were invited to systematically enter an integrated path of care, including internal medicine assessment, psychodiagnostic screening, physiotherapeutic assessment and polysomnography (PSG) + multiple sleep latency test. Final diagnosis resulted from a multidisciplinary team discussion. Fukuda criteria were used for the diagnosis of CFS, DSM-IV-TR criteria for psychiatric disorders, ICSD criteria for sleep disorders.

Results: Out of 378 patients referred during the study period, 298 (78.8%) were included in the study after informed consent [84.9% female; mean age 38.8 years (SD ± 10.3; range 18–63)].

Only a quarter of the patients (n = 77; 25.8%) had a final diagnosis of pure CFS, while in 15.4% a validated diagnosis of CFS was associated with either a primary sleep disorder or psychiatric comorbidity, which did not invalidate the diagnosis of CFS. Fifty-two patients (17.4%) had a single diagnosis of a psychiatric disorder, 28 patients (9.4%) a primary sleep disorder, 50 patients (16.8%) a combination of both. Burn-out or surmenage was diagnosed in 16 patients (5.3%), from which seven also had a sleep disorder. Only seven patients (2.4%) had a diagnosis of a classic internal pathology. In the total sample, a psychiatric disorder (primary or as a comorbidity) was diagnosed in 117 patients (39.3%) (24.2% Axis I diagnosis, 4.7% Axis II diagnosis, 10.4% combination of both). A sleep disorder was found in 41.3% (n = 123) of the sample. The distribution of primary sleep disorders included psychophysiologic insomnia (36.6%), periodic limb movement disorders (31.7%) and obstructive sleep apnea syndrome (23.6%). In 90.7% of the other patients, PSG showed aspecific abnormalities.

Conclusions: A wide range of different diagnostic categories was found in patients referred to a tertiary care centre for otherwise unexplained chronic fatigue with a working hypothesis of CFS. Systematic PSG in this patient population revealed a high incidence of primary sleep disorders, contributing to the constellation of somatic symptoms previously labeled as CFS. This finding validates systematic PSG screening.

O306

Health, social and economic consequences of sleep-disordered breathing: a controlled national study evaluating the societal effect on patients and their partners

P. JENNUM[1], R. IBSEN[1] and J. KJELLBERG[2]
[1]Danish Center for Sleep Medicine, Glostrup, DK, [2]Danish Institute for Health Services Research, Copenhagen, DK

Objectives: The objective direct and indirect costs of obstructive sleep apnea (OSA) and obesity hypoventilation syndrome (OHS) on patients and their partners are incompletely described.

Methods: Using data from the Danish National Patient Registry (1998–2010), 30278 OSA and 1562 OHS patients and their partners were identified. Four matched citizens based on age, gender and social status matched served as controls.

Direct costs were extracted from the Danish Ministry of Health, Danish Medicines Agency and National Health Security, and indirect costs from the Coherent Social Statistics.

Results: 66.2%/63.4% of all OSA/OHS patients was co-living versus 65.4%/65.6% of controls. OSA/OHS showed higher rates of health-related primary and secondary care, medication, unemployment, and other socioeconomic costs. The income level of OSA/OHS patients were lower. The annual mean excess total direct and indirect health-related cost for each patient was €2821 before and €5060 (P < 0.001) after an OSA diagnosis and €10463 before and €15001 after an OHS diagnose.

Partner's total health expenses and the public transfer income were higher, whereas the employment rate and income level were lower than controls. The annual mean excess total cost for each partner was €2639 before diagnosis and €3058 (P < 0.001) after the pts OSA diagnosis, €3523 before and €4068 (P < 0.001) after the pts OHS diagnose. These effects were present 11 years prior to an OSA/OHS diagnose in patients and partners, and increased with disease advancement.

Conclusion: OSA and especially OHS are associated with a major health and social effect affected employment and income level affecting the patients and partners.

O307

Effects of a lifestyle intervention in obese obstructive sleep apnoea patients treated with continuous positive airway pressure

J. MOSS[1], G. A. TEW[1], R. J. COPELAND[1], J. M. SAXTON[2], E. M. WINTER[1] and S. M. BIANCHI[3]
[1]Sheffield Hallam University, Sheffield, UK, [2]University of East Anglia, Norwich, UK, [3]Northern General Hospital, Sheffield, UK

Objectives: Continuous positive airway pressure (CPAP) is the primary treatment for obstructive sleep apnoea (OSA) and lifestyle changes are recommended. This study assessed responses to an intervention that comprised exercise, dietary advice and behaviour change counselling. We hypothesised that the intervention would have a positive effect on anthropometry, functional capacity, cardiovascular risk and quality of life that would be maintained after 3 months of independence.

Methods: With local research ethics committee approval 60 CPAP-compliant OSA patients were recruited from local sleep clinics and randomised into either an intervention (n = 30) or control group

($n = 30$). Assessments occurred at weeks 0, 13 and 26. The intervention involved supervised exercise sessions, dietary advice and behaviour change counselling delivered between weeks 0 and 13. Exercise sessions comprised 40 min of aerobic exercise and 15 min of conditioning and flexibility exercises. The effectiveness of the intervention was determined by assessing changes in body mass/composition, incremental shuttle walk distance (ISWD), cardiovascular risk, and health-related quality of life between weeks 0, 13 and 26 using a mixed-design factorial ANOVA and 95% confidence intervals (CIs) of the net change in groups over time. Data were attributed a qualitative inference depending on the proportion of the change exceeding the minimal clinically important difference (defined as one third of the pooled standard deviation at baseline).

Results: At 13 weeks, the intervention group improved body mass (-1.7 [-0.7, -2.8] kg; $P = 0.001$) and body fat percentage (-1.1 [-0.2, -2.0]%; $P = 0.001$) relative to the control group, although CIs between groups over time indicated changes were not clinically important. Changes in resting heart rate (-6 [-9, -2] beats/min; $P = 0.002$) and ISWD (+91 [52, 130] m; $P < 0.001$) were possibly beneficial. There were no changes in cardiovascular risk. At 26 weeks, changes in resting heart rate were likely trivial (-3 [-8, 1] beats/min; $P = 0.250$) and ISWD was probably beneficial (+110 [71, 149] m; $P < 0.001$).

Conclusion: Our lifestyle intervention improved several outcome measures, however most improvements were deemed clinically trivial. ISWD improved over the course of the intervention, and was maintained at 26 weeks. These data suggest behaviour change towards exercise has occurred and such programmes should play a role in the holistic management of OSA patients.

O308

Preliminary findings for SDB in the Penn State child cohort: relative impact of weight gain/loss

E. BIXLER, A. VGONTZAS, D. LIAO, M. SHAFFER, S. CALHOUN, J. FERNANDEZ-MENDOZA and A. VELA-BUENO

Penn State University, Hershey, US

Objectives: The epidemiology of sleep-disordered breathing (SDB) in children from general population samples has received little attention, with the incidence of SDB in adolescent children even less well studied.

Methods: The Penn State Child Cohort (PSCC) is a representative general population sample of 700 children aged 5–12 years. Our preliminary results are based on an average 8 year follow up of the initial 199 prospective subjects (~28%) from this ongoing cohort study. A forward stepwise conditional logistic regression was used to assess the association between potential risk factors and SDB.

Results: This sample had a mean age of 17.2 ± 0.1 years, an average BMI percentile of 64.6 ± 2.0 and 57.3% were boys. At baseline 1.5% of this subsample had SDB and surprisingly, there was no persistence of SDB. Incident SDB was observed to be 11.1%. The average AHI in those with incident SDB was 13.7 with a maximum of 92.4. Incident SDB was similar for girls (10.6%) and boys (11.4%). Those with SDB were older than those without (18.3 versus 17.0 years, $P = 0.005$) and girls with SDB were older than boys with SDB (19.3 versus 17.5 years, $P = 0.003$). Those with SDB were more obese (BMI percentile = 78.4 versus 62.9, $P = 0.017$), had a greater change in BMI percentile (9.5 versus 0.02, $P = 0.017$) and had an increased waist circumference (91.2 versus 80.2 cm, $P < 0.001$.). In contrast, those that had SDB at baseline but not at followup had a loss in their BMI percentile (-3.2 versus 1.1, $P = 0.109$). Only two variables were included in the final equation of the logistic regression these were, in the order of entry, waist circumference (OR = 1.05 (1.02, 1.08) $P = 0.003$) and age (OR = 1.3 (1.0, 1.7) $P = 0.021$).

Conclusion: In this preliminary sample of an 8 year followup of children from The Penn State Child Cohort, the incidence of SDB is high in adolescents, whereas childhood SDB does not appear to persist into adolescence. Further, the results indicate that robust risk factors for SDB in adolescents are waist circumference and increasing age. Obesity and weight loss appear to be the primary factors associated with the presence or remission of SDB in adolescent children.

Support: NIH: R01 HL603772, R01 HL97165, UL1 RR033184, C06 RR16499.

O309

Sustained improvement in mild obstructive sleep apnoea by lifestyle intervention – post-interventional follow-up of a randomised, controlled trial (5-year follow-up upcoming)

H. TUOMILEHTO, M. UUSITUPA and J. SEPPÄ on behalf of the Kuopio Sleep Apnoea Group

Objectives: Obesity is the most important risk factor for obstructive sleep apnoea (OSA). In the first randomised study conducted, we demonstrated that lifestyle intervention lasting 1 year including an early weight reduction program is a feasible and effective treatment for the vast majority of overweight patients with OSA. Most importantly, although these data are encouraging and weight loss is recommended in all clinical guidelines, thus far it is not known, whether these favourable changes sustain after discontinuation of the intervention. The aim of the study was to assess long-term efficacy of lifestyle intervention in randomised, controlled 2-year post-intervention follow-up in patients with mild OSA.

Methods: Eighty-one consec, Coimbra, PT utive overweight (BMI 28–40 kg/m^2) adult patients with mild OSA were recruited. The intervention group completed the 1-year lifestyle modification including an early 12-week weight reduction program with very low calorie diet. The control group received routine lifestyle counselling. During the second year no intervention was offered. Change in AHI was the main objective outcome variable and change symptoms were used as subjective measurement.

Results: Seventy-one patients completed the 2-year follow-up. The changes in lifestyles and weight reduction were found to result in sustained improvements in findings and symptoms of OSA even after the discontinuation of active counselling. The mean amount of weight loss in the intervention group was -7.3 kg (SD 6.5). After 2 years, the reduction of AHI was significantly more in the intervention group ($P = 0.049$). The intervention lowered risk of OSA at follow-up. The adjusted odds ratio for OSA was 0.35 (95% confidence interval 0.12–0.97, $P = 0.045$).

Conclusions: Our 2-year follow-up study demonstrates that favourable changes achieved by 1-year lifestyle intervention with weight reduction sustain in overweight patients with mild OSA after the termination of supervised lifestyle counselling. Weight reduction also results in an improvement of obesity related risk factors for cardiovascular diseases. Most importantly, at the time of the congress, we have the results after 5-year follow-up ready to be presented.

O310

Examining the mechanism of action of a new device using oral pressure therapy for the treatment of obstructive sleep apnoea

R. SCHWAB[1], C. KIM[1], L. SIEGEL[2], J. BLACK[3], M. FARID-MOAYER[4], J. PODMORE[2] and M. VASKA[2]

[1]University of Pennsylvania, Philadelphia, US, [2]ApniCure, Redwood City, CA, US, [3]Stanford University, Stanford, CA, US, [4]Peninsula Sleep Center, Burlingame, US

Objectives: A novel oral pressure therapy (OPT) system (Winx (TM), ApniCure, Inc.) has been shown to be an effective treatment for patients with obstructive sleep apnoea (OSA). This new therapy provides negative pressure confined to the oral cavity presumably increasing the size of the retropalatal airway by drawing the soft palate and tongue forward. We hypothesized that the OPT system would: (i) increase the mean, minimum and maximum airway area in the retropalatal region; (ii) increase both the retropalatal anterior-posterior and lateral airway dimensions, and (iii) move the centroid of the soft palate and anterior segment of the tongue anteriorly and superiorly.

Methods: Six adults [67% men, mean BMI 31.1 ± 3.3 (SD) kg/m^2, age 64.0 ± 6.6 years] with OSA (4 severe, 1 moderate, 1 mild) underwent upper airway MRI and polysomnography with and without the activated OPT device. Amira 4.2.1 software was used in the MRI analysis of the upper airway, surrounding soft tissues, and centroid. Within subject, differences between baseline and treatment were examined using a Wilcoxon sign-rank test.

Results: The baseline AHI (39.8 ± 22.5 events/h) was significantly reduced (AHI 6.3 ± 4.2 events/h) by OPT treatment. Application of the OPT system on patients with OSA led to the following changes in the retropalatal region: (i) the average airway area per slice increased by 65.0 ± 54.2% (P = 0.09); (ii) the maximum cross-sectional area increased by 101.0 ± 141.0% (P = 0.18); (iii) the dimensions of the minimum airway increased by 4.60 ± 7.73% (P = 0.34) laterally and by 52.8 ± 99.4% (P = 0.44) in the anterior-posterior direction; (iv) the dimensions of the maximum airway increased by 13.4 ± 8.9% (P = 0.06) laterally and by 16.5 ± 18.1% (P = 0.10) in the anterior-posterior direction; (v) the centroid of the soft palate moved anteriorly 14.1 ± 11.8 mm (P = 0.02) and superiorly 17.4 ± 11.2 mm (P = 0.004); and 6) the centroid of the anterior segment of the tongue moved forward, towards the teeth, 5.57 ± 5.73 mm (P = 0.05).

Conclusions: Oral pressure therapy, a novel treatment for sleep apnea, increases the size of the retropalatal airway by moving the soft palate and anterior segment of the tongue forward, towards the teeth. OPT increases airway caliber in both the anterior-posterior and lateral dimensions. Our data suggest that patients manifesting an enlarged soft palate or exhibiting retropalatal airway collapse would be ideal candidates for this implementation of oral pressure therapy.

Support: ApniCure, Inc.

O311

What role does the magnitude of the ventilatory response to arousal play in predisposing to upper airway collapse on the return to sleep?

A. S. JORDAN[1], J. M. CORI[1], C. L. NICHOLAS[1], F. J. ODON-OGHUE[2], P. CATCHESIDE[3], D. J. ECKERT[4], D. MCEVOY[3] and J. A. TRINDER[1]

[1]University of Melbourne, Parkville, AU, [2]Institute for Breathing and Sleep, Heidelberg, AU, [3]Adelaide Institute for Sleep Health, Daw Park, AU, [4]Neuroscience Research Australia, Randwick, AU

Arousals from sleep commonly occur at the end of respiratory events in obstructive sleep apnea (OSA). Arousals could perpetuate cyclical breathing via hyperventilation, hypocapnia and dilator muscle hypotonia leading to airway collapse on the return to sleep. However, several studies have not shown reduced dilator muscle activity following the return to sleep after induced arousal. The magnitude of hyperventilation at arousal varies between individuals and it is possible the proposed sequence of events only occur in individuals with large responses.

Objectives: (i) to assess the variability of the magnitude of the ventilatory response to arousal (VRA) and (ii) to compare dilator muscle activity changes following arousal between individuals with large and small ventilatory responses to arousal.

Methods: Thirty-eight healthy individuals have been recruited. Subjects were instrumented with: EEG, EOG and chin EMG, a nasal mask and pneumotachograph, an epiglottic pressure catheter and two intramuscular genioglossus electrodes. CO_2 was sampled from the mask and the end tidal value (PETCO2) determined. Once more than 2 min of stable supine N2-N4 sleep was achieved, auditory tones (40–100dB, 0.5 s, 1000 Hz) were played to induce brief 3–15 s arousals.

Results: Adequate data were obtained in 21 subjects to date. The peak VRA ranged from 7% to 58% above the pre-arousal level of ventilation (median 32%). Physiologic data were compared between four subjects with large VRA (>50% increase in ventilation) and five subjects with small VRA (<25% increase in ventilation). The mean (SEM) duration of arousal did not differ between large and small VRA groups [6.3 (0.9) and 7.4 (0.9) s respectively]. By design, post arousal ventilation was significantly different between groups [9.4 (0.8) versus 6.6 (0.3) L/min], but no other variables differed significantly. However, PETCO2 and peak inspiratory genioglossus muscle activity tended to show a greater reduction on the 2nd and 3rd breaths following arousal in the large VRA group (Breath 2: -1.1 (0.3) versus -0.1 (0.5) mmHg and 111 (7) versus 131 (11)% baseline activity respectively), although genioglossus activity was not reduced below baseline following the return to sleep in either group.

Conclusions: More data are required before firm conclusions can be made. However, if the results persist in a larger population they would suggest that reduced activity of the genioglossus muscle does not occur on the return to sleep following arousal, even in individuals with a large VRA.

O312

Impact of long-term CPAP use on co-morbidities in the obstructive sleep apnoea/hypopnoea syndrome: a 30-year prospective cohort study

M. VENNELLE[1], N. J. DOUGLAS[1] and R. L. RIHA[2]

[1]University of Edinburgh, Edinburgh, UK, [2]NHS Lothian, Edinburgh, UK

Previously, we reported on 1211 patients on long-term CPAP, in particular determinants of use; apnoea/hypopnoea index (AHI), and Epworth Sleepiness Score (ESS) being the strongest predictors.(1)

Aim: To assess the impact of CPAP on morbidity and mortality in OSAHS followed prospectively over 30 years.

Method: A prospective cohort study of 6472 patients referred for sleep studies at a tertiary sleep centre from 1982 to 2003. Patients were sent a questionnaire to update their health status, CPAP use and other demographic and medical data, including medication use. Minimum follow-up time was 7 years. Standard statistical analysis was undertaken using SPSS v.17 (Chicago, IL).

Results: Of 6472 patients referred to the centre, 3567 (55%) had OSAHS as their primary sleep diagnosis. At time of analysis (March 2012), 906 (26%) had died. Thousand six hundred and thirty-seven patients returned the questionnaire, with 515 being valid for full analysis: 406 men, 109 women.

Age ranged from 33 to 89 years (mean 64 SD 11 years). Two hundred and eighty-nine continued to use CPAP; length of time on CPAP was 13 SD 3 years with an average compliance of 6sd2 h/night. Compared to those who had ceased CPAP, continued users had a higher AHI at baseline (46sd32 versus 27sd16; $P < 0.0001$), higher ESS (13sd5 versus 12sd5; $P = 0.017$), higher BMI (32sd6 versus 28sd5; $P < 0.0001$) with age at commencement being similar (50sd9 versus 51sd11; $P = 0.33$). There was no significant difference in smoking history between those who stopped CPAP and those continuing ($P = 0.42$), nor was there any reported change in weight, either up or down ($P = 0.8$). Cardiovascular disease at baseline was present in those continuing on CPAP to a significantly higher level compared to those who had ceased CPAP ($P = 0.02$). Those still on CPAP had a higher reported rate of type II diabetes (74 versus 8; $P = 0.001$), and hypertension (95 versus 15; $P = 0.015$). There was no significant difference in terms of other cardiovascular or cerebrovascular morbidity.

Conclusion: In a sub-cohort of over 500 patients followed up prospectively, overt cardiovascular disease was more prevalent in those who continued CPAP use over the long-term. This may be a reflection of underlying differences between the two groups intrinsically, or sleep-disordered breathing as an incidental finding that was less likely to require treatment in the first place. The analysis is ongoing.

Refererece:

1. McArdle N. et al. AJRCCM 1999;159:1108–1114.

O313

Nocturnal gastroesophageal reflux, respiratory symptoms and obstructive sleep apnoea, before and after CPAP treatment: the Icelandic Sleep Apnea Cohort study

T. GISLASON[1], E. S. ARNARDOTTIR[1], C. JANSSON[2], B. BENEDIKTSDOTTIR[1], S. JULIUSSON[1], Ö. I. EMILSSON[1] and A. PACK[3]
[1]Landspitali, Reykjavik, IS, [2]Akademiska, Uppsala, SE, [3]Center for Sleep, Philadelphia, US

Objectives: To estimate the prevalence of reported nocturnal gastroesophageal reflux (nGER) in obstructive sleep apnea (OSA) subjects compared to the general population. Also to evaluate what characterizes those who report nGER and whether it changes in OSA patients with continuous positive airway pressure (CPAP) treatment.

Methods: Eight hundred and twenty-two newly diagnosed subjects with OSA [The Icelandic Sleep Apnea Cohort (ISAC)], referred for CPAP treatment. Of those, 741 subjects have had a 2 year follow-up visit with objective CPAP compliance data collected ($n = 475$ CPAP users, $n = 266$ nonusers). The control group consisted of 939 subjects randomly selected from the general population (81% response rate). Both groups answered the same questionnaires, including reporting of nGER, sleep, respiratory symptoms, general health and quality of life measured by SF-12. A sleep study was performed in ISAC participants only.

Results: Altogether 18.6% of OSA females and 13.6% of males ($P = 0.07$) compared to 7.5% of controls ($P < 0.001$) reported nGER (≥1× a week). Wheeze during the last 12 months was more common among OSA subjects with nGER compared to those without nGER (42.5% versus 29.3%, $P = 0.005$). Bringing up phlegm in the morning ≥3 months the last year was also associated with reporting nGER (35.7% versus 24.8%, $P = 0.02$). Among OSA patients prevalence of nGER was not related to smoking, obesity, general health (hypertension, diabetes) or OSA severity. SF-12 showed that among those with nGER both physical component scores (40.7 ± 0.9 versus 37.4 ± 0.3, $P = 0.003$) and mental scores (49.0 ± 0.8 versus 44.1 ± 11.1, $P < 0.0001$) were significantly lower. At 2 year follow-up nGER was only reported by 6.2% of the 618 subjects who have been followed and was lowest (3.8%) among full CPAP users ($P < 0.0001$).

Conclusion: nGER is a common clinical symptom of OSA and often related to respiratory symptoms. Prevalence of nGER decreases with CPAP treatment in a majority of OSA patients.

Support: NIH grants HL72067 and HL94307, the Eimskip Fund of the University of Iceland and the Landspitali University Hospital Research Fund.

O314

Residual sleepiness in obstructive sleep apnoea patients on CPAP: not only a symptom but rather a true syndrome?

M. GASA, R. TAMISIER, M. SAPENE, F. MARTIN, B. STACH, Y. GRILLET, P. LÉVY and J.-L. PÉPIN on behalf of the scientific council of The Sleep registry - French Federation of Pneumology

Background: Hypoxic brain damage might explain persistent sleepiness in some CPAP compliant obstructive sleep apnoea (OSA). Since residual sleepiness (RES) on CPAP remains not fully understood, wake promoting dugs in RES are no longer allowed by the European Medicines Agency.

Aim: To describe RES phenotype in a large prospective sample of OSA patients.

Methods: RES was defined by an Epworth Sleepiness Scale (ESS) ≥11. One thousand forty-seven patients from the French National sleep registry (www.osfp.fr) attending follow-up CPAP visit were eligible. Patients using CPAP <3 h ($n = 275$), with residual apnea + hypopnea index >15/h ($n = 31$) and major depression were excluded ($n = 150$).

Results: RES prevalence in CPAP treated OSA was 13% and significantly decreased with CPAP use (9% in ≥6 h/night users, $P < 0.005$). Although patients with RES at the time of diagnosis had a worse subjective appreciation of their disease (general health scale, ESS and fatigue score) and complained more frequently from CPAP side effects, RES prevalence was lower in severe OSA than in mild-moderate OSA (11% when AHI >30/h versus 18% when AHI between 15 and 30, $P < 0.005$). Moreover, there was no relationship between RES and BMI, cardiovascular co-morbidities or diabetes. CPAP did improved symptoms but to a lower extent (Fatigue scale: -5.2 versus -2.7 in RES- and RES+ patients respectively, $P < 0.001$).

Conclusions: The CPAP adherence threshold associated with the lower RES prevalence was 6 h/night. Hypoxic insult is probably not the explanation for RES since OSA severity does not seem to be critical. Residual symptoms are not limited to sleepiness and this true 'CPAP resistant syndrome' may justify treatment by wake promoting drugs.

Oral Session 13 – Insomnia: Assessment and Treatment

O315

Cognitive-behavioural self-help treatment for insomnia is effective regardless of baseline depression score

J. LANCEE[1], J. VAN DEN BOUT[1], A. VAN STRATEN[2] and V. SPOORMAKER[3]
[1]Utrecht University, Utrecht, NL, [2]VU University, Amsterdam, NL, [3]Max Planck Institute of Psychiatry, Munich, DE

Insomnia is a prevalent and distressing sleep disorder that can be effectively treated with cognitive-behavioral therapy (CBT-I). Randomized controlled trials have shown efficacy of self-help CBT-I. It is unclear whether excluding depressive patients may have boosted treatment effects. To examine whether CBT-I is also effective for subjects with high depression levels, we administered self-help CBT-I to insomniacs with low, mild, and high depression levels. Based on the validated CES-D, the sample (N = 479) was divided into three groups: low depression scores (n = 198); mild depression scores (n = 182); high depression scores (n = 99). Intention-to-treat analyses showed that self-help CBT-I had an equal effect for all groups on insomnia ratings and sleep measures and these effects where comparable to previous effects of self-help CBT-I. The only difference among groups was that the high/mild depression groups improved more on depression and anxiety scores than the low depression group. In the mild and high depression group, about 60% of the participants progressed to a more favorable cutoff score. In the low/mild depression groups 10% deteriorated a cutoff score. This study showed that CBT-I is effective regardless of baseline depression levels. These data may help us understand the relationship between insomnia and depression and they indicate that self-help CBT-I is a promising addition to regular depression treatment.

O316

Characteristics of treatment responders and analysis of treatment effects on secondary measures following cognitive behaviour therapy for insomnia

K. BOTHELIUS[1], K. KYHLE[2], C. ESPIE[3] and J.-E. BROMAN[2]
[1]Uppsala University Hospital, Uppsala, SE, [2]University of Uppsala, Uppsala, SE, [3]University of Glasgow Sleep Center, Glasgow, UK

Objectives: (i) To identify patients likely to benefit from cognitive behavior therapy for insomnia (CBT-I), (ii) to identify the number needed to treat to get a clinical meaningful effect, and [3] to investigate the effects of improved sleep on secondary daytime measures.

Methods: In a randomized controlled study of the clinical effectiveness of protocol-driven CBT-I, delivered by primary care personnel (nurses and social workers) in general medical practice to unselected patients, 66 subjects entered either immediate or delayed treatment.

Results: Number needed to treat was 2.4, with an absolute risk reduction of 0.41. There was a significant association between pre-treatment total sleep time (TST) and treatment response ($\chi^2(1) = 9.14$, $P = 0.003$). The odds of being a responder were five times higher for people sleeping more than 350 min per night before treatment.

Responders did not differ from non-responders on age, number of times they had visited a physician during the last 6 month, mental distress, fatigue, sleepiness, or any other sleep related measures at pre-treatment assessment.

The responder group differed significantly from the non-responders on the Insomnia Severity Index (ISI) directly after treatment ($P \leq 0.001$, d = 1.99) and at follow-up assessment after 1 year ($P = 0.001$, d = 0.79–1.28). There were also significant differences on the sleep-onset latency (SOL), wake time after sleep onset (WASO), and sleep quality (SQ) (all $P \leq 0.001$) directly after treatment, and at follow-up a difference in WASO ($P = 0.014$) and SQ ($P = 0.023$) but not in SOL.

Responders reported less daytime sleepiness after treatment ($P = 0.007$, $d = 0.36$), better mental but not physical health ($P = 0.013$, d = 0.49). There was no difference between the two groups at follow-up. There were no significant differences in fatigue or mental distress

Conclusion: From this study, it is not easy to identify who will have a greater chance to gain from treatment, but having an initially longer total sleep time seems to be beneficial.

Two of every five treated subjects exhibited clinically relevant effects on sleep related measures and this improvement was associated with less daytime sleepiness, and better general mental health. These effect sizes on secondary outcomes were however small and there was no difference between groups after 1 year, even though the differences in the (primary) sleep measures persisted. Changes in sleep did not affect fatigue and effects on mood are somewhat ambiguous.

O317

Instrumental sensorimotor-rhythm conditioning: a non-pharmacological treatment alternative for insomnia?

M. SCHABUS[1], H. GRIESSENBERGER[1], D. P. J. HEIB[1], J. LECHINGER[1], A. PAWLIZKI[2], A. B. KUNZ[3] and K. HOEDLMOSER[1]
[1]University of Salzburg, Salzburg, AT, [2]University of Munich, Munich, DE, [3]University Salzburg, Salzburg, AT

Introduction: EEG recordings over the sensorimotor cortex show a prominent oscillatory pattern in a frequency range between 12 and 15 Hz (sensorimotor rhythm, SMR) under quiet but alert wakefulness. This frequency range is also known to be abundant during light non-rapid eye movement sleep, and is overlapping with the sleep spindle frequency band. Some earlier findings indicated that instrumental conditioning of SMR during wakefulness can influence subsequent sleep and cognitive performance. In the present study we tested whether such training can serve as a non-pharmacological treatment alternative for people suffering from primary insomnia.

Methods: Twenty-four subjects (M = 34.8) with clinical symptoms of primary insomnia (cf. Edinger et al., 2004) were tested in a counterbalanced within-subjects design (19 lab visits over the course of 3–6 weeks). Each patient participated in a SMR- as well as a sham- conditioning training block. Polysomnographic sleep recordings were scheduled before and after the training blocks.

Results: Analysis confirms a significant increase of 12–15 Hz activity over the course of ten SMR training sessions. In addition the number of awakenings decreased and slow-wave sleep increased after SMR conditioning only. Likewise sleep onset latency showed a trend towards a reduction following SMR training. Subjectively sleep quality (PSQI) as well as life quality (WHO-QOL) improved over the whole study period. Last but not least, SMR-training enhancement was also found to be associated with overnight

memory consolidation and (fast) NREM sleep spindle change indicating a beneficial cognitive effect of the SMR training protocol.
Conclusion: Current results indicate that besides healthy individuals also people suffering from primary insomnia can benefit subjectively as well as objectively from SMR conditioning.

O318

An ecological momentary assessment of daytime symptoms in insomnia during brief sleep restriction therapy

C. B. MILLER[1], S. D. KYLE[2] and C. ESPIE[2]
[1]University of Sydney, Sydney, AU, [2]University of Glasgow, Glasgow, UK

Objectives: Sleep Restriction Therapy (SRT) is a highly utilised and effective Cognitive Behavioural Therapy for Insomnia. However, little is known about how and when this intervention may work. In this study, the Daytime Insomnia Symptom Scale (DISS) was employed within an Ecological Momentary Assessment (EMA) technique to examine the daytime impact before (1 week) and during SRT (3 weeks) at four time points per day.
Method: Nine participants (six females; mean age = 46.4) highly screened for Psychophysiological Insomnia completed paper-based versions of the DISS at Risetime, Noon, 18:00, and Bedtime, for 1 week before the intervention (Baseline) and for 3 weeks during the intervention (Weeks: 1, 2, and 3).
Results: Insomnia Severity Index scores were found to significantly decrease pre-to-post treatment [M = 18 (5) versus 7 (5), $P < 0.05$]. The completion rate for the DISS was high at 94.62%. Four previously validated factors from the DISS were examined; Alert Cognition, Positive Mood, Negative Mood, and Sleepiness/Fatigue. A mixed model analysis was implemented for each of the factors (fixed effects for week and time of day, and random effects for between subject variation).
Alert Cognition initially decreased ($P < 0.05$) compared to Baseline at Week 1, subsequently returning to Baseline levels by Week 3 of SRT. Within the Day Time points; Alert Cognition reduced at Bedtime and increased at Risetime by Week 3 compared to Baseline.
Negative Mood remained stable across the weeks.
Positive Mood initially decreased compared to Baseline at Week 1 ($P < 0.05$). At Week 2, scores returned to Baseline levels, and by Week 3 scores generally increased compared to Baseline ($P = 0.06$).
Sleepiness/Fatigue initially increased at Week 1 compared to Baseline ($P < 0.001$). Scores then slightly reduced at Week 2 compared to Baseline ($P = 0.143$). At Week 3 scores significantly decreased compared to Baseline ($P < 0.001$).
Conclusion: This study represents the first attempt to profile the daytime experience of insomnia during SRT, via EMA methods. Changes at Risetime and Bedtime for Alert Cognition and Sleepiness/Fatigue seem like candidates for further study as mechanisms of action in SRT treatment response; potentially reflecting changes to the input and output of the sleep homeostat. This study demonstrates the value of assessing symptoms at multiple time-points throughout insomnia treatment.

O319

Mindfulness-based therapy for insomnia in an Australian population

A. PETERS[1], M. JUNGE[1], D. CUNNINGTON[1], J. ONG[2] and K. GREENWOOD[3]
[1]Melbourne Sleep Disorders Centre, Melbourne, AU, [2]Rush Medical Center, Chicago, IL, US, [3]Edith Cowan University, Perth, AU

Objective: This study investigated group delivery of a mindfulness-based intervention for primary insomnia in an Australian population. Mindfulness Based Therapy for Insomnia (MBT-I) offers an alternative approach to the current gold standard, non-pharmacological approach to insomnia, CBT-I, with a focus on reducing sleep-related arousal. Findings have indicated reductions in several subjective sleep measures following MBT-I treatment (Ong, Shapiro, & Manber, 2008). This study aimed to investigate the outcome of MBT-I in an Australian population recruited from a sleep clinic to examine the generalizability in a diverse sample. Participants: 30 participants, consisting of 21 females (M age = 50, range = 26–72) and nine males (M age = 45, range 34–59) who met criteria for primary insomnia.
Methods: Treatment consisted of six sessions of MBT-I (Ong, Shapiro, & Manber, 2008) delivered in groups of 7–8 with each session lasting 2 h in duration. The primary outcome measure was the Insomnia Severity Index (ISI) and secondary the Pittsburg Sleep Quality Index (PSQI). Outcome measures were recorded at four time-points (screening, baseline, post-treatment and 3 month follow-up).
Results: The average severity of insomnia as measured by the ISI reduced significantly from a moderate level of insomnia (M = 18.74) to sub-clinical insomnia (M = 12.79, $P < 0.01$) indicating that on average, participants no longer met the criteria for insomnia following treatment. The Pittsburgh Sleep Quality Index (PSQI) overall score reduced significantly (M = 13.1 to M = 9.2, $P < 0.01$) reflecting an increase in sleep quality following treatment. All 7 PSQI component scores reduced significantly. The largest change was the component score assessing sleep efficiency (the proportion of average sleep compared to time in bed), which increased from 72% to 83% ($P < 0.01$) following treatment.
Conclusion: Analysis of data collected in response to a group treatment of MBT-I for insomnia delivered over 6 weeks revealed significant reductions in insomnia symptoms, and improvements in sleep quality and sleep efficiency. This suggests that MBT-I can be delivered in a sleep clinic setting with indications of effectiveness.

O320

Daytime driving performance and cognitive evaluation of untreated insomniac patients

J. PERRIER[1], F. BERTRAN[2], C. COUQUE[2], P. DENISE[1] and M.-L. BOCCA[1]
[1]INSERM U 1075 COMETE, Caen, FR, [2]CHU de Caen, Caen, FR

Sleepiness is one of the most causes of road accidents and may be linked to sleep disorders, circadian problem or hypnotic consumption. Among sleep disorders, insomnia is one of the most prevalent sleep complain as it reaches about 30% of general population. Although epidemiological studies have showed that sleepiness increases the risk of driving accidents, the effects of insomnia on driving performance are unknown. The purpose of this work was thus to assess the driving performance of untreated insomniac patients.
To date, twenty insomniacs and 15 good sleepers matched in age and sex were recruited. Monotonous driving performance was evaluated with a mono-screen driving simulator. Subjects had to

ensure lateral stability of the vehicle and respect driving at 110 km/h. The driving task was followed by a Psychomotor Vigilance Test (PVT). In addition, participants completed subjective driving performance and Karolinska Sleepiness scales. The main driving parameter was the standard deviation of the lateral position (SDLP), which is an index of driving safety. The standard deviation of speed (SDS) and the number of road exits were also calculated. The performance at the PVT test was analyzed with the mean reaction time and the percentage of lapses.

Our results revealed that untreated insomnia patients drive worse than good sleepers, with an increased SDLP ($P < 0.005$) and the number of road exits ($P < 0.008$). However, there is no difference in SDS between insomniacs and good sleepers ($P = 0.25$). Subjective scales confirmed behavioral performance decrements because insomniac patients felt driving worse ($P < 0.05$) and felt drowsier ($P < 0.01$) than did good sleepers. No significant difference were found for both the% of lapses and the mean RT of the PVT ($P = 0.11$ for both).

These results revealed that insomnia lead to impaired driving performance in comparison to good sleepers. Interestingly, the patients were aware having an impaired driving. We can hypothesize that by increasing both groups of participants, impaired performance at the PVT should be statistically revealed. All these results will be interpreted in light of polysomnography and actimetry recordings.

O321

Eveningness, knowledge of healthy sleep behaviours and chronic insomnia

B. I. VOINESCU and A. SZENTAGOTAI
Babes-Bolyai University, Cluj-Napoca, RO

Introduction: Poor sleep hygiene is a risk factor for poor sleep quality and chronic insomnia and its improvement is one of the main components in the cognitive-behavioural therapy for insomnia. Also, eveningness has been reported to be more frequently found in insomnia patients.

Objectives: To determine the chronotype and to measure the knowledge on healthy/unhealthy sleep behaviours and the self-reported sleep quality in individuals suspected of chronic insomnia compared to those that report a healthy sleep.

Methods: Three hundred nine adults aged 18–83 (mean age 32.0, standard deviation 12.9), most of them women ($N = 236$, 77%), were recruited via online adverts and invited to fill in a battery of tests consisting in the Romanian translations of the Sleep Condition Indicator (SCI), Sleep Disorders Questionnaire (SDQ), Sleep Beliefs Scale (SBS) and Composite Scale of Morningness (CSM). The survey was hosted on Surveygizmo.

Results: Based on SDQ responses, we identified $N = 124$ individuals complaining of chronic insomnia symptoms, of which $N = 50$ were highly likely to meet the criteria for insomnia disorder. Evening types were significantly more frequent amongst this latter group ($P < 0.001$) compared to those without sleep problems (34% versus 5%). Also, evening types reported significantly poorer sleep (18.2 ± 7.6) compared to both morning (10.4 ± 6.9, $P < 0.001$) and intermediate types (11.3 ± 6.7, $P < 0.001$). Those complaining of chronic insomnia showed better sleep knowledge as they scored significantly higher ($P = 0.02$) in SBS (13.3 ± 2.9) compared to those reporting sound sleep (12.4 ± 3.2). Compared to women, men revealed significantly poorer sleep knowledge, both in the whole sample (11.8 ± 3.5 versus 13.0 ± 2.8, $P = 0.003$), 'sound sleep' sample (11.4 ± 3.5 versus 12.8 ± 3.0, $P = 0.014$) and insomnia one (12.4 ± 3.4 versus 13.5 ± 2.6, n.s.). They also failed to identify eating late ($P = 0.001$), working late ($P = 0.02$) and smoking before going to bed ($P = 0.04$) as being detractors for sleep. Quality of sleep was not associated with sleep knowledge, either in the whole sample or when divided by insomnia complaints. In men, poor sleep was linked with poor sleep knowledge ($r = 0.269$, $P = 0.02$).

Conclusions: Eveningness is significantly more prevalent amongst individuals likely to suffer from insomnia disorder. Knowledge of healthy/unhealthy sleep behaviours was rather modest in our sample, despite higher education, and was better in those reporting chronic poor sleep, as well as in women.

Support for this work was provided by the Sectorial Operational Programme for Human Resources Development 2007–2013, co-financed by the European Social Fund, POSDRU 89/1.5/S/60189 'Postdoctoral Programs for Sustainable Development in a Knowledge Based Society'.

O322

The relative importance of insomnia versus objective short sleep duration in predicting the incidence of hypertension and diabetes: a longitudinal, population-based study

A. VGONTZAS, J. FERNANDEZ-MENDOZA, I. KRITIKOU, S. CALHOUN, M. BASTA, D. LIAO and E. BIXLER
Penn State College of Medicine, Hershey, US

Objective: Cross-sectional studies have shown that objective short sleep duration and insomnia are associated with hypertension and diabetes. The aim of this study was to examine the association of insomnia and objective short sleep duration with incident hypertension and diabetes.

Methods: From a random, general population sample of 1741 adults of the Penn State Cohort, 1102 without hypertension and 1267 without diabetes were followed-up after 7.5 years. All subjects underwent 8-h polysomnography and medical and sleep history at baseline. Sleep apnea was defined as an apnea/hypopnea index ≥5. We used the median percent of sleep time to define short sleep duration (i.e., <6 h). Chronic insomnia was defined as a complaint of insomnia lasting ≥1 year. Medical and sleep history was reassessed at follow-up.

Results: Chronic insomnia (OR = 2.3; $P = 0.004$) and objective short sleep duration (OR = 1.6; $P = 0.003$) were both significantly associated with incident hypertension. There was a significant positive interaction between chronic insomnia (OR = 4.0; $P = 0.027$) with sleep duration on the incidence of hypertension. Chronic insomnia (OR = 3.9; $P = 0.002$) with short sleep duration was significantly associated with incident hypertension, whereas normal sleep with short sleep duration was not (OR = 0.9; $P = 0.556$). Objective short sleep duration was significantly associated with incident diabetes (OR = 2.4; $P = 0.001$), whereas chronic insomnia was not (OR = 1.4; $P = 0.431$). There was no significant positive interaction between chronic insomnia and objective sleep duration on the incidence of diabetes (OR = 0.4; $P = 0.254$). Normal sleep (OR = 2.2; $P = 0.010$) and chronic insomnia (OR = 3.0; $P = 0.050$) with short sleep duration were significantly associated with incident diabetes after controlling for gender, race, age, and sleep apnea.

Conclusion: Chronic insomnia with short sleep duration appears to be a stronger factor compared to objective short sleep duration in predicting incident hypertension. In contrast, objective short sleep duration appears to be a stronger factor compared to insomnia with short sleep duration in predicting diabetes. Sleep restriction and

chronic insomnia are associated with different pathophysiological abnormalities which may explain their differences in predicting hypertension versus diabetes.

O323

Insomnia in sleep apneoa patients before and after treatment with continuous positive airway pressure

E BJORNSDOTTIR[1], C. JANSON[2], J. F. SIGURDSSON[3], P. GHERMAN[4], M. PERLIS[4], E. S. ARNARDOTTIR[3], A. I. PACK[4], T. GISLASON[3] and B. BENEDIKTSDOTTIR[3]

[1]University of Iceland, Reykjavik, IS, [2]Uppsala University, Uppsala, SE, [3]National University Hospital of Iceland, Reykjavik, IS, [4]University of Pennsylvania, Philadelphia, US

Objectives: The aim of this study was to assess the changes of insomnia symptoms among patients with obstructive sleep apnea (OSA) before starting treatment with continuous positive airway pressure (CPAP) and at a 2-year follow up.

Methods: Altogether, 822 untreated OSA patients underwent a medical examination, type 3 sleep study and answered questionnaires on health and sleep before starting on CPAP treatment. The majority of the sample was men (81%) and the age range was 30.6–71.6 years with the mean age of 54.9 ± 7.6 years. Symptoms of difficulties initiating sleep (initial insomnia), difficulties maintaining sleep (middle insomnia) and early morning awakening (morning insomnia) were explored using the Basic Nordic Sleep questionnaire. Two years after treatment initiation, patients were assessed again and treatment adherence examined. Altogether, 90.1% (n = 741) of the sample finished the 2-year follow up.

Results: At baseline, the prevalence of initial insomnia was 15.6%, middle insomnia was 58.3% and morning insomnia was 27.9%. Middle insomnia improved more among patients who were adherent with CPAP treatment (follow up prevalence was 30.1% among users compared to 45.8% among non users P = 0.001). The follow up prevalence of initial insomnia was 9.3% among CPAP users compared to 16.4% among non-users but the improvement from baseline to follow up was not significantly greater among CPAP users. Morning insomnia was however more likely to improve among subjects that were not using CPAP (P = 0.05). Patients with initial and morning insomnia at baseline were less likely to be adherent with CPAP at follow up [(initial insomnia = OR 0.63 (0.42–0.95), P = 0.029, morning insomnia = OR 0.51 (0.37–0.71) P < 0.0001].

Conclusion: The prevalence of middle insomnia is high among untreated OSA patients but if patients are adherent with CPAP treatment, these symptoms generally improve. Initial and morning insomnia however, tend to persist regardless of CPAP use and have a negative effect on CPAP adherence. Therefore, additional intervention may be needed when treating patients with OSA plus either initial or morning insomnia.

O324

Efficacy and safety of suvorexant, an orexin receptor antagonist, in patients with primary insomnia: a 3-month phase 3 trial (trial #1)

K. CONNOR[1], K. BUDD[1], D. SNAVELY[1], K. LIU[1], J. HUTZELMANN[1], R. BENCA[2], A. KRYSTAL[3], T. ROTH[4], D. MICHELSON[1] and W. J. HERRING[1]

[1]Merck, Whitehouse Station, US, [2]University of Wisconsin, Madison, US, [3]Duke University Hospital, Durham, US, [4]Henry Ford Hospital, Detroit, US

Objectives: Suvorexant is a potent orexin receptor antagonist being developed for the treatment of insomnia. Suvorexant was effective and well-tolerated in a 4-week study in patients with primary insomnia. Here we report results from one of two 3-month Phase 3 trials.

Methods: This trial (Trial #1) was a randomized, double-blind, placebo-controlled, parallel-group, 3-month trial in non-elderly (18–64 years) and elderly (≥65 years) patients with primary insomnia. There was an optional 3-month double-blind extension, and a 1-week double-blind run-out period at the conclusion of double-blind treatment (core 3-month phase or optional extension) to assess withdrawal/rebound. Two doses were evaluated in each age group: (i) 40 mg for non-elderly patients and 30 mg for elderly patients, and (ii) 20 mg for non-elderly patients and 15 mg for elderly patients. The elderly dose adjustments were made to match non-elderly exposures. Efficacy was assessed at Week 1, Month 1, and Month 3 by patient-reported outcomes (PRO) of subjective total-sleep-time (sTST), time-to-sleep-onset (sTSO), and wake-time-after-sleep-onset (sWASO), and at Night 1, Month 1, and Month 3 by polysomnographic (PSG) endpoints of Latency-to-onset-of-Persistent-Sleep (LPS) and Wakefulness-After-persistent-Sleep-Onset (WASO).

Results: A total of 1021 patients were treated (40/30 mg = 383, 20/15 mg = 254, placebo = 384). Suvorexant 40/30 mg was significantly superior to placebo on all PRO and PSG endpoints at Night 1/Week 1, Month 1 and Month 3. Differences from placebo in change from baseline at Month 3 for suvorexant 40/30 mg were: sTST = 19.7 min, sTSO = -8.4 min, sWASO = -6.9 min, LPS = -9.4 min, WASO = -22.9 min. The magnitude of effect of suvorexant 20/15 mg compared to placebo was smaller than that of suvorexant 40/30 mg. Differences from placebo in change from baseline at Month 3 for suvorexant 20/15 mg were: sTST = 10.7 min, sTSO = -5.2 min, sWASO = -2.4 min, LPS = -8.1 min, WASO = -16.6 min. All doses of suvorexant were generally well-tolerated, with low treatment phase rates of discontinuation due to adverse events: 3.9% for 40/30 mg, 2.4% for 20/15 mg, and 5.5% for placebo. Overall, no clinically important rebound or withdrawal was observed following discontinuation from suvorexant.

Conclusions: In this Phase 3 trial, suvorexant improved sleep onset and maintenance over 3 months of nightly treatment, without clinically important rebound or withdrawal effects following discontinuation.

Support: Merck

Oral Session 14 – Circadian Rhythms and Light: Clinical Perspectives

O325

Melatonin treatment effects on adolescent students' sleep phase and sleepiness in a placebo-controlled cross-over study

A. LOWDEN[1], B. ECKERBERG[2] and T. ÅKERSTEDT[1]
[1]Stockholm University, Stockholm, SE, [2]Leksand School Health Organization, Leksand, SE

Objectives: During the last few decades the incidence of sleep-onset insomnia, due to delay of circadian sleep phase, has increased substantially among adolescents all over the world. We wanted to investigate whether a small dose of melatonin as a single treatment, administered in the afternoon, could advance the sleep phase in teenagers. Twenty-one students, aged 14–19 years, with sleep-onset difficulties during school weeks were recruited.

Methods: The study was a randomized, double blind, placebo-controlled crossover trial, lasting 5 weeks. During the first 6 days in week 2 and 4 the students received either placebo or melatonin (1 mg) capsules between 16:30 h and 18:00 h. During the first 6 days of week 5 all students received melatonin. Weeks 1 and 3 were capsule-free. In the last evening of each week and the following morning the students produced saliva samples at home for later melatonin analysis. The samples were produced the same time each week, as late as possible in the evening and as early as possible in the morning. Both the student and one parent received automatic mobile text messages 15 min before saliva sampling times and capsule intake times agreed upon. Diaries with registration of presumed sleep, subjective sleepiness during the day (Karolinska Sleepiness Scale, KSS) and times for capsule intake and saliva samplings were completed each day.

Results: Primary analysis over 5 weeks gave significant results for melatonin, sleep and KSS. *Post-hoc* analysis showed that reported sleep onset times were advanced after melatonin school weeks compared with placebo school weeks ($P < 0.005$) and that sleep length was longer ($P < 0.05$). After the last melatonin school week the students fell asleep 68 min earlier and slept 62 min longer each night compared with the baseline week. Morning melatonin values in saliva diminished compared with placebo ($P < 0.001$) and evening values increased ($P < 0.001$), indicating a sleep phase advance. Compared with placebo school weeks the students reported less wake up ($P < 0.05$) and school daytime ($P < 0.05$) sleepiness and increased evening sleepiness ($P < 0.005$) during melatonin weeks.

Conclusion: A small afternoon dose of melatonin could advance the sleep phase and make the students more alert during school days even if they continued their often irregular sleep habits during weekends.

O326

Shift work sleep disturbances predict depressive symptomatology

S. PUTTONEN[1], K. VIITASALO[2] and M. HÄRMÄ[1]
[1]Finnish Institute of Occupational Health, Helsinki, FI, [2]Finnair Health Services, Helsinki, FI

Objectives: Sleep disturbance is associated with cardiometabolic and mental health, including depression. Knowledge on effects of sleeping problems and fatigue related to working in shifts on health and well-being is scarce. We studied whether sleeping problems related to working shift work and irregular hours predict future depressive symptomatology.

Methods: Participants were 703 full-time shift workers (395 men), aged 25–65 years, working in an airline company. Depressive symptoms were assessed using the Depression Scale (DEPS). Participants with increased symptomatology (>9 points) at baseline were excluded from the analysis. During a mean follow-up period of 2.5 years, 51 new cases with increased depressive symptoms were observed. Sleep and fatigue related questions were self-rated at baseline. Age and gender were included as covariates in the analyses.

Results: Participants with frequent (>1 times/week) shift-related sleep disturbances or excessive tiredness were at increased risk of developing depressive symptoms during the follow-up (OR 1.8, 95%CI, 1.02–3.28). Sleep disturbances and excess fatigue with a debilitating influence on work performance (scored as yes or no), was marginally significantly associated with depressive symptoms (OR, 2.2, 95%CI, 0.98–5.05). Typical symptoms of poor sleep, such as difficulties in initiating sleep, frequent awakenings or sleep dept were not associated with depressive symptoms. However, daytime fatigue (>1 times/week) predicted increased depressive symptoms (OR 2.2, 95%CI, 1.21 -4.01).

Conclusion: We were able to show that workers who experience frequent sleep difficulties in relation to their working hours may be at high risk poorer mental health. In addition, the data suggests that common sleep symptoms may not adequately capture the particularities of sleep and fatigue among shift workers.

O327

Why should salivary melatonin be measured in patients to be treated with melatonin?

M. G. SMITS, H. KEIJZER and L. M. G. CURFS on behalf of the Governor Kremers Centre, University Maastricht, the Netherlands

Introduction: Several pharmacopoeas recommend that melatonin should be administered 1 or 2 h before desired bed time although a meta-analysis showed that melatonin is not effective if administered in this way. When melatonin is administered at a time related to Dim Light Melatonin Onset (DLMO) it improves sleep. To establish the clinical relevance of measuring DLMO we reviewed the literature.

Methods: PubMed and Embase were searched between January 1990 and May 2011 using 'human', 'melatonin', 'dim light melatonin onset', 'treatment' and their combinations.

Results: 1. Diagnosis: DLMO is the best characterisation of the 24-h melatonin rhythm, which is strongly associated with the circadian sleep-wake rhythm. Knowledge of DLMO improves the accuracy of Delayed Sleep Phase Disorder diagnosis with 32.5%. Melatonin treatment before measuring DLMO may delay optimal treatment several months. 2. Optimal treatment success: Two meta-analyses of studies where melatonin was administered at a time related to DLMO showed that sleep in insomnia patients improved considerably, while a meta-analysis of studies where melatonin was administered without knowing DLMO did not show improvement of sleep. Exogenous melatonin, administered 5 h before DLMO phase advances melato-

nin rhythm and the sleep-wake rhythm which is associated with it maximally. These effects are dose-depended. 3. Prediction of DLMO. Sleep onset measured with sleep log or polysomnograpy does not predict DLMO reliably in patients with possible circadian sleep-wake rhythm disorder. 4. Clinical reliability of DLMO measurements: In home situations salivary DLMO can be measured reliably in 76.2% of patients with possible circadian sleep-wake rhythm disorders. In the remaining patients additional measurements reveal DLMO. 5. Salivary melatonin measurements after melatonin treatment. Measuring salivary melatonin concentrations the day after administration of exogenous melatonin diagnoses slow melatonin metabolisation, an important reason for inefficacy of melatonin treatment.

Conclusion: Our literature search showed that DLMO is crucial both for optimally diagnosing circadian rhythm sleep disorders and for optimally timing of melatonin treatment, an important pillar of treatment of circadian rhythm sleep disorders. Measuring salivary melatonin during the day after administration of melatonin reveals if the patient is a poor melatonin metabolizer. If so melatonin dose should be lowered considerably.

O328

Integrated mathematical model of sleep for exploration of adaptation to night shifts

S. POSTNOVA and P. A. ROBINSON
University of Sydney, Sydney, AU

Objectives: The number of work-related injuries incurred by shift workers is nearly twice higher than that of non-shift workers. This is possibly related to disturbed sleep-wake cycles due to atypical work times and the thereby increased sleepiness. It is likely that sleepiness and the overall quality of life of shift workers can be improved by proper scheduling of forced wake intervals and adjusting light exposure. An integrated mathematical model of sleep-wake cycles has been developed in order to examine the mechanisms underlying sleepiness and entrainment during various sleep disturbances. The objectives of the present work are: (i) To explore the potential of the integrated model of sleep-wake cycles to quantitatively predict ease of adaptation to shift work; and (ii) To examine the effects of shift light intensity, shift onset, and internal circadian period on entrainment and sleepiness on night shifts.

Methods: The integrated model is combined of the sleep-wake switch model of the ascending arousal system of Phillips and Robinson (2007) and the model of the human circadian pacemaker of St. Hilaire et al. (2007). This model predicts sleep-wake times, levels of sleepiness, and circadian phase depending on individual parameters, such as internal circadian period and homeostatic time constants, and environmental inputs, such as light exposure. The validity of the model for prediction of adaptation to shift work is examined on a number of published experimental protocols.

Results: Simulations show that the model successfully reproduces the results for sleep-wake patterns and circadian re-entrainment on all experimental protocols examined. Exploration of the dynamics of the model on a schedule of 3 days with 8 h night shifts with bright light during the shifts predicts that: (i) light intensity of 3000 lux during night shifts is sufficient for re-entrainment of the circadian pacemaker after 3 days on the shift schedule, (ii) For the internal circadian period of 24.2 h the lowest mean sleepiness during shift on the third day is observed for the schedule with shifts starting at 22:00, and the highest for the shift starting at 01:00, (iii) Longer internal circadian period (24.3 versus 24.1 h) leads to easier adaptation to night shifts starting at 01:00.

Conclusion: This study shows that the dynamics of the integrated model of sleep-wake cycles agree well with experimental observations and make predictions that can be tested in future experiments.

O329

A comparison of sleep and health at the start and end of a 14-day work period among Norwegian oil rig workers

S. WAAGE, S. PALLESEN, B. E. MOEN and B. BJORVATN
University of Bergen, Bergen, NO

Objectives: Shift work and extended work hours are associated with adverse health effects. The aim of the present study was to compare sleep and subjective health complaints among Norwegian oil rig workers, at the start and at the end of a 14 days work period offshore.

Methods: One hundred and eighty-three workers (178 men/5 women, mean age 42.9 years) working either 2 weeks of 12 h day shift ($n = 90$) or 2 weeks of a swing shift schedule ($n = 93$) (1 week of 12 h night shift, followed by 1 week of 12 h day shift) participated in the study. Sleep quality was measured by the Pittsburgh Sleep Quality Index (PSQI), insomnia was measured by the Bergen Insomnia Scale (BIS), and subjective health complaints were measured by the Subjective Health Complaints Inventory (SHC). The workers' sleep and health were investigated in the beginning of the 2 week work period after a 4 week free period at home, and compared with the workers' sleep and health at the end of the 2 week work period using paired samples t-tests. In addition we compared the two shift work schedules (day versus swing shift) by using a mixed between-within ANOVA.

Results: The workers reported significantly poorer sleep (PSQI global score 4.5 versus 5.7, $P < 0.0005$) and more complaints of insomnia (BIS score 7.5 versus 12.5, $P < 0.0005$) at the end of the 2 week work period compared to at the start of the 2 week work period. However, there was no significant difference in subjective health complaints (SHC total score 7.2 versus 6.7, $P = 0.123$). Furthermore, there were no significant differences in sleep quality (day shift: 4.6–5.4, swing shift: 4.5–5.9, interaction effect $P = 0.080$), insomnia (day shift: 7.9–11.2, swing shift: 7.1–13.8, interaction effect $P = 0.101$) or subjective health complaints (day shift: 6.7–5.8, swing shift: 7.6–7.6, interaction effect $P = 0.135$) between day shift and swing shift workers.

Conclusion: In this study among Norwegian oil rig workers, both sleep quality and insomnia became worse during the 2 week work period offshore. There was no difference between the two work schedules, suggesting that 12 h day shift offshore affected sleep to a similar degree as the schedule that involved night work.

O330

Chronic sleep reduction in adolescents with delayed sleep phase syndrome and effects of melatonin treatment

A. VAN MAANEN[1], J. F. DEWALD[1], M. G. SMITS[2] and A. M. MEIJER[1]
[1]University of Amsterdam, Amsterdam, NL, [2]Hospital Gelderse Vallei, Ede, NL

Background: Chronic sleep reduction, resulting from insufficient and/or poor sleep over a long time period, is a common phenomenon in adolescents. This increasing social problem has severe negative psychological and behavioral daytime consequences. As it is often caused by an interaction of biological and social factors, it is most likely also related to the biological clock and a delayed melatonin rhythm. Well timed and well dosed exogenous melatonin treatment might therefore be able to diminish chronic sleep reduction.

Objectives: 1. To investigate whether adolescents with Delayed Sleep Phase Syndrome (DSPS) have more chronic sleep reduction than adolescents from the general population. 2. To examine whether melatonin treatment affects chronic sleep reduction in adolescents with DSPS.

Methods: One hundred and sixteen adolescents diagnosed with DSPS (55.2% boys, mean age 15.4 years, mean DLMO = 22:23 h) completed the Chronic Sleep Reduction questionnaire (CSRQ; Meijer, 2008) at baseline (before treatment). To date, 38 adolescents also completed the CSRQ after 2 months of 1–5 mg melatonin treatment, administered 3–5 h before DLMO.

Results: 1. Adolescents with DSPS had a mean score of 44.21 on the CSRQ at baseline. This was significantly higher (t = 12.088, $P < 0.001$) than the mean score that was found in a group adolescents from the general population (mean score = 33.69; Dewald et al., 2012). 2. In comparison to baseline, chronic sleep reduction was significantly diminished after melatonin treatment (t = -11.145, $P < 0.001$) in adolescents with DSPS. Furthermore, this reduction was present on all CSRQ subscales (shortness of sleep t = -11.211, $P < 0.001$), irritation (t = -2.168, $P = 0.037$), loss of energy (t = -7.602, $P < 0.001$) and sleepiness (t = -6.578, $P < 0.001$). 3. After melatonin treatment, adolescents with DSPS scored 31.40 on the CSRQ. This was lower than adolescents in the general population, although not statistically significant (t = -1.530, $P = 0.133$).

Conclusion: Adolescents with DSPS have more chronic sleep reduction than adolescents from the general population. Melatonin treatment in adolescents with DSPS significantly decreases chronic sleep reduction to a level that is comparable to that of adolescents in the general population. Apparently, chronic sleep reduction is an important characteristic of DSPS.

O331

Optic nerve and melanopsin retinal ganglion cells involvement in relation to circadian dysfunction in Alzheimer's disease

C. LA MORGIA[1], F. N. ROSS-CISNEROS[2], B. PAN[2], R. GALLASSI[1], L. SAMBATI[1], F. PROVINI[1], P. AVANZINI[3], G. CANTALUPO[3], P. BARBONI[1], J. HANNIBAL[4], A. SADUN[2] and V. CARELLI[1]

[1]University of Bologna, Bologna, IT, [2]University of Southern California, Los Angeles, US, [3]University of Parma, Parma, IT, [4]University of Copenhagen, Copenaghen, DK

Objective: Optic nerve involvement and circadian rhythm disturbances are reported in Alzheimer disease (AD). We aimed at characterizing optic nerve involvement with particular reference to melanopsin retinal ganglion cells (mRGCs) in relation to the occurrence of rest-activity rhythm dysfunction in AD.

Methods: Ophthalmologic evaluation and retinal nerve fiber layer (RNFL) thickness measurements by optical coherence tomography (Stratus OCT) were performed in 18 AD patients (age 71.8 ± 11.2) and 74 age-matched controls (age 69.1 ± 8.1). Actigraphic monitoring for 7 days was performed in 15 AD patients (age 70.9 ± 10.3) and 10 controls (age 65.8 ± 7.5). Non-parametric methods were applied to assess interdaily stability (IS), intradaily variability (IV) and relative amplitude (RA) of rest-activity rhythm. Sleep minutes and sleep efficiency were also retrieved. We also performed immunohistochemical analysis of mRGCs in post-mortem retinas and axonal counts in optic nerve cross-sections of 11 AD (age 81.7 ± 13.1) and 11 controls (age 78.5 ± 15.1). Comparison between AD patients and controls was performed by ANCOVA for OCT and unpaired t-test for actigraphic measurements. Correlation analysis was performed with Pearson test ($P < 0.05$).

Results: OCT evaluation demonstrated reduced average ($P = 0.034$), superior ($P = 0.009$) and nasal ($P = 0.016$) RNFL thickness in AD patients. Average ($P = 0.005$), superior ($P = 0.05$) and nasal ($P = 0.04$) RNFL thickness correlated with age in AD patients. Actigraphic monitoring demonstrated a tendency towards an increased IV ($P = 0.098$) and reduced RA ($P = 0.057$) and a significant reduction of sleep efficiency ($P < 0.001$) in AD patients. No significant correlation was detected between OCT measurements and actigraphic data. However, considering only patients with at least one circadian parameter outside 2 SD from the mean of controls, we found a significant correlation between IV and average ($P = 0.035$), superior ($P = 0.045$) and inferior ($P = 0.017$) RNFL thickness. Melanopsin RGCs density was significantly reduced in AD patients compared to controls ($P = 0.008$) and loss of axons in AD optic nerve cross-sections was nearly significant ($P = 0.067$). Thus, mRGCs/RGCs ratio was similar in AD (1.4%) and controls (1.3%).

Conclusions: We demonstrated subclinical optic nerve pathology, correlated to abnormal rest-activity circadian rhythm in a subgroup of AD patients. We also found that mRGCs are lost in AD supporting their contribution to circadian dysfunction in AD.

O332

Cognitive behaviour therapy: a novel treatment for delayed sleep phase syndrome

K. DANIELSSON[1], M. JANSSON-FRÖJMARK[2], J.-E. BROMAN[1] and A. MARKSTRÖM[1]

[1]Neuroscience, Uppsala, SE, [2]Psychology, Stockholm, SE

Objectives: Delayed sleep phase syndrome (DSPS) is the most common circadian rhythm disorder and yet there are still no established treatments with enduring effects. The aim was to examine if light therapy (LT) with cognitive behaviour therapy (CBT), relative to LT only, improves diurnal rhythm, depressive and insomnia symptoms in DSPS.

Methods: Thirty subjects (15 women) with a mean (±SD) age of 22 ± 2 years participated. All subjects fulfilled the criteria for DSPS according to ICSD-2. The study was a randomised controlled trial. Group I received LT for 2 weeks followed by a sleep diary for 4 weeks. Group II was administered LT for 2 weeks and then CBT in group once a week for 4 weeks. All patients filled out a sleep diary, the Hospital Anxiety and Depression scale (HADS) and the Insomnia Severity Index (ISI) at pre-treatment, after 2 weeks and after 6 weeks.

Results: For Group I baseline mean sleep onset was 2:41 ± 1:45 h and sleep offset was 10:20 ± 2:17 h. During the second week of LT sleep onset and sleep offset were advanced by (m ± SD) 74 ± 84 min and by 127 ± 101 min, respectively relative to baseline. At the 6-week follow-up sleep onset and sleep offset were advanced by 44 ± 88 min and by 26 ± 88 min, respectively relative to baseline. A decrease in ISI was observed from baseline to the 2-week follow ($P = 0.071$) and this was maintained at the 6-week follow-up. Depression was reduced ($P = 0.032$) from baseline to the 2-week follow-up. However, depression increased from the 2 to 6-week follow-up at a trend level ($P = 0.080$).

For the Group II baseline mean sleep onset were 3:10 ± 1:28 h and sleep offset were 10:22 ± 1:44 h. During the second week of LT sleep onset and sleep offset were advanced by 122 ± 86 min and by 142 ± 89 min, respectively relative to baseline. At the 6-week follow up sleep onset and sleep offset were advanced by 107 ± 101 min

and by 59 ± 103 min, respectively relative to baseline. ISI was reduced ($P < 0.001$) from baseline to the 2-week follow-up and the result was maintained at the 6-week follow-up. A decrease in depression from the 2-week follow-up to the 6-week follow-up was seen at a trend level ($P = 0.068$).

Conclusion: LT improved diurnal rhythm in both groups. Further, in the LT and CBT combination group a significant decrease in ISI was observed after 2 weeks and was also maintained at the 6-week follow-up.

O333

The expression of the Per2 clock gene is up-regulated in non-treated OSAS patients and normalises its mRNA levels upon positive pressure treatment

S. MOREIRA[1], R. RODRIGUES[2], J. VALENÇA RODRIGUES[1], A. BUGALHO DE ALMEIDA[1] and L. MOITA[2]

[1]Santa Maria Hopital, Lisbon, PT, [2]Instituto de Medicina Molecular, Lisbon, PT

The obstructive sleep apnea syndrome (OSAS) is a frequent sleep disorder that constitutes an independent risk factor for the development of metabolic syndrome and cardiovascular diseases. Nuclear receptors (NRs) are critical integrators of key cycles and metabolic pathways of human physiology. Most exhibit circadian variation at the mRNA and protein levels that can be controlled or influenced by master clock genes, which in turn are modulated by sleep/vigilance cycles.

Objectives: Our goal was to investigate if the expression levels of mRNA coding for clock genes is altered in non-treated OSAS patients and if it can be corrected by standard positive pressure treatment.

Methods: Peripheral blood was collected from male patients diagnosed with severe OSAS (AHI ≥30/h) before treatment initiation. Collections were always performed between 8 and 10 am. Blood was then used to perform routine biochemical analyses and to isolate peripheral blood mononuclear cells (PBMCs). RNA was isolated and qPCR used to measure mRNA levels of genes associated with the central circadian pacemaker including Clock, Bmal1 and three Period genes (Per 1, 2, 3). The selected patients were then followed up at 1, 3 and 6 months after therapy initiation with positive pressure and the mRNA level of relevant genes tested at these points. Patients with addiction habits, cancer, hematological disorders, shift work were excluded from analysis.

Results: After testing the mRNA expression levels of clock genes in non-treated OSAS patients, we found Per2 to be reproducibly over-expressed in six out of eight patients (75%), from 1.5 to 2.5-fold over a reference control. Strikingly, in all six patients found to have Per2 increased levels we observed positive pressure treatment-induced decrease of expression of this gene beginning at 1–3 months post-treatment initiation and normal expression values at 6 months.

Conclusion: We have identified the Per2 clock gene as possible marker of OSAS because it is over-expressed in non-treated patients and its expression levels normalize upon positive pressure treatment. This finding is likely the first molecular marker of the disease and can possibly be used to monitor therapy efficacy. It remains to be determined if Per2 is directly associated with the increased susceptibility of OSAS patients to the development of metabolic syndrome and cardiovascular disease.

O334

Enhancing sleep in hospitals with patient room lighting

M. C. GIMÉNEZ[1], L. M. GEERDINCK[1], M. VERSTEYLEN[2], P. LEFFERS[2], G. J. B. M. MEEKES[3], H. HERREMANS[1], B. DE RUYTER[1], P. M. J. C. KUIJPERS[2] and L. J. M. SCHLANGEN[1]

[1]Philips Research, Eindhoven, NL, [2]Maastricht University Medical Center, Maastricht, NL, [3]Philips Lighting, Eindhoven, NL

Objectives: Impaired sleep has negative consequences for health. Unfortunately, sleep within most hospitals is less optimal as compared to the home situation. The 24 h sleep-wake pattern is strongly influenced by light. Furthermore, light is known to have a broad impact on health and well-being, also within healthcare settings. Lighting standards for hospitals prescribe a horizontal illuminance of at least 300 lux. This is relatively modest as compared to the natural daytime illuminance outdoors that easily exceeds 2000 lux, even on a cloudy day.

The present study investigates how an electrical lighting system that enhances the daytime light exposure within hospital patient rooms by means of a 24 h, ambience providing, dynamic light cycle, influences total sleep duration (TSD), sleep onset latency (SOL), depression-, anxiety- and satisfaction-scores of hospitalized patients.

Methods: Cardiovascular patients ($n = 171$) of the Maastricht University Medical Center were assigned to a control room with standard lighting, or to an intervention room equipped with a prototype of the Philips HealWell lighting system. This system provides general lighting with automated gradual changes in correlated color temperature and illuminance across the day. The maximum vertical illuminance at eye level exceeds 750 lux. Moreover, the system comprises (multicolor) lighting elements for a pleasant ambience with bedside control for the patients.

Sleep was measured by means of Actiwatch-Spectrum® devices. Questionnaires were used to evaluate depression- & anxiety- (HADS) and satisfaction-scores.

Results: Mixed-effect linear regression analysis revealed a significant intervention by time interaction. After 7 days in the intervention room TSD increased by 8% and SOL reduced by 32% as compared to the first night, whereas both parameters hardly changed in the control room. Satisfaction scores of patients and staff for the intervention lighting system were significantly higher as compared to the control condition.

Conclusions: The present lighting intervention achieves modest benefits on various sleep parameters of cardiovascular patients. The intervention is positively appreciated by patients and nursing staff.

Philips Lighting has financially supported this research.

Oral Session 15 – Information Processing

O335

Sleep and synaptic plasticity

G. WANG, L. APPELBAUM, D. COLAS and P. MOURRAIN
Stanford University, Stanford, US

Sleep is a fundamental and evolutionarily conserved aspect of animal life. Studies have shed light on the role of sleep in synaptic plasticity. Demonstrations of memory replay and synapse homeostasis suggest that one essential role of sleep is in the consolidation and optimization of synaptic circuits to retain salient memory traces despite the noise of daily experience. In living zebrafish larvae, we used time-lapse two-photon imaging of the presynaptic marker synaptophysin in hypocretin/orexin (HCRT) neurons to determine the dynamics of synaptic modifications during the day and night. We observed circadian rhythmicity in synapse number in HCRT axons. This rhythm is regulated primarily by the circadian clock but is also affected by sleep deprivation. Furthermore, NPTX2, a protein implicated in AMPA receptor clustering, modulates circadian synaptic changes. Nptx2b is a rhythmic gene that is mostly expressed in hypothalamic and pineal gland cells. Arrhythmic transgenic nptx2b overexpression (hcrt:NPTX2b) increases synapse number and abolishes rhythmicity in HCRT axons. Finally, hcrt:NPTX2b fish are resistant to the sleep-promoting effects of melatonin. This behavioral effect is consistent with NPTX2b-mediated increased activity of HCRT circuitry. These data provide real-time *in vivo* evidence of circadian and homeostatic regulation of structural synaptic plasticity.

O336

Sleep duration and risk of ischaemic heart disease and all-cause mortality: a 30-year follow-up in The Copenhagen Male Study

A. H. GARDE[1], Å. M. HANSEN[2], A. HOLTERMANN[1], F. GYNTELBERG[3] and P. SUADICANI[3]
[1]National Research Centre for the Working Environment, Copenhagen, DK, [2]Copenhagen University, Copenhagen, DK, [3]Bispebjerg University Hospital, Copenhagen, DK

Objectives: Sleep duration is thought to be associated with risk of all-cause mortality (ACM) in a U-shaped manner, whereas the association to ischemic heart disease (IHD) mortality remains controversial. We tested if sleep duration was an independent risk factor for IHD mortality and ACM in a prospective cohort study with 30 year follow-up.

Methods: The Copenhagen Male Study of 5249 gainfully employed men (40–59 years) was used after exclusion of 274 men with cardiovascular disease history at baseline. Sleep duration and confounders related to lifestyle and medical conditions, were obtained in 1970–1971 together with measurement of blood pressure, weight, height and physical fitness. Relative risks were estimated in a Cox's proportional hazards regression model with the maximum likelihood ratio method.

Results: Five hundred and eighty-seven men (11.9%) died due to IHD and 2663 (53.9%) from ACM during the 30-year follow-up. Three groups were formed: Short sleepers: <6 h (n = 276), medium sleepers: 6–7 h (n = 3837), and long sleepers ≥8 h (n = 828). Referencing medium sleepers, short sleepers had an increased risk of IHD mortality (Hazard ratio (HR) = 1.59, 95% confidence interval: 1.18–2.15). The association was attenuated [HR = 1.41 (CI: 1.02–1.93)], but remained significant after adjustment for confounders. Among the older half of the population (>48 y), short [HR = 1.58 (1.09–2.30)] and long [HR = 1.32 (1.02–1.71)] sleep duration was associated with increased risk even after control for confounders. No associations were found for ACM after adjustment for confounders.

Conclusion: Our results supported the hypothesis that men with either short or long sleep duration have an increased risk of IHD mortality.

O337

Daytime sleep specifically enhances consolidation of hippocampal-dependent motor sequence memory: an fMRI study

G. ALBOUY[1], S. FOGEL[1], V. NGUYEN[1], L. PATENAUDE-VEILLEUX[1], A. BOUYOUCEF[1], F. JEAY[1], J. CARRIER[1], E. ROBERTSON[2] and J. DOYON[1]
[1]University Montreal, Montreal, CA, [2]Harvard Medical School, Boston, US

Objectives: The acquisition of a new sequential motor skill requires the simultaneous learning of both allocentric (spatial) and egocentric (motor) representations of the sequence. The aim of this study was to explore the influence of nap on the cerebral correlates of consolidation of these two representations.

Methods: In a first behavioral study, 44 young healthy volunteers were trained on a 5-item finger sequence learning task. After training, they were divided according to whether (i) they were subsequently tested on an allocentric (ALLO) or egocentric (EGO) representation of the sequence, and (ii) were then re-tested on such a representation after a 90-min nap (N) or after quiet wakefulness (W), hence producing four groups: ALLO-N, ALLO-W, EGO-N and EGO-W (n = 11 in each group). In a subsequent study, this protocol was adapted to fMRI, and cerebral activity of 57 new participants was recorded in the four groups (n = 15, n = 13, n = 14 and n = 15) while subjects practiced the motor task. Functional data were analysed using SPM8. Nap and no-nap periods were monitored using polysomnography.

Results: Behavioral study: An ANOVA performed on performance speed revealed significant gains in performance in the ALLO group after nap, but not after wake; the latter being correlated with spindle density during NREM sleep of the post-training nap. In contrast, no significant gains were observed in the EGO group, regardless of the sleep/wake condition.

fMRI study: Behavioral data acquired in the scanner replicated our previous results, i.e., a sleep-dependent gain in the ALLO group that was not observed in the EGO group. Polysomnographic data analyses are still in progress. Brain imaging data acquired while executing the ALLO representation of the sequence revealed bilateral activations in the intraparietal sulci (IPS), motor cortices and hippocampi. In contrast, practicing the EGO representation recruited bilateral sensorimotor cortices. Finally, while sleep did not induce any cerebral reorganization in the EGO group, a decrease in activity in the IPS and the motor cortex was observed after nap in the ALLO group.

Conclusions: Our findings specify the crucial role of the hippocampus in sleep-dependent procedural memory consolidation. Our results show that consolidation of hippocampal-dependent motor memory trace specifically requires sleep and is related to spindle activity. This process is accompanied by a decrease in cerebral resources needed to optimize motor behavior after nap.

O338

Strengthening procedural memory by reactivation in sleep

M. SCHÖNAUER, T. GEISLER and S. GAIS
LMU Munich, Munich, DE

Objectives: There is robust evidence that sleep facilitates procedural memory formation. The exact mechanisms, however, that mediate this process are still unclear. A process of active systems consolidation has been proposed for the declarative memory domain. In that framework, off-line reactivation and replay of prior waking experience during sleep strengthen hippocampal memory traces acquired during periods of wakefulness and integrate information into neocortical long-term memory networks. However, no similar mechanism has yet been proposed for the procedural memory system. We tested the hypothesis that an active replay of prior experience underlies sleep effects on procedural memory. In two additional experiments, we tested whether the duration of sleep affects performance on the task.

Methods: Subjects learned a 12-element finger sequence task during which tones were played for each keypress. Half of the tone sequence was replayed to the subjects during a 3-h period of sleep or wakefulness to see whether this can enhance memory consolidation. In additional experiments, we compared the effect of 3-h and 8-h periods of sleep on performance in the same task.

Results: Only subjects who slept during the consolidation period, benefited from sequence replay in that the number of errors was reduced. Furthermore, this effect could be observed only for the reactivated part of the motor sequence (interaction sleep × reactivation, $P = 0.01$). This demonstrates an active, sequence-specific, and sleep-related consolidation process. A 12-h consolidation period, including a night of sleep, resulted in sleep related gains comparable to the 3-h period with additional external reactivation ($P = 0.04$). A 3-h consolidation period without reactivation did not yield a significant benefit of sleep.

Conclusion: Our findings show that reactivation enhances procedural memory when present during sleep but not during wakefulness. Moreover, this effect is specific to the reactivated part of a sequence. The additional experiments show that a boost in performance after procedural motor learning can either come from longer sleep periods or from additional external stimulation. Thus, we can confirm the functional significance of an active replay process during sleep for the consolidation of procedural motor skills, and show that external triggering can effectively accelerate this inherent processing mechanism.

O339

The timing of learning before night-time sleep differentially affects declarative and procedural long-term memory consolidation in adolescents

J. HOLZ, H. PIOSCZYK, N. LANDMANN, B. FEIGE, K. SPIEGELHALDER, D. RIEMANN, C. NISSEN and U. VODERHOLZER
University Medical Center Freiburg, Freiburg, DE

Objectives: Sleep after learning has been shown to foster the consolidation of new memories. However, fundamental questions on the best timing of learning before night-time sleep persist. The authors tested the hypothesis that learning directly prior to night-time sleep compared to 7.5 h prior to night-time sleep provides better conditions for the consolidation of declarative and procedural memories.

Methods: Fifty healthy adolescents (all female, aged 16–17 years) were trained on a declarative word-pair and a procedural finger-tapping task at 3 PM (afternoon group, $n = 25$) or at 9 PM (evening group, $n = 25$), followed by a sleep laboratory night. Retrieval was assessed 24 h and 7 days after initial training.

Results: Subjects trained in the afternoon showed a significantly elevated retention rate of word-pairs compared to subjects trained in the evening. In contrast, off-line gains in finger-tapping performance were significantly higher in subjects trained in the evening compared to those trained in the afternoon.

Conclusion: In conclusion, our results indicate that learning directly before night-time sleep preferentially promotes procedural memory consolidation, whereas learning in the afternoon, 7.5 h before night-time sleep, provides better conditions for the long-term consolidation of declarative memories in adolescents.

O340

Radio-frequency electromagnetic field stimulation affects sleep-dependent performance improvement

C. LUSTENBERGER[1], M. MURBACH[2], R. DÜRR[3], M. R. SCHMID[3], N. KUSTER[2], P. ACHERMANN[3] and R. HUBER[1]
[1]University Children's Hospital Zurich, Zurich, CH, [2]Foundation for Research on Information Technologies, Zurich, CH, [3]University of Zurich, Zurich, CH

Objectives: Sleep-dependent performance improvements have been linked to sleep spindles and sleep slow-wave activity (SWA, EEG power in the 0.75–4.5 Hz range). Pulse-modulated radiofrequency electromagnetic fields (RF EMF) are capable to modulate these electroencephalographic (EEG) characteristics of NREM sleep. Thus the aim of our study was (i) to explore possible mechanisms how RF EMF affects cortical activity during sleep and (ii) to test whether such effects on cortical activity during sleep interact with sleep-dependent performance changes.

Methods: Sixteen male subjects (18–21 years, 19.9 ± 0.2, mean ± SEM) underwent two experimental nights, one of them with RF EMF exposure (intermittently pulsed at 0.25 or 0.8 Hz), one with sham exposure. All-night EEG was recorded, power spectra during NREM sleep for frequencies up to 15 Hz were calculated for the first four sleep episodes. We also analysed event-related spectral power of single RF EMF pulses. Changes in overnight performance improvement were assessed with a motor sequence finger tapping task (training in the evening, retesting next morning) for both nights.

Results: RF EMF exposure affected EEG power in the SWA range. We found increased SWA in the 4th NREM sleep episode during exposure compared to sham (+44.0 ± 17.9%, $P < 0.04$). Our intermittent pulse modulation design of the RF EMF allowed us to investigate whether single RF EMF bursts directly evoke EEG responses during sleep. Indeed, during the 4th NREM episode subjects showed increased event-related responses in the SWA range. The decrease of SWA across the sham night was correlated with the corresponding overnight performance improvement ($r = 0.63$, $P < 0.01$). No such correlation was found during exposure ($r = 0.15$, $P < 0.59$). Moreover, subjects showed a reduced overnight performance improvement during RF EMF exposure (-20.08 ± 10.57%, $P = 0.03$).

Conclusion: Very-low frequency pulse-modulated RF EMF exposure increased SWA towards the end of the sleep period and reduced sleep-dependent motor performance improvement. We provide first evidence that this increased SWA resulted from an induction of sleep slow waves by RF EMF pulses. The negative

impact of this increased SWA on sleep dependent performance improvement might reflect an interaction of RF EMF with the normalization of cortical excitability during sleep.
Work supported by the Swiss National Science Foundation and the Swiss Research foundation on Mobile Communication.

O341

Different patterns of motor cortex activity during phasic and tonic REM sleep: an intracerebral electrophysiological study

F. DE CARLI[1], E. MORRONE[1], P. PROSERPIO[2], F. MORONI[3] and L. NOBILI[2]

[1]Institute of Molecular Bioimaging and Physiology – C.N.R., Genoa, IT, [2]Niguarda Ca' Granda Hospital, Milan, IT, [3]Sapienza University, Rome, IT

Objectives: Characterization of the electrophysiological activity of the motor cortex as compared to pre-frontal cortex during tonic and phasic REM sleep.

Methods: Quantitative analysis was applied to intracerebral EEG (iEEG) data recorded from six patients with drug-resistant focal epilepsy during pre-surgical investigation. Selected recordings included contact leads in the primary motor cortex controlling limb movements and in pre-frontal cortex. Both structures were free of pathological activity. An overnight polysomnogram with iEEG was recorded for each subject after adaptation, followed by a 3–5 min recording during voluntary limb movements. Polysomnogram was scored into standard sleep stages; rapid ocular movements (REMs) were marked and REM stage was divided into tonic (without ocular movements) and phasic epochs (with ocular movements). Bipolar IEEG from adjacent contacts was processed by short-time spectral analysis. Tonic and phasic REM sleep were compared as for the mean frequency by paired t-test.

Results: During tonic REM a mild peak (at about 8 Hz) corresponding to mu activity could be found, followed by a lower peak (at about 20 Hz) in the beta band. During phasic REM we observed a decrease of EEG power including mu activity and an extension of beta activity towards higher frequencies (peaking at about 24 Hz) reflected by the significant increase of mean frequency ($P < 0.01$). A similar change was observed in a weaker form around the onset of ocular movements and in a stronger form around the onset of voluntary limb movements recorded during wakefulness. Voluntary movements were indeed preceded by mu rhythm while EEG desynchronization and beta frequency shift followed movement onset. This pattern was characteristic of the motor cortex and was not found in the dorso-lateral frontal cortex where the frequency shift of beta activity was not observed.

Conclusion: Phasic REM is characterized, with respect to tonic REM, by specific changes of electrophysiological activity in the motor cortex. These changes seems to suggest that during phasic REM sleep the motor cortex is activated as during wake related movements. These findings can be of particular interest for the understanding of movement disorders during sleep such as REM Behavior Disorder.

O342

Poor sleep quality and unbalanced diet in female elite athletes

M. R. SILVA and T. PAIVA

University of Lisbon, Lisbon, PT

Introduction: The mutual relations between sleep, exercise and nutrition are particularly relevant at young ages. Data concerning sleep/energy intake of high competition athletes during high competition levels are scarce.

Objectives: The main purpose of this study was to evaluate sleep quality, energy intake and body composition in female elite gymnasts during an international championship.

Methods: Sixty-seven rhythmic gymnasts [18.67 (2.93) years old] of high performance level [36.60 (7.56) hours of training/week] were evaluated by a questionnaire, which collected: training data; medical and gynecological history; sleep was assessed by the Epworth Sleepiness Scale and the Pittsburgh Sleep Quality Index; energy intake from the previous 24 h and; body composition (weight, height, body mass index, fat mass and muscle mass) was measured.
Descriptive and linear regression analysis was used to specify relations between two continuous variables. Pearson correlation coefficient was used to determine associations between categorical and continuous variables. The significance level was 5% ($P < 0.05$). Data was analyzed using SPSS, version 18.0.

Results: Gymnasts began training at age 7, being subjected to an intense training regime based on a weekly average of 36.60 (7.56) hours. Menarche was delayed [15.25 (1.31) years] and all menstruating gymnasts had menstrual irregularities. Most athletes presented mild somnolence ($n = 45$; 67.2%) and poor sleep quality ($n = 52$; 77.61%) and a minority had severe somnolence ($n = 9$; 13.5%) and a good sleep quality ($n = 15$ athletes; 22.39%). Gymnasts slept more hours at weekend than during the week. The diet was nutritionally inadequate. The energy content from lipids and proteins was higher than recommended and carbohydrate was significantly lower for this type of athletes. The dietary fiber, omega-3, omega-6, vitamins D and K, calcium, iron, boron, magnesium, and water consumption was lower than that recommended. Moreover, the consumption of vitamins A, B1, B2, B3, B6, B12, C, manganese and zinc was higher than recommended. They had a higher body density, with reduced fat mass and muscle mass.
With intensity training 25–54 h per week there were some disturbances in sleep, food intake and body composition.

Conclusion: These results show important abnormalities in energy intake, in sleep disturbances and in endocrine function in elite young female athletes; they imply the need of future care and recommendations in their orientation training.

O343

Detailed and specific shift work exposures, sleep and fatigue in a representative sample of Swedish shift workers

M. INGRE, G. KECKLUND and T. ÅKERSTEDT

Stockholm University, Stockholm, SE

Objectives: Shift-work studies are often based on a convenience sample from a specific company, or a representative sample with primitive exposure data (sometimes just a single item of night work). This may question the validity of such findings and does not provide good insight in the consequences of specific shift-work exposures in the general population.
The present study combined a representative sample with a detailed collection of exposure data (all work hours during one work week) to estimate the effect of specific shift sequences on sleep and fatigue in the general population.

Methods: A questionnaire with questions of work hours and sleep, fatigue and social complaints was completed by 2029 shift workers in a representative sample of the working population in Sweden. Response rate was 73%. Data was weighted to account for stratification. Shift sequences were quantified and used to predict

complaints the same day using a logistic regression model accounting for clustering within individuals adjusted for age, sex, marital status, education and blue color work.

Results: A total of 10.061 shifts and 8409 free days were analysed with 10% of the shifts classified as morning shifts (start <6 h), 26% evening shifts (end >22 h), 11% nightshifts (3 h, 00-05) and 52% day shifts (the rest), 10% of the shifts were preceded by a short rests (<11 h) and 13% was long shifts (>10 h).

We used free days as a reference in a multivariate model with all shift types up to a sequence of 3 days in a row together with short rests and long shifts to predict sleep problems and fatigue.

The results showed that working day (OR = 2.4, 95% CI: 1.9–3.1), morning (OR = 7.0, 4.7–10.2), evening (OR = 5.5, 4.2–7.1) and night (OR = 11.5, 7.7–17.2) increased sleep complaints compared to days off. Sleep complaints were stable at the second morning shift in a sequence but decreased at the third morning shift (OR = 0.54, 0.34–0.86) suggesting adaptation to the early hours. Long shifts did not predict sleep problems but short rest did (OR = 3.1, 2.5–4.0).

The risk for fatigue also increased for all shift types (OR = 4.2–8.3) in addition to an increase the second day of night (OR = 1.6, 1.3–2.1), morning (OR = 1.4, 1.0–1.9), day (OR = 1.3, 1.1–1.5) and evening (OR = 1.3, 1.1–1.7) work.

Conclusion: Detailed analysis of work schedules in a representative sample of shift-workers suggest sleep problems increase for any workday but most for night shift. After two morning shifts in a row sleep improves but fatigue accumulates.

O344

The fate of incoming stimuli during deep sleep is determined by spontaneous NREM sleep features

M. SCHABUS[1], D. P. J. HEIB[2], T. T. DANG-VU[1], M. BOLY[1], G. ALBOUY[1], S. GAIS[1], C. PHILLIPS[1], C. SCHMIDT[1], G. VANDEWALLE[1] and P. MAQUET[1]

[1]Cyclotron Research Centre, Liège, BE, [2]University of Salzburg, Salzburg, AT

Introduction: The present study aimed at identifying the neurophysiological responses associated with auditory stimulation during non-rapid eye movement (NREM) sleep using simultaneous EEG/fMRI recordings. It was reported earlier that auditory stimuli produce bilateral activation in auditory cortex, thalamus, and caudate during both wakefulness and NREM-sleep. However, due to the spontaneous membrane potential fluctuations cortical responses may be highly variable during NREM. Here we now examine the modulation of cerebral responses to tones depending on the presence or absence of sleep spindles and the phase of the slow oscillation.

Methods: Thirteen healthy young subjects were scanned successfully during stage 2–4 NREM sleep in the first half of the night in a 3T scanner. Subjects were not sleep-deprived and sounds were *post-hoc* classified according to (i) the presence of sleep spindles or (ii) the phase of the slow oscillation during (±300 ms) tone delivery. These detected sounds were then entered as regressors of interest in fMRI analyses.

Results: Interestingly wake-like responses – although somewhat altered in size and location – persisted during NREM sleep, except during present spindles and the negative going phase of the slow oscillation during which responses became less consistent or even absent. While the phase of the slow oscillation did not alter brain responses in primary sensory cortex, it did modulate responses at higher cortical levels. In addition EEG analyses show a distinct N550 response to tones during the presence of light sleep spindles and suggest that in deep NREM sleep the brain is more responsive during the positive going slope of the slow oscillation. The presence of short temporal windows during which the brain is open to external stimuli is consistent with the fact that even during deep sleep meaningful events can be detected.

Conclusion: Altogether, our results emphasize the notion that spontaneous fluctuations of brain activity profoundly modify brain responses to external information across all behavioural states, including deep NREM sleep.

Symposium – Why Obesity and OSA are Such Good Dancing Partners

S346

Increased tongue fat in patients with obstructive sleep apnea

A. KIM, A. PACK and R. SCHWAB
University of Pennsylvania, Philadelphia, US

Objectives: Obstructive sleep apnea (OSA) is closely associated with obesity. However, the mechanism by which obesity leads to OSA is currently unknown. An autopsy study has shown that there is fat in the tongue. We hypothesized that excess fat is deposited in the tongue in obese sleep apneics. Our specific objectives were to determine whether tongue fat is increased in obese subjects with sleep apnea compared to obese subjects without sleep apnea.

Methods: Using three-point Dixon magnetic resonance imaging with sophisticated volumetric reconstruction algorithms, we studied the size and distribution of upper airway intramuscular fat deposits in apneics and obese controls in the tongue and masseter muscles.

Results: We examined the intramuscular fat deposits in 31 obese control subjects (apnea-hypopnea index, 4.1 ± 2.7 events/h) and 90 apneics (apnea-hypopnea index, 43.2 ± 27.3 events/h). The data supported our a priori hypotheses that after covariate adjustment for age, BMI, gender, and race, the tongue in apneics compared to controls was significantly larger ($P = 0.001$) and had an increased amount of intramuscular fat ($P = 0.002$). Our data also demonstrate that within the apneic and normal tongue, there are regional differences in fat distribution with larger fat deposits at the base of tongue.

Conclusions: Increased tongue size and deposition of intramuscular fat at the base of tongue are independent risk factors for OSA. Increased tongue fat may explain the relationship between obesity and OSA.

Symposium – Sleep, Insomnia & Emotion

S349

Distinct roles for SWS and REM in emotional memory consolidation

P. LEWIS[1], S. CAIRNEY[1] and S. J. DURRANT[2]
[1]University of Manchester, Manchester, UK, [2]University of Lincoln, Lincoln, UK

Recent research has demonstrated that sleep mediates the reorganisation of emotional memories, but it is unclear which specific aspects of sleep support this process. Here, we examine this issue by studying memory for emotional pictures with functional magnetic resonance imaging (fMRI) both immediately after encoding, and after a night of carefully monitored sleep.

Sixteen participants undertook two experimental sessions. In the first (3 pm), participants encoded 90 (30 pos, 30 neg and 30 neutral) images. At 10 pm, participants slept overnight until 8 am and were monitored with polysomnography (PSG). In the second session (24 h later), participants repeated the procedures of session one, but with a new batch of 90 images. Thirty minutes later, participants completed a recognition test of all learned images plus 90 previously unseen images (30 pos, 30 neg and 30 neutral) in the MRI scanner.

Behaviourally, a 2 × 3 repeated measures ANOVA on the sensitivity index (d') with factors 'Image' (remote/recent) and 'valence' (pos/neg/neutral), showed no difference in memory performance for images encoded 24 h or 30 min prior to the retrieval test ($F_{1,15} = 0.02$; $P = 0.89$), no effect of valence ($F_{2,30} = 0.42$; $P = 0.66$), and no interaction $F_{2,30} = 0.07$; $P = 0.94$). Functionally, the time spent in SWS predicted an overnight reduction in right hippocampal activity during remote memory retrieval across all three valences, and this was especially strong for negative items (s.v.c. ($P < 0.05$)). While time spent in REM sleep did not predict any specific change in localised brain activity, it did predict an increase in hippocampal-cortical connectivity across retention, both when all valences were combined, and for negative items in isolation ($P < 0.001$ uncorrected).

Our observation that SWS predicted disengagement of the hippocampus, while REM sleep predicted increased hippocampal-cortical connectivity fits well with the idea that these sleep stages may play complimentary roles in consolidation. Specifically, SWS may be critical for the consolidation of individual episodic memories, while REM sleep may be important for the integration of distant concepts. Interestingly, neither behavioural findings nor neuroimaging results supported the selective consolidation of emotional memories across sleep, instead positive, negative, and neutral memories appeared to consolidate along similar trajectories.

S350

Stress and sleep

T. ÅKERSTEDT, H. PETERSEN and G. KECKLUND
Stockholm University, Stockholm, SE

This presentation reviews new work on the relation between stress and sleep. It is concluded that self-reported stress is associated with disturbed sleep cross-secionally and prospectively. Social support and control/influence will reduce the effects. The relation is also present in PSG data from prospecive field studies with comparisons of moderately high and low periods of everyday stress. The effects concern mainly sleep efficiency, WASO, Stage 1 or arousals. Effects of stress is also seen on TST and self-reported sleep quality the next day in a prospective daily measurement approaches across 42 days. Patients on sick leave after long periods of excessive stress show highe levels of impaired sleep. Overall, the studies show that stress impaires sleep even at modest levels, but particularly efter very high parially chronic levels.

S351

The role of emotion regulation in the relationship between insomnia and eating disorders

C. LOMBARDO
'*Sapienza*' *University of Rome, Rome, IT*

Objectives: Emotion Regulation (ER) is the set of processes used for modulating the quality, intensity or duration of an emotion (Gross e Thompson, 2007). Several strategies (e.g. suppression of the emotions) have been demonstrated to negatively influence mental health (Aldao et al., 2010). Previous evidence indicate that poor sleep is associated to higher level of emotion instability and greater experience of negative emotions (e.g. Baglioni et al., 2010). Similarly, people vulnerable to eating disorders have been shown to experience intense negative emotions and to turn to food for up-regulating them (Polivy and Herman, 2002). Moreover, both people with insomnia and people with AN show personality features of emotional dysregulation and inhibition, social avoidance and affective liability (Van de Laar et al., 2010; Holliday, et al. 2006). It is thus possible that emotion dysregulation is one of the factors that promote the development of both insomnia and eating disorders or a factor that promote the comorbidity among them.

Methods: Results of three studies will be presented. The first includes a community sample of 1019 female university students (Lombardo et al., submitted); the second (Lombardo et al., in prep.) includes a community sample of 568 female university students. In both studies valid and reliable questionnaires were used for assessing insomnia and eating disorders symptoms and emotion dysregulation. In the third study (Lombardo et al., in prep.) 105 female participants were enrolled and both self-report and physiological measures (facial EMG, HR, SCL) recorded.

Results: Results of the first study evidence that people reporting insomnia symptoms also show higher disordered eating even after having controlled for depression. Results of the second study evidence that the use of suppression mediates the relationship between insomnia symptoms and eating restriction. The third study evidence that suppression is related to high rates of co-occurrence of insomnia, eating disorders, anxiety and depression symptoms. Moreover, the more severe simptomatology is also related to different psychophysiological responding to emotional stimuli pertinent or not with the main symptoms.

Conclusions: The role of emotion suppression and the clinical implications of the relationships evidenced will be discussed.

S352

Brain reactivity to emotional stimuli in primary insomnia

C. BAGLIONI[1], K. SPIEGELHALDER[1], W. REGEN[1], B. FEIGE[1], C. LOMBARDO[2], C. NISSEN[1], C. VIOLANI[2] and D. RIEMANN[1]
[1]University of Freiburg Medical Center, Freiburg, DE, [2]'Sapienza' University of Rome, Rome, IT

Objectives: Insomnia is highly comorbid with psychiatric disorders and, at least with respect to major depression, it has been found to be

a clinical predictor. The psychobiological mechanisms, however, underlying this relationship are not yet fully understood. Heightened emotionality has been proposed to be a possible mediating factor. Supporting evidence refer to sleep deprivation studies and studies evaluating the role of sleep with respect to emotional memory. Moreover, studies on individuals exposed to chronic life stresses have shown that this condition is associated with sleep disturbances and increases the risk for emotional exhaustion. Neverthless, there is a surprising lack of studies evaluating emotion using physiological indeces in clinical samples of insomnia. Our main objective was to evaluate brain reactivity to emotional stimuli in patients with primary insomnia and in good sleepers.

Methods: Patients with primary insomnia ($n = 22$) and healthy controls ($n = 40$) were presented with different blocks of neutral, negative, and sleep-related negative pictures during an fMRI task. Neutral and negative pictures were taken from the International Affective Picture System (IAPS), while sleep-related negative pictures were previously validated. Stimuli were matched for valence and arousal levels. All participants previously underwent two consecutive nights of polysomnographic recordings in order to exclude those with other sleep disorders.

Results: Preliminary results are consistent with the hypothesis that people with insomnia present altered emotional responses in limbic areas to negative stimuli especially when related to the experience of the symptoms. Specifically, we found that patients with primary insomnia responded with increased amygdala activity to sleep-related negative stimuli as compared with good sleepers.

Conclusion: People with insomnia might develop an emotional bias to stimuli related to sleep which would be associated to increasing rumination and preoccupation about the consequences of bad sleep. Clinical implications of the present findings, which need confirmation by further investigation, suggest that adding an emotional regulation component to standard therapy for insomnia might be effective to ameliorate sleep and to prevent the development of depression as a public health priority.

The study ‘Brain reactivity to emotional stimuli in primary insomnia’ has received funding from the European Community’s Seventh Framework Programme (People, Marie Curie Actions, Intra-European Fellowship, FP7- PEOPLE-IEF-2008) under grant agreement n_ 235321.

Symposium – Cataplexy: an Intriguing Symptom

S353

Phenomenology of human cataplexy and its triggers

S. OVEREEM
Radboud University Nijmegen Medical Centre, Nijmegen, NL

Cataplexy is the most specific symptom of narcolepsy. In its typical form, cataplexy shows as attacks of bilateral muscle weakness with preserved consciousness, triggered by an emotional context. However, the clinical spectrum of cataplexy is extremely wide. Cataplexy can can affect all skeletal muscles except those subserving respiration and eye movements. While attacks can be complete, cataplexy is often partial, preferentially affecting the face, the neck and the lower legs. Partial attacks can be subtle and sometimes only recognized by experienced observers such as the patient's partner. The duration of cataplexy is generally short with most attacks lasting only seconds. However, attacks lasting several minutes have been reported. Although the central characteristic of cataplexy is atonia, positive motor phenomena are quite often observed, with muscle twitching or small jerks, particularly of the face. The emotional triggering is a defining feature. Although the whole gamut of emotions can potentially lead to cataplexy, those associated with mirth are usually the most potent. Laughing out loud, telling a joke or making a witty remark are typical examples with some reporting the anticipation of laughter, typically as a punch line approaches, to be the most effective precipitant. However, in some patients 'negative' emotions such as anger or startle are the most provoking. The frequency of cataplexy is variable, ranging from less than one attack per month to more than 20 attacks per day. Many patients reporting warning signs such as 'strange' feelings in the head, or sensations of warmth or nervousness.

In recent years, increasing attention has been given to the clinical presentation of narcolepsy in childhood. Several studies have now shown that cataplexy in children can appear phenotypically different to typical episodes seen in adulthood. Although cataplexy in children can present very similar to the adult phenotype, it may also take the form of a more generalized hypotonia. The muscle weakness can be very pronounced in the face, with opening of the mouth and ptosis. A peculrar protrusion of the tongue is often observed, leading to a characteristic facial expression that has been coined as 'cataplectic facies'. Finally, childhood cataplexy seems to be associated with several positive motor phenomena, including perioral dyskinesias, dystonic movements and stereotypies. Preliminary follow-up data seems to suggest that the striking childhood form of cataplexy may gradually develop into the more typical adult phenotype over several years.

S354

Identification of the neuronal network generating muscle atonia during cataplexy and REM sleep in mice

C. PEYRON, S. ARTHAUD, N. GAY, M. NOUVIAN, C. YA, S. MEFTAH and P.-H. LUPPI
CRNL, CNRS UMR5292, INSERM U1028, Lyon, FR

Narcolepsy is characterized by excessive daytime sleepiness and cataplexy (loss of muscle tone during wakefulness triggered by emotions), along with hypnagogic hallucinations and sleep paralysis. It is accompanied with a short latency to rapid-eye-movements sleep (REM; also called paradoxical sleep) and sleep onset REM periods (SOREMS). Symptoms highlight a deregulation of REM regulation. Cataplexy is very similar to REM muscle atonia suggesting that part of the network generating REM is activated during cataplexy. Extensive work has been done to identify REM atonia network in cats and rats. However, it has not been identified in mice, a model of choice for the study of cataplexy thanks to the availability of genetically modified animals.

CFos is an immediate early gene expressed in a wide range of neurons when they experience a sustained activity, and is commonly used as a neuronal activation marker. It has been used in rats to identify the neuronal populations specifically active during REM. As REM amounts are low in basal condition, a protocol of homeostatic challenge (i.e. a REM deprivation followed by REM hypersomnia) was used to trigger CFos expression in REM active neurons.

The combined use of CFos immunostaining, pharmacological microinjections and electrophysiological recordings demonstrated in rats that the neurons generating REM are glutamatergic and localized in the pontine sublaterodorsal tegmental nucleus (SLD). In addition, we showed that the SLD send direct projections to glycinergic neurons of the medullary ventral gigantocellular reticular nucleus previously shown to be responsible for motoneurons' hyperpolarization during REM.

Using a similar paradigm of specific REM hypersomnia combined with double immunostaining of Cfos with several markers such as tyrosine hydroxylase, acetylcholine transferase, hypocretin-1 or melanin concentrating hormone, we evaluated the similarities and discrepancies of the network generating REM in mice compared to rats. We found a small region just ventral to the periaqueductal gray, corresponding to the rat SLD, which is immunoreactive for CFos after REM hypersomnia. We also found activated neurons in the ventrolateral part of the periaqueductal gray, in the ventral medulla and the tuberal hypothalamus (including the melanin concentrating hormone neurons). Like in rats, the pontine cholinergic neurons were not Cfos positive.

Our observations indicate that the neuronal network generating REM is similar in mice to rats with some variations in the precise localization of the structures.

S356

Rapid eye movement sleep and cataplexy: distinct regulatory processes revealed by stress and pharmacological treatments in a mouse model of narcolepsy

V. FABRE[1], A. RACHALSKI[1], M. CIZERON[1], G. VODJDANI[1], J. S. LIN[2], S. BERRARD[1] and J. ADRIEN[1]
[1]CRICM, Paris, FR, [2]Neuroscience Research Center, Lyon, FR

Narcolepsy is a sleep disorder characterized by excessive daytime sleepiness, cataplexy, hypnagogic hallucinations and sleep paralysis. Cataplexy is defined as the sudden loss of muscle tone triggered by emotions. In humans, antidepressants, including aminergic reuptake inhibitors, are commonly used to treat cataplexy. Because these compounds are well known to inhibit the occurrence of rapid eye movement (REM) sleep, cataplexy has been proposed to be controlled by mechanisms similar to those producing REM sleep atonia.

Here, we have addressed this question by challenging cataplexy and REM sleep amounts with pharmacological treatments that target REM-on cholinergic and REM-off serotonergic neurotransmissions or

with an acute stress. To this goal, we used a validated mouse model of narcolepsy exhibiting cataplexy-like attacks, i.e. mutant mice that do not express the hypocretin precursor preprohypocretin (pphcrt–/–).

Thus, pphcrt–/– and pphcrt+/+ mice were injected at 7:00 P.M. with the cholinesterase inhibitor physostigmine (0.025 and 0.05 mg/kg), the nicotinic acetylcholine receptor agonist nicotine (1 and 2 mg/kg) and the serotonin reuptake inhibitor citalopram (1–1 mg/kg) or were submitted to restraint stress from 5:30 to 7:00 P.M. Sleep-wake states and cataplexy were monitored from 7:00 P.M. to 7:00 A.M.

In pphcrt-/- mice, enhancement of the cholinergic neurotransmission by physostigmine increases the number and duration of cataplexy-like attacks, but has no effect on REM sleep amounts. Conversely, nicotine inhibits REM sleep without affecting cataplexy-like attacks. Enhancement of the serotonergic neurotransmission by citalopram dose dependently decreases both REM sleep amounts and cataplexy-like attacks in pphcrt-/- mice. Finally, restraint stress session induced strong modifications of REM sleep in pphcrt-/- mice: initially, a dramatic decrease during 2 h and secondarily, an increase during 6 h. It also markedly inhibits the occurrence cataplexy-like attacks during 12 h.

Altogether, these findings show dissociation between the regulatory mechanisms that control cataplexy-like attacks and REM sleep in pphcrt-/- mice, a mouse model of narcolepsy, thus suggesting that the mechanisms that govern REM sleep atonia and cataplexy are, at least partially, distinct.

Symposium – Sleep and Circadian Interactions with Thermoregulation and Cardiovascular Function: Basic Research and Clinical Implications

S357

Circadian clock control of body temperature and cardiovascular function: implications for health and disease

F. A. J. L. SCHEER
Harvard Medical School, Boston, US

Optimal adaptation of the body to the varying physical demands across the day and night requires dynamic and anticipating neuro-endocrine control of thermoregulation and cardiovascular function. Recent evidence has shown that even in the absence of the sleep/wake, rest/activity, and fasting/feeding cycle, the cardiovascular function has robust endogenous circadian rhythms, including those in blood pressure, heart rate, cardiac vagal modulation, plasma epinephrine, cortisol and norepinephrine, and platelet activation, that are synchronized with core body temperature. Animal experimental work has demonstrated the presence of multi-synaptic projections from the suprachiasmatic nucleus of the hypothalamus (SCN), the central circadian pacemaker, to the myocardium and that lesioning the SCN abolishes the circadian rhythm in resting heart rate and core body temperature. In addition, the same molecular clock work as driving the SCN has been demonstrated in peripheral tissues, including the heart and vasculature. Furthermore, the circadian system also interacts with behavioral stressors such as exercise and postural stress, causing endogenous circadian rhythm in stress reactivity. While adaptive in healthy individuals, the dynamic changes may contribute to the morning peak in adverse cardiovascular events in vulnerable populations and to an increased risk for postural hypotension at night, possibly explaining vasovagal syncope interrupting sleep. Furthermore, circadian disruption such as with shift work, may lead to increased cardiovascular risk in these populations. Understanding the fundamental circadian mechanisms may help in the development of novel therapeutic approaches against adverse cardiovascular events.

F. A. J. L. S. was supported by National Institute of Health Grants P30-HL101299 and R01 HL094806.

S358

Deep hypothermia-induced changes in sleep and cardiovascular function

R. AMICI[1], A. AL JAHAMANY[1], M. CERRI[1], F. DEL VECCHIO[1], M. LUPPI[1], D. MARTELLI[1], M. MASTROTTO[1], E. PEREZ[1], D. TUPONE[2] and G. ZAMBONI[1]
[1]University of Bologna, Bologna, IT, [2]Oregon Health & Science University, Portland, US

Objectives: The Rostral Ventromedial Medulla (RVMM) is a key area in the control of autonomic function and metabolism, promoting thermogenesis (1). In the present study, the effects on sleep and cardiovascular parameters of the induction of a torpor-like state by the pharmacological inhibition of RVMM were investigated in the rat.

Methods: Male Sprague–Dawley rats (n = 18, 300–350 g) adapted to an ambient temperature (Ta) of 25°C, were implanted, under general anaesthesia (diazepam, 5 mg/kg, i.m., ketamine, 100 mg/kg, i.p.), with electrodes for EEG and EMG recording, a thermistor for detecting hypothalamic temperature (Thy), a catheter for arterial blood pressure recording, and a microcannula within the RVMM. After a week of recovery, animals were kept for 3 days at Ta 15°C and then they were microinjected within the RVMM (1 injection/h, for 6 h) with either the GABAA agonist muscimol [1 mM, 100 nl; Group 1 (n = 6) and Group 2 (n = 6)] or saline [0.9%, 100 nl, Group 3 (n = 6)]. In order to favour the return to normothermia, 1 h after the last injection Ta was raised to 28°C for Groups 1 and 3 and, for Group 2, to 37°C, which was kept for 1 h and then taken to 28°C.

Results: Muscimol induced a deep hypothermia (Thy: 22.8 ± 0.8°C) which was accompanied by: (i) a reduction of EEG activity; (ii) a decrease in heart rate (HR), from 440 ± 13 to 201 ± 12 bpm; (iii) a substantial maintenance of mean arterial pressure (MAP) at normal levels. Group 2 recovered normothermia faster than Group 1. Recovery was characterized by: (i) a progressive normalization of HR; (ii) the occurrence of a peak in MAP compared to saline (Group 3, 92 ± 4 mmHg), that was larger ($P < 0.01$) in Group 2 (125 ± 4 mmHg) than in Group 1 (116 ± 2 mmHg); (iii) the building up, in Groups 1 and 2, of a large SWS rebound in NREM sleep and of a not significant rebound in REM sleep.

Conclusion: The effects of RVMM inhibition on cardiovascular and sleep parameters resembled those observed in natural torpor (2, 3). The increase in MAP observed during the recovery may be favoured by an excess in sympathetic activity. The effects on sleep observed after the recovery of normothermia indicate that the hypothermic bout and/or the rewarming generated a homeostatic need for SWS, but not for REM sleep.

References:

1) Morrison S, Nakamura K. Front Biosci (2011) 16: 74–104.
2) Swoap SJ, Gutilla MJ. Am J Physiol RICP (2009) 297:R769–774.
3) Deboer T, Tobler I. Sleep (2003) 26: 567–72.

S359

Skin temperature-induced changes in sleep and vigilance and implications for insomnia

B. H. W. TE LINDERT
Netherlands Institute for Neuroscience, Amsterdam, NL

Objectives: We hypothesized that sleep and vigilance are more closely associated with changes in skin temperature than with changes in brain temperature (1–3).

Methods: Skin temperature manipulations, actigraphy and MRI studies.

Results: We confirmed the hypothesis by showing that the induction of minute changes in skin temperature causally affected sleep and vigilance in healthy young and elderly people, insomnia and narcolepsy (4–10). Furthermore, the spontaneous fluctuations in skin temperature are of value in the detection of sleepiness and lapses of attention (11) during the day and greatly improve the reliability of actigraphic sleep estimates during the night.

We addressed possible abnormalities in skin temperature and its association with sleep and vigilance. In healthy subjects, sleep deprivation disrupts coordination of fluctuations in thermoregulatory

skin gradients. In narcolepsy, we demonstrated an insufficient skin vasoconstriction response to attaining an upright posture (12). The less the response, the shorter the sleep onset latency during multiple sleep latency tests (MSLT).

In a voxel-based morphometry MRI study in insomnia, severity of sleep complaints correlated with gray matter volume in the orbitofrontal cortex, a key area for the evaluation of thermal comfort (13). Indeed, we confirmed deficits in the subjective evaluation of thermal comfort in insomnia patients (8). Recently, we demonstrated that early morning awakening in healthy subjects is associated with a relatively low orbitofrontal gray matter density (14)

Conclusion: Concertedly, our studies indicate a close link between thermoregulation and vigilance regulation, and provide new avenues for the development of treatments for disorders of sleep and alertness.

References:

1. Romeijn N et al (2012) Sleep, vigilance, and thermosensitivity. Pflügers Archiv Eur J Physiol 463:169–176.
2. Van Someren EJW (2004) J Therm Biol 29:437–444.
3. Van Someren EJW (2006) Prog Brain Res 153:309–324.
4. Raymann RJEM et al (2005) Am J Physiol 288:R1589–R1597.
5. Raymann RJEM and Van Someren EJW (2007) Sleep 30:96–103.
6. Raymann RJEM et al (2007) Physiol Behav 90:257–266.
7. Raymann RJEM et al (2008) Brain 131:500–513.
8. Raymann RJEM and Van Someren EJW (2008) Sleep 31:1301–1309.
9. Fronczek R et al (2008) Sleep 31:233–240.
10. Fronczek R et al (2008) J Neurol Neurosurg Psychiatry 79:1354–1357.
11. Romeijn N and Van Someren EJW (2011) J Biol Rhythms 26:68–77.
12. Fronczek R et al (2006) Sleep 29:1444–1449.
13. Altena E et al (2010) Biol Psychiatry 67:182–185.
14. Stoffers D et al (2012) Front Neurol in press.

S360

Sleep-induced changes in cardiovascular function and skin temperatures: diagnostic implications for cardiovascular disease

K. KRÄUCHI

Centre for Chronobiology, Basel, CH

The cardiovascular system plays a central role in both temperature (T) and blood pressure (BP) regulation. It has long been recognized that diurnal rhythms of core body and skin T, heart rate and BP are influenced by the sequence of rest (sleep) and activity. Sleep initiation is tightly coupled with a reduction in sympathetic nerve activity, heart rate and arterial BP and an increase in skin blood flow and skin T (most expressed in distal skin regions), whereby all these changes start after lights out and before appearance of sleep stage 2. In a series of experiments (some with melatonin or warmth administration) we studied distal and proximal skin T together with core body T, BP, heart rate and sleepiness/EEG-sleep measures under controlled lab protocols and some of these parameters under ambulatory conditions. Under constant routine conditions distal skin T, salivary melatonin secretion and sleepiness increase at the beginning of the subjective night together with a decline in proximal skin T, core body T and heart rate. In contrast, systolic and diastolic BP exhibits minor endogenous circadian variation, if any. Under ambulatory real life conditions proximal and more pronounced distal skin T increase at the beginning of the sleep phase and BP and heart rate decline. The distal–proximal skin T gradient (DPG) exhibits nearly a mirror image of mean arterial BP (MAP). Lower DPG level during daytime (reduced distal skin blood flow dSBF) significantly predicts larger sleep induced decline in MAP indicating possible diagnostic implications (e.g. for over- and non-dipping – BP profiles). Preliminary path analysis suggested that outdoor air temperature may act on MAP via changed dSBF (e.g. cold air in winter reduces DPG, increases MAP and hence cardiovascular risk). Data of seasonal and environmental influences (e.g. in air T, humidity, atmospheric pressure) on MAP, pulse wave velocity, augmentation index, heart rate, wrist activity and skin T will be presented of an ongoing study carried out during winter and summer in women with predisposition for cold extremities (vascular dysregulation) and controls.

In summary, dSBF seems to play not only an important role in sleep initiation but might have an impact on individual cardiovascular risk prediction with respect to diurnal, seasonal and weather variations.

Supported by SNF 3100A0-102182/1, 3200B0-116504/1 and Schwickert-Stiftung.

Keynote Lecture

S361

Sleep and synaptic homeostasis

C. CIRELLI

University of Wisconsin–Madison, Madison, US

The function of sleep remains an unsolved biological puzzle. Understanding the function of sleep is obviously important both scientifically and from the perspective of human health. Sleep is a pervasive, universal, and fundamental behavior: It occupies a third of our life, and an even larger proportion in infants; it is present in every animal species where it has been studied, from fruit flies to humans; it is tightly regulated, as indicated by the irresistible mounting of sleep pressure after prolonged wakefulness; and even partial deprivation of sleep has serious consequences on cognition, mood, and health. A recent hypothesis about the function of sleep, the synaptic homeostasis hypothesis, states that plastic processes during wakefulness (and development) result in a net increase in synaptic strength in many brain circuits; such increased synaptic strength comes at the expense of increased metabolic consumption and higher demand for cellular supplies such as proteins and lipids, and reduces the informativeness of neuronal signals. Stronger synapses are also closer to their level of saturation, which may prevent further learning. According to the hypothesis during sleep synaptic strength is globally renormalized to a baseline level that is energetically sustainable and beneficial for memory and performance. Sleep is thus the price we pay for plasticity, and its core function is the homeostatic regulation of synaptic weight impinging on neurons. I will review recent experiments in flies, rodents and humans that provide molecular and electrophysiological evidence for the hypothesis and discuss limitations and future challenges.

Poster Session – Attention, Aronsal and Vigilance

P362

A double interference Stroop task: effect of nocturnal alertness reduction

M. SEBASTIANI[1], D. MARTELLA[2], A. MAROTTA[1], L. MACCARI[1], F. COSCO[1], A. SPAGNA[1], L. J. FUENTES[3] and M. CASAGRANDE[1]
[1]University of Rome 'Sapienza', Rome, IT, [2]Basque Center on Cognition, Brain and Language, San Sebastian, ES, [3]Universidad de Murcia, Murcia, ES

Objectives: This study points to evaluate the effect of a reduction of alertness, obtained by sleep reduction as well as circadian phase, on the inhibition of automatic behavior to allow a voluntary one. One of the most used task to this purpose is the Stroop Task (Stroop, 1935). In the scientific literature mixed results have been reported about this subject (Sagaspe et al., 2006).

Methods: A modified version of the Stroop Task has been used (Besner & Stolz (1999). Stimuli were words naming colors, and letters compounding them were colored in two different colors. Participants have to name the central letter's color, which was congruent or incongruent as respect to the meaning of the word (e.g. 'rosso', Italian word for red, presented with the central S in red or in green). The other letters were in a different color as respect to the central letter. One hundred and fifty millisecondsearlier the word presentation, a small circle (spatial cue), surrounded the central letter (valid condition), the letter on the right or the left of the central one (invalid condition) or the entire word (neutral condition). Participants have been invited to ignore the cue. Participants have performed the task at 12.00 p.m. and 2.00 a.m.

Results: An ANOVA 2 Session × 2 Conflict × 2 Cue on the average of the vocal responses (RT) has revealed main effects of Session ($F_{1,8}$ = 11,45; $P < 0.01$), Conflict ($F_{1,18}$ = 23,9; $P < 0.001$), and Cue ($F_{3,24}$ = 13,86; $P < 0.001$). The Session × Cue ($F_{3,24}$ = 3,36; $P < 0.03$) interaction was also significant. In the 'Night' Session RT were slower in the invalid condition (664 ms) as respect to the valid condition (620 ms; $P < 0.00004$).

Conclusion: Reading a word and the attentional capture by a spatial cue have been considered as automatic process, which must be inhibited to allow the voluntary task of naming the central letter's color. In the task presented here there was no need to move the focus of attention from the center of the word, because the color of the letter to be named was always presented in the same position. Nevertheless, in the night session, Participants seem to be more sensitive to the effect of the attentional capture exerted by invalid cue.

P363

Counteracting low alertness during the main sleep gate: effects on attentional networks

D. MARTELLA[1], A. MAROTTA[2], L. MACCARI[2], M. SEBASTIANI[2], A. SPAGNA[2], L. J. FUENTES[3] and M. CASAGRANDE[2]
[1]Basque Center on Cognition, Brain and Language, San Sebastian, ES, [2]University of Rome 'Sapienza', Rome, IT, [3]Universidad de Murcia, Murcia, ES

Objectives: Sleep loss and its interaction with time of day probably exerts the most critical effects on sustained operations, causing a decrease in functioning of attentional networks (alerting, orienting and executive control). Specifically, in such conditions the strong decrease of the tonic component of alertness (A) impair both attentional orienting and executive functions (Martella et al., 2011). This study was aimed to verify whether an increase of phasic A is able to contrast the effects of A decrease produced by both nighttime and sleep loss (SD) on attentional systems. The two components of A (tonic and phasic) were contemporarily manipulated, on one part by reducing the tonic level of it through a SD, on the other by increasing the phasic level of A, through the random presentation of an auditory warning (W). The attentional performance has been assessed by using the Attention Network Test that allows evaluating at the same time the efficiency and the relationship among the three attentional systems.

Methods: Eighteen healthy volunteers (mean age: 22.3 ± 1.9) had to discriminate the direction of a left- or right-point arrow, which was flanked on either side by two arrows pointing either in the same direction, or in the opposite direction. Before the target four visual cue conditions could be equally present: valid, invalid, double-cue, no-cue. A W was presented in 25% of the trials. After participants slept their usual 8 h, they were kept awake for 24 h and were required to perform the ANT at 5.00 p.m. (BSL) and 4.00 a.m. (SD).

Results: ANOVAs separately performed on reaction times of the W and No-W conditions showed a significant effect for the Session (W: F = 20; $P < 0.001$; No-W: F = 28; $P < 0.0001$); with slower RTs in the SD than in BSL. All the other main effects were significant ($P < 0.0000001$). In the W conditon no interaction was present, while in the No-W condition the Session × Cue (F = 4; $P < 0.02$) and the Cue × Flanker (F = 3; $P < 0.02$) interactions were significant. Furthermore only in this condition, there were significant variations of Orienting (F = 7; $P < 0.02$), Alerting (F = 5,8; $P < 0.03$) and Executive (F = 5; $P < 0.05$).

Conclusion: The results induce interesting considerations on the effects of the two components of the A in a SD condition. In fact, if a low level of A reduces the efficiency of each attentional system, modulating their mutual interaction; the increase of the phasic A seems counteract theseeffects, ensuring the independence of the three systems.

P364

Sleep deprivation affects attentional orienting triggered by central un-informative gaze and arrow cues

A. MAROTTA[1], M. SEBASTIANI[1], D. MARTELLA[2], L. MACCARI[1], A. SPAGNA[1] and M. CASAGRANDE[1]
[1]University of Rome 'Sapienza', Rome, IT, [2]Basque Center on Cognition, Brain and Language, San Sebastian, ES

Objectives: Behaviour and neuroimaging studies have shown that Sleep Deprivation (SD) negatively affects exogenously cued selective attention. However, it is an open question as to whether all subtypes of reflexive attention are similarly affected. The aim of this study was principally to assess the impact of partial SD and nighttime performance on reflexive attentional orienting triggered by central un-informative eye-gaze and arrow cues. Subjective mood and interference performance in Emotional Stroop task was also investigated.

Methods: Twenty healthy volunteers (4 M/16 F; mean age: 24.3 ± 2.3) performed spatial cueing tasks using central directional arrow and eye-gaze as a cue to orient attention. The target was a colour word written in different coloured inks. The subject's task was to identify the colour of the ink whilst ignoring the semantic content of the word (with negative or neutral emotional valence). The experi-

ment took place on two consecutive days. On the first day, each participant performed a 20 min training session of the spatial cueing task. On the second day, participants remained awake for 24 h during which time cueing tasks were performed once at 4:30 p.m. (BSL) and once at 6:30 a.m. (SD).

The experiment had a four-factor repeated measure design: Session (BSL, SD) × Cue Type (gaze and arrow) × Cueing (Cued, Uncued) × Valence (negative, neutral).

Results: Analyses of variance revealed that mean reaction time performance on the spatial cueing tasks was worsened by sleep deprivation ($F_{1,19} = 79.05$, $P < 0.001$). The Session × Cueing interaction was also significant ($F_{1,19} = 5.45$, $P < 0.03$), showing a significant Cueing effect only in the BSL ($F_{1,19} = 6.17$, $P < 0.03$). No differences were found between cued and uncued trials in the SD ($F < 1$). Moreover, ANOVA revealed that self-assessment of mood on a visual analogue scale was worsened by sleep deprivation ($F_{23,437} = 6.03$, $P = 0.001$). No other effect was significant.

Conclusion: Sleep Deprivation negatively affects attentional orienting triggered by central un-informative gaze and arrow cues. Moreover prolonged wakefulness affect self-reported mood but does not affect interference control in Emotional Stroop Task.

P365

Baseline neural predictors of working memory Impairment during sleep deprivation

A. M. TUCKER[1], Y. GAZES[2], R. C. BASNER[2], C. HABECK[2], J. STEFFENER[2] and Y. STERN[2]

[1]University of Colorado, Boulder, US, [2]Columbia University, New York, US

Introduction: Individual differences in the cognitive consequences of sleep loss are sizable, spanning an order of magnitude. This study examines whether baseline fMRI can be used to predict which individuals will demonstrate resilience in maintaining working memory throughput during sleep loss.

Methods: Healthy young adults aged 20–35 years were continuously monitored and kept awake in a laboratory in two sleep deprivation experiments ($N = 17$ and $N = 20$). Participants were scanned while they performed a delayed letter recognition task, once at 9:00 am and a second time after 48 h of total sleep deprivation (TSD). An event-related design allowed us to use SSM to search for networks of brain regions whose activation changed with increasing memory set size for each of three trial phases: encoding, retention, and retrieval.

Results: At baseline we were able to identify networks of activation for each trial phase. After 48 h TSD participants were slower, less accurate, and had more failures to respond on the recognition task; a PCA was used to combine these variables into a latent variable representing working memory throughput. Baseline activation during the encoding and retention phases, but not the retrieval phase, correlated with the magnitude of the performance changes seen with sleep loss ($r^2 = 0.20$ and $r^2 = 0.13$, respectively). In a multiple regression, only the network expressed during the encoding phase remained a significant predictor of performance impairment ($r^2 = 0.25$). This network involved greater activation of dlPFC and SMA and reduced activation in extrastriate cortex and the insula.

Discussion: Neural activation during the encoding phase of a working memory task during baseline was predictive of resilience in maintaining working memory throughput during sleep deprivation. The activation patterns suggested that resilient individuals were able to exert more top-down control over both external and internal incoming sensory information. This adds to behavioral evidence that the working memory deficits seen during sleep deprivation may be due to difficulties in encoding information while aspects of memory retrieval seem to be intact during TSD. In summary, these results suggest that those individuals with better top-down control of sensory regions important for detecting and encoding information at baseline may be better able to withstand working memory impairments during sleep loss.

P366

Validating a 3-min psychomotor vigilance task for sleep loss-induced performance impairments

E.-.M. ELMENHORST, D. ROONEY, S. PENNIG, M. VEJVODA and J. WENZEL

German Aerospace Center, Cologne, DE

Objectives: Psychomotor performance degradation is a sensitive marker for sleep loss related vigilance deficits. However, tests with a typical duration of 10 min + are usually not feasible in operational settings. Therefore, the DLR-Institute of Aerospace Medicine developed a 3-min Psychomotor Vigilance Task (PVT) on a handheld computer to be operated in the working environment of aviation and transportation. The aim of the current study was to assess the validity of this test.

Methods: We investigated 47 subjects (21 female, mean age 27 ± 5 years) during 12 days in the DLR-sleep laboratory. Subjects executed performance tests every 3 h during wake time (in total 63 sessions). Sleep restriction (38 h awake, 4h sleep, and 4 h sleep after moderate alcohol intake) was applied to induce different levels of performance degradation. In nights with 4 h sleep 24 of the subjects slept in a crew-rest-compartment in the DLR-pressure chamber in a realistic flight simulation (atmosphere, noise), whereas 23 of the subjects slept in the sleep lab in normobaric and silent conditions. Each intervention was followed by 2 recovery nights and administered in a crossover design. We calculated Pearson's correlation between the 3-min PVT and a computer-based 10-min PVT as well as between the 3-min PVT and an Unstable Tracking Task (UTT). UTT reflects typical operator demands and is a validated task sensitive for sleep loss induced performance decrements.

Results: Ten-minute PVT and UTT were highly significantly correlated with 3-min PVT regarding all experimental conditions ($P < 0.001$). During 38 h awake correlation was r = 0.714 for PVT mean reaction time (RT), r = 0.592 for lapses, and r = 0.498 for UTT root mean square error. After 4 h of sleep restriction the correlation was r = 0.808 for RT, r = 0.611 for lapses, and r = 0.561 for UTT in the sleep lab group and r = 0.804 for RT, r = 0.546 for lapses, and r = 0.526 for UTT in the pressure chamber group. After 4 h of sleep restriction with alcohol intake the correlation was r = 0.808 for RT, r = 0.542 for lapses, and r = 0.606 for UTT in the sleep lab group and r = 0.850 for RT, r = 0.619 for lapses, and r = 0.540 for UTT in the pressure chamber group. The overall correlation of all test sessions during the study was r = 0.814 RT, r = 0.634 for lapses, and r = 0.550 for UTT.

Conclusion: The 3-min PVT detected performance impairments after different degrees of sleep restriction reliably and consistently, thereby tracking the impairments in the parallel 10-min PVT and in UTT.

P367

Night-time, sleep loss and change blindness: how low arousal affects a very engaging task

L. MACCARI[1], D. MARTELLA[2], A. MAROTTA[1], M. SEBASTIANI[1], A. SPAGNA[1] and M. CASAGRANDE[1]

[1]University of Rome 'Sapienza', Rome, IT, [2]Basque Center on Cognition, Brain and Language, San Sebastian, ES

Objectives: Some tasks are most affected by sleep deprivation (SD) than others. A recent meta-analysis (Lim, & Dinges, 2010) considering several cognitive fields show that the effect sizes ranged from small and non significant to large. Interestingly, performance do not significantly decrease on the more complex cognitive tasks over the night of sleep deprivation (Pilcher et al., 2003). So, if the task encourages to remain attentive to and engaged in the task, performance is less affected by SD. According to this, it could be relevant to test this hypothesis using a really engaging task like the flicker task FT. It requires subjects to find a change occurring when two version of the same scene alternate repeatedly, separated by a brief gray screen. The pictures are identical except in a specific detail, the change to find. Based on the scene characteristics, there are changes first and easily found (of Central Interest: CI) and others requiring more time (of marginal interest: MI).

Methods: Eighteen healthy volunteers (3 M/15 F; mean age: 24.3 ± 2.3) executed the FT. They had to find a CI or MA change in complex scenes. The experiments were run on two consecutive days. In the morning of the first day, participants performed the training task. On the second day, after participants slept their usual 8 h, they were kept awake for 24 h and were required to perform the FT at about 3.00 p.m. (Baseline: BSL) and 5.00 a.m. (SD). The order of BSL and SD conditions were balanced across subjects.

Results: The ANOVA performed on RT shows an effect of TypeChange ($F_{1,17} = 88.23$; $P < 0.0001$; partial eta 2 = 0.84), with slower RT in detecting CI changes (9915 ms) than MA changes (17781 ms). The Session × TypeChange interaction ($F_{1,17} = 82.39$; $P < 0.0001$; partial eta 2 = 0.83) shows that SD improves CI detection (BSL: 12789 ms versus SD: 13981 ms; $P < 0.0001$) and worsens MI detection (BSL: 7041 ms versus SD: 21581 ms; $P < 0.0001$).

Conclusion: Our results show that SD affects differently the detection of CI and MI changes. This findings support the notion that a moderate sleep deprivation affects voluntary attentional processes to a greater degree than automatic processes (Trujillo, Kornguth, & Schnyer, 2009).

P368

Disturbances of visual-motor coordination during decreased the arousal level caused by monotony performance

G. N. ARSENYEV, O. N. TKACHENKO, T. P. LAVROVA and V. DOROKHOV

Institution of Russian Academy of Sciences Institute of Higher Nervous Activity and Neurophysiology of RAS, Moscow, RU

Aim of our studies was to develop a way to investigate influence of monotonous activity on visually-motor coordination during the moments before appearance of behavioural errors, caused by decrease of wakefulness level is a work problem.

The experimental model looked as follows: target object is a small round spot (diameter 13 mm) which moved with constant slow rate (12 mm/s) on a circular orbit (diameter 80 mm) and 20 s period.

We have performed four series of experiment. The first series (without the satellite) has been designed to cause a state of monotony in a subject. In second series we added a satellite constantly orbiting the main target. In the fourth series subjects slept 50% from a usual sleep one night prior to experiment.

Eyes movements were registered by a non-contact videosystem for eye movements research. The trajectories mouse cursor and eyegaze where registered with the time resolution -120 Hz. Electroencephalogram C 3, C 4) was registered to assess where level of a wakefulness.

In the first (preliminary) series we have found out the mistakes associated with monotony development. In the second series ($N = 10$) besides errors, characteristic for the first series, the augmentation of a latent period (LP) pressing the mouse button from 643 ± 157 to 678 ± 259 ms was also observed.

In the third series ($N = 13$), during the decrease in wakefulness level, we observed the augmentation of eyegase LP (time between appearance of the satellite and the beginning of fast eye movement – saccades) from 291 ± 110 to 342 ± 144 ms, cursor movement LP from 440 ± 121 to 463 ± 136 ms and mouse button pressing LP when cursor got to the satellite 1296 ± 365 to 1408 ± 322 ms.

In the fourth series ($N = 19$), at depression in wakefulness level we observed significant increase in reactions LP: 380 ± 130 to 490 ± 110 ms for saccade beginnings, 430 ± 190 to 483 ± 212 ms for mouse movement LP and 1236 ± 331 to 1385 ± 343 ms for pressing the mouse button LP.

Thus in three series LP by comparison third and fourth series, eyegase LP at with sleep deprivation subjects in state without monotony was bigger, than subjects at without sleep deprivation (291 ± 110 ms against 380 ± 130 ms). Cursor movement LP wasn't differ (440 ± 121 ms and from 430 ± 190 ms). But mouse button pressing LP when cursor got to the satellite was differ (1296 ± 36 ms and 1236 ± 331 ms).

P369

Fading of consciousness and executive functions during sleep onset: behavioural and EEG evidence from Go (-No-Go) tasks

V. NOREIKA, T. BEKINSCHTEIN and A. OWEN

MRC Cognition and Brain Sciences Unit, Cambridge, UK

Objectives: The onset of sleep provides a unique window to investigate psychophysiology of consciousness and its fading. Within several minutes or even tens of seconds, consciousness may fluctuate between alertness, relaxation, drowsiness and unresponsiveness, each of which is associated with varying capabilities of executive functioning. The aim of the present study was to investigate psychophysical and neurophysiological markers of these transitions of consciousness.

Methods: Two daytime EEG experiments were carried out in which participants performed a Go-Left/Go-Right task and a decision-wise more challenging Go-No-Go task. Participants were encouraged to enter drowsiness by setting the lights dim and asking participants to relax and close their eyes. Behavioural and EEG analyses of these tasks allowed us to investigate attention and decision making across the brief cycles of consciousness fading and regaining.

Results: Error rates, reaction times and their variability increased from alertness to drowsiness to unresponsiveness. However, participants differed regarding their performance in time: one group of participants showed increasing drowsiness pattern, whereas another group showed more cyclic pattern of performance. Behavioural findings were supported by changes in the Go-left versus Go-right and Go-No-Go-specific ERP components. Furthermore, we found

that certain pre-trial spectral EEG markers, such power ratios between different frequency bands, may predict behavioural pattern of post-stimulus responding.

Conclusion: Inhibition of auditory awareness and executive functions during transition from wakefulness to drowsiness to unresponsiveness is a complex, temporary extended process, which can be characterized by specific EEG and behavioural markers.

P370

Analysis of EEG changes during microsleep with open eyes associated with lapses in psychomotor test performance

O. TKACHENKO, T. LAVROVA, V. DOROKHOV and I. SILKIS
IHNA RAS, Moscow, RU

Mistakes in visuomotor performance that are often associated with behavioral microsleep episodes can have catastrophic consequences. We put forward a hypothesis that one of mechanisms of lapses during microsleep is a spontaneous generation of ponto-geniculo-occipital (PGO) waves that suppress transmission of visual information from the retina via lateral geniculate nucleus to primary visual cortical areas and the striatum, and thus significantly impair visual perception and attention. If this hypothesis is correct it must manifest itself in specific changes of spectrum of electroencephalogram (EEG) in occipital areas (O1, O2) wherein primary visual cortical areas are located. The goal of the present work was to test this hypothesis. Six healthy subjects (18–26 years) were selected to participate in this study. Experiments were performed during the nighttime. Monotonic testing during performance of the two-alternative psychomotor test invoked participants into a state defined as a microsleep with open eyes (25 experiments). Polysomnographic recordings included EEG, vertical and horizontal electrooculogram (EOG), and galvanic skin response (GSR) were made for all subjects during the whole experiment. For each participant a comparative analysis was made for intensity of EEG spectrum before, during, and after the state of microsleep with open eyes when lapses in test performance were occurred, and during accurate performance in waking state. Following criteria were used for identification of intervals that include microsleep: four error-free responses, one lapse, and four error-free responses. Those 30-s intervals with open eyes that included a lapse were considered as a microsleep episodes. GSR data were used as additional criterion for microsleep occurrence. Following trends in changes of EEG spectrum were found: increase in intensity of low alpha-range, and decrease in intensity of high alpha- and beta-ranges. Changes in theta-, low beta- and gamma-ranges were differently directed. Taking into account the known data observed EEG changes specify a decrease in activation of primary visual cortical areas. Revealed data could support our hypothesis concerning mechanism of visual-motor disturbances during microsleep with open eyes. If additional evidence for PGO generation during microsleep will be obtained by noninvasive methods, artifical suppression of their generation could be useful to prevent dangerous consequences of microsleep during monotonous work.

Supported with RFH grant No 10-06-00019a.

Support: Russian Humanitarian Science Foundation 12-36-01293; 12-06-00927.

P371

Losing your left side of the world during sleep onset: auditory spatial neglect-like effects in drowsy normal participants

C. A. BAREHAM[1], T. MANLY[1], S. K. SCOTT[2] and T. BEKINSCHTEIN[1]
[1]MRC Cognition and Brain Sciences Unit, Cambridge, UK, [2]Institute for Cognitive Neuroscience, UCL, London, UK

Objectives: To investigate potential shifts in spatial attention in states of low arousal such as during sleep onset.

Methods: Normal participants performed an auditory spatial localisation task while transitioning in and out of sleep. They were asked to judge the laterality of tones presented between 0 and 60 to the left and right of midpoint. EEG correlates of theta-alpha ratios from 16 s preceding each tone, across 129 electrodes, were reduced to the first principal component to form an objective Drowsiness Index, (DI). Trials were divided into those in the upper and lower DI quartiles.

Results: A significant interaction between drowsiness (sleep stage 1) and laterality of errors was found ($F_{1,29} = 29.00$, $P = 0.01$). Participants were dramatically more likely to report left tones as having occurred on the right, and to show a modest reduction in equivalent right tone errors, during drowsy relative to alert trials. No bias to either side was evident during wakeful trials.

Conclusion: The results therefore confirm, for the first time using direct EEG measurement, that states of lowered alertness (sleep onset) are generally associated with a change in response tendencies consistent with a rightward shift in attention. These findings mirror that of clinical spatial neglect; a stroke-related condition whereby patients fail to attend to stimuli on one side of the body or environment not due to a deficit in sensation. Sleep-wake transitioning seems to change spatial attention and awareness in normal participants.

P372

Do we really know what we know? Awareness of performance during sleep to wake transitions

S. GEORGIEVA and T. BEKINSCHTEIN
Medical Research Council – Cognition and Brain Sciences Unit, Cambridge, UK

Objectives: Driving on a long and monotonous road in the middle of the afternoon, are we aware that our ability to assess another vehicle's distance is compromised? Or do we think that our perceptual judgments are as accurate as that in the morning after a refreshing night sleep? The aim of the current study is to investigate how our capacity to discriminate two categories changes not only with the level of ambiguity of stimuli, but with changes in drowsiness. Moreover, we investigate whether people are able to assess accurately their performance on a perceptual judgment task and whether confidence in their perceptual judgments is modulated by alertness.

Methods: Participants were asked to judge whether morphed word-stimuli were one of two words (tone/cone). The stimuli varied in the degree of morphing (from 95/5% to 45/55% in steps of 10%), rendering the words perceptually ambiguous. Additionally, the morphs were merged with white noise. Forced-choice discrimination was followed by self-paced confidence rating (1–10). EEG during task provides a direct measure of drowsiness state.

Results: The preliminary findings replicated previous results indicating that people form a sharp discrimination boundary between the two word stimuli, usually around the 55–45% morph. Almost all the 'miss' trials (i.e., trials on which people indicated tone when the word

contained over 50% cone) are at 55–45% morph. Accordingly, participants give lowest ratings of confidence around this condition, and corresponding reaction time is at its lowest. Overall, people rate confidence lower on miss trials (M = 4.96, SD = 1.88) compared to hit ones (M = 7.04, SD = 1.51). Using an EEG drowsiness index, we expect to see that when people become drowsier the categorical judgment curve flattens, coupled with increases in reaction time and decrease in confidence.

Conclusions: If we find a general decrease in confidence on all trials with transition to sleep, this will indicate that sufficient alertness is necessary to perform the task effectively. However, it is possible that during transition into sleep, confidence changes independently of perceptual ambiguity, indicating worse insight of task performance. This finding would be coherent with reports of overconfidence dissociated from objective performance estimation when drowsy, i.e. when driving sleepy. In any case, either outcome is informative with respect to awareness of self-performance during transitions into sleep.

P373

Attentional bias distorts sleep quality perception of good sleepers

J. WUYTS[1], E. DE VALCK[1], N. MARCOEN[1], M. VANDEKERCKHOVE[1], A. BULCKAERT[2], V. VERHAERT[2], J. VERBRAECKEN[3] and R. CLUYDTS[1]

[1]Vrije Universiteit Brussel, Brussels, BE, [2]Katholieke Universiteit Leuven, Leuven, BE, [3]Antwerp University Hospital, Antwerp, BE

Objectives: Cognitive models of insomnia and experimental studies suggest that an attentional bias towards sleep related and sleep disturbing cues can result in distorted perception of the level of sleep disturbance. Our aim was to communicate a finding on different experimental manipulations in which the induction could not be blinded (i.e. light and noise) compared to nocebo-experiments, in which creation of a negative expectation about upcoming night was the only induction. This way, we wanted to investigate to which level expectation plays a role in explaining differences found between experimental and pla/nocebo-conditions in investigating sleep quality.

Methods: In two studies subjects [n = 14 (22.43 year ± 0.82) and n = 15 (23.73 year ± 0.92)] slept each four nights in the laboratory. All were good sleepers. After an habituation night, reference (RE) and two different induction nights were counterbalanced. The following manipulations were induced: 1st study: (i) nightly periodical presentation of dimmed light (≤ 40 lux) positioned at the head of the bed (LI), (ii) continued presentation of recorded traffic noise (NO) (<55dB) and 2nd study: (iii) expectation of a sound, said to be presented at unpredictable moments during the night (SO), (iv) expectation of a suboptimal bedding system (BS). However, both SO and BS were nocebo inductions, neither sound nor suboptimal bedding system were present. Overnight polysomnogram was recorded and morning sleep quality (SQ) and feelings of refreshment (FR) were assessed by means of visual analog scales.

Results: No significant alterations in sleep stage distribution were found in none of the conditions when compared to the RE-night. For all conditions a significantly lower SQ (LI: z = 2.80; $P < 0.01$; $n < 14$; NO: z = 2.80; $P < 0.01$; $n = 14$; SO: z = 2.51; $P < 0.05$; $n = 15$; BS: z = 2.22; $P < 0.05$; $n = 15$) and FR (LI: z = 2.59; $P < 0.01$; $n < 14$; NO: z = 2.09; $P < 0.05$; $n < 14$; SO: z = 1.99; $P < 0.05$; $n = 15$) score were observed. For BS no difference in FR score was observed (z = 1.48; $P < 0.05$; $n = 15$).

Conclusion: A consistent pattern was observed in conditions for which blinding of the induction is impossible: for good sleepers, subjective sleep quality was reduced, although there was no change in sleep macrostructure. First, this suggests that expectation might play a dominant role in experiments with subjective findings which are not supported by objective results. Second, this supports the role attributed to attentional bias by models of insomnia.

P374

Individual differences in psychomotor vigilance during an Antarctic winter-over

O. MAIRESSE, A. CORTOOS and N. PATTYN

Royal Military Academy, Brussels, BE

Objectives: The overall adverse effect on sleep and performance of being exposed to constant darkness and in isolated and confined environments (ICE), is fairly undisputed. However, reports show evidence of individuals with stable or even increased performance during Antarctic winter-over campaigns. The purpose of this study is to assess the stability and the composite nature of the inter-individual differences in psychomotor performance in a sample of Antarctic over-winterers.

Methods: Thirteen male volunteers (36.7 ± 9.4 years) from the Concordia Research Station performed a 10-min psychomotor vigilance task every 6 weeks during the 2011 Antarctic winter. The stability of the inter-individual differences was quantified by intra-class correlation (ICC). Outcomes showing substantial or perfect stability (ICC > 0.60) were subjected to a functional principal component analysis (fPCA).

Results: Z-adjusted mean response speed shows the largest ICC (0.612), suggesting a substantial stability in inter-individual variability. 77.8% of the individual variance in response speed profiles is accounted for by two functional components. The first functional component explains 57.15% of the variance and characterizes the individual variability from the mean response speed function. High (low) scores on the first component raise (lower) the mean response speed profile. The second functional component explains 20.6% of the variance and is characterized by a downward functional trend over time. Individuals scoring high (low) on the second component show a more decreasing (increasing) trend in response speed profiles in comparison to the mean response speed function.

Conclusion: Most of the variability in response speed profiles is accounted for by stable inter-individual differences in mean reaction speed, irrespective from any state-dependent decline during the winter-over period. An additional proportion of the variability is explained by differences in the rate of decline/improvement of response speed. It is suggested that this component reflects the adaptive capacity of the individual to conditions of isolation and confinement under constant natural darkness.

P375

The effects of daytime nap on mental fatigue

A. PUCHKOVA, O. TKACHENKO and V. DOROKHOV

IHNA RAS, Moscow, RU

A person performing a mentally demanding task becomes increasingly fatigued which, in turn, may lead to decreased performance and higher probability of mistakes. Daytime nap is reported as an effective way to restore working performance A contactless eye-tracking method does not interfere with normal working activity as much as EEG and may be a better option in development of a performance monitoring system.

Our aim was to study the possible benefits of a daytime nap for a person fatigued by a purely cognitive task. To evaluate changes in productivity and eyegaze parameters caused by mental fatigue we have developed an experimental design allowing us to induce moderate levels of mental fatigue and monitor subject's performance. Each subject took part in two experiments – with and without a nap, both after a normal night sleep. They had to solve arithmetic sums (four different double-digit numbers, two pluses, and one minus) as quickly and as accurately as possible for two working sessions separated by a rest period. When the subject solved the sum, he had to click on it and then quickly find the correct answer among the two appearing options. After the first session subjects had a lunch and either had a nap or stayed awake for 1 h. The rest period occurred at the time of increased daytime sleepiness (about 3 p.m.). During the nap a polysomnogram was recorded. After the rest subjects had a second working session with the same task. During every working session mouse movements, eyegaze movements, and EEG (6 channels) were recorded.

Right-handed volunteers of both sexes took part in the study. Subjects successfully performed the presented task and reported low to moderate levels of fatigue after the first working session. All subjects fell asleep during the nap period and reached stages 2 or 3 NREM sleep. During the first working session subjects' productivity and eyegaze parameters did not change as moderate workload was successfully compensated. Some of subjects also developed a strategy of 'anticipatory saccades' towards the place where an answer should appear. However, for some subjects mental fatigue manifested during the second working session. In experiment with simple rest during the second session their speed decreased and after a nap they maintained stable performance. The nap was beneficial for recuperation after mental fatigue, but its effectiveness was individual.

Supported by RFH grant RHSF 12-36-01296 and RHSF 12-06-00927

Poster Session – Molecular and Genetic

P377

Elimination of RXFP3 signalling causes reduced circadian voluntary wheel running in mice: implications for Relaxin-3 networks in arousal and sleep control

I. T. HOSKEN[1], C. SMITH[1], A. BLASIAK[2] and A. L. GUNDLACH[1]
[1]Florey Neuroscience Institutes, Melbourne, AU, [2]Jagiellonian University, Krakow, PL

Objectives: Relaxin-3 is expressed by neurons in the nucleus incertus and adjacent brainstem nuclei that widely innervate forebrain areas containing high levels of its cognate receptor, RXFP3. Experimental evidence suggests relaxin-3/RXFP3 signalling is involved in arousal-related behaviours including feeding, motivation and reward, and sleep. Furthermore, relaxin-3 knockout (KO) mice display a hypoactive phenotype reflected by reduced running wheel activity accompanied by an apparent increase in sleeping [1–3]. Our objective was to study the behaviour of RXFP3-KO mice and their wild-type (WT) littermates and assess the possible presence of a circadian activity phenotype.

Methods: Behaviour of C57BL/6J backcrossed RXFP3-KO mice (n = 24; Johnson & Johnson PR&D LLC, USA) was compared to WT littermates (n = 24) in a battery of acute tests. Levels of chronic circadian voluntary running wheel activity were measured in separate cohorts of RXFP3-KO (n = 15), RLN3-KO (n = 15), and their WT littermates (n = 15/15).

Results: No differences were detected between RXFP3-KO and WT mice in the acute tests, suggesting comparable levels of motor coordination, spatial and recognition memory, anhedonia, basal fear and anxiety, sensorimotor gating, and locomotor activity in novel environments. Notably though, RLN3-KO and RXFP3-KO mice were markedly hypoactive (20–30%, $P < 0.05$) on voluntary running wheels during the dark/active phase.

Conclusion: Recapitulation of the circadian hypoactive phenotype observed in RLN-3 KO mice in the RXFP3 KO strain supports its association with deficits in relaxin-3/RXFP3 signalling; and highlights the potential of these mice to better elucidate the role of these networks in arousal and sleep control. Thus, studies are underway using EEG/EMG telemetry to assess differences in sleep architecture resulting from the deficits in relaxin-3 and RXFP3 KO mice and to examine the effect of acute or chronic 'restoration' of relaxin-3/RXFP3 signalling using RXFP3-selective peptides and lenti- and adeno-associated viral vectors both globally throughout the brain and in specific brain regions.

References:

1. Ryan PJ et al. (2011) Nucleus incertus – an emerging modulatory role in arousal, stress and memory. Neurosci Biobehav Rev 35: 1326–41.
2. Smith CM et al. (2011) Relaxin-3 systems in the brain – the first 10 years. J Chem Neuroanat 42: 262–75.
3. Smith CM et al. (2012) Relaxin-3 null mutation mice display a circadian hypoactivity phenotype. Genes Brain Behav 11: 94–104.

P378

Sleep regulation and brain energy metabolites in genetically modified loss-of-function and gain-of-function brain-derived neurotrophic factor mice

H.-K. WIGREN, J. C ZANT, A. SANDERS, E. CASTREN and T. PORKKA-HEISKANEN
University of Helsinki, Helsingin yliopisto, FI

Objectives: Previous studies show that the expression of cortical brain-derived neurotrophic factor (BDNF) is causally linked to homeostatic regulation of sleep slow wave activity and correlates with expression of other plasticity related cortical transcripts. In addition to cortical mechanisms, the activating arousal systems including the cholinergic basal forebrain (BF) are crucially involved in the regulation of sleep homeostasis. In the present study we investigated if BDNF also plays a role in the BF mediated regulation of arousal and sleep homeostasis. Particularly, we were interested if genetic modifications affecting BDNF function modulate extracellular levels of lactate and adenosine in the BF.

Methods: Loss-of-function C57BL/6 mice (n = 6) heterozygous for BDNF-null gene and gain-of-function C57BL/6 mice (n = 6) overexpressing neurotrophic tyrosine kinase receptor, type 2 (TrkB) gene and their wildtype (wt) littermates (n = 6 + 6) were under general anesthesia implanted with cortical EEG electrodes and unilateral microdialysis quide cannulae aimed at the BF. After recovery and habituation microdialysis probes were inserted into the BF and continuous sampling of microdialysates and EEG was initiated the next day. A 24 h baseline experiment followed by a 6 h sleep deprivation (SD; by gentle handling) with 18 h recovery period was performed. Adenosine and lactate concentrations were measured from microdialysates whereas EEG was processed for vigilance stage scoring and power spectral analysis. After the experiments mice were sacrificed and half of the brain was used for verification of probe location while the other half was processed for quantification of plasticity related transcripts.

Results: No significant differences were found in the overall amount of vigilance stages in transgenic mice as compared to their wt siblings. However, the heterozygous BDNF-null mice had significantly higher overall levels of lactate in the BF than their wt siblings. During SD BF lactate levels in the wild types exceeded their active dark period values whereas in the BDNF-null heterozygote mice lactate levels did not reach dark period values.

Conclusions: Lactate is neuronal activity-dependent energy metabolite, previously shown to increase in the BF during SD and particularly during active waking. Our results showing a blunted lactate response to sleep deprivation indicate that BDNF may be involved in the regulation of sleep homeostasis also at the subcortical level.

P379

Upstream transcription factor 1: a novel regulator of sleep and metabolism

K-M. RYTKÖNEN[1], H. M. OLLILA[2], J. C. ZANT[1], H.-K. WIGREN[1], T. PAUNIO[2] and T. PORKKA-HEISKANEN[1]

[1]University of Helsinki, Helsinki, FI, [2]National Institute for Health and Welfare, Helsinki, FI

Objectives: Sleep problems and metabolic disorders are extremely prevalent and thought to be related to each other, with sleep loss inducing metabolic changes that promote diabetes and obesity. Upstream transcription factor 1 (USF-1) regulates genes involved in the control of lipid and glucose metabolism. A genetic variation in the USF-1 gene predisposes humans to hyperlipidemia and elevated levels of blood triglycerides; known risk factors for metabolic syndrome and type 2 diabetes. USF-1 influences metabolism in USF-1 over-expressing mice and is also implicated in the regulation of the circadian clock, making USF-1 an exciting new candidate gene at the crossroad of sleep and metabolism. Our aim was to characterize effects of the USF-1 on sleep and the circadian rhythm.

Methods: We used a USF1-1 knockout (KO) mouse model in the study. Video-monitoring, sleep electroencephalography (EEG) recordings and gene expression analysis of the brain were carried out in knockout (KO), heterozygous (HT) and wild-type (WT) mice to characterize the physiological function of the USF-1 gene in the regulation of sleep and circadian rhythm.

Results: Mice lacking the USF-1 gene (USF-1 KO mice) have decreased movement activity, flattened circadian rhythm and increased sleep-wake fragmentation compared to their wild-type littermates. Many of these alterations, indicating disrupted sleep-wake regulation, have been described in other animal models with changed metabolic or circadian function.

Conclusion: USF-1 gene is a promising new regulator of sleep and provides additional support for the link between sleep and metabolism.

P380

Sleep-wake cycle alterations in transgenic mice carrying the murine homologue of the mutation linked to fatal familial insomnia

F. DEL GALLO[1], S. MANTOVANI[2], R. CHIESA[2] and L. IMERI[1]

[1]University of Milan Medical School, Milan, IT, [2]Mario Negri Institute for Pharmacological Research, Milan, IT

The prion protein (PrP) is a glycoprotein anchored to cell membrane and expressed in most cell types, including neurons and glia. The physiological role of PrP is not yet clarified. The D178N/M129 mutation of the PrP gene leads to fatal familial insomnia (FFI). FFI is a rare neurodegenerative disease characterized by major alterations in sleep-wake cycle, vegetative control and circadian rhythms (Montagna et al, Neurology, 2: 167–76, 2003).

Objectives: The first animal model of FFI was described in 2009 (Jackson et al, Neuron, 63:438–450, 2009), but no polygraphic evaluation of sleep-wake behavior was performed. Aim of this study was to polygraphically investigate the sleep-wake patterns of transgenic mice carrying the murine homolog of the PrP mutation that leads to FFI.

Methods: To this purpose, 12-months old male mice of four strains were instrumented for chronic polygraphic recording of sleep-wake activity, according to standard techniques. Strains were: i) C57BL/6J, wild-type mice (WT, $n = 8$); ii) PrP KO mice ($n = 10$); iii) mice expressing both wild type and mutant PrP (FFI+/0, $n = 8$); iv) mice expressing only mutant PrP (FFInull, $n = 9$). Animals were maintained under a 12–12 h light-dark cycle, at a constant temperature of 26 ± 1°C. After recovery from surgery, EEG and gross body activity were recorded for 24 h in undisturbed conditions.

Results: (i) during the light period, in mice expressing only the mutant PrP (FFInull) REM sleep amount was significantly reduced to about half that observed in the other strains ($P < 0.001$); (ii) the reduction of REM sleep in FFInull was due to a decrease of the number of REM bouts ($P < 0.001$), whereas no significant differences were found in the duration of REM bouts between strains; (iii) both transgenic mouse strains (FFInull and FFI+/0) showed a significant increase in the number of transitions between states compared to control mice (FFInull and FFI+/0 versus WT, $P < 0.001$).

Conclusion: These data suggest that transgenic mice carrying the murine homolog of the PrP mutation linked to FFI represent an useful animal model of the disease. The co-expression of wild type and mutant PrP influences the phenotype, since REM sleep amount was not reduced in FFI+/0 mice. This observation also suggests that the expression of wild type PrP may protect against changes produced by mutated PrP.

P381

Cardiovascular and sleep alterations in mice lacking the cannabinoid receptor-1

S. BASTIANINI, C. BERTEOTTI, V. LO MARTIRE, R. MAZZA, U. PAGOTTO, C. QUARTA, A. SILVANI and G. ZOCCOLI

University of Bologna, Bologna, IT

Objectives: The inhibition of the endocannabinoid system (ECS) prevents the development of diet-induced obesity through the increase in thermogenesis and sympathetic activity. On the other hand pharmacological stimulation of ECS reduces blood pressure (BP) value and induces sleep in rats. Drugs acting as antagonists of the ECS showed promising results in reducing body weight whereas data on their impact on cardiovascular and sleep regulation are not clear. Aim of the study was to assess whether the increased sympathetic activity resulting from ECS inhibition leads to cardiovascular and sleep alterations.

Methods: Cannabinoid receptor-1 knockout mice (KO) and their wild-type (WT) littermates were maintained on 12:12 light-dark cycle and fed *ad libitum* with high-fat or low-fat diet (HFD and LFD, respectively). Animals (KO-LFD $n = 10$; WT-LFD $n = 7$; KO-HFD $n = 9$; WT-HFD $n = 10$) were implanted with a telemetric pressure transducer (TA11PA-C10, DSI) and electrodes for discriminating wakefulness, non rapid-eye-movement sleep (NREMS), and REMS. Two weeks later, recordings were continuously performed for 2 days with the mice left undisturbed and freely moving. Mean BP and heart rate (HR) values were computed in each wake-sleep state and analyzed by ANOVA and t-test with significance at $P < 0.05$; data are presented as mean ± SEM.

Results: During the light period, no cardiovascular alteration or difference in the amount of time spent in NREMS or REMS was found between KO and WT mice either on HFD or LFD. On the contrary, during the dark (activity) period, KO mice spent significantly less time in NREMS than WT controls irrespective of the diet. However, during the dark period, KO mice showed higher BP (+7.0 ± 2.4 mmHg) and HR (+29.1 ± 10.4 beats/min) values than WT controls only if fed with HFD.

Conclusion: Our data indicate that chronic ECS inhibition may lead to cardiovascular and sleep derangements. In particular interaction between ECS inhibition and HFD produced hypertension and tachycardia during the dark (activity) period probably because of

activation of the sympathetic nervous system. These cardiovascular alterations are, at least in part, consequent to the lower sleep propensity in KO mice during the dark period.

P382

Sleep ontogeny and the melanocortical system in barn owls (Tyto alba) in the wild

M. F. SCRIBA[1], A. ROULIN[1], I. HENRY[1], A.-L. DUCREST[1], A. L. VYSSOTSKI[2] and N. C. RATTENBORG[3]

[1]Department of Ecology and Evolution, Lausanne, CH, [2]ETH Zurich, Zurich, CH, [3]Max Planck Institute for Ornithology, Seewiesen, DE

Objectives: The melanocortin system is implicated in the expression of many phenotypic traits. Activation of the melanocortin MC1 receptor by melanocortin hormones induces the production of black eumelanic pigments, while activation of the four other melanocortin receptors affects other physiological and behavioural functions including stress response, energy homeostasis, anti-inflammatory and sexual activity, aggressiveness, resistance to oxidative stress and sleep.

In our study we examine the link between the melanocortin system and sleep in barn owls living in the wild. Additionally, we were interested in determining whether REM sleep in birds – the only non-mammalian taxonomic group to exhibit slow-wave sleep (SWS) and rapid-eye movement (REM) sleep – is negatively correlated with age, as observed in mammals.

Methods: We conducted the first study of sleep in barn owl nestlings ($N = 50$) in the field using a minimally invasive method for recording the electroencephalogram and sleep-related behaviour. Additionally, we measured melanin-based coloration, mass and size of the chicks, as well as proopiomelanocortin (POMC) gene expression.

Results: In contrast to adult owls, chicks were not nocturnal, but could be awake or asleep any time of day and night. On average chicks spent 54.0% awake, 33.7% in SWS and 12.3% in REM sleep. We found strong correlations between sleep states, coloration, age and sex. The time spent in REM sleep was negatively correlated with age. Darker eumelanic individuals showed more REM sleep and less SWS and wakefulness compared to lighter nestlings.

Conclusion: In mammals, the wake-like brain activity occurring during REM sleep is thought to direct normal brain development. We show that in an altricial bird species time spent in REM sleep decreases with age. Therefore REM sleep might play a similar role in brain development in birds.

We provide the first evidence for a link between variation in the melanocortin system and sleep in a naturally occurring organism. Determining the effect that color associated variation in REM sleep has on brain development and behaviour may ultimately provide insight into the function of sleep. Moreover, given that the melanocortin system is highly conserved in the vertebrate lineage, and involved in several genetic diseases, behavioural ecology studies of this sort may have implications for sleep medicine.

P383

Sleep restriction alters gene expression in peripheral leukocytes – a microarray study on healthy young men

V. AHO[1], H. M. OLLILA[2], W. M. A. VAN LEEUWEN[3], S. MATIKAINEN[3], S. RIPATTI[2], M. HÄRMÄ[3], M. SALLINEN[3], M. JAUHIAINEN[2], H. ALENIUS[3], T. PAUNIO[2] and T. PORKKA-HEISKANEN[1]

[1]University of Helsinki, Helsinki, FI, [2]National Institute for Health and Welfare, Helsinki, FI, [3]Finnish Institute of Occupational Health, Helsinki, FI

Objectives: Sleep loss is an increasing problem in modern societies. Short or insufficient sleep has been associated with an elevated risk of cardiovascular diseases and mortality in epidemiological studies. There is also strong evidence that the development of these diseases has an immunological component.

To elucidate the mechanisms underlying the detrimental effects of sleep loss, we designed a simulation of a working week with restricted sleep and a weekend of recovery, and assessed changes in the gene expression profiles of leukocytes.

Methods: Thirteen healthy young men spent a week in laboratory conditions. After baseline sleep of two nights (8 h time in bed / night), sleep was restricted in the experimental group ($n = 9$) to 4 h / night for five nights followed by two nights of recovery sleep (8 h / night). The control subjects ($n = 4$) spent 8 h / night in bed. Leukocyte RNA expression was analysed at baseline, after sleep restriction, and after recovery period, using Affymetrix whole genome microarrays complemented with pathway and transcription factor analysis of differentially expressed genes.

Results: Altogether, the expression of 117 genes was altered ($P < 0.05$) after sleep restriction. The up-regulated pathways included those for B cell activation ($P < 0.001$), NFkB signalling ($P < 0.005$), and T helper cell 2 differentiation ($P < 0.05$). STAT1 and IRF2 transcription factor binding sites were enriched among the up-regulated transcripts and the RNA expression of these transcription factors was increased in sleep restriction ($P < 0.05$). Several lipid transport and synthesis pathways were down-regulated ($P < 0.05$). Many of the detected expression patterns did not return to baseline during the recovery period.

Conclusion: Our data suggests that cumulative sleep restriction alters the regulation of the immune system, also at the level of gene expression. These changes may lead to low-grade inflammation through NFkB-mediated signalling. The changes in the bidirectional interplay of sleep and the immune system may at least partly explain how prolonged sleep restriction can contribute to the pathogenesis of cardiometabolic diseases.

We wish to thank the Academy of Finland, Työsuojelurahasto, and the EU (project LSHM-CT-2005-518189) for funding this study. The authors claim no conflict of interest.

P384

Genetic factors in evolution of sleep length in adult humans

C. HUBLIN[1], M. PARTINEN[2], M. KOSKENVUO[3] and J. KAPRIO[3]

[1]Finnish Institute of Occupational Health, Helsinki, FI, [2]Helsinkin Sleep Clinic, Helsinki, FI, [3]University of Helsinki, Helsinki, FI

Objectives: Genetic factors affect many aspects of sleep such as sleep length. Studies on the contribution of genetic factors to stability and change of sleep length over time are rare. We assessed the contribution of genetic factors to sleep length in adults over a 15 year period.

Methods: Finnish adult twins responded to questionnaires administered to the Finnish Twin Cohort in 1975 (response rate 89%, 11 041 twin pairs; age 18 years or more), 1981 (84%, 9323; age 24 or more) and 1990 (77%, 4507; age 33–60 years). Subjects were categorized as short (<7 h), average, or long (>8 h) sleepers. Pairwise similarity in MZ and DZ pairs was examined at each survey by age-group and sex. Quantitative genetic modelling was used to estimate cross-sectional and longitudinal genetic effects in sleep length.

Results: Average sleepers formed the majority in all age and gender groups, and their proportion varied from 47.4 to 80.0%, being higher in the younger groups. The proportion of variance in sleep length

accounted for by genetic effects was very stable over time, being 0.31 (95% confidence intervals 0.27–0.33) in 1975, 0.32 (0.29–0.35) in 1981, and 0.30 (0.24–0.34) in 1990. Longitudinal modelling indicated that the correlations of genetic effects between the three measurement points were high: 0.85 (0.77–0.95) between 1975 and 1981, 0.93 (0.85–0.98) between 1981 and 1990, and 0.76 (0.70–0.88) between 1975 and 1990. In contrast, despite a high contribution of environmental effects at each time point (about 0.7), their correlations over time were modest: 0.31 (0.29–0.33) between 1975 and 1981, 0.33 (0.30–0.37) between 1981 and 1990, and 0.18 (0.14–0.21) between 1975 and 1990.

Conclusion: Genetic factors have a relative low but stable effect on the evolution of sleep length in adults, which indicates that multiple measures of sleep length would be a superior measure in genetic analyses than a single cross-sectional measure. On the other hand environmental factors have relative high effects with low stability over time, which would suggest that there are major external effects on sleep length, which have, however, little temporal stability over a long (15 year) time span.

P385

Transcriptional correlates of an *in vitro* model of sleep

C. MIKHAIL, V. HINARD, S. PRADERVAND and M. TAFTI
University of Lausanne, Lausanne, CH

Introduction: Sleep is a vital function. However, the functions of sleep remain elusive. Although many theories have been proposed, none is accepted with large consensus.

Methods: To study and understand the function of sleep, we developed a model of sleep *in vitro*. In this study we investigated the molecular correlates of sleep: the transcriptional marker of sleep *in vitro*. For this purpose, we used dissociated cortical cultures harvested for 12–14 days *in vitro* until they matured in a sleep-like firing state. To mimic wakefulness, we used a physiological cocktail of excitatory neurotransmitters and analysed the transcriptome of waking-neurons versus sleeping neurons.

Results: Microarray data showed that stimulated cortical cultures have a highly similar gene expression pattern to that of the cortex of sleep deprived living animals. We also demonstrated that the homeostatic process of sleep can be reproduce in culture by a dose-response experiment.

Conclusion: In conclusion, we have shown that an *in vitro* neuronal assembly can nicely mimic sleep and wakefulness. Therefore, a major advantage of this *in vitro* model is to open up new avenues in investigating sleep at cellular and molecular levels.

P386

Heterozygosity of P2RX7 with depression-associated risk allele alters sleep architecture

V. JAKUBCAKOVA, S. WALSER, C. FLACHSKAMM,
F. HOLSBOER, J. M. DEUSSING and M. KIMURA
Max Planck Institute of Psychiatry, Munich, DE

Objectives: Recently, a single-nucleotide polymorphism (SNP) identified in the gene of the purinergic P2X7 receptor (P2X7R) was found to be associated with depression. In search for the functional relevance of this SNP as a susceptibility marker for depression, we investigated changes in sleep architecture of humanized mouse mutants in which the murine P2rx7 gene was substituted by the wild-type or the disease-associated human P2rx7 variants (P2rx7h). In addition, we attempted to examine whether chronic partial sleep deprivation (CHPSD) exerts an antidepressant effect in mice carrying depression-associated risk allele, since studies in patients suggested that the repeated SD treatment leads to improve depressive episodes.

Methods: All mouse lines (wild-type P2rx7hWT, heterozygous P2rx7hWT/hMT, homozygous P2rx7hMT; n = 8–11 each) habituated into 12:12 h light-dark cycles were implanted with EEG-EMG electrodes for polygraphic sleep recordings. Spontaneous sleep-wake states were monitored for 24 h before and after 7 days of 6 h SD starting with the light onset.

Results: The amount of wake, nonREM sleep (NREMS) or REMS did not differ between genotypes during the baseline recording. However, significantly decreased activity of slow waves during NREMS, reduction of time spent in SWS2 and frequent entries into the REMS episodes were observed in heterozygous P2rx7hWT/hMT mice. Following CHPSD, the amount of REMS decreased in all genotypes whereas the amount of NREMS and wakefulness did not differ when compared to corresponding baseline quantities. During the light period, the episode number of REMS significantly decreased in P2rx7hWT/hMT mice while the duration of REMS episodes was not affected after CHPSD.

Summary: Only heterozygous P2rx7hWT/hMT mice carrying both human P2RX7 variants show a reduced quality of sleep similar to that seen in human depression. Strong drives toward REMS and altered homeostasis of NREMS regulation are unique sleep characteristics observed in the heterozygous mice expressing the depression-associated risk allele. Interestingly, 7 days of CHPSD induced a notable decline of REMS entries in these mice. Therefore, a repeated application of enforced wakefulness might have worked to reduce a REMS drive, which could be readout of its antidepressant effect. Altogether, we suggest the feasibility of P2rx7hWT/hMT mouse line as a new heterozygote disadvantage model of depression to study sleep disorders caused by the same variation in humans.

P387

Notch dependent neuroglia signalling and sleep regulation

A. AGUIRRE and L. SEUGNET
Lyon Neuroscience Research Center, Lyon, FR

Maintenance of neurotransmission, regulation of energy metabolism, and learning and memory processing have been identified as potential sleep functions. Importantly, all these processes are modulated by glial cells in response to neuronal signals. Neuron-glia interactions may thus play a key role in sleep function. We have previously identified a neuroglial signaling pathway dependent on the Notch receptor (in glia) and its ligand Delta (in neurons). Notch and Delta modulate sleep homeostasis and performance following sleep deprivation in Drosophila. Here we dissected the function of this signaling pathway using Drosophila molecular genetic tools to understand its role in sleep regulation.

Using the Gal4-UAS system to target gene expression in astrocyte-like glia, we evaluated the role of Notch signaling in the regulation of the expression of the glutamate transporter dEaat1, and its potential interactions with the epidermal growth factor receptor (EGFR) signaling pathway, another sleep regulator in Drosophila. dEaat1 expression was assessed using a dEaat1-Gal4 construct coupled to GFP expression. Our results indicate that dEaat1 is independently regulated by Notch and EGFR at the transcriptional level. The influence of Notch signaling on brain dopamine and octopamine levels will also be presented.

P388

The genetic basis of mammalian sleep

C. MUHEIM[1], R. DALLMANN[1], T. SARTORIUS[2], C. KABAGEMA[2], R. HUBER[3], I. TOBLER[1], P. RUTH[2] and S. BROWN[1]
[1]University of Zurich, Zurich, CH, [2]University of Tuebingen, Tuebingen, DE, [3]Children's Hospital University of Zurich, Zurich, CH

For more than 150 years, sleep has been studied extensively, but very little is known about the genetic components underlying its complex structure. Nevertheless, evidence has begun to accumulate suggesting that single genes can dramatically affect sleep architecture. For example, a forward screen in Drosophila identified the potassium channel mutation shaker as having a dramatic sleep phenotype when mutated (Cirelli et al., 2005), and similar results have been documented in mice (Douglas et al. 2007). Given the fact that potassium channels broadly regulate membrane potential in neurons (reviewed in Johnston et al., 2010) other ion channels might also be important key players for sleep. However, much remains to be discovered.

In our study we aim to conduct a large scale screen of all ion channels present in the neocortex for their importance in local homeostatic sleep. As model we use adult mice, which are unilaterally injected with an shRNA-system for site-directed knockdown in a very restricted area. Subsequently, sleep in the two hemispheres will be compared by EEG analysis. This screen should give information about the function of ion channels in rest-wake behavior. Because of the targeted nature of the injection, it will also provide insights about local development of sleep independent of broader developmental changes.

Preliminary data using an adenosine kinase overexpression-vector has already revealed promising data: a local effect on delta sleep could be documented that mimics the sleep phenotype found in an ADKtg mouse model (Palchykova et al., 2010). Moreover, a first set of candidate genes, including the BK channel of the Ca-activated subfamily and some members of the voltage-gated potassium channel family have also revealed interesting sleep-specific functions of those channels.

P389

Astrocytes display different pattern of gene expression related to neuro-metabolic coupling in anterior and posterior hypothalamus of mice

A. MIKHALEVA[1], J. GYGER[1], P. J. MAGISTRETTI[2] and J.-M. PETIT[2]
[1]EPFL, Lausanne, CH, [2]EPFL-CNP, CHUV-UNIL, Lausanne, CH

Objectives: The posterior hypothalamus (PH) is crucial for maintaining wakefulness whereas the anterior hypothalamus (AH) constitutes a sleep-promoting region. Consequently, the energy needs of AH and PH should probably change throughout the sleep-wake cycle. The glycogen mobilization altogether with the astrocyte-neuron lactate shuttle (ANLS) likely constitutes the main mechanism by which astrocytes ensure neurometabolic coupling to maintain the neuronal activity. Therefore, we hypothesized that astrocytes of AH and PH may display differences in genes expression involved in the neurometabolic coupling during the sleep-wake cycle. The striatum (ST) was taken as a control region.

Methods: We used transgenic mice (P28-P31) expressing the fluorescent protein GFP under the control of the astrocyte-specific gene GFAP promoter. Mice were sacrificed at two time points corresponding to light-on (ZT0) and light-off (ZT12). After brain dissection, 'punches' of AH, PH and ST were micro-dissected from slices. Cell suspensions of AH, PH and ST were obtained from a pool of 3 samples by enzymatic digestion and cell trituration. Then, GFP-positive cells (GFP+), which are highly enriched in astrocytes, were sorted by FACS. Total RNA was extracted from harvested cells and levels of mRNA encoding proteins involved in ANLS and glycogen metabolism were assayed by qRT-PCR and normalized by cyclophylin mRNA levels.

Results: Four genes related to ANLS were tested: the alpha 2 subunit of the Na-K ATPase (Atp1a2), the Glutamate transporter 1 (GLT1) and two monocarboxylate transporters (MCT1 and MCT4). Results showed that, excepted for MCT4, their levels of expression exhibited some differences in all regions. AH and PH displayed similar levels of gene expression except for Atp1a2 which was highly regulated in AH with an increase in 40% relative to ST levels from ZT0 to ZT12. GLT1 was more present in ST.

Levels of expression of genes encoding the Glycogen Phosphorylase (Gphos), the Glycogen Synthase (GS) and the Protein Targeting to Glycogen (PTG) did not display major regional change. However an increase in GS expression was observed in all regions at ZT12.

Conclusion: This study shows that astrocytes displayed some transcriptional regulation in different hypothalamic areas. The different pattern of expression of ANLS-related genes in AH and PH suggests that neuro-metabolic coupling capacity of each structure might play a functional role in the sleep-wake regulation.

P390

Regulation of astrocytic connexins following sleep deprivation in mice

J.-M. PETIT[1], J. GYGER[2], X. LIU[3], C. GIAUME[3] and P. J. MAGISTRETTI[1]
[1]EPFL-CNP, CHUV-UNIL, , Lausanne, CH, [2]EPFL, Lausanne, CH, [3]Collège de France, Paris, FR

Objectives: In addition to synapses, gap-junctions (GJ) play an active role in the neuronal as well as in glial cell coupling. GJs are formed by apposition of intercellular channels composed by hexameric assemblies of intra-membrane proteins named connexins (Cxs). In the brain, different subtypes of Cxs are present with a cellular specific distribution. The Cx43 is mainly expressed by astrocytes but also by developing neurons, while Cx30 is only present in astrocytes. The Cx36 is almost exclusively present in neurons. Moreover, it has been recently described that in astrocytes Cxs can also form hemichannels, possibly involved in gliotransmission. Interestingly, gliotransmission has been involved in sleep regulation (Halassa et al. 2009), suggesting the potential involvement of GJs in sleep mechanisms. To test this hypothesis, we assessed the effects of a 'gentle' sleep deprivation (GSD) followed or not by 3 h of sleep recovery (SR) on the levels of mRNA encoding the Cx30, Cx36 and Cx43 in the cortex and hippocampus.

Methods: GSD was performed by incorporating objects or bedding materials to stimulate C57BL6j mice. For SR, mice were sacrificed 3 h after GSD. Control mice were left undisturbed during 6 or 9 h from the beginning of the light phase until sacrifice. At the end of the GSD, SR or control periods, mice were decapitated and cerebral cortex and hippocampus were dissected out. Levels of mRNA encoding Cx43, Cx30 and Cx36 were determined by qRT-PCR. In addition we also assay the Cx 30 and Cx43 proteins by Western-Blot 3 h after GSD.

Results: We observed that Cx30 mRNA was increased after GSD in cortex and hippocampus (+35 ± 5% and +72 ± 12% respectively) but also after 3 h of SR (+36 ± 6% and +48 ± 10% respectively)

while no significant changes were observed for the other tested genes. In spite of these transcriptional changes, protein levels were not increased for the Cx30 and Cx43 3 h after the end of the GSD.
Conclusion: The transcriptional induction of Cx30 underlines that astrocytes are directly impacted by GSD. The lack of CXs protein increase might be due to rapid turnover of the GJs described on *in vitro* models. Measurements of Cxs proteins at different time points after GSD together with assessments of astroglial networks following GSD should help us to delineate the role of glial CXs in sleep regulation.
(Halassa et al., Neuron 61:213, 2009).
Supported by FNRS grant 3100AO-108336/1 to PJM.

P391

Biochemical properties of insufficient sleep and recovery sleep

C. A. EVERSON, A. E. FOLLEY and N. HOGG
The Medical College of Wisconsin, Milwaukee, US

It is generally understood that severe sleep deprivation (SD) impairs health and that recovery sleep is physically restorative. However, there is little tangible evidence of the specific physical properties that underlie having slept. In laboratory rats, severe SD results in hypercatabolism, immune deficits, and hormonal declines which can cause death. Structural damage has not been found, indicating mediation by biochemical reactions and altered functions. We previously provided evidence that uncompensated oxidative stress is a consequence of SD which is expected to result in cell injury. The objective of the present study was to start fingerprinting the oxidative damage.

Adult male rats (N = 4–10/group) were studied. Baseline (BL) was a 7 day period prior to SD. SD was produced by the Rechtschaffen-Bergmann method for 10 days by means of a 6-s ambulation requirement upon sleep onset. Control rats received consolidated ambulation requirements (AC) to provide periods for uninterrupted sleep. Recovery rats (SD-Rec) were deprived for 10 days and then allowed 2 days of sleep. Measurements of oxidative stress markers included carbonyl (oxidative protein damage), nitrotyrosine (nitrative stress), F2-isoprostane (lipid peroxidation), and caspase-3 (executioner caspase). Data were analyzed by two-tailed *t*-tests.

SD resulted in increased carbonyls in the liver and heart (versus AC, each $P < 0.001$); increased liver caspase-3 (versus BL, $P = 0.02$); decreased nitrated proteins (versus AC, $P < 0.003$); and, deceased plasma isoprostane (versus BL, $P < 0.02$). SD-Rec was marked by increased liver nitrotyrosine (versus SD, $P < 0.04$) and decreases in both liver and plasma isoprostane (versus BL, $P = 0.04$ and $P < 0.003$). Splenic caspase-3 was significantly increased during recovery sleep (versus BL, $P < 0.004$).

Lipids as targets appeared protected, especially during recovery. In contrast, general protein damage was evident in association with increased caspase-3 in the liver during SD. These signs are expected to reflect cell injury. Increases in oxidative stress markers also occurred during sleep recovery, which may seem counterintuitive. However, increased amounts of nitrated tyrosine could mean increased proteolysis of proteins modified by prior sleep loss. Increased splenic caspase-3 during sleep recovery hints at the dismantling of selective cell types. These possibilities are consistent with our previous observations that extraordinary increases in antioxidant enzymes appear to be a property of sleep recovery.

Research supported by the National Heart, Lung & Blood Institute, NIH.

P392

Effect of an acute sleep deprivation and recovery sleep on metabolic, hormonal, immune and inflammatory parameters in healthy men

M. CHENNAOUI[1], C. DROGOU[1], F. SAUVET[1], S. BANZET[1], T. GALLOPIN[2], D. GOMEZ-MERINO[1] and B. NINDL[3]
[1]IRBA, Bretigny, FR, [2]ESPCI ParisTech, Paris, FR, [3]USARIEM, Natick, US

Objectives: Mounting evidence from both observational and experimental research suggests that sleep disturbance and short sleep duration adversely impact human physical health and increase mortality risk. The mechanism by which altered sleep duration affects health are unclear, but experimental studies suggest altered sleep may impact levels of cytokines known to be important in regulating inflammation.

The mechanisms related sleep loss and health are unclear, but experimental studies suggest that altered sleep may impact levels of cytokines implicated in inflammation regulating.

Methods: To assess the effects of an acute total sleep deprivation (TSD) under constant and well controlled conditions, on hormone and cytokine assays such as TNF-alpha, IL-6, TLR-4 mRNA levels; 12 healthy men (29 ± 3 years) participated in a 5-days sleep deprivation experiment (two control nights followed by a night of sleep loss and one recovery night). At 8:00 a.m, blood sampling were completed before (day 2: D2), after (day 4: D4) one night of sleep loss and after (day 5: D5) one night of sleep recovery.

Results: Our main results have shown that after 25 h of continuous wakefulness (D4), a significant increase in amounts of mRNA encoding TNF-alpha ($P < 0.01$) and an increasing trend of TLR4 mRNA levels ($P = 0.07$). We also observed at D4 a decrease in free IGF-1 levels ($P < 0.001$) and in PGE2 levels ($P < 0.05$).

Conclusion: We conclude that in healthy men, under our experimental conditions, an acute exposure to 25 h of TSD is associated with increased pro inflammatory cytokine mRNA such as TNF-alpha. This expression of TNF-alpha significantly higher in D4 could be explained by the existence of a period ranging between 16 and 24 h of continuous wakefulness (night in D3) in which modifications immunoinflammatory and endocrine-related deprivation sleep will induce an increase of proinflammatory proteins such as TNF-alpha resulting in the increase of its own expression. High free IGF-1 levels could be identified as possible mediators of the enhancing and suppressing actions of nocturnal sleep on pro- and anti-inflammatory cytokines.

P393

Sleep in a monozygotic pair and a dizygotic pair of twins: an actigraphic case report

M. MARQUES[1], S. BOS[1], B. MAIA[2], M. J. SOARES[1], A. PEREIRA[1], M. H. AZEVEDO[1] and A. MACEDO[1]
[1]University of Coimbra, Coimbra, PT, [2]Higher Institute of Social Service of Porto, Porto, PT

Present actigraphic and subjective data on the sleep of a pair of identical twins and a pair of fraternal twins, at 3 months postpartum. A pair of monozygotic twins (boys) and a pair of dizygotic twins (girls) wore an actiwatch, on their ankle, for a period of respectively seven and six consecutive days and nights to measure their sleep–wake patterns. Actiwatches (Cambridge Neurotechnology) were set to record activity in 1-min intervals. Several sleep parameters were calculated: sleep efficiency, mean activity score, among others. Mothers answered questions regarding weeks of gestation when the

babies were born and their's babies sleep. Both pairs were born at 35 weeks of gestation. Identical twins (Jo and A) and fraternal twins (L and Ju) presented, respectively, a sleep efficiency of 64.86 and 66.00, and of 75.14 and 80.29. Jo and A and L and Ju mean activity scores were, respectively, of 43.43 and 46.14, and 22.43 and 32.29. Jo and A and L and Ju actual sleep time were, respectively, of 06:30 and 06:37 and of 08:29 and 07:56. Regarding actual wake time, Jo and A and L and Ju showed the following values: 02:40 and 02:36; 01:21 and 01:46. Jo and A. presented 63.57% and 63.71% of immobile time; L and Ju of 81.86% and 78.86%. Finally, Jo and A and L and Ju showed, respectively, a moving time of 35.57% and 35.29%, and 17.29% and 20.29%. According to the mothers, J. and A. had none to one and one to two night awakenings, respectively at 06:00 am (half an hour) and 03:00 and 06:30 am (40 min); L. and Ju. had none to one night awakenings at 07:00 or 08:00 (10 min). Concerning daytime naps, J. and A. presented three naps (2:45 and 2:30 h, respectively), at 7:30, 11:30 and 15:30; L. and Ju presented three naps (45 min to 1 h, respectively), at correspondingly, 10:00, 13:30 and 17:00 and 9:30, 13:00 and 18:00. Twin studies show that sleep is extremely similar in identical twins, while in fraternal twins, it seems only to exist familial relatedness. Using actigraphic data, in only a pair of identical and a pair of fraternal twins, we found greater similarity in all sleep parameters in the identical pair, comparing with the fraternal pair. Financial support: AstraZeneca Foundation.

Poster Session – Neurophysiology: EEG

P394

Increase in cortico-thalamo-cortical connectivity during human sleep slow wave activity

C. KUSSÉ, R. LEHEMBRE, A. FORET, L. MASCETTI, P. MAQUET and M. BOLY
Cyclotron Research Centre, Liège, BE

Objectives: Slow waves are the hallmark of non-rapid eye movement (NREM) sleep and are quantified by slow wave activity (SWA). The neural mechanisms of these oscillations in the human brain remain incompletely understood. Dynamic causal modelling (DCM) for steady state responses uses a mathematical neural model to infer the changes in functional interactions between brain regions likely underlying observed changes in power spectrum. The present study used DCM to investigate changes in effective connectivity between NREM and wakefulness in default mode network areas involved in SWA generation.

Methods: We recorded 64-channel electroencephalographic (EEG) night-time sleep in 20 healthy human volunteers. Five-minute clean EEG epochs from wakefulness, stage 2 and stage 3 NREM were selected for further analysis.

Results: The two regions of interest selected from the source-reconstructed analysis were located in posterior cingulate (PCC) and medial prefrontal/anterior cingulate (MPFC). Bayesian comparison revealed that the best model for explaining power spectral changes in our data across vigilance states contained both cortical areas and a reciprocally connected thalamus. Repeated measures analysis of variance revealed significant changes across vigilance states in connection strength from MPFC to thalamus and from thalamus to PCC ($P < 0.05$, corrected for multiple comparisons). Post-hoc analysis revealed increased corticothalamic and thalamocortical connectivity along this anteroposterior axis, induced by NREM sleep. We also identified increased excitability (intrinsic connectivity) in MPFC and thalamus in NREM. Changes in connectivity mirrored the changes in scalp EEG SWA: while a significant increase in scalp delta power and significant connectivity differences were observed between stage 3 and both stage 2 sleep and wakefulness, scalp power and connectivity in stage 2 sleep and wakefulness did not significantly differ from one another.

Conclusion: The effective connectivity changes identified during NREM sleep in the present study are reminiscent of the preferential anteroposterior spread reported for individual sleep slow waves. Our results suggest that the increased EEG synchronisation during NREM sleep is mediated through changes in cortico-thalamo-cortical interactions rather than through a substantial change in corticocortical connections. These results are in line with a suggested role of thalamocortical interactions in NREM sleep slow wave generation.

P395

Sleep spindle harmonic: experimental observation and theoretical explanation

R. G. ABEYSURIYA, P. A. ROBINSON and C. J. RENNIE
University of Sydney, Sydney, AU

Objectives: This pilot study explores the origins of sleep spindles using new experimental data and comparisons with an established mean-field model of the brain. Understanding the production of sleep spindles at a large-scale dynamical level explains new phenomena that are not predicted by existing theories, and provides a context in which single neuron or local field measurements of sleep spindles can be interpreted.

Methods: An established mean-field model of the brain is used, which predicts the EEG power spectrum from dynamics of the cortex, thalamic relay nuclei, and thalamic reticular nucleus. Spindle activity in the model arises when the feedback loop between the reticular nucleus and the relay nuclei is strong. Neurons exhibit a nonlinear firing response, and this nonlinearity in the relay nuclei is found to be significant during sleep spindle activity, resulting in a spindle harmonic at double the frequency of normal spindle activity. By analytically deriving the relationship between the normal spindle activity and the harmonic activity, power and phase correlation is predicted.

To confirm these predictions, polysomnograms of nine healthy controls are examined, and spindle activity is automatically detected and isolated. The Fourier transform is computed to provide the power spectrum for each burst of spindle activity. The powers in the spindle peak and in the harmonic are measured, and the bicoherence is calculated to detect phase relationships.

Results: All nine subjects have strong spindle activity around 12–14 Hz, and show a harmonic at 24–28 Hz. A correlation between peak powers is observed, with the harmonic peak increasing in strength as spindle activity increased. These preliminary results are consistent with model predictions, although due to the nature of spindle activity (a small number of events, which are short in duration thus limiting spectral resolution) additional data will be required to verify predictions more rigorously. The bicoherence of the spectra shows a clear phase relationship between the spindle activity and its harmonic.

Conclusion: Neural field theory predicts sleep spindles will be accompanied by a harmonic due to nonlinear effects in the brain. A harmonic spindle was discovered in experimental data, confirming modeling results.

P396

Cordance as a biomarker in sleep EEG for treatment response in depression – a naturalistic study after antidepressant medication

M. PAWLOWSKI, M. ADAMCZYK, M. DRESLER and A. STEIGER
Max Planck Institute of Psychiatry, Munich, DE

Introduction: Cordance is a relatively new quantitative EEG-method, which has shown usability as a biomarker for depression within the waking-state. Cordance has not been tested within sleep yet. We wanted to examine whether differences in cordance derived from sleep EEG exist between responders and non-responders to antidepressant medication. Additionally we wanted to compare cordance in depressed patients with healthy subjects.

Methods: Twenty in-patients (15 women, five men) with a depressive episode were treated with various antidepressants according to doctor's choice. No significant differences in age (mean 45 ± 22 years versus mean 49 ± 12 years), medication or Hamilton Depression Rating Scale score (23.8 ± 4.5 versus 24.5 ± 7.6) were found between responders and non-responders at inclusion shortly before drug treatment. Response to treatment was defined as a ≥ 50% reduction of Hamilton score between inclusion and the end of four weeks of active medication. Cordance values for the prefrontal theta-EEG were calculated from sleep EEG during the first week with

active medication. Furthermore seven healthy young subjects (five women, two men, mean 23 ± 2 years) have been included to calculate the same and to compare depressed patients versus healthy subjects.

Results: Eight responders compared to 12 non-responders showed higher cordance values in prefrontal EEG sites (z-score -1.52 ± 0.98 versus -2.52 ± 0.71, $P = 0.006$). Z-scores and Hamilton scores of all patients are moderately correlated (Spearmans Rho: R = -0.5; $P = 0.025$). The healthy subjects showed cordance values similar to the responders, but not to the non-responders.

Conclusion: These results suggest that cordance derived from sleep EEG provides a predictor for treatment response in patients with depression.

P397

The use of Kalman filter in sleep EEG analysis

F. WALLNER

Institut für Schlafmedizin, Passau, DE

Objectives: In order to improve the accuracy of EEG results, it might be useful to enhance Borbély's and Daan's mathematical two process model of sleep with spectrum analysis. The aim of this method is to achieve more exact and realistic results of the EEG measurement by including 'natural' errors of measurement and fuzzy effects with Kalman filtering technics.

Methods: The Kalman filter method enables prognoses about the developing of power density spectra, which are compared and correlated with really surveyed data. With the aid of this method, spectral changes can be indicated in physical units, and the effect of psychotropic can be analysed.

Results: Compared to results based on Borbély's and Daan's conventional model, the inclusion of fuzzy effects via Kalman filter makes errors of measurement determinable and produces results which reflect the actual phases of sleep in a more exact and realistic way. This improved mathematical model of sleep might be useful e.g. in order to quantify effects of therapeutic treatment and makes sleep density measurable.

Conclusion: The Kalman filter method is an excellent method in order to verify or to falsify predicted model assumptions based on measured data. It might provide valuable services at the issue of a mathematical model of sleep.

This Poster Article is puplished as a thesis in mathematics at the Univerity of Passau

P398

The effects of transcranial magnetic excitation and inhibition on vigilance

A. MENSEN[1], C. GORBAN[2], M. NIKLAUS[3], E. KUSKE[3] and R. KHATAMI[3]

[1]Clinic Barmelweid, Barmelweid, CH, [2]University of Zurich, Zurich, CH, [3]University of Berne, Berne, CH

Introduction: Previous animal and human research has shown that cortical stimulation using transcranial magnetic and electrical stimulation can affect vigilance levels. Both stimulation and inhibition of the prefrontal cortex using transcranial magnetic stimulation (TMS) have a significant effect on subcortical dopamine levels. In this experiment we examined whether excitation and inhibition of the dorso-lateral prefrontal cortex (DLPFC) could have opposing modulatory effects on vigilance levels.

Methods: Twenty healthy participants (17 male), restricted a night of sleep to a maximum of 4 h prior to the experimental day. We used a combined MSLT/MWT variant to measure the participants ability to fall asleep or to stay awake. A post-nap Psychomotor Vigilance Test (PVT), assessed sustained vigilance performance. Prior to each nap, continuous or intermittent theta-burst TMS was used to either hyper-excite (10 participants) or inhibit (14 participants), the activity of either the DLPFC or a control region of the occipital cortex (OC).

Results: Mixed design ANOVA analysed the differences between TMS-type and target-site order. A significant effect was found for participants' mean sleep latencies to stage N1 and N2 with stimulation being associated with longer latencies and inhibition showing shorter latencies. TMS also significantly affected total sleep duration with longer sleep duration after inhibition of DLPFC. Reaction times on the PVT were also significantly affected. Some measures showed a significant modulation with time of stimulation.

Conclusion: Neuronavigation-guided TMS excitation and inhibition of the DLPFC can have significant opposing effects on participants' ability to fall and remain asleep during a daytime nap test and modulate participants' post nap performance reaction time during a sustained vigilance test. These effects may be mediated by TMS induced subcortical dopamine release.

P399

Effect of oscillatory stimulation tDCS (<1 Hz) on low-frequency EEG activity

E. DE SIMONI[1], M. GORGONI, F. MORONI[2], C. MARZANO[1], M. FERRARA[3], F. FERLAZZO[1], P. M. ROSSINI[4] and L. DE GENNARO[1]

[1]Sapienza University of Rome, Rome, IT, [2]University of Bologna, Bologna, IT, [3]University of L'Aquila, L'Aquila, IT, [4]Catholic University of Rome, Rome, IT

Introduction: Transcranial Direct Current Stimulation (tDCS) is a non-invasive method to modulate cortical excitability, depolarizing (anodal tDCS) or hyperpolarizing (cathodal tDCS) neurons, by continuous current (c-tDCS), or oscillatory current (so-tDCS). We used the so-tDCS (<1 mA and 0.75 Hz for 10 min) to actively induce changes in electrophysiological measures (EEG) of sleepiness.

Methods: Waking EEG was recorded from 28 derivations before and after stimulation (5 min with eyes-closed and 5 min with eyes-open) in 10 subjects for the anodal tDCS and sham (control), and 7 subjects for the cathodal tDCS. Mean EEG power was calculated for the following bands: delta (1–4 Hz), theta (5–7 Hz), alpha (8–12 Hz), beta1 (13–15 Hz) and beta2 (16–24 Hz). The two conditions (after versus before), for each band and for each derivation, were compared by t-tests, and corrected for multiple comparisons by the Bonferroni test.

Results: In the eyes-open condition, the results point to an increase in theta activity at the left parietal area after cathodal tDCS, and an increase of the beta1 activity at the right parietal region after anodal tDCS. In the eye-closed condition, the increased theta activity was confirmed at the left parietal area after cathodal tDCS, while an increase of beta1 activity was found at the frontal region.

Conclusions: According to the a priori hypothesis, cathodal stimulation affects spontaneous EEG activity in both conditions (i.e., eyes-closed and open), because it mainly facilitates the increase in the theta activity, that is the EEG marker of diurnal sleepiness. On the other hand, the anodal stimulation seems inducing opposite effects, by relatively increasing the low-beta activity.

P400

Effects of different rocking movements on relaxation in a supine position

X. OMLIN, F. CRIVELLI, L. TAROKH, R. RIENER and P. ACHERMANN
University of Zurich, Zurich, CH

Objectives: Rocking movements appear to have effects on sleep and examples can be found in everyday life: Commuters doze off in a rattling train and babies fall asleep when being rocked in a cradle. Recent research suggests a facilitated transition from wake to sleep in the presence of lateral rocking movements. However, the effects of other movement axes have not been explored. The aim of this study was to investigate the effect of six different movement directions on relaxation and their potential to promote sleep.

Methods: Movements were induced using a bed on a platform, which was driven by a rope robotic system. This system allows movements in six degrees of freedom. Translations along the x-, y-, and z-axis and rotations around the roll-, pitch-, and yaw-axis were tested in 25 healthy subjects (eight female, age: 23–47 years). Movements were presented in random order and were performed with a frequency of 0.3 Hz. Baselines without movement were also recorded. Subjects completed a questionnaire rating how pleasant and relaxing each movement was. EEG, ECG and respiration were recorded throughout the experiment. Heart rate was calculated using beat detection and respiration rate was estimated with spectral analysis (fast Fourier transform routine, Hanning window, averages over 60-s epochs). Waking EEG alpha power (8–12 Hz), alpha peak power, and theta power (5–8 Hz) were also calculated (fast Fourier transform routine, Hanning window, averages over 2-s epochs).

Results: With regards to relaxation, the best questionnaire ratings were found for movements along the z-axis while the worst were found for the roll-axis. Heart rate showed no changes between the movement conditions and baseline. Respiration frequency increased in all movement conditions compared to baseline, reaching values close to the movement frequency. Preliminary analysis comparing the most and least pleasing condition showed no changes in EEG parameters.

Conclusion: Movements along the z-axis appear to be most promising for promoting relaxation. Further EEG analysis will be conducted to compare the analyzed conditions with the other movement conditions and baseline. As respiration frequency was influenced by the movement frequency, further studies are planned to elucidate whether respiration frequency can be reduced when applying slower movement frequencies.

P401

Sleep at moderate altitude resulted in reduced low-frequency power in the EEG and increased spindle peak height

K. STADELMANN[1], T. D. LATSHANG[2], C. M. LO CASCIO[2], N. TESLER[3], A.-C. STOEWHAS[2], M. KOHLER[2], K. E. BLOCH[2], R. HUBER[3] and P. ACHERMANN[1]
[1]University of Zurich, Zurich, CH, [2]University Hospital Zurich, Zurich, CH, [3]University Children's Hospital Zurich, Zurich, CH

Objectives: As alpine tourism has become very popular, examining the effects of altitude on sleep is of increasing importance. Several studies have reported a shift towards lighter sleep with an ascent to high altitudes. Changes in sleep resulting from stays at moderate altitude, however, are difficult to detect. The aim of the present study was to examine changes in the sleep EEG spectra concurrent with changes in blood gas concentrations and the occurrence of central apneas/hypopneas at three different altitudes.

Methods: In a randomized cross-over design, 44 men underwent polysomnography on a baseline night at 490 m and two consecutive nights at two higher altitudes (1630 and 2590 m). EEG power density spectra of frontal (F3A2) and central (C3A2) derivations were calculated and averaged over the minimal common length of NREM sleep within individuals.

Results: Exposure to hypobaric hypoxia decreased NREM sleep slow-wave activity (SWA, 0.8–4.6 Hz) by 15% on both nights at 2590 m (C3A2 and F3A2) and 4.4% on the first night at 1630 m (F3A2 only). At the highest altitude a 10% decrease in spectral power was also found in theta activity (4.6–8 Hz). SWA also decreased during REM sleep, although the decline was less pronounced than that observed during NREM sleep (15% versus 3%). SWA at 2590 m was negatively correlated with the central apnea/hypopnea index (AHI; r = -0.4), while theta activity was positively correlated with mean oxygen saturation (SpO2; r = 0.4). In addition, spindle peak height tended to increase on the first night by 6%, ($P = 0.07$) and increased by an additional 5% on the second night at 2590 m compared to baseline ($P < 0.001$). On the first night at 2590 m, the increase in spindle peak height and decline in SWA and theta activity were correlated (C3A2: r = 0.4).

Conclusion: SWA – a marker of sleep intensity and homeostasis – was reduced at altitude in both NREM and REM sleep. The greater decline in SWA during NREM sleep may be explained by increased central AHI during this sleep state. The stage non-specific reduction in low-frequency power and the increase in spindle peak height may be due to a common mechanism.

Funding: Zurich Center for Integrative Human Physiology and Schweizerische Unfallversicherungsgesellschaft (SUVA).

P402

Cyclic alternating pattern is associated with brain haemodynamic variation measured by near-infrared spectroscopy in healthy humans

J. TOPPILA[1], T. NÄSI[2], J. VIRTANEN[2], T. SALMI[1] and R. J. ILMONIEMI[2]
[1]Helsinki University Central Hospital, Helsinki, FI, [2]Aalto University, Espoo, FI

Objective: Within non-rapid eye movement (non-REM) sleep there is typical oscillatory variation in the cortical electroencephalographic activity called cyclic alternating pattern (CAP). CAP is formed from transient phasic events (phase A) and background activity (phase B) lasting 2–60 s each. According to literature the increased CAP proportion during non-REM sleep is probably connected to micro arousals and minor sleep discontinuity due to sleep apnea, periodic leg movement disorder, and even sleeping in suboptimal conditions. The brain hemodynamic counterpart of the CAP activity has not yet been as-sessed in healthy subjects.

Methods: Near-infrared spectroscopy (NIRS) is a non-invasive, safe, and painless method to measure brain hemodynamics with sufficient temporal resolution for finding alterations associated with CAP. Scalp and cortical hemodynamics were measured with NIRS from the forehead, systemic hemodynamics with a finger pulse oximeter, and CAP activity with simultaneous polysomnography in 11 healthy subjects during 23 nights altogether.

Results: CAP sequences were associated with oscillatory alteration in both cortical and systemic hemodynamic signals: oxyhemoglobin (HbO_2), deoxyhemoglobin (HbR), and heart rate. The magnitude of

the alteration was biggest during the cycle of subtype A3 + B. Subtypes A2 + B and A1 + B had parallel but weaker effects on hemodynamics compared to A3 + B. During the first half of phase A there was an immediate increase in heart rate and HbO2 level. During the last half of phase A, HbO_2 turned into longer and deeper transient decrease continuing also in subsequent phase B. Simultaneously there was a slight increase in cortical HbR and a decrease in extracerebral HbR.

Conclusion: We found that CAP is associated with alterations in brain hemodynamics that correspond to the ones seen in sleep apnea. In line with earlier reports of autonomic arousals connected to CAP, the systemic hemodynamics changed as well. We have reported earlier parallel cortical and systemic hemodynamic changes associated with sleep-wake transition in healthy subjects. Increased number of CAP cycles during non-REM sleep associated with minor sleep disturbances seems to affect the cerebral hemodynamics in a similar manner as sleep apnea.

P403

Functional brain connectivity across sleep stages and sleep EEG frequencies

F. JURYSTA[1], J.-P. LANQUART[1], P. LINKOWSKI[1] and D. MARINAZZO[2]

[1]Academic Erasmus Hospital, Brussels, BE, [2]Faculty of Psychological and Pedagogical Sciences, Ghent, BE

Objectives: Functional connectivity reflects the statistical dependencies among even remote brain regions. We studied the functional brain network across sleep stages for each relevant sleep EEG frequency band.

Methods: The first 20 epochs of each sleep stage (awake, sleep stages 1–4 and REM sleep) of nine healthy young men were analysed. Sleep stages were visually scored in accordance with the Rechtschaffen and Kales criteria. All subjects were free from somatic, psychiatric and sleep disorders. In regard of specific sleep EEG frequencies as delta, theta, alpha, sigma and beta, coherence analysis (COH) and generalized partial directed coherence (GPDC), which allows to detect directional influences, were applied between each electrode and each other of the 19 EEG electrodes.

Results: COH showed high values for right or left hemisphere without interconnectivity between both right and left regions across awake and stage 1. During sleep stages 2, 3 and 4, high coherence values were observed around all central electrodes with an increased interaction between both hemispheres. During REM, COH values were observed between awake and sleep stage 2 values. COH remained stable between stage 2 and stages 3 and 4. These results were similar for all frequency bands. GPDC showed an increased interdependency between electrodes as well as a larger area of interactions from awake to stage 4 for all EEG frequencies. GPDC increased from delta to alpha and remained unchanged between alpha, sigma and beta. At delta frequency, the information flowed from frontal to parietal electrodes for awake, stage 1 and REM. This flow was also observed to occipital regions during stage 1 and REM. During stage 2, an additional flow was observed from half posterior central brain region to parietal and occipital regions. The source of this flow moved progressively to right parieto-occipital region during stages 3 and 4 while parietal activity decreased. Results of flow information were similar between sleep EEG frequencies. Nevertheless, the flow from frontal to occipital regions during REM at delta frequency disappeared progressively with increasing EEG frequencies.

Conclusions: The functional connectivity demonstrated major changes between awake, sleep stages 1 and 2 while connectivity remained stable across stages 3 and 4. REM sleep could be considered as a particular sleep stage between awake/stage 1 and the other sleep stages. Similar changes were observed across sleep EEG frequencies.

P404

Hippocampal sleep spindles preceding neocortical sleep onset in humans: an intracerebral EEG study

S. SARASSO[1], P. PROSERPIO[2], F MORONI[3], M. FERRARA[4], L. DE GENNARO[5], A. PIGORINI[1], M. MASSIMINI[1] and L. NOBILI[2]

[1]University of Milan, Milan, IT, [2]Ospedale Niguarda, Milan, IT, [3]University of Bologna, Bologna, IT, [4]University degli Studi dell' Aquila, L'Aquila, IT, [5]'La Sapienza' University of Rome, Rome, IT

Objectives: Human sleep is considered a global phenomenon, orchestrated by specialized and diffuse neuronal networks modulating the whole-brain activity. Recent clinical as well experimental evidence suggest that sleep-and sleep/wake transitions- may be regulated locally. As an example, intracerebral electroencephalographic (EEG) recordings showed that thalamic deactivation precedes neocortical sleep onset by several minutes. Along the same lines, here we aim at investigating whether some cortical regions, such as the hippocampus, also shows sleep EEG features before others.

Methods: Six patients (4 M, 2 F; mean age 29.3 ± 10.8) diagnosed with drug-resistant focal epilepsy underwent intracerebral EEG investigation (Stereo-EEG, SEEG) for the presurgical assessment of the epileptogenic zone. Inclusion criteria encompassed the presence of at least one bipolar SEEG lead investigating the hippocampal formation and the absence of sclerosis as well as of pathological EEG activity in the hippocampus. Recordings begun at lights off and sleep onset (SO) was determined as the first occurrence of a K-complex or a sleep spindle at the scalp derivation. SEEG leads containing epileptiform activity were discarded and the remaining (Mean: 14; SEM:1.6), together with hippocampal derivations, were then analyzed by means of spectral signal decomposition (FFT routines) and automatic detection algorithms aimed at identifying sleep spindles.

Results: Automatic detection algorithms, validated by visual inspection, showed that, in every patient, hippocampal sleep spindles occurred before SO (Mean: 13 min; SEM: 2.5; $P < 0.001$) and preceded sleep spindles occurring in other neocortical structures (Mean: 4.5 min; SEM:1.6; $P < 0.05$).

Conclusion: Our results support the notion that sleep onset is a dynamic event, progressively involving distinct cortical structures. This observation, although preliminary, suggests that the transition from wakefulness to sleep may follow a phylogenetic determined pathway involving, at first, the archicortical hippocampal formation and, only later, neocortical structures. Also, our finding may help understanding the cognitive consequences of sleepiness. In fact, the occurrence of sleep-like sign in the hippocampus together with preserved neocortical wake patterns, may produce a covert form of 'dormiveglia' characterized by attentive as well as mnestic deficits.

P405

Effective brain connectivity during sleep

D. MARINAZZO[1], J.-P. LANQUART[2], P. LINKOWSKI[2] and F. JURYSTA[2]

[1]Faculty of Psychological and Pedagogical Sciences, Ghent, BE, [2]Academic Erasmus Hospital, Brussels, BE

Objectives: A great insight on brain function can come from the investigation of the directional pathways of information flow across its regions (effective connectivity). We used Granger Causality (GC) to infer the effective connectivity brain network across sleep stages during nocturnal sleep.

Methods: The 20 first sleep stage epochs (awake, sleep stages 1–4 and REM) of nine healthy young men were analysed. Sleep stages were visually scored in accordance with Rechtschaffen and Kales criteria. All subjects did not suffer from somatic, psychiatric or sleep disorders and did not take any medication. Connectivity matrices between the 19 EEG electrodes were obtained for each sleep stage using multivariate GC.

Results: During wake, hetero-hemispherical activity was observed reciprocally in frontal, occipital and occipito-parietal regions. Across 1–4 sleep stages, the information flow decreased in the posterior brain regions while activity was increased in anterior and central brain regions. During REM sleep, connectivity was limited to occipital and left fronto-temporal regions. Changes in GC values were observed between each sleep stage except for stages 3 and 4. During these last sleep stages, the pattern of information flow is analogous to stage 2.

Conclusions: GC changed across sleep stages. During stage 2 and deep sleep, major connectivity was observed in central brain regions and remained unchanged. The effective connectivity network architecture in sleep stage 1 reflected a transitional state between awake and stage 2, while during REM sleep, GC revealed a specific pattern. In conclusion, effective brain connectivity could suggest 3 different sleep states in comparison to wake: a transitional state as Stage 1, a sleep state as Stages 2, 3 and 4, and a specific state as REM.

P406

Mapping distinct waves of sensory-evoked K-complexes: a high-density EEG study in humans

M. LAURINO[1], D. MENICUCCI[2], P. ALLEGRINI[2], F. MASTORCI[2], A. PIARULLI[3] and A. GEMIGNANI[1]

[1]University of Pisa, Pisa, IT, [2]National Research Council (CNR), Pisa, IT, [3]Scuola Superiore Sant'Anna, Pisa, IT

Objectives: Sensory stimulation during NREM sleep elicits the K-complex (KC), which consists of distinct EEG waves reflected by peaks with different polarity and latency. Traditionally, the evoked KC is considered to be sensory-modality independent. Our aim is to verify this statement by means of high-density (HiDe) EEG recordings of evoked KCs using different sensory modalities.

Methods: We have collected HiDe-EEG recordings (128 channels) from 14 volunteers (age 23 ± 3 years). During N2 and N3 stages of sleep, auditory (brief 1000 Hz pure tones of 20 dB; 50 ms duration), somatosensory (constant mechanical vibrations of 600 Hz delivered at the middle finger of the right hand; 50 ms duration) and visual (brief full-field flashes; 10 μ s duration) stimuli have been administered to each subject. Each evoked KC has been segmented into distinct waves: the positive peak around 200 ms after the stimulation (P200), the negative peak N550, corresponding to KC downstate, and the positive peak P900, corresponding to KC upstate.

Results: The P200 waves show the lowest latencies in the primary sensory areas wired to the stimulation modality, and behave as travelling waves. The N550 waves have a latency distribution with differences among sensory modalities: an antero-posterior gradient with a minimum in the fronto-central areas (without any topological difference between the two sensory modalities) has been detected for acoustic and somatosensory stimulations, while for the visual stimulation the latency detected in visual areas is comparable to those observed in frontal and central ones. Higher amplitudes and shorter latencies have been found for the P900 in medio-frontal areas, for all stimulations.

Conclusion: P200 is the KC wave most strictly dependent on the specific sensory stimulation, since both its origin location and propagation pathways depend on the eliciting modality. The N550 latency map also shows a sensory-modality-dependent topology, although less specific than the P200, discriminating visually elicited KCs. Finally, the P900 waves turned out to be completely independent of the sensory eliciting modalities. In conclusion, each wave of sensory-evoked KC shows distinct topological and dynamical behaviors, aimed at preventing the emergence of conscious sensory processing.

P407

Quantative analysis of electrodermal activity during sleep

A. SANO and R. PICARD

Massachusetts Technology of Institute, Cambridge, US

Objectives: The objective is to quantitatively characterize electrodermal activity (EDA) during sleep. EDA is widely used as a measure of sympathetic nervous system (SNS) activity, where the SNS is one of the main branches of the autonomic nervous system. Prior studies have reported that high frequency peaks in EDA occur during slow wave sleep (SWS) and non-REM2 sleep (NREM2, however high frequency peaks do not necessarily occur corresponding to those sleep stages. Quantitative analysis is needed to clarify the characteristics of the EDA peaks.

Methods: We analyzed EDA patterns of 15 healthy adults on over 200 nights. We gathered data using the Affectiva QTM wrist sensor, which comfortably logs skin conductance, skin temperature, and actigraphy. We measured two conditions: (i) 1-night for each of eight adults with concurrent polysomnography (PSG) in a sleep lab; (ii) 30-nights for each of 7 adults at home, sans PSG. We applied zero-crossing and Cole's function to the actigraphy data to discriminate sleep and wake. After low-pass filtering the EDA (cutoff 0.4 Hz, 32nd order FIR), we took the first derivative and marked peaks where the slope exceeded 0.09 micro Siemens/s. When 30-s epochs having peaks were adjacent to or within 5 min of each other, they were combined into a 'storm'.

Results: We found 29% of SWS and 13% of NREM2 epochs had EDA peaks (average over eight lab nights). Four people had maximum mean EDA amplitude in NREM2 and the rest had maximum mean EDA amplitude in SWS. EDA peak frequency was highest in NREM2 for three nights, in SWS for four nights and in NREM1 for one night. The mean and standard deviation for the number of peaks per 30-s epoch was 2.8 ± 1.7 in NREM2 and 2.9 ± 0.9 in SWS across the eight lab nights. We analyzed the temporal pattern of EDA peaks for both the home and lab data. The highest frequency peaks were observed after the first hour of sleep for two thirds of the participants and just after sleep onset for the rest, with decreasing EDA amplitude as the night passed. Of all storms, 57% had only 1 peak, and 49% lasted only 30 s. Histograms of the

number of peaks in storms and duration of storms showed logarithmic decay.

Conclusion: We quantitatively characterized EDA for over 200 nights from home and lab sleep and described a basic taxonomy of EDA peaks and amplitude, validating their tendency to occur in NREM2 and SWS. EDA peaks showed the highest frequency either after the first hour of sleep or right after sleep onset. Picard is co-founder, chief scientist, and chairman of Affectiva, the company who manufactures the Q™ sensors we used.

P408

Respiratory disturbances reduce slow-wave and spindle activity during non-REM sleep and decrease slow wave sleep

K. STADELMANN[1], T. D. LATSHANG[2], C. M. LO CASCIO[2], N. TESLER[3], A.-C. STOEWHAS[2], M. KOHLER[2], K. E. BLOCH[2], R. HUBER[3] and P. ACHERMANN[1]

[1]University of Zurich, Zurich, CH, [2]University Hospital Zurich, Zurich, CH, [3]University Children's Hospital Zurich, Zurich, CH

Objectives: Patients with mild sleep disordered breathing show less slow wave sleep, sleep EEG sigma activity and spindle density when compared to controls. Correspondingly, ascent to altitude has been shown to result in more central apneas and a shift toward lighter sleep in healthy individuals. Our aim was to gain a better understanding of how respiratory disturbances at moderate altitude may impact sleep.

Methods: Fifty-one healthy young men spent one baseline night at 490 m and one night at 2590 m. Fourteen nights with at least 40 artifact-free epochs of stage 2 sleep containing a respiratory disturbance (central/obstructive apnea, hypopnea, periodic breathing) were included in the analysis. Mean power spectra of epochs with and without respiratory disturbance were compared. Furthermore, all-night EEG spectra of non-REM sleep, stage 2 and slow wave sleep were calculated and sleep at altitude was compared with baseline sleep (n = 14).

Results: Epochs of stage 2 sleep with respiratory disturbances exhibited less slow-wave (0.8–4.6 Hz) and spindle activity (13–13.2 Hz) and more beta activity (14.6–15 Hz) compared to epochs without respiratory disturbances. Slow-wave sleep was decreased (-13%) at altitude compared to baseline. At altitude slow-wave activity (SWA, 0.8–4.6 Hz) was decreased in non-REM (-17%) and stage 2 sleep (-18%), but not in slow wave sleep.

Conclusion: Our findings demonstrate that respiratory disturbances lead to decreased slow-wave and spindle activity and increased beta activity, maybe due to a disruption of stage 2 sleep by e.g. micro arousals or EEG activation. In support of this, we find a decrease in SWA during stage 2 sleep. The disturbances of stage 2 sleep may account for the suppression of slow waves observed by altitude induced central apneas. By inhibiting the transition into deep sleep, central apneas may lead to a reduction of slow wave sleep and a decrease in SWA during non-REM sleep.

Funding: Zurich Center for Integrative Human Physiology and Schweizerische Unfallversicherungsgesellschaft (SUVA).

P409

Cerebral cortex and sleep onset: an asynchronous process?

C. MARZANO[1], F. MORONI[2], L. GAGLIOSTRO[1], M. FERRARA[3] and L. DE GENNARO[1]

[1]Sapienza University of Rome, Rome, IT, [2]University of Bologna, Bologna, IT, [3]University of L`Aquila, L`Aquila, IT

Objectives: Sleep onset period is characterized by large regional and frequency-specific EEG differences. In order to assess the topographical EEG features of wake-sleep (W-S) transition, the full-scalp EEG power either for baseline (BSL) and recovery (after 40-h of sleep deprivation, REC) night has been analyzed. Moreover, the temporal dynamics of regional cortical oscillations across W–S transition have been investigated.

Methods: Pre- and post-sleep EEG of 40 subjects (20 M and 20 F; age = 23.75 ± 2.92 years) were recorded from 19 derivations. The EEG power values were calculated by Fast Fourier Transform routine applied across the 0.5–24.75 Hz frequency range. The Better OSCillation (BOSC) detection method was used to detect rhythmic oscillatory activity within EEG signals.

Results: Statistical comparisons between pre- and post-sleep, computed separately for BSL ($t \geq 3.82$; $P \leq 0.0005$) and REC ($t \geq 3.80$; $P \leq 0.0005$) night considering each scalp derivation and each 1 Hz frequency bin, revealed the presence of: (i) an increase of delta activity concomitant with a reduction of beta activity during sleep onset in almost all derivations, (ii) a specific prevalence of occipital theta activity, of centro-parietal sigma and anterior alpha activity after sleep onset, and (iii) a greater extent of these phenomena in REC night. The spatio-temporal dynamics showed a progressive increase in the fronto-central slow-frequency activity and in the centro-parietal sigma activity, that paralleled the generalized decrease of beta activity. The temporal dynamics point to a shift from the posterior predominance of alpha activity during pre-sleep period to the anterior predominance during sleep onset.

Conclusion: This study documented, in a large sample of subjects, state- and frequency-specific changes of cortical oscillations during sleep onset period and the presence of an asynchronous process of EEG synchronization in different brain areas while falling asleep. An orchestrated pattern emerges by our Results: the slow wave activity shows a progressive increase over the more anterior scalp derivations, while the alpha band exhibits a posterior dominance during pre-sleep wakefulness and an anterior prevalence at sleep onset.

P410

Spindles throughout the stages of sleep

R. S. NADER[1], C. T. SMITH[1], A. MURKAR[1] and M. SABBAGH[2]

[1]Trent University, Peterborough, CA, [2]Queens University, Kingston, CA

Introduction: This study examined the prevalence of three spindle types throughout the various stages of sleep. Slow (11–13.5 Hz), fast (13.51–16 Hz) and super-fast (16.01–18.5 Hz) spindles were examined in each stage.

Method: Participants were 32 healthy adolescents (17 female) aged 12–19 years (M = 15.36 years). In home recordings of EEG were obtained. Spindles were counted using PRANA®. Minimum spindle duration was 0.5 s; spindles were counted separately in 11–13.5 Hz, 13.51–16 Hz, 16.01–18.5 Hz bins.

Results: All three types of spindles were found to exist in Stage 2, REM and SWS. Densities were highest in Stage 2 for all three types and lowest in REM sleep. At FZ, the mean numbers of spindles in stage 2 were: 1776.09 (Slow), 365.66 (Fast), and 42.31 (Super). In SWS at FZ, the following means were found: 1019.88 (Slow), 126.63 (Fast), and 12.28 (Super). In REM at FZ the following means were observed: 19.63 (Slow), 19.06 (Fast) and 18.12 (Super). The number of slow spindles in Stage 2 was significantly correlated with the number of slow spindles in SWS (e.g. FZ: $r(30) = 0.57$, $P = 0.001$), but not as consistently with the number of slow spindles in REM (e.g.

C3: r(29) = 0.56, $P = 0.001$; FZ: r(30) = 0.27, $P = 0.138$). The number of slow spindles in SWS and REM were not consistently related (FZ: r(30) = 0.25, $P = 0.166$). The number of Fast spindles in Stage 2 was significantly correlated with the number of fast spindles in SWS (e.g. FZ: r(30) = 0.72, $P < 0.001$), but not as consistently with the number of fast spindles in REM (e.g. C3: r(29) = 0.39, $P = 0.031$; FZ: r(30) = 0.14, $P = 0.438$). The number of fast spindles in SWS and REM were not consistently related (e.g. C3: r(29) = 0.36, $P = 0.048$; FZ: r(30) = 0.008, $P = 0.965$). The number of Super spindles in Stage 2 was significantly correlated with the number of Super spindles in SWS (e.g., FZ: r(30) = 0.57, $P = 0.001$), and with the number of Super spindles in REM (e.g. FZ: r(30) = 0.80, $P < 0.001$). The number of Super spindles in SWS and REM, were not related (e.g., FZ: r(30) = 0.25, $P = 0.176$).

Conclusions: The numbers and types of spindles in SWS and REM were substantial and suggest that the focus on Stage 2 sleep when examining spindles may be too limiting. There were substantial numbers of spindles in the Super (16.01–18.5 Hz) range. Spindle density in Stage 2 is positively related to density in the other stages, suggesting that they have similar underlying mechanisms.

P411

Travelling slow waves in the avian brain

G. J. L. BECKERS, J. VAN DER MEIJ, J. A. LESKU and N. C. RATTENBORG

Max Planck Institute for Ornithology, Seewiesen, DE

Objectives: Recent studies have shown that slow waves propagate across the neocortex as a traveling wave during mammalian slow wave sleep. Although waves tend to originate in frontal regions, they can originate in virtually any part of the neocortex. To determine whether the behavior of slow waves described in mammals reflects a fundamental aspect of slow wave sleep, we examined whether slow waves also act as traveling waves in birds, the only other taxonomic group to exhibit unequivocal slow wave sleep.

Methods: Adult female zebra finches (Taeniopygia guttata) were anesthetized with 1–1.25% isoflurane. Local field potentials (LFP) and multiunit activity (MUA) were recorded using a 64-channel NeuroNexus silicon probe (8×8, 200 micro-m grid of 413 micro-m^2 electrodes) inserted into the anterior hyperpallium and underlying mesopallium and nidopallium. LFP and MUA were recorded (sampled at 14 kHz) while the birds remained under anesthesia. Probe placement was verified histologically using a fluorescent tracer.

Results: The LFP recordings revealed high amplitude slow waves associated with bursts of MUA across most recording sites. This activity swept across the plane of the electrode array as a traveling wave. Although activity tended to appear first in deeper sites, it could appear first in any part of the array. The wave usually reached all electrode sites, but in some cases only involved specific brain regions. The speed with which the waves crossed the array varied from wave to wave.

Conclusions: Several characteristics of avian slow waves are similar to those described in mammals; (i) slow waves are associated with alternating periods of MUA and neuronal quiescence, (ii) slow waves are more likely to appear first in certain electrode sites, but can appear first in virtually any part of the brain covered by the electrode array, and (iii) slow waves propagate as traveling waves. In addition, the apparent variable propagation speed across the 2-D array suggests that the waves actually propagate in three dimensions with some wave fronts occurring orthogonal and others parallel to the surface of the array. Wave propagation in three dimensions is consistent with the nuclear arrangement of stellate-shaped neurons in the avian pallium. The traveling nature of slow waves appears to be a fundamental feature of slow wave sleep.

P412

Age-related changes in sleep spindle characteristics following sleep deprivation

Z. SEKEROVIC, M. LAFORTUNE, N. MARTIN and J. CARRIER

University of Montreal, Montreal, CA

Objectives: Sleep spindles are one of the main oscillatory events defining non-rapid eye movement (NREM) sleep in humans. The mechanisms underlying spindle generation involve transient rhythmic bursts (~11–15 Hz; >0.5 s) of thalamocortical neurons, which contribute to sleep protection and brain plasticity. Aging affects spindle dynamics as studies have shown a decrease in spindle density, duration and amplitude in older subjects. Results from sleep deprivation (SD) studies in young subjects suggest an inverse homeostatic relationship between the increase in slow waves (SW) and the decrease in spindle density during recovery sleep. Moreover, our group recently showed that, compared to young individuals, middle-aged subjects show a blunted SW rebound following SD. However, whether enhanced homeostatic sleep pressure after SD impacts spindle characteristics differently in young and older subjects remains unknown. This study evaluated the effect of SD and topography on spindle characteristics in young and middle-aged subjects.

Methods: Twenty-eight young (14W; mean = 27.3 years, SD = 5.1) and 32 middle-aged (19W; mean = 51.7 years, SD = 5.1) healthy subjects participated in a baseline (BSL) nocturnal sleep and a daytime recovery (REC) sleep (after a 25-h SD). Spindles (11.1–14.9 Hz) were detected on artefact-free NREM sleep epochs. Spindle density (nb/min), duration (s), amplitude (microV) and frequency (Hz) were analyzed for Fp1, F3, C3, P3 and O1 (linked-ears) derivations.

Results: In young subjects, spindle frequency increased during REC sleep as compared to BSL in all derivations whereas middle-aged subjects showed spindle frequency enhancement only in the Fp1 derivation. No other interaction between age group and SD was found. Spindle density decreased during REC sleep as compared to BSL in all derivations, although the effect was less prominent in Fp1. As compared to BSL sleep, spindle duration increased in C3 and P3 during REC sleep but decreased in Fp1. Inversely, spindle amplitude decreased in C3, P3, and O1 during REC sleep but increased in Fp1.

Conclusion: Older subjects showed a lower impact of daytime recovery sleep than young subjects on spindle frequency only. Both groups showed a similar decrease in spindle density during recovery sleep, despite previous findings of lower SW density rebound in middle-aged subjects. Impact of daytime recovery sleep on spindle density, amplitude and duration varied across derivations, particularly in the prefrontal area.

P413

Spectral EEG indicators of the kinetics of the hypothetical processes S and W during prolonged wakefulness and wake-sleep transitions

A. PUTILOV

Research Institute for Molecular Biology and Biophysics, Novosibirsk, RU

Objectives: The cyclic transitions between wakefulness and sleep might be ultimately delineated as oscillations between opposing

neurobiological processes, i.e., those promoting arousal and inhibiting sleep and those promoting sleep and inhibiting arousal. The major aim of the present analysis was to uncover the electroencephalographic (EEG) indicators of the hypothetical opponent processes underlying the wake-sleep transitions.

Methods: Data included 315 EEG recordings of the attempts to stay permanently awake for 43–61-h periods in 15 subjects, and 356 EEG recordings of the sleep positive attempts to fall asleep during multiple naps in 32 subjects. Principal component analysis was performed on the sets of 16 single-Hz log-transformed EEG powers (frequency range from 1 to 16 Hz).

Results: A close resemblance was demonstrated between the patterns of changes in the EEG indexes during prolonged wakefulness and during transitions between wakefulness and sleep. Time course of score on the 1st principal component of the EEG spectrum was characterized by a small decline before sleep onset followed by a rapid rise after sleep onset. Such a pattern was interpreted as indicating the kinetics of the process S, a regulator of accumulation and repayment of sleep debt during wakefulness and sleep, respectively. The opponent of this process can be labeled the process W and associated with time course of the 2nd principal component score. It showed a decline both before and after sleep onset, and the fastest decline was observed on the boundary between wakefulness and sleep. Time courses of spectral powers in separate frequency bands were interpreted as reflecting the combined action of the processes S and W. Given that both components load positively on alpha and sigma ranges, high frequency activity can serve as a representative of the additive action of the two processes. In contrast, low frequency activity can reflect their differential effect because the 1st component load positively and the 2nd component load negatively on delta and theta ranges.

Conclusion: Brain activity in separate frequency ranges reflects the combined action of the two hypothetical processes, while the calculation of scores on the 1st and 2nd principal components of the EEG spectrum allows the separation of the time courses of these processes.

Poster Session – Sleep Across Lifespan

P414

Long-term EEG/EMG recordings from chick embryos

D. MARTINEZ-GONZALEZ[1], N. C. RATTENBORG[1], S. DI PASCOLI[2], E. BALABAN[3] and M. POMPEIANO[3]

[1]Max Planck Institute for Ornithology, Seewiesen, DE, [2]University of Pisa, Pisa, IT, [3]McGill University, Montreal, CA

Objectives: Birds and mammals both possess two sleep states, slow-wave sleep (SWS) and rapid eye movement (REM) sleep. The chicken chick (Gallus gallus domesticus) embryo offers three key advantages relative to mammals for studying the relationship between brain development and the emergence of the sleep-waking cycle: (i) physiological independence of the embryo from its mother, (ii) well-characterized brain development, and (iii) easy accessibility for experimental manipulations at all stages of development. Our goal was to record chick embryo EEG and neck muscle EMG continuously during the final 5 days prior to hatching under the least invasive conditions possible in order to better understand how EEG patterns resembling sleep and waking states emerge developmentally.

Methods: We utilized a miniature microprocessor-based wireless EEG/EMG recording system (6 channels of data with a maximum sampling frequency of 500 Hz and a resolution of 12 bits) attached to the egg shell. Eggs incubated for 16 days (hatching at day 21) were implanted with brain dura electrodes (affixed to the skull), consisting of 38-gauge gold-plated copper wires (MWS Wire Industries, Westlake Village, CA, USA) overlying the visual wulst of the dorsal pallium and the posterior-lateral part of the pallium of each hemisphere. The EMG was recorded with an electrode placed over the neck muscle. The egg was placed on a custom-made device for recording embryo movements from the egg shell, inside of a Faraday cage on top of a vibration-isolation table. The embryo was recorded continuously in a dark, heated and humidified chamber.

Results: Continuous recording of embryos during their last five days prior to hatching revealed a gradual increase in EEG power between 1 and 10 Hz, with the emergence of cyclic variation in power correlated with variations in the self-similarity of the EEG waveform reminiscent of SWS-like and REM sleep-like activity appearing in the final period prior to hatching.

Conclusions: The strength of the brain EEG signal emerges slowly and gradually over the final 30% of chick embryonic development, with cyclic variation reminiscent of SWS- and REM sleep-like brain states emerging towards the final stages of embryonic development.

Supported by the Fondazione Cassa di Risparmio di Pisa.

P415

Brain connectivity assessed by sleep EEG coherence spectra: region- and frequency-specific maturation during early childhood

S. KURTH[1], T. RUSTERHOLZ[1], P. ACHERMANN[2] and M. LEBOURGEOIS[1]

[1]University of Colorado, Boulder, US, [2]University of Zurich, Zurich, CH

Objectives: Across early childhood, the sleep EEG undergoes major maturational changes. Developmental changes in slow-wave activity (SWA, 1–4.5 Hz) during NREM sleep have been proposed to reflect cortical thickness maturation. Brain morphology in early childhood also experiences major increases in myelination. We propose that coherence in the sleep EEG may reflect myelination of cortico-cortical connectivity.

Methods: All-night sleep EEG recordings were obtained in eight children (3 m) at three ages (2.5–3 years, T1; 3.5–4 years, T2; 5.5–6 years, T3). Standard sleep stage scoring and artifact removal were performed before computing all-night EEG coherence spectra on 30-s epochs (Hanning window, Welch's averaged periodogram) for (i) interhemispheric central (C4A1-C3A2) and occipital (O2A1-O1A2), and (ii) intrahemispheric left (C3A2-O2A1) and right (C4A1-O2A1) derivations. Fisher's z-transformation was applied to the square root of coherence for statistical analyses.

Results: Overall, interhemispheric coherence was higher in occipital than central derivations (0.25–25 Hz, NREM sleep, 2-way ANOVA; $P = 0.003$ for 'region'; $P =$ ns for 'age'). Coherence was larger in the left than right hemisphere ($P = 0.007$) and increased across age ($P = 0.0001$). Coherence averaged over selected frequency bands uncovered maturational changes (T1–T3) in a region and frequency specific manner: SWA revealed an increase in intrahemispheric coherence (left 14%, right 18%), while theta activity (4.75–7.75 Hz) showed an interhemispheric coherence increase (occipital 14%). Spindle activity (10–14 Hz) exhibited both inter- (occipital 15%, central 21%) and intrahemispheric coherence increases (left 10%, right 13%).

Conclusion: Similar to reports of region-specific early maturation of coherent waking EEG activity, coherence of the sleep EEG also follows a frequency-specific maturational pattern during early childhood. Such findings might identify age-specific programmed unfolding of cortico-cortical connections. Regional differences in interhemispheric coherence may reflect corpus callosum maturation, the largest white matter tract connecting the hemispheres. Whether coherence of the sleep EEG parallels myelination and associated development of cognitive function in early childhood remains an important unanswered question.

P416

Dynamic properties of sleep states in children and adults

L. IMBACH[1], E. WERTH[1], S. KURTH[2], M. LEBOURGEOIS[3], R. HUBER[2] and C. R. BAUMANN[1]

[1]University Hospital, Zurich, CH, [2]University Children's Hospital, Zurich, CH, [3]University of Colorado, Boulder, US

Background: Behavioral states in human sleep are conventionally described by subsequent analysis of characteristic EEG-patterns, representing the sleep architecture in a rather static way. In this approach, however, the dynamic properties of sleep – e.g. transitions between behavioral states – are poorly represented. Two-dimensional state space analysis (a novel frequency-based EEG analysis method) offers the possibility to measure behavioural state instability quantitatively using state space velocity as a comparable indicator of sleep stability. Using this technique, we addressed the question, whether sleep stability is enhanced during childhood by comparing sleep recordings of healthy children with those of healthy adult volunteers.

Methods: We analyzed sleep EEG-recordings (8 channels, whole-night polysomnography) in 6 healthy volunteers (three children: two female, one male, 4.4 ± 0.3 years old and three adults: three female, 34.6 ± 6 years old). For each EEG channel (F1 F2 C3 C4 P3 P4 01 02) an automated state space analysis was performed and average velocities in state space were determined.

Results: Using this approach, we observed a uniform characteristic distribution of stable state space clusters with low inter-individual variability for all examined volunteers independent of age or gender. Therefore, we were able to compare state space velocities between the two sub-groups (children versus adults). We then found significantly lower overall velocities in state space for children as compared to adults in all EEG derivations. By analysis of regional velocities we found that this effect was most pronounced in frontal, as compared to occipital derivations.

Conclusion: The uniform distribution of sleep patterns in all volunteers shows that state space analysis is a reliable tool for automated sleep analysis, providing comparable data even between subjects with large age differences (4.4 versus 34.6 years old). Considering the lower overall velocities in children, we conclude that childhood sleep is indeed considerably more stable and consolidated as compared to adults. For future projects, velocity analysis might therefore be used as a novel potentially diagnostic criterion not accessible by conventional polysomnography techniques in healthy and pathological sleep.

Funding: Swiss National Science Foundation Grant PP00A-114923, RH

P417

Topographical differences in sleep spindles between children and young adults

S. FRENETTE[1], R. GRUBER[2], N. MARTIN[1] and J. CARRIER[1]
[1]Montreal University, Montreal, CA, [2]Douglas Mental Health University Institute, Montreal, CA

Objectives: Spindles are a hallmark of NREM sleep and play a role in brain plasticity and sleep protection. Differences in spindles between childhood and adulthood may reflect modifications in NREM sleep brain mechanisms since thalamic and cortical networks, in which spindles are involved, are modified with age. Human EEG studies have shown higher spindle density and amplitude as well as longer spindle duration in children compared to adults. However, most of these results are derived from the central derivation. This study aims to identify topographical differences in spindles between children and young adults.

Methods: Sleep was recorded with standard polysomnography (PSG) in 31 children (12M, 19W; 8.3 years ± 1.1) and 25 young adults (8M, 17F; 22.6 years ± 2.3). Spindle detection was performed with an automatic algorithm using a bandpass filter (-3dB at 11.1–14.9 Hz), then thresholding the RMS values of the filtered signal at the 95th percentile. Spindle number, mean density (nb/min), duration (s), amplitude (μV) and frequency (Hz) were analysed on artefact-free sections of NREM sleep for F3, C3, P3, and O1 derivations (linked-ears). Two-way ANOVAs (two Age groups; four Derivations) were performed, and resulting interactions were analysed with post-hoc Tukey HSD tests.

Results: Children showed more spindles but lower spindle density than young adults in all derivations. Compared to young adults, children demonstrated longer spindle duration and this effect was more prominent in the frontal derivation and less prominent in the occipital derivation. Spindle amplitude was higher in children than in young adults but only in frontal and central derivations. Finally, children showed slower spindle mean frequency than young adults in all derivations but this effect was stronger in posterior cerebral areas (P3, O1).

Conclusions: These results demonstrate that differences in spindle characteristics between children and young adults are topographically specific. Future research should investigate mechanisms underlying age-related changes in spindle topography and their functional significance for cognitive development.

P418

Night-time sleep macro and microstructure changes in overweight children

R. CHAMORRO[1], R. FERRI[2], C. ALGARÍN[1], M. GARRIDO[1], L. CAUSA[1], J. CAUSA[1], C. HELD[1], B. LOZOFF[3] and P. PEIRANO[1]
[1]University of Chile, Santiago, CL, [2]OASI Institute, Troina, IT, [3]University of Michigan, Ann Arbor, US

Objectives: To compare sleep organization in overweight (OW) and otherwise healthy normal weight (NW) 10-year-old children.

Methods: We studied 96 children average age 10.3 ± 0.2 years, 65.6% male. Nutritional status was evaluated by body mass index (BMI) z-score adjusted for age and sex, according to WHO criteria. Two groups were compared: 37 normal-weight (>-1 BMI z-score < 1) and 59 OW (BMI z-score ≥ 1) children. All were participants in an ongoing cohort follow-up study since infancy. A polysomnographic (PSG) recording was assessed in the laboratory following children's usual sleep routines. Actigraphics recordings were performed continuously for 1 week preceding PSG. Sleep-waking stages (non-REM sleep N1, N2 and N3, REM sleep, and waking) were visually scored according to international criteria. Conventional sleep parameters, total amount, and number and duration of sleep stage episodes were established. In addition, a visual detection of the Cyclic Alternating Pattern (CAP) during non-REM sleep was conducted in a subsample of 28 normal-weight and 45 OW children.

Results: Groups showed similar timing of sleep onset, time in bed, and sleep period time. There were no differences regarding the length of previous waking or sleep respiratory disorder index. Compared to NW, the OW group showed lower total sleep time (460.5 ± 74.2 versus 426.8 ± 79.0 min, $P < 0.03$) and sleep efficiency (93.3 ± 6.8 versus 88.9 ± 10.1%, $P < 0.01$). Sleep organization was also different between groups: OW children had lower amount of non-REM sleep N1 and N2 ($P < 0.05$) and REM sleep ($P < 0.05$), and higher amount of WASO ($P < 0.02$). The CAP analysis showed a similar total NREM CAP rate between the subgroups (40.7 ± 12.4 versus 42.7 ± 13.2, respectively, however, OW children presented higher number, time, and mean duration of CAP during non-REM sleep N3 episodes (all $P < 0.02$).

Conclusion: Our results indicate that OW children have both lower sleep quality and lower sleep amount than normal-weight children, adding support to previous epidemiological findings. Nighttime sleep organization was also modified, with several differences between groups, but without involving non-REM sleep N3. However, CAP results indicated higher instability of non-REM sleep N3 episodes in OW children. Further research is needed to better understand the role of both macro- and microstructure of sleep within the obesity epidemic

Support: NIH HD 33487 and Fondecyt 1110513 & 1120319 grants. (*)CONICYT PhD program fellowship

P419

Sleep patterns and child body weight in the first six months: a birth cohort study in Taiwan

C. P. KUO, W. C. LIAO, S. H. LEE and M. C. LEE
Chun Shan Medical University, Taichung, TW

Objectives: Sleep pattern plays a critical role in children development. This paper was to explore the relations with child body-weight

at age 6 months determine by sleep patterns and demography factors from Taiwan Birth Cohort Study (TBCS).

Methods: Using a cross-sectional design, incorporate subjects drawn from the Taiwan Birth Cohort Study (TBCS) from 2005. Through completed interviews and surveys with 12 174 parents, differences in child's body-weights (low or normal) of 6 months age and demography factors, sleep patterns (single or co-sleep type, total sleep time) were analyzed.

Results: A total of 902 low body-weight (15%) and 11272 normal body-weight (15%) children's mothers had completed questionnaires during the study period. There was a significantly higher incidence of male children, low birth weight, premature, immigrant mother and mothers' education level Senior high school and below in the low body-weight group of 6 months age. When adjusted for covariates in the multiple logistic regression models, compared with children, maternal factors and sleep patterns for low and normal body-weight groups. When adjusted for mothers' age, premature and breastfeeding variables in the model?, male children had 1.73 times than female children for low body-weight in 6 months old (OR = 1.73, CI 1.50, 2.00). Similarity, low birth weight children had 4.08 times (OR = 4.08, CI 2.73, 6.10), immigrant mother had 4.08 times (OR = 1.32, CI 1.09, 1.60) than normal birth weight children for low body-weight in 6 months old. Additionally adjusted for sleep type and total sleep time in the model?, male children had 1.74 times than female children for low body-weight in 6 months old (OR = 1.74, CI 1.51, 2.20). Similarity, low birth weight children had 4.05 times (OR = 4.05, CI 2.71, 6.06), immigrant mother had 1.33 times (OR = 1.33, CI 1.09, 1.61) than normal birth weight children for low body-weight in 6 months old.

Conclusion: In our study, children gender, low birth weight and immigrant mother those factors speculated that child's low body weights of 6 months age in Taiwan. Sleep patterns that cross cultures result from a variety of health problems, but in our results not significant with children body weight. Future we may explore the associations between children body-weight growth and unique sleeping patterns in Taiwan.

P420

Infants' sleep-wake cycle and temperament

S. C. BOS, M. MARQUES, M. J. SOARES, A. PEREIRA, B. MAIA, M. H. AZEVEDO and A. MACEDO
University of Coimbra, Coimbra, PT

Objectives: to investigate infant's sleep-wake cycle at 3 and 6 months of age and to explore its association with infant's temperament.

Methods: Mothers were asked to complete the Brief Infant Sleep Questionnaire (Sadeh, 2004), the Difficult Infant Temperament Questionnaire (Azevedo & Bos, 2005; Macedo et al., 2011) and the Beck Depression Inventory-II (Beck et al., 1996, Coelho et al., 2002) twice, i.e. when the infant was 3 months (Time 1) and 6 months (Time 2) of age. Data from 45 infants (62.2% boys) were obtained.

Results: Sleep-wake cycle parameters were similar between time assessments. However, analyses within the same subject revealed that at 3 months infants had later bedtimes (M = 22:23, SD = 01:27 versus M = 22:02, SD = 00:57, $P = 0.023$), longer time awake during the night (M = 01:02, SD = 00:46 versus M = 00:46, SD = 00:33, $P = 0.013$), longer awakenings during the night (M = 00:35, SD = 00:21 versus M = 00:22, SD = 00:21, $P < 0.001$), longer daytime sleep (M = 04:46, SD = 02:10 versus M = 03:48, SD = 01:14, $P = 0.006$) and higher number of daytime naps (M = 3.4, SD = 0.86 versus M = 2.7, SD = 0.65, $P < 0.001$) than at 6 months of age. Mother's perception of having a difficult infant was positively associated with the number of night awakenings at both time assessments (Time 1, r = 0.56, $P < 0.01$; Time 2, r = 0.38, $P < 0.01$) and with longer time awake during the night at Time 1 (r = 0.52, $P < 0.01$). Temperament items associated with the number of night awakenings and longer time awake during the night at 3 months included: is your baby irritable or fussy?, does your baby cries excessively?, is your baby difficult to comfort or calm down?. Controlling for mother's depressive symptomatology, the number of night awakenings and time awake during the night still predicted mother's perception of having a difficult baby [$R^2 = 0.14$, $F_{1,41} = 7.28$, $P = 0.010$; R2 = 0.12, $F_{1,39} = 5.59$, $P = 0.023$, respectively].

Conclusion: Results of the present study suggest that the development of infant's sleep is an important feature of temperament and can influence mothers' perceptions of their baby temperament. Parental education on how to improve infant's sleep may help parents coping with a difficult baby.

Financial Support: AstraZeneca Foundation.

P421

Continuity and change of poor sleep from chilhdood to pre-adolescence

A. PESONEN, K. RÄIKKÖNEN, S. MARTIKAINEN AND K. HEINONEN for the DEPSY (the Developmental Psychology Research Group in the University of Helsinki)

The content of the concept of 'poor sleep ' in children and adolescents is vague. In terms of questionnaire-based data, it often refers to heterogeneous variety of different sleep problems, and in actigraph studies poor sleep is usually defined as short sleep duration and low sleep efficiency. In the absence of absolute cut-off values for poor sleep in actigraph studies, the lowest 10th percentiles of the given data have generally been used for defining poor sleep. Actigaphy- and questionnaire-based poor sleep, albeit often not correlating even modestly, have both been associated with compromised psychological and somatic well-being in children and adolescents. However, most of these studies, actigraph-based studies in particular, base on cross-sectional data on sleep. Consequently, there is an enormous need for longitudinal investigation of poor sleep in children, and specifically in the transition phase from childhood to adolescence. In this study, we examined the continuity and change of poor sleep from childhood to pre-adolescence, from 8-year-olds to 12-year-olds i n an epidemiological data of 180 children. We measured their sleep with actigraphs for one week at both follow-ups. The pubertal stage was evaluated on the Tanner scale. We found modest to average correlations between the actigaph-based measures of sleep at 8- and 12-years follow-ups (r's from 0.33–0.60). Poor sleep as defined by 10th percentile cut-offs in different actigraph parameters showed also significant continuity for most children from 8- to 12-years. There were only few cases of increasing poor sleep in the entire data; for most children poor sleep was either persistent or declining. Parent-rated sleep problems did not correlate strongly, if at all, with actigraph parameters, but enabled equally the identification of different developmental trajectories. This study contributes to the understanding the developmental continuity of poor sleep from childhood to pre-adolescence, a topic often neglected in prior pediatric sleep studies.

P422

Impaired sleep-related consolidation of non-verbal declarative memory in benign childhood epilepsy: a preliminary study

S. GALER, C. URBAIN, X. DE TIÈGE, P. PEIGNEUX and P. VAN BOGAERT

Université Libre, Brussels, BE

Objectives: Sleep-related consolidation of declarative memories has been demonstrated both in healthy adults and children. Benign childhood epilepsy with centro-temporal spikes (BECTS) is a syndrome characterized by unfrequent seizures and frequent focal interical discharges (IED). IEDs are present in the awake state but more abundant during non-rapid eye movement sleep, thus potentially disrupting the plastic processes underlying memory consolidation. In this respect, sleep-dependent impairment in the consolidation of verbal declarative memory was shown in 8–10 years old children with epilepsy (Urbain et al., 2011). However, investigation of sleep-dependent declarative memory deficits at an earlier age or in different languages is difficult using verbal material. We investigated in this pilot study the impact of nocturnal focal IEDs on sleep-related declarative memory consolidation using a non-verbal paradigm (2D object location task) in which sleep-dependent maintenance of performance was demonstrated in healthy 6–8 years old children (Wilhelm et al.,2008).

Methods: Two 7-year old girls diagnosed with BECTS participated in this preliminary study. In the evening, they learned the location of 12 pairs of objects presented on a grid. After presentation of the 12 pairs, immediate memory for the location of the second exemplar was tested by presenting the first element of each pair (cued recall). The whole procedure was repeated until children reached a 60% learning criterion. The next morning after a night of sleep, memory for object locations was tested using the same cued recall procedure. Memory performance was measured as the difference between the number of items recalled at retrieval minus the number of items memorized to reach the learning criteria.

Results: At variance with results previously reported in the healthy 6–8 years old population, in whom retention of object locations was maintained over sleep but declined over wakefulness periods (see Wilhelm et al. 2008), both BECTS patients presented diminished memory scores after a night a sleep (differential scores -3 and -2).

Conclusion: Results of this pilot study indicate that IEDs in BECTS may disrupt the plastic processes underlying sleep-related consolidation for non verbal declarative memory. The 2D object location task is a suitable tool to investigate sleep-related disruption of non-verbal declarative memory consolidation in young epileptic children.

P423

Sleep-dependent automation of procedural learning in children

C. URBAIN[1], E. HOUYOUX[1], G. ALBOUY[2] and P. PEIGNEUX[1]

[1]Université Libre, Brussels, BE, [2]Institut Universitaire de Gériatrie de Montréal, Montreal, CA

Objectives: Sleep participates in the off-line consolidation of declarative and procedural memories. Although the hypothesis was corroborated in adults, it remains debated whether sleep similarly contributes to procedural memory consolidation during the developmental period of childhood. Especially, it was argued using motor sequence learning and mirror tracing tasks (e.g. Prehn-Kristensen et al. 2009, 2011; Wilhelm et al. 2008) that sleep might not benefit procedural memories in healthy children. Here we investigated these effects using a rotation adaptation task previously used in adults (e.g. for opposite findings Huber et al., 2004; Debas et al. 2010).

Methods: Healthy 10–12 years old children were tested under two experimental conditions: Wake (n = 16, eight boys) where learning (L) took place in the morning (>1 h 30 after awakening) and retest (R) in the evening, and Sleep (n = 16, eight boys) in which learning took place in the evening and retest in the morning. In the learning session, participants performed 14 blocks of 16 trials, in which they had to move a pointer from a central starting point to one of eight targets disposed in a circle. The cursor position was systematically rotated clockwise relative to the hand position by a fixed angle of 60°, eventually leading to an automatic adaptation of the movement to reach the attended target. At retest session, subjects performed 20 blocks of 16 trials, in which the imposed rotation was clockwise (learned) again but was anticlockwise (unlearned) for blocks 3, 6, 9, 12, 15 and 18. Dependent measures were directional error (DE), time to target (TT), area under the curve (AC), and the AC/TT ratio, as in prior studies.

Results: Both groups similarly improved on all measures at learning (ps < 0.005). Decreased performance on L rotations was found at retest (2 last L versus 2 first R blocks; ps < 0.005 but RT P > 0.65), without interaction with the sleep factor (ps > 0.45). Still, presentation of the unlearned rotation elicited significant increase in all parameters (ps < 0.001), higher in the Sleep than in the Wake condition (interaction effects ps < 0.005, but DE P > 0.03).

Conclusions: Besides lack of sleep-dependent change in performance for L rotations, our results suggest their better integration and/or automation after post-training sleep, eventually resulting in a higher proactive interference effect on untrained material. Hence, sleep may contribute in the consolidation of procedural memories in children. CU was supported by special grants from Fondation Vigneron and the ULB-ARC project 'Pathophysiology of memory consolidation processess'

P424

The effects of intensive cognitive training on cognitive performance and sleep EEG topography in children

F. PUGIN[1], A. METZ[2], M. STAUFFER[3], A. RAUCH[3], L. JÄNCKE[3], P. ACHERMANN[3], M. WOLF[2], O. JENNI[1] and R. HUBER[1]

[1]University Children's Hospital Zurich, Zurich, CH, [2]University Hospital Zurich, Zurich, CH, [3]University of Zurich, Zurich, CH

Ojectives: Several studies have shown an association between the major EEG characteristics of NREM sleep – slow waves and spindles – and cognitive performance. More specifically, the activity of slow waves (SWA, EEG spectral power between 0.75 and 4.5 Hz) seems to reflect local plastic changes, e.g. as found after visuomotor learning. Sleep spindles which are generated by the thalamocortical system have been linked to measures of intelligence. In this ongoing study, we investigate the effects of an intensive cognitive training on fluid intelligence test performance and regional aspects of brain activity during sleep in a population of young male subjects.

Methods: We recorded high-density sleep electroencephalography (hd EEG, 128 electrodes) during two nights separated by three weeks (n = 16, 13.1 ± 1.2 years). In the afternoon before each night recording, the subject's fluid intelligence was assessed with a standardized matrices test (TONI-IV, test of non-verbal intelligence). Between the two sleep sessions, nine of the subjects (13.2 ± 1.3 years) performed an intense cognitive training using the BrainTwister software (University of Bern).

Results: In a first step we confirmed the positive correlation between sleep spindle activity and fluid intelligence. The nine subjects of the training group showed an increase in fluid intelligence (test score 1, 36.6 ± 9.8 (mean ± SD, test score 2, 42.1 ± 5.8; $P < 0.05$, paired t-test). No significant increase was found in the control group. First results of the sleep EEG topography in the training group indicate an increase of SWA by 12.1% ± 9.3% (mean ± SD, $P < 0.005$) over the left temporal cortex.

Conclusions: In line with the literature, our preliminary results show that intensive cognitive training improves fluid intelligence test performance. This finding is accompanied by a local increase of sleep SWA which is suggested to be closely related to learning induced cortical plasticity. We anatomically localized this increase of SWA to brodman area 2, 6 and 22, areas involved in perception, attention and cognition.

This work was supported by the Zurich Center for Integrative Human Physiology and the Anna Müller Grocholsky foundation.

P425

Do reading or playing a video-game before going to bed influence sleep?

I. FIETZE, A. BLAU, S. ZIMMERMANN, M. HOLTERDORF, C. GARCIA and T. PENZEL

Charité University Hospitals, Berlin, DE

Objectives: Reading or playing video-games before going to bed is a common behavior especially in adolescents. Playing video-games could be associated with somatic complaints, attention problems, and family interaction problems. There is limited evidence about the effects on sleep of playing video-games before going to bed. The aim of this study was to investigate the effects of playing a video-game on adolescent sleep.

Methods: Twenty-two adolescents (age 14.6 ± 0.4 years, 16 females) were included in this study. Healthy participants were selected from one school and grade. We asked them to rate their habitual sleep quality and exposed them 2 h before bedtime randomly, to a not aggressive jump and run video-game or to read a youth magazine (control group) in our sleep lab. Watching TV, drinking caffeinated drinks or sleeping was prohibited in the evening. A polysomnogram according to the AASM standards was conducted to measure sleep. On the second day the groups switched the tasks.

Results: Ten participants rated thier habitual sleep quality as always restorative and 12 as predominantly restorative. Video-game playing resulted in a significant reduced amount of slow-wave sleep (N3 44.6 ± 9.6 versus 49.1 ± 6.6 min, $P = 0.01$) and increased lighter sleep (N1 and N2: 201.0 ± 40.2 versus 182.9 ± 42.9 min, $P = 0.04$). We found no significant trend of increased arousals (17.4 ± 5.6 versus 19.7 ± 6.6/h, n.s.) or decreased REM sleep (66.0 ± 24.2 versus 62.6 ± 20.6 min, n.s.). Sleep-onset latency, total sleep time and wake time after sleep onset were unaffected.

Conclusion: Most adolescents in our study rated their sleep quality as predominantly restorative. Playing video-games before sleep in our sleep lab resulted in reduced slow-wave sleep and an increase of lighter sleep in adolescents. Our results support the hypothesis of an influence of behavior before sleep on sleep-architecture in healthy adolescents.

P426

Social jetlag and its association with life style variables and academic achievement among Swedish adolescents

K. SCHRAML, J. F. A. SCHWARZ, M. SÖDERSTRÖM and A. PERSKI

Stress Research Institute, Stockholm, SE

Objectives: Social jetlag (indicated by a high discrepancy in sleep times between work and free days) has been associated with psychological distress and mood disorders among adults. However, social jetlag might be even more relevant in adolescents because they have a higher prevalence of being an evening chronotype and it is known that late chronotypes are especially prone to social jetlag. The aim was to investigate (i) the prevalence of social jetlag, (ii) the associations between social jetlag and stress related life style variables, and (iii) the role of social jetlag in predicting academic achievement in a sample of Swedish adolescents.

Methods: In total, 961 16 years old high school students (533 boys and 428 girls) answered questions about sleep times, regarding both free and school days. Moreover, participants answered a questionnaire about life style variables which have been associated with stress. Two years later, objective indicators of academic achievement, the final high school grades of 351 participants were available.

Results: The mean chronotype, defined as the sleep-corrected mid-sleep on free days, was 5.20 am local time (SD = 1 h 12 min). The mean social jetlag was 3 h 10 min (SD = 18 min). Of 118 students had a social jetlag of <2 h, 184 students' social jetlag exceeded more than 4 h, most of the participants ($n = 659$) showed a social jetlag between 2 and 4 h. As expected, the chronotype correlated positively with social jetlag ($r = 0.785$; $P < 0.001$), indicating that late chronotypes have more social jetlag. Social jetlag was a significant predictor of subsequent academic achievement (worse final grades) two years later ($r = -0.156$; $P = 0.003$). Social jetlag was significantly correlated with more perceived stress symptoms ($r = 0.085$), skipping breakfast more often ($r = -0.157$), smoking more frequently ($r = -0.205$) and increased alcohol consumption ($r = -0.211$). Furthermore, participants with more social jetlag perceived their sleep quality as slightly worse ($r = -0.069$) and were on sick leave more often ($r = -0.085$).

Conclusion: Social jetlag is very common in adolescents. Stress related life style habits were more frequent in participants with social jetlag. Social jetlag was associated with worse academic achievement and thus might have a negative influence young people's future career prospects. The present findings emphasize the importance of reducing social jetlag in young age groups.

P427

The differential effects of sleep and depression on school functioning and school performance in Dutch adolescents

J. F. DEWALD, A. M. MEIJER, F. J. OORT and S. M. BÖGELS

University of Amsterdam, Amsterdam, NL

Objectives: Sleep and depression are by definition interrelated (DSM-IV-TR), however, sleep problems are only one aspect of the complex phenomenon depression, which includes different symptom clusters (e.g., affect, behavior, somatic symptoms, social interaction). To gain more insight into the unique contribution of both depression and sleep, we investigated their differential effects on school functioning (achievement motivation, teacher-child relationship, academic self-concept) and school performance.

Method: The total sample consisted of 733 students (57.4% girls; 11.03–17.98 years) who completed online questionnaires on total

sleep time, sleep quality, sleepiness (Epworth Sleepiness Scale), depression (Children's Depression Inventory), school functioning (achievement motivation (PMT-K), teacher-child relationship and academic self-concept (School Perception Questionnaire), and school performance.

Results: Principal component analysis identified four clusters of depressive symptoms (Negative affect with somatic aspects, Negative self-image, Social problems and anhedonia, and Behavioral problems). Preliminary results reveal that sleep and the four depressive symptom clusters differently contributed to school functioning and to school performance, however, in general depressive symptoms were more influential than sleep. Larger proportions of variance were explained in the models for school functioning than for school performance, raising the idea that school performance may be affected via school functioning rather than by sleep or depression directly (Meijer, 2008).

Conclusion: Although our cross-sectional design does not allow causal conclusions addressing the 'chicken and egg' question of the interplay between sleep and depression, we were able to show that sleep and the depressive symptom clusters both contribute to adolescents' school functioning. Our results demonstrate that, in opposite to school functioning, the impact of sleep and depression is rather small when looking at school performance. Despite the need for longitudinal research in the future, we believe that our study is a first step in understanding the complex effects of sleep and depression on adolescents' daytime functioning.

P428

The relationships among hall residence, sleep and psychological well-being in college students

E. Y. Y. LAU[1], M. L. WONG[1], E. C. W. NG[1], C. H. HUI[1], S. F. CHEUNG[2] and D. S. Y. MOK[2]

[1]University of Hong Kong, Hong Kong, HK, [2]University of Macau, Macau, MO

Objectives: College students have been reported to have insufficient sleep, poor sleep quality and eveningness chronotype, which are related to negative mood and lower quality of life. Few studies have addressed the role of hall residence in college students' sleep and daytime functioning. By studying sleep behaviours, mood and quality of life in students living on- versus off-campus, we aim to assess the contribution of hall residence to sleep and psychological wellbeing.

Methods: College students (N = 1078, 32.1% male, mean age = 20.87) from 16 universities in Hong Kong and Macau completed online questionnaires measuring sleep behaviours Sleep Timing Questionnaire, Composite Scale of Morningness (CSM), Pittsburgh Sleep Quality Index), mood (Depression Anxiety Stress Scale), quality of life (World Health Organization Quality of Life Measures), and demographics (age, sex, year of study, part-time job, relationship status and type of residence).

Results: Analysis of covariance (ANCOVA) was used to test the between-group differences on sleep, quality of life and mood with demographics controlled. Hall residents had less sleep debts, $F_{1,878} = 4.360$, $P = 0.037$, shorter sleep latency, $F_{1,878} = 4.482$, $P = 0.035$, and fewer sleep disturbances, $F_{1,881} = 5.364$, $P = 0.021$. Chi-square analysis revealed that morningness chronotype was more prevalent among hall residents, χ^2 (1, N = 459) = 4.063, $P = 0.044$. In addition, hall residents had less stress symptoms, $F_{1,876} = 7.159$, $P = 0.008$, and better quality of life across different domains: physical health: $F_{1,956} = 4.235$, $P = 0.040$; psychological health: $F_{1,950} = 21.596$, $P < 0.001$; social relationship: $F_{1,949} = 7.042$, $P = 0.008$; and environment: $F_{1,951} = 13.035$, $P < 0.001$. Partial correlation analyses (demographic variables controlled) revealed that morningness-chronotype, less sleep debts, shorter sleep latency and fewer sleep disturbances were correlated positively with quality of life (r = 0.07–0.24) and negatively with stress and mood symptoms (r = -0.09 to -0.39).

Conclusion: Our results showed that hall residents have better sleep, mood and quality of life than their non-hall peers. While we demonstrated that sleep variables among hall residents were correlated with quality of life and mood measures, future studies with longitudinal design are needed to verify the directional relationship between hall residence, sleep and daytime outcomes. Mediators and moderators that contribute to better sleep and psychosocial functioning in hall residents also warrant further investigation.

P429

Exploring the complex pathways among specific types of technology, sleep duration and body mass index in UK adolescents

T. ARORA, S. HUSSAIN, G. N. THOMAS and S. TAHERI

University of Birmingham, Birmingham, UK

Objectives: Technology devices are widely accessible and increasingly utilised by adolescents. Several studies have suggested that short sleep duration is associated with both increased body mass index (BMI) and the use of technology devices. We examined the independent associations between sleep duration, four common technologies (computer use, mobile telephones, TV viewing and video gaming) and BMI z-score. We also proposed a theoretical path model showing the direct effects of these four technologies on BMI z-score and sleep duration as well as the indirect effects of each technology on BMI z-score whilst considering sleep duration as a mediating factor of the relationship.

Methods: A sample of 632 adolescents (63.9% girls, mean age 13.9 ± 2.0 years) were recruited to the Midlands Adolescents Schools Sleep Education Study. Previously developed age-appropriate questionnaires (School Sleep Habits Survey, Technology Use Questionnaire) were used and objective measures of height and weight were obtained for BMI z-score calculation.

Results: Weekday use of all types of technology at bedtime was significantly associated with reduced weekday sleep duration after adjustment, beta (computer use) = -0.38, $P \leq 0.001$; beta (mobile telephone) = -0.27, $P \leq 0.01$; beta (TV viewing) = -0.35, $P \leq 0.001$; beta (video gaming) = -0.39, $P \leq 0.001$. Use of all types of technology at bedtime during the week, with the exception of mobile telephones, was significantly associated with an increased BMI z-score after adjustment, beta (computer use) = 0.26, $P < 0.01$; beta (TV viewing) = 0.31, $P < 0.001$; beta (video gaming) = 0.40, $P < 0.001$. Our path model suggests that weekday sleep duration was significantly and negatively associated with BMI z-score. Furthermore, our path model demonstrates that weekday sleep duration mediates the effects of computer use and mobile telephones on BMI z-score.

Conclusion: If confirmed in other samples and longitudinally, improving sleep through better management of technology use by adolescents could be an achievable intervention that could have important public health implications in attenuating the current obesity epidemic.

P430

The effects of technology types on sleep and its associated parameters in contemporary UK adolescents

T. ARORA, E. BROGLIA, G. N. THOMAS and S. TAHERI
University of Birmingham, Birmingham, UK

Objectives: Technology has rapidly advanced in recent decades and multiple device ownership is increasingly common. Technology is widely accessible and increasingly utilised, particularly by adolescents. Studies suggest technology can have adverse effects on adolescent sleep duration, a group who experience sleep loss due to physiological changes that occur alongside puberty. The effects of technology on other sleep parameters, however, have not yet been fully explored. We examined six types of technology (TV, video gaming, PC for studying, music, internet for social networking and mobile telephones) on eight sleep parameters [sleep duration, sleep onset latency (SOL), difficulty switching off, number of night-time awakenings, difficulty falling to sleep, nightmares, sleepwalking, insomnia (early awakening with inability to initiate sleep again)].

Methods: A sample of 722 adolescents (54% boys), aged 11–13 years were recruited to the Midlands Adolescents Schools Sleep Education Study. Previously developed age-appropriate questionnaires (School Sleep Habits Survey, Technology Use Questionnaire) were used.

Results: Frequent use (usually/always) of all technologies were significantly associated with reduced sleep duration after adjustment, B (TV) = -0.36, $P < 0.01$; B (video gaming) = -0.57, $P < 0.01$; B (mobiles) = -0.77, $P < 0.001$; B (music) = -0.37, $P < 0.01$; beta (PC) = -0.48, $P < 0.01$; beta (internet) = -0.87, $P < 0.001$, compared to never users. Usually/always listening to music was associated with increased SOL B = 7.03, $P < 0.05$ compared to never listeners. Frequent use of mobiles, TV, internet and music was significantly associated with more frequent (several times/every night) insomnia B = 4.22, beta = 2.98, B = 3.39 and B = 3.49, all $P < 0.05$, respectively, compared to non-users. Frequent users of mobiles, music and the internet showed greatest difficulty falling to sleep compared to non-users: B = 1.91, B = 3.49 and B = 2.75, all $P < 0.05$, respectively. Those who sometimes watched TV, usually/always used a PC or the internet had the greatest risk of difficulty falling to sleep: B = 1.90, B = 2.04 and B = 1.51, all $P < 0.05$, respectively. Sometimes or usually/always watching TV at bedtime was significantly associated with sleepwalking: B = 2.29 and B = 3.71, $P < 0.05$, respectively.

Conclusion: If confirmed in other samples and longitudinally, improving sleep hygiene habits through better management of technology use could enhance the health and wellbeing of adolescents.

P431

In middle adolescence, emotion regulation and emotion expression, but not emotion recognition is related to sleep deprivation

N. KALAK, M. GERBER, S. LEMOLA, U. PÜHSE, E. HOLSBOER-TRACHSLER and S. BRAND
University of Basel, Basel, CH

Background: Sleep deprivation is related to cognitive, emotional and behavioral impairment. However, for middle adolescence, no studies focused on the relation between sleep deprivation and emotional information processing so far.

Method: In three separate studies, a total of 460 adolescents (mean age: 17 years old) reported on sleep and emotional information processing.

Results: Irrespective from the sample, poor sleep was associated with poor regulation and expression of own emotions. Relative to male participants, female participants showed an increased performance in recognizing, regulating, and expressing their own emotions. By contrast, emotion recognition of other people was not affected by sleep deprivation.

Conclusions: The pattern of results suggests that as in adults, in adolescents poor sleep is associated with decreased processing of emotional information; however, processing emotional signals of other people was not related to sleep. The underlying mechanisms remain unclear, though it is highly conceivable that emotional information of one's own and of other people is processed by two separate neuronal structures.

P432

Sleep in early adolescence

S. MARTIKAINEN, A. PESONEN, K. HEINONEN and K. RÄIKKÖNEN
DEPSY – the Developmental Psychology Research Group in the University of Helsinki, Helsinki, FI

Objectives: Sleep architecture and the timing of sleep undergo notable changes during puberty. This is expected to be due to various psychosocial and biological factors related to the onset of adolescence. The best documented change in adolescent sleep is the delayed sleep phase which may result in reduced sleep duration due to the demands of everyday life. However, studies in younger children currently experiencing the transition to puberty are still few; further understanding on the relations between sleep and the onset of puberty is clearly warranted.

Methods: In this study, we examined the associations of pubertal maturation with sleep timing, and the difference between weekday and weekend sleep in 12-year-old children ($N = 297$). Sleep was measured with actigraphs for an average of a 1 week period. The pubertal stage was evaluated on the Tanner scale. We hypothesized that pubertal maturation would result in later bedtimes and greater discrepancy between weekend and weekday sleep, but would not affect the actual quality of sleep.

Results: We found that the children within a higher stage of pubertal maturation had a trend for later sleep onset as well as larger discrepancy between weekday and weekend sleep. Pubertal maturation was associated with shorter sleep during the weekdays, whereas no association was not found for the weekend sleep.

Conclusion: These results are in line with earlier studies stating that pubertal maturation is associated with a delayed sleep phase and shorter sleep during the weekdays. Our study adds to previous knowledge by showing that the maturational changes in sleep associated with puberty are visible already in children transitioning to adolescence. These results provide further understanding to the developmental changes in sleep associated with puberty, and support the proposition that the puberty-related vulnerability of sleep should be recognized already in the early adolescence.

P433

Risk factors and protection in school and the prevalence of alcohol and tobacco use among Brazilian and Spanish students: its influence on sleep quality

K. STANCATO[1], M. PÉREZ SOLÍS[2], I. GARRIDO GUTIÉRREZ[2], A. C. GABAN[1] and O. L. DE FIORE[3]

[1]Universidade Estadual de Campinas, Campinas, BR, [2]Universidad Complutense de Madrid, Madrid, ES, [3]Secretaria de Saúde de Sumaré, Sumaré, BR

Objectives: to know the similarities and differences in consumption patterns, experiences, information and belief, the influence of protective factors and risk of legal drug in sleep quality of Brazilian and Spanish children.

Method: A multicenter survey sampling intentional comparing public and private schools in central and peripheral areas. Participants 1012 children, 720 Spanish and 292 in Brazil, aged 11 years. The six questionnaires were administered to students after the study was approved by the Ethics in Research of the Faculty of Medical Sciences, Unicamp (number protocol 633/2008).

Results: the level of participants' age, protective factors and risk do not work, but did not specify the subject as the various factors exert their effect on their sleep behavior related to alcohol and tobacco. Once the protective factors and risk work in relationships, to modulate and interfere with each other, so it is difficult to figure out how to relate to each other.

Conclusion: it is supported by the fact that we found a very small number of significant differences when analyzing gender differences in the binding of protective factors with no consumption and risk factors of tobacco use. Descriptors: risk factors; smoking; alcoholism; child; alcohol drinking; tobacco; sleep.

P434

Subjective sleep quality effect on cognitive functioning in institutionalised elderly

H. ESPÍRITO-SANTO, M. MARQUES, I. PENA, J. MATRENO, S. FERMINO, F. RODRIGUES, E. ANTUNES, D. SIMÕES, Â. CONDE, A. COSTA, A. CORREIA and A. PIMENTEL

Instituto Superior Miguel Torga, Coimbra, PT

We wish to describe subjective sleep aspects in institutionalised elderly and examine the extent to which subjective sleep quality and subjective sleep aspects are related to cognitive functioning, controlling educational level. Ninety-nine institutionalised elderly (mean age, M = 78.65, SD = 6.92; 44.4% without schooling; 52.5% schooling above 4 years) from Coimbra Council filled in a test battery, including socio-demographic questions, subjective sleep questions (daytime napping and sleepiness, sleep routines, physical exercise, pain during night, sleeping with someone, sleep disease and medication), neuropsychological tests (Mini Mental State Examination; MMSE; Montreal Cognitive Assessment, MoCA; Frontal Assessment Battery, FAB; Semantic fluency tests; copy and 3-min recall of Rey-Osterrieth figure; modified Stroop interference test) and a subjective sleep quality index (SSQI). The SSQI assesses sleep latency, difficulty in falling asleep, number of night awakenings, waking up spontaneously too early, subjective perception that waking up too early constitutes a problem, general subjective sleep quality and sleep depth. Some elderly reported daytime napping (48.5%) and sleepiness (45.5%), sleeping routines (91.8%), physical exercise practice (44.9%), pain during night (34.7%), having someone in the room that disturbs sleep (22.2%), sleeping disease (45.9%) and sleep medication intake (62.8%). Regarding SSQI, we found prolonged sleep latency (37.5%), trouble falling asleep (41.4%), sleep fragmentation (greater nighttime wakefulness and frequent, long wake episodes) (66.3%), short sleep duration (49.1%) and global poor sleep quality (48.5%). Controlling education, SSQI was associated with clock drawing task; sleeping with somebody with better result on FAB abstraction task; physical exercise practice with MoCA fluency task; sleeping medication with MoCA abstraction task; and having pain during night with the Stroop task. Concluding, napping, daytime sleepiness, physical exercise practice and sleeping disease were fairly prevalent. Sleep medication intake and sleeping routines were very common. Sleep disturbances prevalence, including poor sleep quality, was relevant. Controlling education, some executive functions were associated with sleep subjective quality and other subjective sleep aspects. Future studies should address education level when assessing the association of cognitive functioning with sleep variables.

P435

Associations between sleep quality and different correlates in the elderly

H. ESPÍRITO SANTO, M. MARQUES, J. MATRENO, S. FERMINO, I. PENA, F. RODRIGUES, E. ANTUNES, D. SMÕES, Â. CONDE, A. COSTA, A. CORREIA and A. PIMENTEL

Instituto Superior Miguel Torga, Coimbra, PT

Describe subjective sleep quality and explore the associations between several correlates and sleep quality in an elderly sample. Ninety-nine institutionalised elderly (mean age, M = 78.65; SD = 6.92; range = 60–95) from Coimbra Council filled in voluntarily a test battery (or whose relatives/caregivers gave consent), including socio-demographic questions, initial sleep assessment (daytime naps, daytime sleepiness, sleep routines, physical exercise, presence of pain/noise during night, sleep diseases and medication, sleep satisfaction), medical problems assessment and of medication that affect sleep, a subjective sleep quality index (SSQI), depressive (Geriatric Depression Scale) and anxious (Geriatric Anxiety Inventory) symptomatology and satisfaction with life (Satisfaction with Life Scale). The SSQI assesses sleep latency, difficulty in falling asleep, number of night awakenings, waking up spontaneously too early, subjective perception that waking up too early constitutes a problem for the person, general subjective sleep quality and sleep depth. Forty-nine percent of the elderly reported poor sleep. Older age was associated with early awakenings and decreased sleep depth, both in men and women. In men, age was associated with early awakenings, decreased sleep depth, diminished sleep satisfaction, and more daytime naps. In women, older age was not associated to any variable. Poor subjective sleep quality was associated with less education, no sleep satisfaction, more daytime sleepiness, pain during night, presence of medical problems that affect sleep, and depressive symptoms, both in men and women. In men, subjective sleep quality was associated with diminished sleep satisfaction, more daytime sleepiness, and pain or noise during night; older women had less sleep satisfaction, more daytime sleepiness, medical problems that affect sleep and more depressive symptoms. Decrease in sleep quality is fairly common in old institutionalised persons, and poor sleep is associated with less education, no sleep satisfaction, more daytime sleepiness, pain during the night, presence of medical problems that affect sleep and higher depressive symptoms. Studies are required to establish whether improvements in these outcomes will ameliorate sleep in institutionalised elderly.

P436

Functional uncertainty in elderlies' sleep

F. CONTE[1], B. M. ERRICO[1], D. IOVINO[1], F. GIGANTI[2] and G. FICCA[1]

[1]University of Naples II, Caserta, IT, [2]University of Florence, Florence, IT

Objectives: The notion of 'functional uncertainty' was formulated in 1997 to describe the inability of the Central Nervous System to maintain coordinated physiological processes [1]. A high degree of functional uncertainty has been hypothesized in the sleep of infants and elderly individuals, as well as in some conditions of disturbed sleep. However, this hypothesis has never received experimental support. We have recently proposed [2] that the level of functional uncertainty is expressed by specific parameters of sleep continuity, stability and organization, such as frequency of awakenings, arousals, state transitions, and 'functional uncertainty periods' (FU periods). Aim of this study is to describe the differences in these sleep measures between young and elderly subjects.

Methods: Sleep recordings of 20 healthy elderly subjects (M = 8, F = 12; age range: 65–85 years) were compared to those of 20 healthy young subjects (M = 7, F = 13; age range: 20–35 years). Scoring was performed through visual inspection according to the AASM manual rules [3], except for: (i) arousals (defined as all transitions to shallower NREM sleep stages and from REM sleep to stage 1), (ii) Slow Wave Sleep, for which the amplitude criterion was not considered [4].

Results: Most measures of functional uncertainty are significantly higher ($P < 0.0001$) in the elderly than in the young subjects, including: frequency of brief awakenings, arousals, state transitions, FU periods; time spent in functional uncertainty both absolute and relative to total sleep time.

Conclusion: Our data support the hypothesis that sleep in aged individuals shows high levels of instability, which is expressed by frequent oscillations in electrophysiological activity, often culminating in behavioural awakenings.

References:

1. Salzarulo P, Formicola G, Lombardo P, Gori S, et al. *Acta Neurol Belg* 1997, 97: 118–122.
2. Conte F, Ficca G. *Sleep Med Rev* 2012, in press.
3. Iber C, Ancoli-Israel S, Chesson A, Quan SF. The AASM Manual for the scoring of sleep and associated events. 2007, Westchester, IL: American Academy of Sleep Medicine.
4. Webb WB, Dreblow LM. *Sleep* 1982, 5: 195–199.

P437

Effect of transcranial direct current stimulation on sleep-dependent memory consolidation in elderly healthy subjects

T. EGGERT, H. DORN, C. SAUTER, M. BAJBOUJ and H. DANKER-HOPFE

Charité University Hospitals, Berlin, DE

Objectives: Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation method leading either to an increased (anodal stimulation) or a decreased (cathodal stimulation) excitability of cortical neurons. Slow oscillations (of <1 Hz) seem to be associated with sleep-dependent consolidation of declarative memories by exerting a synchronizing influence on hippocampal reactivations and thalamic spindle activity. It has been shown that offline consolidation during sleep varies with age resulting in better performances in the young compared to the elderly. Recently, a study in young subjects provided evidence of a positive impact of an anodal time-varied tDCS (0.75 Hz) during sleep on declarative but not on procedural memory. The aim of the present study was to investigate whether sleep-dependent consolidation of declarative memories in the elderly can also be affected by tDCS oscillating with a frequency of 0.75 Hz.

Methods: Twenty-three subjects (14 females) with a mean age of 69.3 (SD: 8.0) years participated. To test for a stimulation-dependent effect on offline consolidation during sleep a declarative memory task (word pair test) and a procedural memory task (finger-tapping) had to be completed before sleep and after awakening. Furthermore, sleep stages were scored and EEG power and spindle densities were computed. Statistical analysis was based upon comparisons between the tDCS and the sham stimulation condition.

Results: Independent of stimulation condition performance in both memory tasks significantly decreased overnight. However, comparisons of the differences between learning and retrieval yielded a trend ($P \leq 0.1$) towards a lower performance reduction under the tDCS stimulation compared to sham in the declarative memory task, while for the procedural memory task such a difference has not been observed. At the physiological level, a significant decrement of the fast sleep spindle density (13–15 Hz) was found under tDCS stimulation.

Conclusion: The results of the present study are in line with many studies showing that offline consolidation during sleep varies with age and is less pronounced in the elderly than in young or middle-aged subjects. Nevertheless, the results also show that tDCS might have an effect on sleep-dependent consolidation in older subjects. Furthermore, the outcomes on the behavioural level could be interpreted as a positive stimulation effect on sleep-dependent consolidation of declarative memories.

P438

The effect of declarative learning on sleep spindles in young and older adults

L. B. RAY, K. R. PETERS and C. T. SMITH

Trent University, Peterborough, CA

Objectives: Sleep architecture and memory ability both show considerable changes with age, suggesting that a relationship may exist between the two. Although many studies have examined the relationship between sleep and memory, most of them have used young adults only. The purpose of this study was to examine changes in spindle density following a declarative learning task in young and older adults.

Methods: A total of nine young female (19–23 years) and 11 older female (60–75 years) participants underwent polysomnographic recording for three consecutive nights in the sleep lab; the data reported here are from the second (Baseline) and third (Post-Acquisition) nights only. On the third evening, participants learned 15 word pairs (the A–B list). The next morning, participants learned word pairs that comprised the same first word as before but a new associate word (the A–C list). Following a 15-min delay, participants were again shown the A-words and asked to recall both the corresponding B- and C-words (retroactive interference paradigm). Independent t-tests were used to compare the recall of B- and C-words for the two age groups. Stage 2 spindle densities were computed from the Fz, Cz, and Pz electrode sites. For all analyses, we divided spindles into slow (12–14 Hz) and fast (14–16 Hz) types. For each spindle type and electrode site, we computed 2 (Group: Young, Older) × 2 (Night: Baseline, Post-Acquisition) mixed ANO-

VAs to assess for age differences across the two nights. Significant interactions were followed up with paired t-tests.

Results: Behaviourally, young adults recalled significantly more of the B- and C-words than older adults ($P < 0.05$ for both). The density of fast spindles was greater in young adults than in older adults at each of the three sites ($P < 0.05$ for all); in contrast, the density of slow spindles was greater in young adults than older adults at Cz only ($P = 0.008$). The group by night interaction was significant for fast spindles at Pz only ($P = 0.042$): there was a significant decrease in spindle density in the young adults ($P = 0.037$) but no significant change in the older adults ($P = 0.880$).

Conclusion: Although preliminary, these results suggest that fast spindles in females may be more affected in older adults than slow spindles. They may also suggest that declarative learning has different effects on spindle density in young and older adults.

P439

An fMRI investigation of sleep-dependent consolidation of episodic memories in older adults

C. HARAND, F. BERTRAN, F. DOIDY, F. GUÉNOLÉ, B. DESGRANGES, F. EUSTACHE and G. RAUCHS

INSERM Research Unit U1077, Caen, FR

Objectives: Sleep, and especially slow-wave sleep (SWS), favours consolidation of episodic memories. During normal aging, several elements, such as the decrease in SWS and the dysfunction of memory-related areas, suggest that sleep-dependent memory consolidation may be impaired or, at least, occurs differently. In this study, we investigated how sleep influences the neural substrates of episodic memory retrieval in older adults using functional magnetic resonance imaging (fMRI).

Methods: On day 1, 11 older, healthy adults (OA group, mean age ± SD: 65.7 ± 4.9 years) were invited to memorize a series of pictures with emotional or neutral valence. Then, they were allowed to sleep regularly at home during the three post-learning nights. On day 4, fMRI data were acquired while they performed a recognition task. fMRI data were analyzed with SPM5. Memory performance and patterns of brain activity were compared to those obtained in young subjects that followed exactly the same procedure [Young-Sleep (YS) group: $n = 18$, 22.6 ± 2 years] and in young adults that were totally sleep-deprived during the first post-learning night (TSD group: $n = 17$; 21.9 ± 2 years). Indeed, some authors suggested that healthy aging results in functional changes close to those observed after acute sleep deprivation in young adults.

Results: Percentage of correct recognitions did not differ between groups (mean ± SD, OA: 83.7 ± 9.3; YS: 84.2 ± 10.1; TSD: 84.7 ± 8.7; $P > 0.96$) but OA made more false recognitions than both young groups (mean ± SD, OA: 36.2 ± 18.8; YS: 14.2 ± 9.2; TSD: 14.6 ± 12; $P < 0.001$). Consequently, the discrimination score (d'), reflecting recognition accuracy, was lower in OA (mean ± SD, OA: 1.51 ± 0.48; YS: 2.35 ± 0.52; TSD: 2.38 ± 0.61; $P < 0.001$). fMRI analyses revealed that OA activated a limited set of brain areas, including frontal and parietal cortices, when recognizing the pictures ($P < 0.001$). No hippocampal activation was detected. However, higher activity in the right inferior parietal lobule (IPL) was observed in OA compared to their younger sleep and sleep-deprived counterparts. Interestingly, a similar activation was reported in TSD subjects, compared to YS participants. Interestingly, our data showed that OA failed to deactivate the IPL, compared to young participants.

Conclusion: The altered pattern of brain activity in the parietal cortex, together with the lack of hippocampal activation, may explain the impairment of sleep-dependent memory consolidation in aging.

Poster Session – Environmental and Life Style

P440

Sleep during days with work stress compared to weekend sleep – home polysomnography in normal life settings

H. PETERSEN, G. KECKLUND, P. DONOFRIO and T. ÅKERSTEDT
Stress Research Institute, Stockholm, SE

Objectives: Very few studies of naturally occurring variations in daily stress and polysomnography (PSG) have been carried out. The aim of the present study was to provide such knowledge and used sleep before the first day off during the weekend as a low stress context and a 'normal' and high stress weekday as a contrast. To the best of our knowledge no previous studies are available on weekend/weekday home recorded sleep in a normal life context.

Methods: Seventeen teachers had their PSG recorded in their own homes on one high stress and one low stress condition during the workweek and on a workday followed by a day off. Sleep diaries and actigraphs were also used.

Results: There were no difference in bedtime (23:06 ± 12min) between high stress (HS), low stress (LS) and weekend (W) but the weekend sleep had longer TST (LS = 403 ± 14.4, HS = 376.1 ± 13.5, W = 447.1 ± 19.4, $P = 0.017$), contained more awakenings (LS = 25.6 ± 1.8, HS = 23.2 ± 2.3, W = 38.5 ± 3.8, $P = 0.004$), stage transitions/h (LS = 15 ± 0.8, HS = 15.5 ± 0.8, W = 25.7 ± 1.6, $P < 0.001$), arousals (LS = 37.5 ± 4.8, HS = 33.5 ± 4.5, W = 49.5 ± 4.3, $P < 0.01$) and more stage 1 (LS = 16.7 ± 3.4, HS = 13.5 ± 2.4, W = 66.4 ± 8.9, $P < 0.001$) and SWS (LS = 26.9 ± 5, HS = 34 ± 5.5, W = 45 ± 5.7, $P < 0.01$). Stress at bedtime as well as preoccupation with work was lower before the day off. There were no differences in subjective sleep quality. Arousal levels rated every 2 h during the day was higher during the high stress period and lowest during the weekend. On the following day cognitive functions were better after the weekend sleep but sleepiness levels was not affected. Based on the FIRST-scale (Ford insomnia response to stress) 2 groups of high and low ratings were compared. There was an interaction effect in REM sleep latency ($P < 0.01$), the group sensitive to stress had an increase in REM sleep latency in the weekend sleep (LS = 77.3 ± 15, HS = 96.2 ± 15.8, W = 146.4 ± 17.2), while the not sensitive group had a decrease (LS = 87 ± 11.1, HS = 83.4 ± 11, W = 77.1 ± 12.7). When the weekend sleep was cut to match the length of the workdays it still contained more SWS, awakenings, arousals and stage transitions.

Discussion and Conclusion: Weekend sleep clearly differed from weekday sleep, resulting in both increased SWS and decreased sleep continuity. The increase in SWS could be a result of lower stress and less preoccupation with work in the evening or a rebound effect of sleep deprivation during the week. The interpretation of increased discontinuity is not clear and needs further confirmation.

P441

Alterations in slow wave sleep characteristics after acute exposure to moderate altitude

N. TESLER[1], T. LATSHANG[2], Y. NUSSBAUMER-OCHSNER[2], C. M. LO CASCIO[2], K. STADELMANN[3], A.-C. STOEWHAS[2], M. KOHLER[2], K. E. BLOCH[2], P. ACHERMANN[3] and R. HUBER[1]
[1]University Children's Hospital Zurich, Zurich, CH, [2]University Hospital Zurich, Zurich, CH, [3]University of Zurich, Zurich, CH

Objectives: Travelling to higher altitudes causes changes in sleep architecture (e.g. Nussbaumer-Ochsner, 2012). However, little is known about the effects of moderate altitude on the characteristics of slow waves (SW; 1–4.5 Hz), the major EEG marker of NREM sleep. Such SW are thought to be involved in memory consolidation and synaptic downscaling (Steriade et al., 2003; Tononi & Cirelli, 2006). We investigated the overnight alterations of SW characteristics, in particular their slope, amplitude and incidence. Since the slope of SW reflects synaptic strength, we measured the overnight re-normalization of synaptic strength (i.e. downscaling) as the decrease in the slope from the first to the last hour of NREM sleep.

Methods: In a randomized cross-over design, 48 healthy men spent one night in Zurich (ZH) and two nights in Davos Wolfgang (WO) and Jakobshorn (JH) (1630 m versus 2590 m). Additionally we investigated 30 patients with obstructive sleep apnea (OSA) using a similar study design. At altitude these patients were treated with acetazolamide, which alleviates the altitude dependent oxygen desaturation level, or placebo. Polysomnographic recordings including central EEG derivations were conducted.

Results: In healthy subjects slope and amplitude of SW were significantly lower at highest altitude ($P < 0.001$) while the incidence did not change. The slope difference between the first and last hour of NREM sleep showed a reduction from ZH and WO to JH ($P < 0.05$). OSA patient's slope difference in ZH and at altitude treated with placebo showed a similar pattern as in healthy subjects. When treated with acetazolamide the SW slope increased from the first to the last hour of NREM sleep. Only heart rate showed a similar altitude and drug dependent alteration.

Conclusion: The overnight decrease of the slope of SW was reduced after acute exposure to moderate altitude. At the same time heart rate increased which likely reflects augmented sympathetic activity, which might have affected our measure of synaptic downscaling. Such a reduction in downscaling may have consequences on sleep dependent performance changes. Thus, in a subgroup of our healthy subjects ($n = 21$) we analysed the overnight performance improvement of a visuomotor learning task in ZH and JH. Preliminary results show less overnight performance improvement in JH compared to ZH.

P442

Association of physical activity level, daily sleepiness and sleep quality in university students

J. ALMEIDA[1], P. P. SIQUEIRA[2], M. S. BRASILEIRO-SANTOS[3] and A. M. LIMA[1]
[1]Federal University of Pernambuco, Recife, BR, [2]FIR, Recife, BR, [3]Federal University of Paraíba, Recife, BR

Aims: The aim of this study was to verify the association among physical fitness level, daily sleepness and sleep quality in universitary students.

Methods: This observational transversal study was approved by a local ethics committee (Integrated Faculties of Recife). Physical fitness level, daily sleepiness and sleep quality were evalueted by International Physical Activity Questionary (IPAQ), Epworth Sonolence Scale (ESS) and Pittsburgh Sleep Quality Index (PSQI), respectively. To verify the association among the analyzed variables chi-square and Fisher exact test were used. A p value < 0.05 was considered statistically significant.

Results: Two hundred and sixty subjects were analyzed [male: $n = 42$ (16.15%); female: $n = 218$ (83.85%), between 18 and

30 years (22.5 ± 2.1 years). When the association between physical fitness level and daily sleepiness ($P = 0.999$) and between physical fitness level and sleep quality ($P = 0.101$) were analyzed, there was no relationship among these variables. In the analysis of the IPAQ, showed that all active individuals, 38 (73.1%) showed no sleepiness (NS), 13 (25.0%) mild sleepiness and only 1 (1.9%) moderate sleepiness. In the irregularly active, 59 (72.8%) had NS, 20 (24.7%) mild sleepiness, and 2 (2.5%) moderate sleepiness; as regards sedentary individuals, 89 (70.1%) had AS, 33 (26.0%) mild sleepiness, 4 (3.1%) moderate sleepiness and 1 (0.8%) severe sleepiness. When we analyzed the PSQI results showed that subjects who had normal sleep quality, 34 (65.4%) were active, 41 (50.6%) were irregularly active (IA) and 61 (48.0%) were sedentary, whereas individuals who had poor sleep quality 18 (34.6%) were active, 40 (49.4%) were IA and 66 (52.0%) were sedentary.

Conclusion: According to the results of this study, we observed that there was no association between physical activity level, daily sleepiness and sleep quality in university students. This study also suggests that the lack of association between these variables, can be related to the average age of the population studied. In Older individuals is more likely to develop sleep disorders and, in this group, it may be that exercise training has a significant action on the sleep quality and daytime sleepiness.

P443

The effect of intermittent fasting on sleep architecture and daytime sleepiness

A. S. BAHAMMAM, M. SHARIF and K. ALMUSAILHI
King Saud University, Riyadh, SA

Objectives: Fasting during Ramadan (Islamic intermittent fasting) is distinct from regular voluntary or experimental fasting. Two theories have been proposed to influence sleep during Ramadan: (i) physiological effects of fasting, and (ii) lifestyle changes during Ramadan. We hypothesized that if a fixed sleep-wake schedule and fixed caloric intake are followed during intermittent fasting, the effect of fasting on sleep architecture and daytime sleepiness will be minimal. Therefore, we designed this study to objectively assess the effect of Islamic intermittent fasting during Ramadan and outside Ramadan (baseline) on sleep architecture and daytime sleepiness.

Methods: In this descriptive study with repeated measures, eight healthy volunteers who were not on vacation during the study period reported to the Sleep Disorders Center on five occasions for polysomnography (PSG) and multiple sleep latency (MSLT) tests: (i) an initial visit for adaptation and data gathering, (ii) 5 weeks before Ramadan (baseline (BL) non-fasting), (iii) 4 weeks before Ramadan while performing Islamic fasting (non-Ramadan Fasting), (iv) during the second week of Ramadan (Ramadan Fasting), and (v) two weeks after Ramadan (Recovery). During 'non-Ramadan Fasting', participatants performed Islamic fasting for one week. Fixed caloric intake and fixed properties of food based on their ideal body weight light exposure to maintain circadian rhythm were maintained during the days of the sleep studies. Daytime sleepiness was assessed using Epworth Sleepiness Scale (ESS), MSLT and the John Drowsiness Scale (JDS) that utilizes infra-red reflectance oculography system.

Results: The participants had a mean age of 26.6 ± 4.9 years, BMI of 23.7 ± 3.5, and ESS of 7.3 ± 2.7. Sleep efficiency and rapid eye movement (REM) sleep percentage were significantly lower during fasting. There was no difference in sleep latency, NREM sleep percentage, arousal index and ESS scores during the four periods and MSLT analysis revealed no difference in sleep latency of individual naps or their mean between the 'BL non-fasting', 'non = Ramadan Fasting', 'Ramadan Fasting' and 'recovery' indicating lack of increased daytime sleepiness. There was no difference in JDS values during the four studies.

Conclusion: Under conditions of fixed sleep-wake schedule and caloric intake, Islamic intermittent fasting results in decrease REM sleep with no impact on other sleep stages, arousal index or daytime sleepiness.

P444

A warm bedroom does not hamper sleep onset

T. E. J. WEYSEN, E. I. S. MØST and R. J. E. M. RAYMANN
Philips Group Innovation, Eindhoven, NL

Introduction: Nocturnal sleep coincides with higher skin temperatures and is affected by ambient temperature. It is commonly advised to keep the bedroom temperature between 19°C and 22°C [1]. Subjective discomfort increases when the temperature deviates from this range. Furthermore, overnight sleep structure is negatively impacted outside the aforementioned temperature range, although this has only been confirmed by studies that applied very high or low temperatures [1,2]. These extremes are commonly not to be expected in the bedroom. Moreover, mild skin warming speeds up the process of falling asleep [3] and skin temperature is dependent on room temperature. Hence we investigated the effect of a relatively warm – but not hot – bedroom on sleep onset.

Methods: Twelve healthy sleepers (6 male) visited the sleep laboratory two times for a sleep onset attempt. Bedroom temperature was set at 18°C in the neutral (N) and 25°C in the warm condition (W). Sleep onset was determined online using PSG and sleep onset latencies (SOL) were scored *post hoc*. Subjective thermal comfort was measured using VAS scales. Paired t-tests (alpha = 0.05, 1-sided) were performed.

Results: The temperature was significantly ($P < 0.001$) higher in the warm bedroom (24.8°C ± 0.1 versus 17.8°C ± 0.1). No differences in SOL were observed (W: 9.4 min ± 2.1 versus N: 12.8 min ± 2.4, $P = 0.14$). The warmer bedroom was considered more comfortable (W: 59.3 ± 4.6 versus N: 39.3 ± 6.0, $P < 0.001$).

Discussion: Although it has been shown that relatively high ambient temperatures negatively impact sleep [2], we show that a warm bedroom does not affect sleep onset and contributes to the comfortable feeling that a bedroom should reflect. Our results stretch the advised bedroom temperature range, but our findings are restricted to the sleep onset period: 18°C–25°C. For the remainder of the sleep, it still holds that a bedroom temperature below 22°C is preferred. In most bedrooms a gradual decline in room temperature will be observed as long as the heating system is turned off before bedtime.

References:

1. Candas V et al. Body temperature during sleep under different thermal conditions, in Indoor Climate: Effect on Human Comfort, Performance and Health P.O. Fanger PO & Valbjorn O, Editors. 1979, Dan Res Ins: Copenhagen.
2. Muzet A et al. Ambient temperature and human sleep. Experientia, 1984, 40(5): 425–429.
3. Raymann RJEM et al. Cutaneous warming promotes sleep onset. *Am J Physiol*, 2005, 288(6): R1589–97.

P445

Promoting sleep using bed warming

T. E. J. WEYSEN, E. I. S. MØST and R. J. E. M. RAYMANN
Philips Group Innovation, Research, Eindhoven, NL

Introduction: Recent studies showed that manipulating skin temperature without affecting core body temperature has beneficial effects for sleep. It has been shown that intermittent skin warming by means of water-perfused thermosuits shortened sleep onset latency, promoted deep sleep and minimized early morning awakenings [1,2]. In the current study, we investigated whether set-point controlled bed warming would result in a faster sleep onset, more deep sleep and less light sleep.

Methods: Eight healthy sleepers (four male) visited the sleep laboratory for two nights. Participants slept one night in a bed warmed to 34°C (W) and one night in a bed that was unwarmed (N). Bed temperature was regulated via a set-point controlled electric blanket developed at our technical department. Sleep was measured using PSG and questionnaires. Paired t-tests (alpha = 0.05, 1-sided) were performed.

Results: Sleeping in the warmed bed suppressed wakefulness by 73% ($P = 0.009$), which was also reflected in the subjective reports on wakefulness (N: 16.8 min ± 7.6 versus W: 7.1 min ± 4.1, $P = 0.033$). The total amount of S1 was suppressed by 37% ($P = 0.036$). Sleep efficiency increased by 2% in the warmed bed condition ($P = 0.004$). Difference in SOL between conditions only reached trend level (N: 16.1 min ± 5.6 versus W: 10.0 min ± 4.7, $P = 0.070$).

Discussion: In the current study, we show that set point controlled bed warming results in better sleep. It has been reported that electric blankets disrupt sleep, mainly due to a heat buildup during the night [3]. Our blanket is feedback controlled and as such stops adding heat to the bed whenever the desired temperature set point is reached. As such it can be regarded as discontinuous warming which has been shown to be sleep-promoting [1,2]. The results indicate that feedback control of the in-bed temperature is an effective, non-pharmacological instrument that could easily be applied as a tool for sleep management.

References:

1. Raymann RJEM et al. Cutaneous warming promotes sleep onset. *Am J Physiol* 2005, 288(6): R1589–97.
2. Raymann RJEM et al. Skin deep: enhanced sleep depth by cutaneous temperature manipulation. *Brain* 2008, 131: 500–513.
3. Fletcher A et al. Sleeping with an electric blanket: Effects on core temperature, sleep, and melatonin in young adults. Sleep 1999, 22(3): 313–318.

P446

Showers close to bedtime facilitate sleep

E. S. GROSSMAN[1] and H. BABKOFF[2]
[1]Bar Ilan University, Ramat Gan, IL, [2]Ashkelon Academic College, Ashkelon, IL

Objective: The sleep-wake cycle closely resembles the circadian temperature cycle. Sleep is usually initiated when body temperature decreases, while waking usually occurs when body temperature begins to rise. A number of studies have reported that passive body heating can improve sleep onset latency, and that the effect can last several hours. Older subjects who are at risk of thermoregulation difficulties as well as young adults fall asleep faster after passive body heating. As sleep may not depend on actual body temperature, but on temperature change, the timing of passive body heating may be significant in regulating sleep onset. Another concern relates to the utility of these manipulations in normal settings. In the current study we were essentially interested in the importance of timing for the benefits of passive body heating and compared the effects of a short hot shower proximal to bedtime with the same procedure 2 h before bedtime.

Method: Thirty-eight subjects [mean age = 25 (2.85) (15 male)], wore acti-watches for four full days and were instructed to take (bearably) hot showers (10 min duration), 2 h before sleep on two nights and a hot shower 15 min before bedtime on the other two nights. The nights with early and late showers were randomized. Oral and room temperature were measured: (i) hourly, beginning 18:00, (ii) before and after the shower, and (iii) when entering bed. Subjects were instructed to mark the actigraph when they decided to go to sleep and mark any wakeup during the night. Upon morning awakening, oral and room temperature were measured and entries were made in the sleep log.

Results: Showers resulted in a temperature elevation of about 0.5°C. When the showers immediately preceded bedtime, there was a slight, but significant, increase over body temperature and a trend for a larger decrease in body temperature just before sleep onset than when showers were taken 2 h prior to bedtime. When showers preceded bedtime: (i) sleep onset latency was shorter, (ii) sleep efficiency was higher, and (3) the number of night awakenings was smaller than when showers were taken 2 h before bedtime.

Conclusions: The timing of passive body heating is an important factor for improved subsequent nocturnal sleep. A short hot shower immediately preceding bedtime can elevate body temperature prior to sleep onset and facilitate subsequent sleep.

P447

Sleep-related symptoms, job burnout and cognitive performance: a P300 study

M. LEINIKKA[1], L. SOKKA[1], C. HUBLIN[1], M. HUOTILAINEN[2] and K. MÜLLER[1]
[1]Finnish Institute of Occupational Health, Helsinki, FI, [2]University of Helsinki, Helsinki, FI

Objectives: Approximately 25–30% of workers report sleeping problems. Acute as well as cumulative sleep deprivation has been shown to cause impairment in cognitive functions such as working memory and attention. Work related burnout, which is conceptualized as a syndrome involving a prolonged response to chronic emotional and interpersonal stressors related to work, is an important cause of sleeping difficulties. Burnout is characterized by three major dimensions: exhaustion, cynicism and reduced professional efficacy. It also has a negative effect on cognitive performance and work capacity. The aim of our study is to investigate the relationship between cognitive performance, job burnout and sleep related symptoms. We studied workers with different degrees of burnout symptoms, some of them having also sleeping problems, and their healthy controls with normal sleep.

Methods: Cognitive performance was studied using a classical auditory oddball paradigm with harmonic tones. The peaks (amplitude and latency) of event-related potential (ERP) P300 were measured in all groups. P300 is elicited after the presentation of unexpected, task relevant stimuli. It is a good estimate of cognitive performance due to the known role of P300 in memory updating. During the study, subjective sleepiness was measured with Karolinska Sleepiness Scale. Sleep symptoms were screened with the symptom check-list questionnaire and classified into four different

dimensions: insufficient sleep, sleep-apnea related symptoms, insomnia and excessive daytime sleepiness. The degree of burnout is measured with Maslach Burnout Inventory General Survey.

Results and Conclusion: In our on-going research of 30 participants, our preliminary results of the first 10 subjects suggest an association between sleep symptoms, diminished cognitive task performance and differences in ERP P300 between the groups. The applicability of this type of diagnostics within occupational health services for evaluating a worker's cognitive performance relevant to modern work-life is also been assessed. This study is a part of SalWe (www.salwe.org) Mind and Body-programme.

P448

The chronic exposure to radiofrequency electromagnetic fields modified the thermopreferendum during sleep in juvenile rats

A. PELLETIER[1], S. DELANAUD[1], J.-P. LIBERT[1], V. BACH[1], G. THUROCZY[2], R. DE SEZE[2] and N. LOOS[1]

[1]University of Picardie Jules Verne, Amiens, FR, [2]INERIS, Verneuil-en-Halatte, FR

Objectives: Sleep disturbances by radiofrequency electromagnetic fields (RF-EMF) emitted by mobile phone base stations type GSM are not well-known. In a previous study, we pointed out that most effects of RF-EMF on sleep were dependent on the thermal environment, suggesting that RF-EMF exposure may modify sleep through interactions with thermoregulatory processes. In the present study, juvenile rats exposed to RF-EMF were allowed to choose their thermal environment corresponding to the thermopreferendum. Sleep was scored as comfort criteria.

Methods: Six Wistar rats (3 weeks-old) exposed to RF-EMF (900 MHz, 1 V/m) during 5 weeks were compared to a non-exposed group ($n = 4$). One week after surgery, sleep was measured (wireless) during the day when animals were allowed to move freely between three similar communicated rooms which differ according to their ambient temperatures (24, 28 and 31°C). Wakefulness (W), Slow Wave (SWS) and Paradoxical Sleep (PS) were scored at 10 s-periods. The time spent in each room, the total durations of sleep stages, the mean durations of episodes and their frequencies were tested using Mann–Whitney and Wilcoxon.

Results: Exposed rats preferred to sleep at 31°C whereas the controls preferred 28°C. At 31°C, the total time sleep was increased (+139 min and +103 min compared to 24°C and 28°C respectively, $P < 0.05$) as a result of longer total durations of SWS (compared to 24°C: +107 min, $P < 0.05$) and of PS (compared to 24°C and 28°C: +10 min and +7 min respectively, $P < 0.05$). The frequencies of SWS and PS episodes also increased at 31°C compared to 24°C (SWS: +167% and PS: +111%, $P < 0.05$).

Conclusion: In sleeping rats, the thermopreferedum was increased by chronic exposure to RF-EMF. The increased sleep duration suggests that the animals exposed to RF-EMF may develop behavioral responses to prevent energy expenditure.

P449

How long may I nap without disrupting my night-time sleep?

M. L. WONG[1], E. Y. Y. LAU[1], C. H. HUI[1], S. F. CHEUNG[2] and D. S. Y. MOK[2]

[1]The University of Hong Kong, Hong Kong, HK, [2]University of Macau, Macau, MO

Objectives: Napping has recently been shown to benefit human's cognition and emotion. Yet, poor nighttime sleep was reported to relate to long naps. It is unclear what the optimal nap duration is to achieve the benefits of a nap without disrupting nighttime sleep. By comparing the sleep behaviours, mood and quality of life in people of different nap duration and people who do not nap, we aim to enrich the knowledge on the relationship between duration of nap, nighttime sleep behaviours and daytime functions.

Methods: A community sample of 972 Chinese adults residing in Hong Kong and Macau (32.0% male, mean age = 22.96) reported their napping habits, sleep behaviours (Composite Scale of Morningness, Epworth Sleepiness Scale, Sleep Timing Questionnaire and Pittsburgh Sleep Quality Index), mood (Depression Anxiety Stress Scale) and quality of life (World Health Organization Quality of Life Measures) online. Based on their duration of nap, nappers were divided into four groups: very short (<30 min), short (30–60 min), medium (1–2 h) and long (>2 h).

Results: Between-group differences on nighttime sleep behaviours, mood and quality of life were studied by analysis of covariance with demographics (age, sex, family income, marital status) controlled. The four groups of nappers and non-nappers significantly differed in daytime sleepiness, $F_{5,940} = 10.394$, $P < 0.001$; sleep debt, $F_{5,901} = 15.139$, $P < 0.001$; sleep quality, $F_{1,826} = 2.815$, $P = 0.024$; and chronotype, $F_{1,894} = 3.657$, $P = 0.006$. Significant differences in physical health, $F_{1,962} = 5.107$, $P < 0.001$; social relationship, $F_{1,960} = 4.238$, $P = 0.002$ and environmental quality of life, $F_{1,962} = 4.071$, $P = 0.002$ were observed. No significant difference in mood was observed. Post-hoc analyses (sidak) showed that non-nappers had significantly (ps < 0.05) lower daytime sleepiness than most nap groups. Long nappers had greater sleep debt, worse sleep quality and worse physical health than non-nappers. Long nappers were also more inclined towards eveningness-chronotype. In contrast, short nappers had significantly better social relationship and environmental quality of life than non-nappers.

Conclusion: Our results suggested that people who nap for <2 h did not seem to have problems in nighttime sleep, mood and quality of life. Short nappers even had higher quality of life in some domains. Future studies with experimental or longitudinal designs will shed light on the causal relationship between napping and different daytime outcomes.

P450

Occurrence of insomnia and sleep characteristics among employed men and women and its association to quality of life

S. SARRAFI ZADEH, S. NIKDAD and K. BEGUM

University of Mysore, Mysore, IN

Objectives: To investigate influence of insomnia on quality of life (QoL) among employed men and women.

Material and Methods: Information obtained included, demographic profile, Sleep behavior and quality of life using standard questionnaires. Of 608 male and female professionals aged 21–45 formed the study group.

Result and Conclusion: Of 41 and 44.1% of the males and females respectively had insomnia. Difficulty falling asleep, staying asleep and trouble getting back to sleep were the common features of insomniacs and appeared in order of occurrence. Feeling un-fresh in morning was the most prevalent symptom. Males (45.2%) were more inflicted than females. Students exhibited high prevalence followed by IT professionals and teachers. Reduced work performance throughout the day due to poor sleep was reported by 33.1% of the insomniacs. Scores for QoL were significantly lower for insomniacs. Insomnia is becoming a public health concern, employed population

are at the risk of developing insomnia. Hence, creating awareness regarding consequences of insomnia and its effective management should be adopted as a population strategy.

P451

Ora et labora, et dormi bene!

N. KALAK, S. LEMOLA, M. GERBER, U. PÜHSE, A. GROB, E. HOLSBOER-TRACHSLER and S. BRAND
University of Basel, Basel, CH

Objective: There is evidence that earlier parental set bedtimes are a protective factor against children's depression and suicidal ideation. To explain the underpinning mechanisms, it is supposed that parental control may confer to a longer sleeping duration, which in turn is associated with increased subjectively perceived restoring sleep and sleep quality; most importantly, sufficient and satisfying sleep are associated with decreased risks for stress and depressive symptoms. The aim of the present study was to verify to which extent set bedtimes are associated with favorable sleep and psychological functioning among a larger sample of adolescents attending boarding schools compared to their class mates living at home. In students attending boarding schools, we expected a higher supervision of students' sleep-/wake-schedules, along with favorable psychological functioning.

Method: A total of 1571 adolescents (age: M = 16.51, SD = 1.83; 55% female participants) took part in the study. All participants were attending boarding schools. Of those, 558 (36%) were living at home, whereas the majority (64%) was living at the boarding schools. Participants completed a series of self-reporting questionnaires related to sleep and psychological functioning.

Results: Set bedtimes decreased with participants' increasing age. Irrespective of age, participants attending boarding schools reported more frequent and thorough set bedtimes, as compared to participants living at home. Participants attending boarding schools indicated slightly longer sleep durations, an increased sleep quality, and more favorable psychological functioning such as less perceived stress, lower sleep disturbances, lower perceived pain, but increased optimism and curiosity and exploration behavior.

Conclusions: Data suggest that compared to their class mated living at home, adolescents attending boarding schools experience a higher supervision as to the sleep schedules, which seems to positively impact on sleep quality and psychological functioning.

P452

In-car countermeasures, open window and music, revisited on the real road: popular but hardly effective against driver sleepiness

J. F. A. SCHWARZ[1], M. INGRE[1], C. FORS[2], A. ANUND[2], J. TAILLARD[3], P. PHILIP[3], G. KECKLUND[1] and T. ÅKERSTEDT[1]
[1]Stockholm University, Stockholm, SE, [2]VTI, Linköping, SE, [3]University of Bordeaux, Bordeaux, FR

Objectives: Approximately 20% of motor vehicle crashes are caused by driver sleepiness. Consequently, effective countermeasures against driver sleepiness could add great benefit to traffic safety. According to a recent survey, listening to music and opening the window are among the most commonly used countermeasures. The aim of the present study was to investigate the effects of these countermeasures during real road driving.

Methods: In total, 24 individuals participated in the study. Eight participants served as control group. Sixteen participants (countermeasure group) received intermittent 10 min intervals of (i) open window, and (ii) listening to music, during both day and night driving on an open motorway. During daytime, the countermeasure was activated 20 min after the start and 20 min after the turnaround. During night time, it was activated 2 min after the participant reported KSS7. Each drive took ca. 90 min. The effects of open window and music on driver sleepiness were investigated using multilevel mixed effects regression modeling for subjective sleepiness (KSS) and physiological sleepiness (log transformed blink duration BDlog).

Results: Both subjective sleepiness ($P < 0.001$) and physiological sleepiness ($P = 0.041$) were estimated to be significantly reduced when subjects listened to music (estimated effects: KSS: -0.37 steps; BDlog: -0.02), but the effect was only minor compared to the pronounced effects of night driving (KSS: +1.83 steps; BDlog: +0.11) and driving duration. Open window had no attenuating effect on either sleepiness measure (KSS: +0.07; BDlog: +0.00). No significant long-term effects beyond the actual countermeasure application intervals occurred as shown by comparison with the control group (KSS: $P = 0.125$; BDlog: $P = 0.403$).

Conclusion: In summary, listening to music showed only slight beneficial effects and opening the window was ineffective in countering sleepiness during real road driving. Thus, these countermeasures are presumably of little practical relevance in overcoming the substantial effects of night-time and prolonged driving.

The study was financed by VINNOVA (a government research funding organization) and coordinated by the EU programme ERAnet.

P453

Reduced sleep quality predicts lower self-esteem

Z. ROGERS[1], M. GARDANI[2] and S. M. BIELLO[3]
[1]University of Glasgow Sleep Centre, Glasgow, UK, [2]Institute of Health and Wellbeing, Glasgow, UK, [3]Department of Psychology, Glasgow, UK

Objectives: Poor sleep quality is highly associated with an increased risk of depression not only as a symptom but also a possible predictor of onset of depression. Low self-esteem is a pervasive factor in depression and anxiety. The present study investigated the relationship between sleep quality and self-esteem independent of depression and anxiety in a student population.

Methods: Participants were screened for medication and alcohol use and those who met inclusion criteria ($n = 310$, F = 229, M = 81) completed the following questionnaires on-line: Pittsburgh Sleep Quality Index (PSQI), Rosenberg Self-Esteem Scale, Hospital Anxiety and Depression Scale (HADS), Perceived Stress Scale (PSS) and Big Five Inventory – 10 (BFI-10) which measures the five factors of personality. Participants were assigned to one of two groups based on their PSQI score: normal sleepers (PSQI $\leq$ 5) and poor sleepers (PSQI > 5).

Results: A univariate ANCOVA indicated that poor sleepers had significantly lower self-esteem ($F_{1,308} = 8.51$, $P < 0.01$) than normal sleepers even when controlling for the covariates of depression and anxiety. Nine variables were included as potential predictors in a backward regression analysis of self-esteem. Of these, perceived stress, depression, extraversion, emotional stability, PSQI score and conscientiousness were shown to be significant predictors of self-esteem, R-squared = 0.65, adjusted R-squared = 0.64, $F_{9,310} = 93.29$, $P < 0.001$. The associations between each of openness, agreeableness and anxiety and self-esteem were not significant in the regression model.

Conclusion: Findings from our study show that sleep quality and self-esteem may be related independently of depression and anxiety

as well as perceived stress and personality. Future research is needed to investigate the direction of causality in this unique relationship between sleep quality and self-esteem and whether sleep-related daytime impairments decrease competence in the self-esteem domains of social acceptance and achievement.

P454

Characteristics of individuals vulnerable to sleep reactivity to stress

H. AZEVEDO[1], A. PEREIRA[1], S. BOS[1], B. MAIA[2], M. MARQUES[3], M. J. SOARES[1], A. GOMES[4] and A. MACEDO[1]

[1]University of Coimbra, Coimbra, PT, [2]Higher Institute of Social Service of Porto, Porto, PT, [3]Higher Institute of Miguel Torga, Coimbra, PT, [4]University of Aveiro, Aveiro, PT

We wish to explore the relationship between pre-sleep arousal, arousability, perceived stress, coping, sleep related aspects, neuroticism/extraversion, self-esteem, perceived health and sleep reactivity to stress, in young adults good sleepers. Of 154 males and 280 females, medical students (mean age 19.24 years), self–defined good sleepers, completed a series of questionnaires that assessed sleep reactivity to stress (Ford Insomnia Response to Stress Test, FIRST), arousability; emotion regulation (cognitive reappraisal/expressive supression); emotional expressivity (negative expressivity, positive expressivity, impulse strength); tendency to worry/lose sleep over worries; neuroticism/extraversion; perceived physical/psychological health; perceived academic stress; positive affect/negative affect; pre-sleep arousal (cognitive arousal; somatic arousal); self-esteem; sleep related aspects (sleep depth, sleep needs, subjective sleep quality, sleeplessness, daytime sleepiness, sleep flexibility, chronotype). In both genders the regression models showed that pre-sleep cognitive arousal (beta values: Males = 0.401, $P = 0.<001$; Females = 247, $P \leq 0.001$), arousability (beta values: Males = 0.362, $P \leq 001$; Females = 0.171, $P = 0.07$), and perceived academic stress (beta values, Males = 0.280. $P = 0.001$; Females = 0.156, $P = 0.014$) all were independent significant predictors of FIRST total scores. Only in males subjective sleep quality (beta = 0.214, $P = 0.001$), negative affect (beta = -0.177, $P = 0.019$), and worry, (beta = -0.192, $P = 0.001$) were independent significant predictors of FIRST total scores and in females lose sleep over worries (beta = 0.192, $P = 0.001$), sleep flexibility (beta = 0.156, $P = 0.003$), and morningness (beta = 0.116, $P = 0.007$), were independent predictors of the same outcome. Although our findings suggest some sex specific factors, pre-sleep cognitive arousal, arousability and perceived academic stress were all associated with sleep reactivity to stress in good sleepers, in both genders.

P455

Evidence that self-reported sleep impacts on momentary affect in daily life, and predicts follow-up depressive symptomatology

J. A. DE WILD-HARTMANN[1], M. WICHERS[1], A. L. VAN BEMMEL[2], J. VAN OS[1] and C. J. P. SIMONS[1]

[1]Maastricht University, Maastricht, NL, [2]GGzE, Eindhoven, NL

Objective: The first aim of the study was to prospectively investigate the day-to-day associations between self-reported sleep and daily affect using the Experience Sampling Method (ESM), allowing for the examination of directionality of sleep-affect associations. The second aim was to examine the association between baseline sleep reports and follow-up depressive symptoms.

Methods: Six hundred and twenty-one women from a population based survey underwent a five day ESM protocol at baseline, assessing prospectively positive and negative affect ten times a day for 5 days, along with daily assessments of self-report sleep. To establish directionality in the day-to-day associations of sleep and affect, sleep variables and affect measures were analyzed in turn as predictor and outcome measures in lagged analyses using mixed regression. Subsequently, the baseline sleep measurements were used as predictor of follow-up depression.

Results: Daily self-report sleep and affect variables were consistently associated, particularly sleep and positive affect. The association between sleep and subsequent affect was stronger than between sleep and prior affect. Baseline sleep predicted depressive symptoms at follow-up.

Conclusion: In the general population, self-report sleep and every day affect were consistently, but not bidirectionally, associated. Sleep appeared to impact on momentary affect the next day, particularly PA, suggesting a role for sleep in (positive) affect regulation. Furthermore, sleep predicted onset of depressive symptoms, reaffirming sleep as causal risk factor rather than as secondary – or epiphenomenon in the onset of depressive illness.

P456

Behavioural lifestyle, personality factors and sleep quality

M. SHARMA and M. BHATIA

Sir Ganga Ram Hospital, New Delhi, IN

Objective: The present study explored the effect of various lifestyle behaviors and personality traits on the quality of sleep.

Methods: Behavioral lifestyle and personality factors were assessed by physical activity, obesity, smoke, alcohol consumption and stress; extraversion and neuroticism respectively. Subjective sleep quality was assessed by the Pittsburg Sleep Quality Index (PSQI). Lifestyle behavior scores were derived from battery of psychological tests designed for this study whereas personality was assessed by Eysenck Personality Questionnaire-Revised. It was hypothesized that healthy lifestyle behavior would be conducive to better sleep quality; neurotic personality trait will adversely affect the quality of sleep. These instruments were given to a sample of 134 subjects from the metropolitan city of India (controls = 33).

Results: Hypothesis framed were partially accepted. Age, marital status, BMI, Alcohol, Smoke, Stress and Neuroticism were seen to be correlating with poor sleep quality (person coefficient correlation). Logistic regression found that high consumption of alcohol and smoke (OR = -3.44; 7.0 respectively, high Stress (OR = -1.08), neuroticism (OR = -1.14), adversely affects the quality of sleep.

Conclusion: The current study has identified lifestyle and personality factors to adversely affect the sleep quality in the general metropolitan population. More research is needed to determine if this overall relationship is 'causal' and there is need to examine further some of the variables that are believed to moderate the overall relationship.

P457

In search of the perfect sleep

M. MARQUES, S. BOS, A. PEREIRA, M. J. SOARES, M. H. AZEVEDO and A. MACEDO

University of Coimbra, Coimbra, PT

Verify if types of perfectionism are associated with various sleep aspects. Of 713 students (Mean age = 19.3, SD = 1.26; 65.6% girls) filled in the two Multidimensional Perfectionism Scales, the Profile of

Mood States, the Pre-sleep Arousal Scale and a questionnaire about sleep-wake behaviours including habitual sleep duration, depth, subjective quality, nighttime awakenings, latency and time to get up in the morning. Sleep depth, quality, latency and awakenings were summed to form a sleep quality index (SQI). Positive perfectionism was measured summing personal standards/PS and self-oriented perfectionism/SOP; negative perfectionism summing doubts about actions/DA, concerns over mistakes/CM and socially prescribed perfectionism/SPP). Based on the mean and standard deviation both positive and negative perfectionism were categorized in low, medium and high groups. Three groups were created: healthy perfectionists, high/medium levels of positive perfectionism and low levels of negative perfectionism; non perfectionists, low levels of positive perfectionism; unhealthy perfectionists, high levels of positive and negative perfectionism. Higher SOP levels were associated with worst subjective sleep quality, more awakenings ($P \leq 0.05$) and shorter sleep duration ($P \leq 0.001$). DA ($P \leq 0.05$), CM and SPP ($P \leq 0.001$) were associated with shorter sleep duration, worst subjective sleep quality and SQI ($P \leq 0.001$). DA and SPP were associated with longer time to get up and DA with more awakenings ($P \leq 0.001$). Negative perfectionism had a similar pattern of results to SPP and DA + CM to DA. Except for PS, all perfectionism variables were associated with negative affect (NA). DA, CM, DA + CM, SPP and negative perfectionism were negatively related to positive affect (PA). All perfectionism variables were associated with pre-sleep cognitive arousal. Healthy perfectionists reported better subjective sleep quality and SQI versus unhealthy perfectionists. They had higher PA levels, lower NA levels, depression and cognitive arousal versus the other groups. Unhealthy perfectionists presented more awakenings, NA, depression and cognitive arousal versus non-perfectionists; lower PA levels and higher NA levels, depression and cognitive arousal versus healthy perfectionists. Cognitive arousal mediated DA + CM relation with subjective sleep quality and DA relation with awakenings. Healthy perfectionism is linked to better sleep quality than unhealthy perfectionism and non-perfectionism.

P459

Colombians refugees in Quebec: influence of sociocultural factors involved in sleep and rest

C. SANCHEZ MACIA, A. BOILARD, E. BASTILLE-DENIS, C. BRISSET, T. ARAUJO, A. VALLIÈRES and Y. LEANZA
University Laval, Quebéc, CA

Introduction: Sleep is intrinsically linked to society and culture, which is mostly neglected in sleep studies. The present project investigates the sociocultural aspects of sleep of Colombian refugees in Quebec-City in relation to circadian rhythm, perceived quality of sleep and acculturation.

Methodology: An exploratory qualitative design was chosen, completed with questionnaires. Twenty Colombians migrants (11 women; Mage = 33.8, SD = 12.04) were recruited. Eighteen of them were political refugees. Average length of stay was six years. Participants went through two interviews. The first one was a non-structured interview focusing on sociocultural factors related to sleep (SAISI). It includes 67 questions such as 'Could you describe your habits when you are about to go to sleep?' The second one was the Insomnia Interview Schedule (IIS), a semi-structured interview used to identify presence of insomnia or other suspected sleep disorders. Then, participants completed three self-reported (validated Spanish versions) questionnaires addressing sleep quality (PSQI), chronotype (MEQ) and acculturation (VIA). Questionnaires' scores and descriptive statistics were produced with SPSS. Thematic analysis, including an interrater reliability procedure, was used for qualitative data (SAISI interviews) using QDA-Miner.

Results: No participants reported sleep disorder. The majority presented an intermediate-eveningness (MEQ Mscore = 42.1 SD = 0.4) which is concordant with the reported bed time in the IIS (average 00:30). Participants reported good sleep quality as assessed with the PSQI (M = 3.28, SD = 0.2). Acculturation average scores demonstrated a strong identification to Colombian culture (M = 8.1, SD = 0.9) and a fair adaptation to Québec culture (M = 5.7, SD = 1.1). Preliminary qualitative analysis showed three main themes on how participants perceive sleep: (i) it is essential for human beings, such as food, and is associated with well-being, (ii) naps are conceived as 'natural' with no positive or negative value, and (iii) sleep is described as a social experience, to be shared with their beloved ones.

Conclusion: For this population, sleep is more than a simple biological function. It possesses a social dimension, which is never accounted for in traditional sleep researches. This sociocultural aspect might have implication for clinical intervention. More analyses are needed to verify if this conception of sleep is related to acculturation level.

P460

Sleep study during an Arctic polar expedition

G. CHAUMET[1], C. INFANTE[2], P. VAN BEERS[3] and O. COSTE[4]
[1]Université de la Méditerranée, Marseille, FR, [2]University Joseph Fourier, Grenoble, FR, [3]IRBA/ENOP, Brétigny-sur-Orge, FR, [4]HIA Desgenettes, Lyon, FR

Introduction: Sleep studies during polar expeditions are not very frequent. Recently, a polar expedition, called Deepsea Under the Pole was performed by a French team. Its main scientific goal was to dive under the ice in the northern polar zone and to measure ice thickness during their progression between the pole and their base camp located at Resolute Bay (Canada). The members of the expedition also friendly accepted to realize a study of their sleep during spring 2010, i.e., in constant light conditions.

Methods: Six young healthy subjects (five men and one woman, Age: 30 ± 3.3 years) were involved in this expedition. Their sleep was studied by wrist actigraphy crossed with a diary giving the level of perceived fatigue and sleepiness.

Results: We observed interdaily significant fluctuations of sleep and subjective parameters reflecting a huge interdaily variability of physical and psychological components. Nevertheless, we observed a significant delay in mid sleep time based on a linear trend analysis.

Conclusion: These results suggested a desynchronization of the sleep-wake cycle due to constant light exposure on sleep-wake cycle. In other words, expedition schedule, physical activity, and social interactions in a small group did not seem to be strong enough to prevent a phase delay induced by constant light exposure.

Support: Rolex fully sponsored this expedition, but without any financial benefit for IRBA's researchers.

P461

Missed appointments at hospital outpatient clinics in Scotland during transitions into and out of daylight saving time

S. D. KYLE, D. ELLIS, R. JENKINS and C. ESPIE
University of Glasgow, Glasgow, UK

Objectives: Transitions into and out of daylight saving time (DST) have been associated with altered rates of myocardial infarction, road traffic accidents, and impairments in mood and cognition; all of which have been attributed to changes in sleep duration/quality and circadian misalignment. In the present exploratory study we investigated the extent to which missed appointments at NHS hospital outpatient clinics varied according to transitions into and out of DST.

Methods: We assessed the percentage of missed appointments at hospital outpatient clinics in Scotland for individuals aged 18–64, during the two weeks before the clock change, the week of the clock change, and the two weeks after the clock change (for both transitions into and out of DST). Incidence ratios (IR) were computed for each weekday × year (2005–2010), for both forward (March) and backward (October) clock-changes, reflecting the% of missed appointments during the week of the clock change (observed) divided by a baseline measure encompassing the 2 weeks pre- and post-clock change (expected). IR > 1 indicates elevations in missed appointments; while IR < 1 indicates a relative decrease in missed appointments.

Results: Total number of appointments given out during the analysed weeks of interest equalled 1 004 641; of which 11.75% were missed. For the week of the spring clock-change, the only reliable change in missed appointments was found on the Thursday, with missed appointments increasing by approximately 6% (IR = 1.056, CI: 1.014–1.099). On the Monday during the autumn clock-change, missed appointments decreased by 8.5% (IR = 0.915, CI: 0.836–0.997). No other reliable weekday differences were observed.

Conclusions: Though preliminary, these modest alterations in the number of missed appointments may reflect changes into and out of DST, through the downstream effects of sleep and circadian disruption on cognition and behaviour. Novel ways of assessing how DST may impact behaviour at a societal level should be considered.

P462

The effect of Intensive Care Unit reproduced noise on the nap

O. MANDAI[1], M. NAKAI[2] and T. KOBAYASHI[1]
[1]Ashikaga institute of Technology, Ashikaga, JP, [2]Tohto College of Health sciences, Fukaya, JP

Objectives: It is very important to apprehend patients' sleep disruption for physical and mental recovery after medical intervention. Our previous study indicated that the important disorder of sleep-wake rhythm, due to the environmental factors: noise, light, nursing acts and so appear just after surgical intervention and reduce all the way through staying in general wards. We investigate, in this study, the effects of environmental noise in ICU (Intensive Care Unit) on the nap with PSG (polysomnography) recording and subjective survey on sleep quality in perspective of the medical nursing.

Methods: Ten healthy male subjects (21.6 ± 1.6 years old) were polygraphically recorded during their nap from 1:00 PM to 4:00 PM for 2 adaptation days (Ad-1 and Ad-2), base-line day (BL) and experimental day (EX) in which the Ss were exposed in the reproduced ICU noise. This sound sequence is recorded in real ICU. The sound pressure level is 48.9 ± 2.1dB. The luminosity of this bed room is under 2.0 lux. The temperature and the humidity are controlled to 25 Co and 55–60%. The order of BL day and EX day is counterbalanced. The PSG record is performed in according to the international 10–20 standard for EEG with EMG, EOG and ECG. The sleep staging is based on the Rechtschaffen and Kale's criteria. The Subjects are asked before and after their nap for each day to complete a japanese questionnaire OSA sleep inventory that explore subjective sleep quality.

Results: We observed no different mean duration of stages 1 and 2 between BL day and EX day However the slow wave sleep (stages 3 and 4) durations show a significant ($P < 0.02$) decrease (20.5 ± 18.4 mn for BL versus 4.1 ± 6.3 mn for EX) as well as for REM sleep duration (20.4 ± 13.5 mn for BL versus 5.9 ± 9.4 mn for EX, $P < 0.02$). The Sleep latency prolongation is observed as 11.6 ± 7.5 mn for BL day versus 21.5 ± 7.6 mn for EX day ($P < 0.01$) and frequent sporadic awakenings lead to a decrease of sleep efficiency (85.1 ± 13.2%for BL versus 67.2 ± 22.1% for EX, $P < 0.05$). The ICU noise reduce also the score of item 'sleep latency and sleep maintenance' in OSA sleep inventory (40.3 ± 6.5 pts. for BL versus 36.7 ± 8.6 pts.for EX, $P < 0.05$).

Conclusion: As indicated above, the ICU's auditory environment noise disturbs sleep structures in particular transition to deep sleep stages for even healthy young subjects. It is obvious that ICU noise reduction is necessary in order to provide sufficient and effective sleep to patients.

P463

In-car nocturnal blue light exposure improves motorway driving as well as caffeine intake: a randomised trial

J. TAILLARD[1], A. CAPELLI[1], P. SAGASPE[1], A. ANUND[2], T. AKERSTEDT[3] and P. PHILIP[1]
[1]University of Bordeaux, Bordeaux, FR, [2]Swedish Road and Transport Research Institute, Linköping, SE, [3]Stress Research Institute, Stockholm, SE

Background: Sleep deprivation induced by prolonged wakefulness highly decreases nocturnal driving performance. The development of in-car countermeasures (in contrast with interventional countermeasure, ie coffee…) is a major issue for the prevention of sleep related accidents.

Methods: Forty-eight subjects (mean age 33.19 ± 1.57) participated in this randomized and controlled study. Participants drove 400 km (250 miles) on the same 2-lane highway for 4 h (from 1:00 AM to 5:15 AM with a 15-min mid-way break). They randomly received either continuous blue light exposure (GOLite, Philips, 460 nm, 20 lux) during driving or 2*200 mg of caffeine or placebo of caffeine before driving and during break with at least 1 week between conditions. Main criteria were the number of inappropriate line crossings (ILC) and the quality, quantity and timing of three subsequent nocturnal sleep episodes determined by actigraphy.

Results: Eight participants complained about dazzle during blue light exposition and were thus removed from analysis. Results from the 40 other participants showed that countermeasures reduced the number of ILC ($F_{2.91.11} = 6.64$; $P < 0.05$). ILC were lower with coffee (12.51 ± 2.08, $P = 0.001$) and blue light (14.58 ± 2.18, $P = 0.003$) than with placebo (26.42 ± 3.86). A significant effect of the moment of driving was also found ($F_{1,103.92} = 11.47$; $P < 0.01$) indicating higher number of ILCs during the 2nd night-time driving session (21.32 ± 2.64) than during the 1st night-time driving session (14.59 ± 2.07, $P = 0.001$). Caffeine, placebo and continuous noctur-

nal blue light exposure did not modify quality, quantity and timing of subsequent sleep.

Conclusions: Despite a lesser tolerance (dazzle), a non-inferior efficacy of continuous nocturnal blue light exposure compared with caffeine suggests that this in-car countermeasure could be used to fight nocturnal sleepiness at the wheel in all drivers, whatever their age.

This research was supported by an ERANET transport ENT 15 grant (Sleepiness at the wheel) from the French Ministry 'Ministère de l'Ecologie, du Développement Durable, des Transports et du Logement (MEDDTL)'. PHILIPS provided 2 portable blue lights (goLITE BLU®) and VINCI autoroute/ASF allowed us to use their highways for our research.

Poster Session – Insomnia: Epidemiology, Measurement and Classification

P464

Subjective sleep quality, insomnia and depression in the Georgian general population: preliminary findings

M. ALKHIDZE[1], L. MAISURADZE[2] and S. KASRADZE[1]
[1]*Tbilisi State University, Tbilisi, GE,* [2]*I.Beritashvili Center of Experimental Biomedicine, Tbilisi, GE*

Objectives: Compared to western countries, very little is known about the distribution of sleep disorders in Georgian general population. This study was aimed to investigate sleep complaints and disturbances in the individuals living in Tbilisi, Georgia.

Methods: A representative sample (n = 501, 90 males and 411 females, aged 16–78 years) of the individuals from the largest district of Tbilisi city was enrolled in the survey. Interview was conducted from March to October 2010 by using following questionnaires: Insomnia Severity Index (ISI), Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), Beck Depression Inventory (BDI), and special constructed questionnaire to evaluate sleep-wake habits considering demographic data and educational level.

Results: According to the ISI responses, it was observed that 18% had borderline insomnia, 5.6% – clinical insomnia and 1.6% – severe insomnia. Clinical and sever insomnia was more prevalent in women than in men. Of 57.0% had no sleep complaints. In general, 60.0% reported difficulties falling asleep; this complaint was more prevalent in the respondents with early bedtime. Fourten per cent indicated that they need more than 30 min to fall asleep. Frequent nocturnal awakenings in parallel to the sleep initiating difficulties three or more nights a week was reported by 5.4% of total sample. Of 18.0% of the respondents suffered of restricted nocturnal sleep. Of 25.0% complained on non-restorative sleep. Although there was no significant difference in the prevalence of excessive daytime sleepiness (17.0%) among men and women, it was more distributed in males (36.0%) with Body Mass Index > 25. According to the BDI, depression was distributed in 20.0% of the sample; it was less prevalent in the respondents with high level of education (24.0%). More men than women had severe depression (7.0% versus 2.0%). Of 2.0% of total sample indicated regular intake of different medications for the sleep improvement following medical consultation and 3% – without prescription.

Conclusion: The findings of the present study clearly indicate that 43% of the urban population of Georgia has had at least one of the major sleep complaints. Unfortunately the most of these respondents never apply for medical consultation. Further research is needed to perform systematic longitudinal epidemiological study on the prevalence of insomnia or other sleep disorders in Georgian general population, and in relation to different comorbid conditions as well.

P465

Headache, chronic musculoskeletal pain and risk of insomnia: longitudinal data from the Nord-Trøndelag Health Study

S. S. ØDEGÅRD[1], T. SAND[1], M. ENGSTRØM[1], L. J. STOVNER[1], J. A. ZWART[2] and K. HAGEN[1]
[1]*Norwegian University of Science and Technology, Trondheim, NO,* [2]*Ullevål University Hospital, Oslo, NO*

Objective: The aim of this longitudinal cohort study was to investigate whether the presence of headache and chronic musculoskeletal complaints (CMSCs) among an insomnia-free population in the second Nord-Trøndelag Health survey (HUNT-2) was associated with an increased risk of insomnia 11 years later in HUNT-3.

Method: HUNT-2 and HUNT-3 were carried out in 1995–1997 and 2006–2008 respectively inviting all inhabitants in Nord-Trøndelag County of Norway aged ≥ 20 years to participate. Among the invited potential participants in HUNT-2 (n = 92 566) and HUNT-3 (n = 94 194) a total of 40 255 subjects participated in both surveys, whereof 27 185 (62%) completed the insomnia-related questions of both surveys. The insomnia, headache and CMSCs diagnoses were based on self report according to the DMS-IV, ICHD-I and ARC criteria respectively. Using logistic regression, we evaluated the association between headache (type and frequency), CMSCs (non-widespread and widespread) and insomnia at follow-up. Trend analyses were done for headache frequency.

Results: The presence of headache <7 days/month at baseline was associated with a 60% increased risk of insomnia at follow up (RR = 1.6, 95% CI = 1.4–1.7), while having headache ≥7 days/month was associated with a doubled risk (RR = 2.0, 95% CI = 1.7–2.4). The results for migraine and non-migraineous headache were similar. There was a significant relationship (P trend < 0.001) between the headache frequency at baseline and the risk of insomnia 11 years later. The combination of headache and CMSCs at baseline, in particular headache on <7 days/month, predisposed more strongly to insomnia (RR = 1.9, 95% CI 1.6–2.1) than headache without CMSCs (RR = 1.3, 95% CI 1.1–1.5).

Conclusion: Headache, with or without coexisting CMSCs at baseline increase the risk for insomnia after 11 years. Headache and CMSCs should be treated not only to relieve pain but also to prevent development of insomnia.

P466

Socioeconomic and gender inequalities in difficulty falling asleep of British, Finnish, and Japanese civil servants: roles of job strain, work hours and work-family conflicts

M. SEKINE[1], T. TATSUSE[1], N. CABLE[2], T. CHANDOLA[3], M. MARMOT[2], T. LALLUKKA[4], O. RAHKONEN[4] and E. LAHELMA[4]
[1]*University of Toyama, Toyama, JP,* [2]*University College London, London, UK,* [3]*University of Manchester, Manchester, UK,* [4]*University of Helsinki, Helsinki, FI*

Objectives: In general, high socioeconomic status (SES) individuals and men have better sleep quality. Research on international variations in SES and gender differences in sleep may provide further understanding of social determinants of health. This study aims to evaluate (i) whether the patterns and magnitude of SES and gender differences in difficulty falling asleep differ among countries, and (ii) whether work and family factors explain the differences.

Methods: The participants were 3611 British employees, 2298 Japanese employees, and 3922 Finnish employees. All the participants were civil servants aged 40–60 years. Participants answered questions that asked about job strain as measured by job demand and control, work hours, family structure, and work-family conflicts. Difficulty falling asleep was evaluated using a single item from

Pittsburg Sleep Quality Index in the Japanese civil servants study and from Jenkins Sleep Questionnaire in the British and Finnish civil servants study. Logistic regression analysis was performed to evaluate whether job strain, work hours, and work-family conflicts explain international variations of SES (employment grade) and gender inequalities in difficulty falling asleep.

Results: In all cohorts, there were SES inequalities in difficulty falling asleep among men (i.e. the higher the SES, the better the sleep). In women, there were no consistent patterns in the associations of SES with difficulty falling asleep. When the work and family characteristics were adjusted for, the SES differences reduced considerably among Japanese men but such reduction in the differences was not observed among British and Finnish men. Gender inequalities in difficulty falling asleep were observed in the British and Japanese cohorts but there were no significant gender inequalities in the Finnish cohort. When the work and family characteristics were adjusted for, the gender inequalities reduced and were no longer significant in the Japanese cohort, while such reduction was not observed in the British cohort.

Discussion: The patterns and magnitude of socioeconomic and gender inequalities in difficulty falling asleep and the contribution of work and family characteristics to the inequalities differed among countries. Although longitudinal study is needed, understanding social patterns of risk factors for poor sleep in each country may be needed to construct and implement health policies aiming at reducing SES and gender inequalities in sleep.

P467

Sleep, quality of life and depression in a Japanese male working population

H. KADOTANI[1] and T. KADOTANI[2]

[1]Kyoto University, Kyoto, JP, [2]Takatsuki General Hospital, Kyoto, JP

Data on 324 middle-aged male subjects were analyzed to report the prevalence of psychiatric disorders and its effects on sleep and quality of life in a Japanese male working population. Structured Clinical Interview for DSM-IV axis 1 disorder Non-patient Edition (SCID-I/NP) was conducted by one physician. Self-rating depression, sleepiness, sleep quality and quality of life were assessed by Self-rating Depression (SDS), Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI) and Medical Outcomes Study 36-Item Short Form health survey (SF-36), respectively. Sleep duration was obtained by sleep diary and actigraphy during one week. No untreated major depressive subjects were found. Of 4, 3 and 18 subjects had major depression with partial remission, minor depression and past depression, respectively. We could not identify statistical differences in SDS, ESS, PSQI or sleep duration according to the depressive status. Five subscales of SF-36 were disturbed in in past depression (General health, vitality, social functioning, role-emotional and Mental Health). Mental Health was also disturbed in minor depression. Prevalence of depression in this population was low, but comparable to other studies in Japanese. Because of the low prevalence rate, number of participants may be not large enough to get statistical power. However, some subscales of SF-36 were significantly disturbed. Quality of life was disturbed not only in current minor depression but also in past major depression. SF-36 may be more sensitive than SDS, PSQI or sleep duration to detect depression.

This work was supported by Special Coordination Funds for Promoting Science and Technology, grants in aid from Ministry of Health, Labor and Welfare of Japan, and research grants from PRESTO JST, Suzuken Memorial Foundation, Takeda Science Foundation, Mitsui Life Social Welfare Foundation, Chiyoda Kenko Kaihatsu Jigyodan Foundation, and Health Science Center Foundation.

P468

Sleep misperception in insomnia: changes in the discrepancy between actigraphy and self-reported total sleep time during a 4-week sleep restriction intervention

M. CRAWFORD[1], S. D. KYLE[1], I. M. CROIJMANS[2], D. J. BARTLETT[3], R. R. GRUNSTEIN[3] and C. ESPIE[1]

[1]University of Glasgow Sleep Centre, Glasgow, UK, [2]Maastricht University, Maastricht, NL, [3]University of Sydney, Sydney, AU

Objectives: Sleep misperception is frequent in insomnia, where reported subjective sleep tends to be underestimated relative to objective sleep. This discrepancy should be given greater attention in relation to therapeutic process and outcome. In the present study we investigated sleep misperception day-by-day during a 4-week sleep restriction treatment (SRT).

Methods: Twenty seven individuals with primary insomnia [mean age = 48; *n* female = 22; baseline Insomnia Severity Index (ISI) = 19] completed a 4-week sleep restriction treatment. We analysed the discrepancy between subjective total sleep time (TST, sleep diaries) and objective TST (actigraphy). A misperception index (MI) was computed [(objective TST – subjective TST)/objective TST], ranging from -1 to +1, with positive values indicating a greater underestimation of objective sleep.

Results: The treatment intervention produced significant reductions in ISI scores from baseline (mean = 19) to post-treatment (mean = 12, $P < 0.01$). The MI was found to vary across the weeks of treatment, [F (1.7, 45.3)=6.8, $P = 0.004$], significantly decreasing from week 1 (+0.11, SD = 0.17) to week 4 [+0.02 (SD = 0.17), $P = 0.006$]. This change in misperception occurred despite no changes to objective sleep over treatment, ($P = 0.15$), while subjective total sleep time significantly improved from 260 (week 1) to 303 (week 4) min ($P < 0.01$). Visual presentation of MI across day of therapy indicated a strong negative correlation, with progression through SRT being associated with a decline in MI (r = -0.7).

Conclusions: Misperception of total sleep time, at least when evaluated against actigraphy, appears to reduce across SRT. Although this report lacks pre-treatment actigraphy data, these results may indicate that sleep restriction exerts some of its effects through a reduction in subjective-objective sleep discrepancies.

P469

REM sleep alterations in primary insomnia

B. FEIGE, K. SPIEGELHALDER, C. BAGLIONI, C. NISSEN and D. RIEMANN

University Hospital Freiburg, Freiburg, DE

Objectives: We previously (2008) found an association between REM sleep duration and perceived wakefulness in 81 patients with primary insomnia (PI) in addition to a clearly increased arousal index in REM sleep. The current study aimed to replicate and extend the previous findings.

Methods: Polysomnogram (PSG) and subjective sleep quality questionnaire (Schlaffragebogen A, SFA) data of PI patients and matched good sleeper controls (GSC) were evaluated for group differences.

Results: One hundred and fifty-six new PI patients could be matched to the same number of GSC (GSC; 60M, 96F; Mean age

PI: 42.6 ± 12.4 years, GSC: 42.2 ± 13.4 years). PI patients had a higher wake time within bed time as well as lower REM and sleep stage 2 time. The association between perceived wake time and REM sleep time could be replicated in this new and larger group, as well as a clearly increased arousal index in REM sleep, while the arousal index in NREM sleep was significantly but less strongly increased.

Conclusion: We postulate that the psychophysiological hyperarousal characteristic for primary insomnia is particularly expressed as a REM sleep alteration. REM sleep appears to be particularly vulnerable to pre-sleep worries, leading to increased retrospective recall of this time as wake time and a lower restorative sleep quality.

P470

The diagnostic value of sleep history due to non-organic insomnia

N. E. NEERINGS-VERBERKMOES, M. H. M. VLAK and H. L. HAMBURGER

Slotervaart Hospital, Amsterdam, NL

Background/Objectives: Video-polysomnography (VPSG) is the golden standard for diagnosing sleep disorders. However, since VPSG is an expensive and time-consuming investigation it is often omitted when non-organic insomnia is suspected after sleep history. We primary aim of this study was to calculate the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of sleep history in identifying non-organic insomnia.

Methods: Data were retrospectively collected from the medical records of the Amsterdam Center for Sleep and Wake disorders (ASWC). We included all patients of 18 years and older who visited the ACSW for the first time in 2010. At their first visit, all patients had undergone an extensive sleep history by a sleep specialist. Detailed data on symptoms of sleep apnea, restless legs (RLS) or periodic limb movements (PLMD), bruxism, parasomnia, bed time schedules, daytime functioning and daytime sleepiness were acquired. Subsequently, all patients underwent VPSG.

Sleep disorders were divided into two groups: organic insomnia (sleep related breathing disorder, RLS, PLMD, bruxism or parasomnia) or non-organic insomnia (psychofysiological insomnia or delayed sleep phase disorder). We compared the provisional primary diagnosis after extensive sleep history with the primary diagnosis after VPSG.

Results: A total of 810 patient were included in this study. Based on sleep history 342 patients were suspected of having non-organic insomnia and 468 of organic insomnia. Based on VPSG, 70 (20.5%) patients with a provisional diagnosis of non-organic insomnia had organic insomnia. Fifty-six patients (16.4%) of them had a sleep related breathing disorder, of whom 41 (12.0%) had an apnea-hypopnea index >15. A total of 136 patients (29.1%) with a provisional diagnosis of organic insomnia had no organic cause of insomnia on their versus PG. We calculated that the sensitivity of sleep history in detecting non-organic insomnia is 66.7% with a specificity of 82.6%. The PPV was 80% and the NPV was 71%.

Conclusions: Detailed sleep history alone is not sufficient in excluding organic insomnia. A considerable percentage of patients with suspected non-organic insomnia has a sleep related breathing disorder, most of whom have moderate to severe sleep apnea. These patients run serious health risks, especially when their insomnia is treated with benzodiazepines.

P471

Familial event-related potentials investigation in primary insomnia

D. WOLYNCZYK-GMAJ, I. NOWOSAD, B. GMAJ, T. PIOTROWSKI and W. SZELENBERGER

Medical University of Warsaw, Warsaw, PL

Objectives: There is converging evidence that insomnia results from stress-vulnerability interaction. Stress amplifies N1 component of event-related potentials (ERP), however, prior research has also demonstrated that visual N1 amplitude and latency are under a strong genetic control and may serve as endophenotypes of psychiatric disorders (Smit et al. 2007). This study tested the prediction that positive family history for primary or psychiatric insomnia may account for variation in N1 amplitude and latency.

Methods: Ten patients with DSM-IV primary insomnia (mean age: 34.8 ± 11.83) and 10 healthy subjects, matched on age and education, participated in the study. Six patients and two controls had relatives afflicted with primary insomnia or depressive disorder. All the subjects underwent two nights of polysomnography (PSG) and were tested on the Athens Insomnia Scale (AIS), the Hyperarousal Scale (HS), the Beck Depression Inventory (BDI) and the Hamilton Depression Rating Scale (HDRS). Visual ERP were recorded from 21 derivations while the subjects performed Continuous Attention Test. For statistical analysis, Glimmix procedure (SAS 9.2) was used. Statistical model included N1 amplitude and latency for nontargets as dependent variables, and age, diagnosis, family history, derivation and hyperarousal score as independent variables.

Results: PSG showed only worse sleep efficiency ($P < 0.0001$) and longer wake after sleep onset ($P = 0.01$) in patients. As expected, insomniacs had higher score on AIS ($P < 0.0001$), higher level of arousal on HS ($P < 0.0001$), and higher scores on depression scales HDRS ($P < 0.0001$) and BDI ($P = 0.01$). N1 amplitude of the posteriorly distributed component ($F = 35.7$, $P < 0.001$) was dependent on diagnosis ($F = 11.8$, $P = 0.001$), HS score ($F = 5.57$, $P < 0.02$) and family history ($F = 5.3$, $P = 0.025$), but not on age. No significant effects on N1 latency were found.

Conclusions: Our preliminary results suggest that visual N1 amplitude is associated with both diagnosis and family history of primary insomnia or other disorders with a shared biological background.

P472

The relationship between PTSD, hypervigilance, and disordered sleep

M. VAN WYK, M. LIPINSKA, S. MUNSON, R. TIMOL and K. G. F. THOMAS

University of Cape Town, Cape Town, ZA

Objectives: Disordered sleep in post-traumatic stress disorder (PTSD) constitutes a major component of the presenting symptomatology. However, the literature on PTSD and sleep is identifiable by discrepancies across studies, especially in terms of utilising either objective or subjective measures of sleep quality. As a result, disordered sleep and its underlying mechanism have not been unambiguously characterised in PTSD. Our research focused on the link between PTSD and disordered sleep using objective and subjective measures of sleep quality. Specifically, we investigated whether prominent hypervigilance symptoms function as one mechanism underlying disordered sleep when compared to individuals without such symptoms. In addition we asked whether hypervigilance affects dream content and themes in individuals with PTSD.

Methods: We recruited four groups of participants: Individuals diagnosed with PTSD with prominent hypervigilance symptoms (HYP+) (n = 10); individuals diagnosed with PTSD without prominent hypervigilance symptoms (HYP-) (n = 10); individuals diagnosed with depression (DEP) (n = 15), and healthy controls (CON) (n = 14). Each individual underwent one night of sleep-adapted EEG recordings, and we measured sleep latency, awakenings, time spent awake after sleep onset (WASO), and sleep efficiency. We also obtained self-reports of general sleep quality and two reports of their most recent dreams.

Results: Analyses of objective measures of sleep quality demonstrated statistically significant between-group differences for sleep efficiency and WASO. A planned comparison revealed that HYP+ individuals tended towards worse sleep quality for sleep efficiency and WASO than HYP- individuals. Subjective measures of sleep quality also revealed statistically significant differences between HYP+ compared to HYP- and CON. Our hypotheses regarding dream content and theme were not confirmed. However, the mean trends were indicative of more negative dream content and theme in the HYP+ group when compared to the other three groups.

Conclusion: Preliminary results of objective and subjective measures tend to support the notion that the HYP+ group experiences worse sleep quality when compared to other groups. These results suggest that prominent hypervigilance symptoms might serve as one underlying mechanism accounting for worse sleep quality in individuals diagnosed with PTSD. Analyses on a bigger sample is ongoing.

P473

Comparison between subjective and actigraphic measurement of sleep in primary insomnia: the accuracy of sleep perception

V. CLEMENTE, H. RODRIGUES, S. VIEIRA and J. MOUTINHO DOS SANTOS

Hospital Center of Coimbra, Coimbra, PT

Objectives: The present study aims to investigate the distribution, consistency, and correlates of sleep time perception in primary insomnia patients. Specifically, this study examines and compares sleep onset latency (SOL), wake time after sleep onset (WASO), total sleep time (TST), sleep efficiency (SE) and objective sleep time estimated (OSE), by comparing the two most important assessment methods in insomnia, actigraphy (A) and sleep logs (SL).

Methods: A total of thirty-two chronic insomnia patients, followed in clinical context, composed our sample (22 males, 10 females, mean age of 49.9 ± 13.4 years). Each patient underwent seven nights of home actigraphy and provided concurrent subjective estimates of their sleep. Minute-to-minute comparison of actigraphy and sleep log data was made. Other psychological and clinical variables were obtained. Descriptive statistics and inferential tests were used to examine the nature of sleep time perception and its correlates.

Results: Consistent with the majority of previous studies, our group of insomnia patients overestimate their sleep onset latency (SOL_SL Mean = 28.167; SD = 21.467 versus SOL_A Mean = 11.135; SD = 7.946; P = 0.000). On the other hand, they underestimate their wake time after sleep onset, significantly, on 4th night (WASO_SL Mean = 50.400; SD = 64.012 versus WASO_A Mean = 86.281; SD = 73.027; P < 0.005). They also underestimate their total sleep time (TST_SL Mean = 320.851; SD = 122.234 versus TST_A Mean = 436.135; SD = 72.790; P = 0.000), and sleep efficiency (SE_SL Mean = 62.728; SD = 24.816 versus SE_A Mean = 82.221; SD = 7.402; P = 0.000). In a similar way, insomnia patients' objective sleep estimated score distributions show a greater propensity to underestimate their sleep time (OSE Mean = -23.798%; SD = 31.250%). We also found that sleep time perception doesn't vary with insomnia severity (P = 0.349), depressed symptoms (P = 0.865), diurnal somnolence (P = 0.846) and sleep medication (P = 0.270).

Conclusion: Subjective perception is of central importance to sleep assessment in primary insomnia. Actigraphy provides only a partial portrayal of the nature of sleep difficulties.

P474

Sensory perception of patients with sleep disorders

T. GRIPPE[1], M. ELBAZ[2], K. YAUY[2], N. DELGADO-RODRIGUES[1] and D. LÉGER[2]

[1]University of Brasilia, Brazil, BR, [2]University Paris Descartes, Paris, FR

Even if it is well known that patients with sleep debt may have sensory deficit and pacients with sleep disorders may complain(ed) of sensory troubles, little literature has been devoted to sensory perception of patients with sleep disorders.

Purpose: To explore sensory perception profile of sleep disorders patients coming to a sleep disorder center.

Methods: Fifty-three patients aged 24–75 years-old and 20 controls aged from 25–65 years.o have been systematically interviewed and the 'Visual/audio/kinesthesic' 25 items scale applied. Sleep of patients and controls was also systematically recorded during an one night polysomnography. Sleep disorders diagnosis was based on the ICSD2d classification.

Preliminary Results: On 33 patients (seven with narcolepsy, eight with sleep apnea, 18 with insomnia) an average visual score of 10.2, audio score of 7.6 and kinesthesic score of 7.2 was found. Patients with insomnia had mostly a visual and kinesthesic preference, patients with narcolepsy presented a visual preference while no specific preference was found for sleep apnea. Future analyses will compare these results to the control group patients and test the association between total sleep time and sensory perception.

Conclusion: Better understanding the sensory perception of patients with sleep disorders may help clinicians in taking better care of their poor quality of life.

P475

Sleep and physical and cognitive performance: National survey of the Institut National du Sommeil. Journée du Sommeil®, France, 2012

F. FAUGERON, A. LOPEZ, J. ADRIEN, F. BECK, A. BRION, C. GRONFIER, J. KRIEGER, A. MUZET, P. PHILIP, M. ELBAZ, M.-F. VECCHIERINI and D. LÉGER

Institut National du Sommeil et de la Vigilance, Paris, FR

Goal: Exploring the association between sleep, sleep disorders and physical and psychological performance.

Method: Telephone call survey, made in January 2012 on a 1 010 subjects from 18 to 60 years old representative of the French national adult population. Questionnaire was built by the scientific committee of the INSV and included: sociodemographic data, detailed sleep and nap schedules, sleep disorders according to the ICSD2nd and sleepiness assessed by the Epworth sleepiness scale (ESS). Performance was described subjectively by the level of physical exercise, several items on physical limitation, items on concentration and fatigue.

Results: Sleep. French adults were sleeping and average 7 h and 5 min during working days and 8 h 11 min during restdays. Thirty-one per cent were sleeping 6 h or less during working days. Twenty-two per cent reported insomnia, 5% sleep apnea, 4% restless leg syndrome. Twenty per cent had an ESS score between 11 and 15 and 6% >/16.

Performance: Forty-eight per cent said they had regular exercises, from which 44% are walking, 27% doing gym, 25% cycling, 17% swimming, 17% gardening, 15% running. Sixty-eight per cent said they had no physical limitation for going to work, 54% to stand up longly, 46% to travel and cope with jet-lag, 41% to bring a heavy thing.

Regarding social and cognitive tasks: Eighty-four per cent said they have a good or very good ability to take care of nearest, 83% to be on time on appointments, 80% to schedule mid-terms professional or personal projects, 77% to achieve professional goals, 62% to remember names, phone numbers, addresses. However 25% of the group had the feeling of fatigue at least 5 times a week. Thirty-five per cent reported a maximum 30 min of concentration on a complex task.

Sleep and performance: We found no significant difference regarding total sleep time on workdays (7 h 7 min versus 7 h 2 min) and resting days between subjects who reported or not regular exercise. Regular exercise was not significantly associated with less sleep insomnia (21% versus 23%) or less restless leg syndrome (3% versus 4%), but with less sleep apnea syndrome ($P < 0.01$). Subjects with sleep disorders had significantly more physical limitation on every item than subjects with no sleep disorders. Insomniacs and subjects with sleep apnea reported significantly more ability to achieve personal and professional goals, to take care of nearest, to schedule mid-term professional or personal projects, to remember names, phone numbers, addresses.

This study was supported by the MGEN (Mutuelle Générale de l'Education Nationale).

P476

The effects of stress and sleepiness during the day on subsequent sleep duration – a prospective study of day-to-day variability across 42 days

T. AKERSTEDT[1], J. AXELSSON[2], N. ORSINI[2] and G. KECKLUND[1]
[1]Stockholm University, Stockholm, SE, [2]Karolinska Institute, Stockholm, SE

Objectives: It is generally assumed that stress impairs and shortens sleep, making sleep initiation difficult and sleep termination premature. This picture is mainly based on clinical observations. Similarly, it is assumed that sleepiness would lead to longer sleep duration. However, there seems to be no empirical field data to support these notions. The present study set out to investigate the relation between stress at bedtime and mean sleepiness during the day (at 8 points) and subsequent sleep sleep duration across 42 days.

Methods: Fifty healthy participants maintained a sleep/wake diary and recorded actigraphy across 42 days. The results were analyzed using a mulitlevel, mixed model approach which makes possible a day-to-day prospective correlative approach while accounting for individuals. In order to control for other factors that might serve as confounders also weekend/workday (next day) was used as a predictor (0/1), as was duration and time of termination of prior sleep, alcohol intake and, finally, subjective health.

Results: Each unit on the stress scale (1–5) reduced sleep duration by 19 min (95% Confidence interval = 14–24 min), while sleepiness increased TST by 11 min (Ci = 7–15 min) per unit (scale: 1–9). Weekend increased sleep duration by 35 min (Ci = 21–49) per unit (0–1). The intercept was 304 min, repreenting weekday sleep with no stress and low sleepiness).

Interestingly, lights out and time of day was predicted by different factors. Lights out was predicted by Sleepiness during the day (ß = -0.22, Ci = -0.28–0.15, $P < 0.0001$) and weekend (ß = 0.86, Ci = 0.62–1.09, $P < 0.0001$), with an intercept at 24.74 (decimal or 0043 h). Time of awakening was predicted by Weekend (ß = 1.38, Ci = 1.09–1.68, $P < 0.0001$) and Stress/worries at bedtime (ß = -0.15, Ci = -0.06–0.24, $P < 0.001$), with an intercept of 6.73 h (decimal, or 0641 h).

Conclusions: The results suggest that sleepiness at bedtime increases sleep duration by phase advancing lights out and that stress/worries at bedtime reduces TST by curatiling sleep prematurely.

Poster Session – Medical Disorders and Sleep

P477

Assessment of relationship between snoring and ischemic heart disease

A. MOZAFARI[1], S. F. HEJAZI[2] and Z. AFRAKHTEH[2]
[1]Islamic Azad University, Qom, IR, [2]University of Medical Scinece, Qom, IR

Introduction: Snoring is common in the general population, with up to 25% of women and 45% of men reporting habitual snoring. Snoring is the main symptom of OSA, one of the most frequent symptom of OSA which affects 4% of middle-aged men and 2% of middle-aged women. Snoring were the associated with a significantly increased risk for acute myocardial infarction and stroke in men and women in some articles. Epidemiologic studies in Caucasian populations have shown association snoring and sleep apnea with vascular disease.

Method: This article was case-control study. All patients who were done cardiac vessel angiography put in two groups. Ninety-three patients were normal or <50% stenosis and another 108 with 1, 2 or 3 vessel disease (>50% stenosis). Then complete demographic and laboratory data, ESS, Berlin questionnaire (risk factor for OSA) and analyze them in according to chi-square and pearson correlation coefficient in SPSS software 18.

Results: Mean age 56.8 ± 12 that 119 (59%) patients were female. There weren't significant difference among snoring with IHD (76.7% and 62.8% in case and control respectively $P = 0.506$), severe snoring with IHD ($P = 0.73$) and snoring with ejection fraction ($P = 0.511$). It was showed significant correlation among IHD with risk factor for OSA ($P < 0.05$), snoring with HTN ($P < 0.0001$), snoring with IDDM ($P < 0.05$) and snoring with ESS ($P < 0.05$).

Conclusion: In this study we showed that there wasn't significant difference between snoring and severity of snoring with IHD.

P478

The effect of obesity levels on sleep quality and quantity

S. C. CHUNG[1], C. C. HUANG[2], W. C. LIAO[3] and H. N. CHEN[2]
[1]Chang Gung University, Taoyuan, TW, [2]Chang Gung Memorial Hospital, Taoyuan, TW, [3]Chung Shan Medical University, Taichung, TW

Background: Obesity has been reported to be associated with different types of sleep problems (or disturbance), such as decreasing sleep time, reduction in sleep quality, and the development of sleep breathing disorders. The relation between obesity and sleep problem is proposed to be mediated by two appetite-related neuropeptides- leptin and ghrelin. The role of leptin and ghrelin on the development of obesity-related sleep disturbance is not fully explored, especially in Taiwanese population.

Objectives: This one-year study was aimed to investigate the effect of different obesity levels on sleep quantity and quality among Taiwanese adults, by taking the proposed mediating hormonal factors- leptin and ghrelin into account.

Method: One hundred and twenty-one participants (aged 20–50, 60 males and 61 females) with different obesity levels were recruited. Participants' demographic, anthropometric, and serum leptin and ghrelin data were collected during their clinical visits; perceived sleep quality and sleep quantity information were recorded for 3 days by using sleep diary and actigraphy.

Results: (i) reduced ghrelin levels and elevated leptin levels were significantly associated with increased BMIs, (ii) a negative association was found between BMI and sleep efficiency, (iii) higher in serum leptin levels were significantly associated with decreased sleep quality and elevated insomnia scores, and (iv) higher ghrelin levels were associated with higher total sleep time and total time in bed.

Conclusion: In this study, we identified that higher obesity levels are associated with elevated leptin, reduced ghrelin, and lower sleep efficiency. Elevated in BMI is also associated with increased frequency of nocturnal awakenings, decreased sleep efficiency, and poor sleep quality while considering the mediating effects of serum leptin and ghrelin levels into account.

P479

Sleep and related factors in older adults with diabetes

W. C. LIAO[1], C. P. KUO[1], C. N. HUANG[2] and S. L. HWANG[3]
[1]Chun Shan Medical University, Taichung, TW, [2]Chun Shan Medical University Hospital, Taichung, TW, [3]National Taipei University of Nursing and Health Sciences, Taipei, TW

Objectives: Sleep is an important indicator for quality of life. Patients with diabetes often have sleep disorders, especially symptoms of insomnia or sleep apnea. To have a better sleep quality during night time and maintain daytime function without excessive sleep, affirming related factors for sleep management is vital. Diabetes associated complications and symptoms may contribute to sleep disorders. This study explored sleep at night and day in older diabetics and examined factors contributed to poor night time sleep and excessive daytime sleep.

Methods: Ninety-nine (41 males and 58 females) type 2 diabetes patients aged 55–81 years (mean ± SD = 66.5 ± 7.1) voluntarily participated in this study. The average duration of diabetes since diagnosed was 10.9 ± 7.5 years. The Pittsburg Sleep Quality Index (PSQI ≥ 5) and the Epworth Sleepiness Scale (ESS ≥ 10) were used to assess sleep quality and excessive daytime sleep. Glycemic control was assessed by hemoglobin A1c (HbA1c). Diabetic complications including vascular disease, retinopathy, neuropathy, and nephropathy were retrieved from medical records.

Results: Of 64.9% of patients had poor glycemic control (HbA1c > 7) and 56.6% had at least one of diabetic complications. The majority of participants slept <7 h (67.7%) and 65.7% were classified as having poor quality of sleep. More female complained of poor sleep (66.2%). In contrast, only 5.1% claimed having more than 9 h of sleep a night, and 29.3% were classified as having excessive daytime sleep. The leading causes to disturb night time sleep perceived by participants were nocturia (68.7%) and cough or snoring (36.4%). Poor night time sleep was associated with retinopathy (OR = 5.28, 95% confidence interval 1.41–19.76) after adjusting for age and gender. Excessive daytime sleep was associated with snoring (OR = 2.94, 95% confidence interval 1.11–7.79) after adjusting for age, gender and BMI.

Conclusion: In our sample, poor night time sleep is more dominate than excessive daytime sleep in older diabetics. Retinopathy may be a leading factor to affect sleep. Since eyes play a major role in receiving light to regulate human sleep-wake cycle, impaired eyes may affect sleep. Further study is needed.

P480

Sleep duration and obesity in asthma

M. TEODORESCU[1], S. FERGUSON[1], D. POLOMIS[1], F. CONSENS[2], R. CHERVIN[2] and M. C. TEODORESCU[1]
[1]University of Wisconsin School of Medicine and Public Health, Madison, US, [2]University of Michigan Health System, Ann Arbor, US

Objective: Obesity is more prevalent in asthmatics. Short sleep duration has emerged as novel risk factor for obesity in general populations. We aimed to test the association of sleep duration and asthma characteristics with obesity.

Methods: Adult asthma patients followed at tertiary Pulmonary/Asthma Clinics were surveyed on demographics, habitual sleep duration and asthma symptom frequency. Medical records were used to help assess asthma severity step, identify current medications and diagnosed comorbid conditions. Obesity was defined as a BMI ≥ 30 kg/m^2. Habitual sleep was categorized as short (<7 h), normal (7–8 h) and long (>8 h). Inhaled corticosteroid (ICS) doses were categorized as low, moderate and high.

Results: Among 611 participants, mean BMI was 30 ± 8; 249 subjects (41%) were obese. In bivariate analyses, short sleep duration, higher asthma step and inhaled corticosteroid doses, oral corticosteroid and long acting beta 2-agonist use, rhinitis and psychiatric disease were associated with obesity. With adjustment for covariates, the statistical significance of the association of short sleep duration (P = 0.008), asthma step (P = 0.02), and psychiatric disease (P = 0.01) with obesity were maintained, with a trend observed for the relationship with high ICS dose (P = 0.10). As compared to normal sleepers, among short sleepers, the odds of being obese were 69% higher [95% confidence interval (1.14–2.48), P = 0.008]. Independent of above covariates, with each one-step increase in asthma severity, the likelihood of obesity increased by 22% [95% confidence interval (1.03–1.43), P = 0.02].

Conclusions: Obesity in asthmatics is associated with short sleep duration, asthma severity, and psychopathology. Although this cross-sectional study cannot prove causality, we speculate that further investigation of sleep may provide new opportunities to reduce the rising prevalence of obesity among asthmatics.

P481

Fatigue in sleep disorders before and after treatment, and in other neurological diseases – Assessment of its severity and its nature

N. T. ECONOMOU[1], M. MANCONI[1], E. BONANNI[2], S. MARELLI[3], C. GOBBI[1], L. PETRINI-KLIEBER[1], M. MAESTRI[2], E. IACOPINI[2], C. ZECCA[1], M. GOLA-BRICALLI[1], C. CEREDA[1], C. LIMONI[1], O. PETRINI[1], L. MURRI[2], L. FERINI-STRAMBI[3] and C. BASSETTI[4]
[1]Neurocenter of Southern Switzerland, Lugano, CH, [2]University of Pisa, Pisa, IT, [3]San Raffaele University, Milan, IT, [4]University of Berne, Berne, CH

Objectives: Fatigue is highly prevalent in a variety of disorders, however it remains an under-diagnosed issue in neurological field and in particular in sleep disorders (SD). Concerning fatigue and SD, several issues need to be addressed: the correlation between fatigue's severity and SD severity, fatigue's amelioration after treatment of SD; moreover it is unknown whether SD sufferers who complain also about fatigue, refer strictly to the fatigue's symptoms or also to its behavioral consequences. The above-mentioned items represent the aims of this study.

Methods: Prospective, observational, multicentre study, carried out on 694 SD patients (447M, 247F, age 54.27 ± 13.13 years), on 131 fatigue-free healthy controls (52M, 60F, age 52.12 ± 11.24 years), on 41 multiple sclerosis (MS) patients (13M, 28F, age 25.24 ± 7.24 years), and on 15 patients with a previous stroke (8M, 7F, age 47.68 ± 10.89 years). SD patients were diagnosed for (%): sleep apnea (44.6), insomnia (21.9), RLS/PLMI (8.1), EDS/Hypersomnia of other origin (8.1), parasomnia (7.4), narcolepsy with cataplexy (1.2), other sleep-wake disorders (1.6) and a combination of more than one SD (7.1). Patients and controls completed two different fatigue scales: the Fatigue Scale (FS) and the Fatigue Severity Scale (FSS). FS aims to detect the fatigue symptoms (both physical and mental), while FSS comprises also questions on fatigue's behavioral impact. SD patients completed both scales before and after specific treatment.

Results: FS and FSS normal cut-offs are 3/4 and 4 respectively. FSS score was beyond the normal value for both SD and MS patients (SD: 4.1 ± 1.7, MS: 4.2 ± 1.7), while FS score was abnormal only for SD patients (SD: 4.5 ± 4.4, MS: 3.2 ± 3.3). Stroke patients and controls had normal fatigue scores (Stroke FS: 2.9 ± 3.4, FSS: 3.9 ± 1.6, Controls FS: 2.3 ± 3.4, FSS: 3.0 ± 1.4). Thus, according to FSS, SD and MS patients reported significantly more fatigue compared to healthy controls (P < 0.05), while based on FS, SD, MS and stroke patients presented more fatigue compared to controls (no significance was achieved). The treatment of SD implied a significant normalization of fatigue in both scales (FS: 2.3 ± 3.8, FSS: 1.9 ± 2.1) (P < 0.01).

Conclusions: Fatigue is a common finding in SD, as common as in MS patients. Following SD treatment, a significant improvement of fatigue was recorded. Finally, in SD assessment, a tool measuring not only fatigue's symptoms but also its behavioral consequences seems to be mostly appropriate.

P482

Type 2 diabetes prevalence increases with sleep-disordered breathing severity in the general population: the HypnoLaus Study

J. HABA-RUBIO[1], D. ANDRIES[1], N. TOBBACK[1], J. VAUCHER[2], P. MARQUES-VIDAL[2], G. WAEBER[2], P. VOLLENWEIDER[2], M. TAFTI[1] and R. HEINZER[1]
[1]Center fo investigation and research in sleep, Lausanne, CH, [2]Internal Medicine Department, Lausanne, CH

Objectives: The prevalence of type 2 diabetes is reportedly increased in patients with sleep disordered breathing (SDB). The aim of our study was to determine the prevalence of type 2 diabetes in a large unselected middle-aged European population according to SDB severity.

Methods: Of 1066 subjects (47.8% women, 50.2 ± 5.7 years old, BMI 25.3 ± 4.1 kg/m^2) participating in an ongoing population-based sleep cohort study (HypnoLaus, Lausanne, Switzerland) underwent complete polysomnographic recordings at home. SDB severity was assessed using the apnea-hypopnea index (AHI) defined according to the AASM 2007 criteria. All subjects had an extensive clinical workup including fasting glucose and insulin level measurements. Type 2 diabetes was defined as a fasting glucose level ≥ 7.0 mM or the use of an antidiabetic treatment.

Results: Mean AHI was 6.4 ± 10/h. Prevalence of SDB defined as an AHI >5/h, >15/h and >30/h was 36.5%, 11.2% and 3.6%, respectively. Mean ESS score was 6.9 ± 4.1. Mean neck circumference was 36.6 ± 5.1 cm. There was a positive correlation between AHI and plasma glucose levels (r = 0.28, P < 0.0001) and between AHI and insulin levels (r = 0.27, P < 0.0001). The prevalence of type

2 diabetes was 3.1% for an AHI<5/h, 7.4% for an AHI between 5 and 14.9/h, 11.0% for an AHI between 15 and 29.9/h and 20.5% for and AHI ≥ 30/h ($P < 0.0001$). Fasting glucose level (mM) was: 5.5 ± 0.6; 5.8 ± 1.0; 6.0 ± 0.9; and 6.5 ± 1.1 ($P < 0.0001$); Insulin level (mU/l) was 6.17; 8.45; 8.81 and 11.94 respectively ($P < 0.0001$) for the corresponding AHI categories. These differences remained significant after adjustment for age, sex, BMI, waist and neck circumference: $P = 0.0014$ (glucose level) and $P = 0.008$ (insulin level).

Conclusion: In HypnoLaus population-based study, there is a positive correlation between AHI and glucose and insulin levels. The prevalence of type 2 diabetes as well as glucose and insulin levels increase with increasing AHI. These differences remain highly significant after adjustment for the main confounding factors.

P483

Differences between patients with arterial hypertension (controlled and resistant) versus control in a population with obstructive sleep apnoea syndrome – a retrospective study

O. C. DELEANU[1], A. E. MALAUT[2], R. ULMEANU[3], D. POCORA[2] and F. D. MIHALTAN[1]

[1]University of Medicine Carol Davila, Bucharest, RO, [2]National Institute of Pneumology Marius Nasta, Bucharest, RO, [3]Oradea University of Medicine, Oradea, RO

Objectives: Resistant hypertension (RTH) is common in obese patients, refractoriness among them is frequently caused by obstructive sleep apnea syndrome (OSAS). A previous study conducted in our clinic showed that controlling blood pressure values leads to erasing excessive daytime somnolence and some other OSAS symptoms. We studied the differences between these two distinctive groups and a control population (without hypertension-HT) in order to understand our previous findings.

Methods: After applying the exclusion criteria (central/mixed sleep apnea syndrome, obesity-hypoventilation/overlap syndrome, obstructive/restrictive respiratory dysfunction, CPAP failure) to 422 patients, we compared 27 patients with controlled HT and OSAS matched up with 27 patients with OSAS but without HT, and similar, seven patients with RHT versus seven patients with OSAS without HT. Patients were matched-up by body mass index (BMI) and gender. We studied differences in demographics, anthropometrics, symptoms, comorbidities, sleep study's report (χ^2 test, T-test, Pearson).

Results: Group I: 27 patients with OSAS and controlled HT versus 27 patients with OSAS without HT: controlled HT patients were older (58.41 years ± 12.12 versus 47.59 ± 10.09, $P = 0.001$), had a lower Epworth Sleepiness Score (ESS = 8.15 ± 7.81 versus 11.69 ± 6.51, $P = 0.044$), suffer from insomnia in a higher rate (52% versus 20%, $P = 0.018$) and associate more cardiovascular and metabolic comorbidities (ischemic heart disease, heart rhythm disorders, stroke, dyslipidemia). Group II: seven patients with RTH and OSAS versus seven patients with OSAS: RTH patients had more nightmares (57.1% versus 0%, $P = 0.018$) and, as controlled HT patients, associate more cardiovascular and metabolic comorbidities: ischemic heart disease and dyslipidemia. Other significant differences were not found probably due to small number of patients in the RTH group. Pearson correlation showed no association between ESS or blood pressure values and any other studied variable.

Conclusion: In controlled HT versus control group a significant lower Epworth score was observed in patients with controlled HT (in concordance with our previous study). These patients suffer from insomnia in a higher percent, consistent to literature data which indicate that certain antihypertensive drugs contribute to insomnia onset. Special attention should be given to patients with treated hypertension, suspecting OSAS even in the absence of excessive daytime sleepiness.

P484

Correlations between pulmonary function and sleep respiratory events – a retrospective study conducted on obstructive sleep apnoea versus overlap syndrome patients

O. C. DELEANU[1], D. POCORA[2], S. MIHAICUTA[3], A. MALAUT[2] and F. D. MIHALTAN[1]

[1]University of Medicine Carol Davila, Bucharest, RO, [2]National Institute of Pneumology Marius Nasta, Bucharest, RO, [3]University of Medicine Victor Babes, Timisoara, RO

Background: Chronic obstructive pulmonary disease (COPD) and obstructive sleep apnea syndrome (OSA) are frequently encountered diseases, their coexistence (overlap syndrome = OS) is due to chance and the prevalence is 0.5–1%. The literature shows (only) that OS is associated with more severe nocturnal desaturation.

Method: We compared two populations, each of 24 patients with smoking history, diagnosed with OSA (apnea-hipopnea index AHI >5/h), one associating COPD matched by gender, smoking status, age and AHI, regarding to anthropometric variables, Epworth scale (ESS), pack-year index (PY), daytime saturation (SaO_2) and sleep study reports. Patients with central apnea syndrome, obesity-hypoventilation syndrome and restrictive ventilatory disfunction were excluded. For the analysis we used SPSS (T test, χ^2 test, Pearson correlation).

Results: OS patients are heavier smokers (43.79 ± 25.97 versus 17.79 ± 12.33YP), more obese (40.3 ± 7 versus 34.3 ± 4.93kg/m^2), more sleepy (ESS = 12.79 ± 6.42 versus 8.75 ± 6.86), have lower daytime SaO2 (91.87 ± 5.39 versus 96.55 ± 1.23%) compared to OSA patients, without any significant differences regarding neck circumference and ENT alterations. After CPAP, OS patients have a higher hypopnea index (23.4 ± 14.47 versus 10.05 ± 11.01/h) and greater nocturnal desaturation (67.76 ± 25.14 versus 13.26 ± 18.82%). Both before and after titration, OS patients have a greater hypopnea index ($P < 0.001$) and smaller apnea index ($P = 0.005$) compared to OSA patients. Pulmonary function (FEV1) correlates with the obesity degree (r = -0.31, $P = 0.03$), oxygen saturation (r = 0.56, $P < 0.001$), minimum nocturnal O2 level (r = 0.83, $P < 0.001$), apnea index (r = 0.44, $P = 0.002$) and hypopnea index (r = -0.72, $P < 0.001$). CPAP properly corrects the respiratory events in both groups of patients, but nocturnal hypoxaemia is still an issue in OS patiens.

Conclusions: Patients with OS are more obese, more sleepy and, at similar values of AHI, have less apnea and more hypopnea events compared to OSA patients; this differences persist under CPAP and are correlated with pulmonary function. There are studies necessary to elucidate the pathophysiology of this peculiarity.

P485

Physical activity and self-care activities among type 2 diabetic patients: the role of insomnia impact and vital exhaustion

R. PISANTI, S. BUCCI, D. COSTANZI, A. NUZZI, V. MARINO, A. CARNOVALE, S. MORANO, C. LOMBARDO and C. VIOLANI

Sapienza University of Rome, Rome, IT

Objectives: Within an health protection framework, we examined in a group of diabetic type 2 patients how and to what extent the impact

of insomnia and negative affect are associated with physical activity and with adherence to important self care activities (monitoring diet, blood glucose, feet, etc); having controlled the role of the perceived severity of diabetes and of the perceived interferences with daily activities.

Methods: We interviewed 147 diabetic type 2 patients (63% male) on the following areas: (i) perceived severity of diabetes and its complications, and perceived interference of diabetes with daily activities, work, and social activities, measured through the Multidimensional Diabetes Questionnaire (Talbot et al., 1997), (ii) Vital Exhaustion measured by the Maastricht Questionnaire (Appels, et al., 1987), (iii) A score of insomnia impact calculated from the Sleep Disorder Questionnaire (Violani et al., 2004), (iv) A score of physical activity derived from the Physical Activity Scale for the Elderly (PASE; Washburn et al., 1993), (v) A global score of self care activities calculated on the basis of the Summary of Diabetes Self-Care Activities Measure (SDSCA, Toobert et al., 2000). We used a series of hierarchical regression analyses for each criterion variable (PASE and SDSCA). Firstly we controlled for interference and severity of diabetes. In the second block we entered: vital exhaustion and insomnia impact. Subsequently, in the third block, we considered the two ways interaction of vital exhaustion and impact insomnia.

Results: Higher levels physical activity were associated with higher scores of perceived severity (Beta = 0.36; $P < 0.000$) and lower levels of interference of diabetes (Beta = -0.19; $P < 0.05$). Furthermore the interaction between vital exhaustion and insomnia impact was significant (Beta = 0.28; $P < 0.05$). Patients characterized by lower levels both of vital exhaustion and insomnia impact were more prone to declare to engage in physical activity. With regards to self care, lower scores of monitoring diet, feet and blood glucose were associated with higher scores of insomnia impact (Beta = -0.29; $P < 0.05$).

Conclusion: Findings suggest that vital exhaustion and insomnia impact play an important role in the adherence to prescribed behaviors among type 2 patients. The process of disease management in diabetic type 2 patients should be integrated with counseling regarding sleep hygiene.

P486

Epidemiology of symptoms of obstructive sleep apnoea and lung function in nocturnal gastroesophageal reflux

Ö. I. EMILSSON[1], C. JANSON[2], B. BENEDIKTSDÓTTIR[1], S. JÚLÍUSSON[3] and T. GÍSLASON[1]

[1]University of Iceland, Reykjavik, IS, [2]Uppsala University, Uppsala, SE, [3]Landspitali University Hospital, Reykjavik, IS

Background: Nocturnal gastroesophageal reflux (nGER) has received increasing interest as a predisposing factor for respiratory diseases and sleep disturbances. The evident association between obstructive sleep apnea (OSA) and nGER is of special interest. The aim of this study was to explore the association between nGER and respiratory diseases, lung function and symptoms of OSA.

Methods: Participants in the Burden of Obstructive Lung Disease (BOLD) initiative in Iceland and Sweden, a random sample from the general population of 1325 adults aged 40+ (>70% response rate), were compared by pre- and post-bronchodilator spirometry, answers to questionnaires about OSA and respiratory symptoms, health, and symptoms of GER.

Results: Altogether 102 participants (7.7%) reported nGER and 249 used medication against GER. Participants were divided into three groups: (i) No nGER ($n = 1040$), (ii) treated GER without nGER ($n = 183$), and (iii) nGER ($n = 102$). The nGER group had a significantly higher prevalence of respiratory and OSA symptoms than subjects without nGER. Observed apneas were twice as common among the nGER group than the no nGER group (5.1% versus 10.8%, $P = 0.02$). The nGER group also had a higher prevalence of COPD (GOLD stage 1 +), (25.0% versus 15.6%, $P = 0.02$) and lower FEV1/FVC ratio (95.9% versus 98.9% of the predicted, $P = 0.01$). These associations remained significant after adjusting for smoking, weight and other possible confounders. No independent association was found between having treated GER and lung function, respiratory or OSA symptoms.

Conclusions: Untreated nGER in a general population is associated with both respiratory and OSA symptoms as well as airflow obstruction.

P487

Onset of symptoms of obstructive sleep apnoea and asthma in persistent nocturnal gastroesophageal reflux

Ö. I. EMILSSON[1], A. BENGTSSON[2], K. A. FRANKLIN[2], K. TORÉN[3], B. BENEDIKTSDÓTTIR[1], A. FARKHOOY[4], J. WEYLER[5], S. DOM[5], W. DE BACKER[5], T. GÍSLASON[1] and C. JANSON[4]

[1]University of Iceland, Reykjavik, IS, [2]Umeå University, Umeå, SE, [3]University of Gothenburg, Gothenburg, SE, [4]Uppsala University, Uppsala, SE, [5]University of Antwerp, Antwerp, BE

Background: Nocturnal gastroesophageal reflux (nGER) is associated with asthma and obstructive sleep apnea (OSA), but prospective studies are lacking. Our aim was to investigate whether nGER is a risk factor for onset of asthma, respiratory and OSA symptoms in a prospective population based study.

Methods: We invited 2640 subjects from Iceland, Sweden and Belgium for two evaluations with a nine years interval. They participated in structured interviews, answered questionnaires, underwent spirometries and methacholine challenges. Blood samples were analyzed for specific IgE.

Results: Subjects with persistent nGER ($n = 123$) had an independent increased risk of new asthma at follow-up [OR (95% CI): 2.3 (1.1–4.9)]. Persistent nGER was independently related to onset of respiratory symptoms [OR (95% CI): 3.0 (1.6–5.6)]. The risk of developing symptoms of OSA was increased in subjects with new and persistent nGER [OR (95% CI): 2.2 (1.3–1.6) and 2.0 (1.0–3.7), respectively]. No significant association was found between nGER and lung function or bronchial responsiveness.

Conclusions: Persistent nocturnal gastroesophageal reflux contributes to the development of asthma and respiratory symptoms. The risk of new onset of OSA symptoms is higher among subjects with nGER. These findings support that nGER may play a role in the genesis of respiratory symptoms and diseases.

P488

Quality of life among sleep apnoea patients before and after treatment with continuous positive airway pressure compared to controls from the general population

B. EYSTEINSDÓTTIR[1], E BJÖRNSDÓTTIR[1], C. JANSON[1], E. S. ARNARDÓTTIR[1], A. PACK[2], B. BENEDIKTSDÓTTIR[1] and T. GÍSLASON[1]

[1]The National University Hospital, Reykjavík, IS, [2]University of Pennsylvania School of Medicine, Philadelphia, US

Objectives: The aim of this study was to compare health-related quality of life between a large group of patients with obstructive sleep apnea (OSA) and subjects from the general population. In addition,

the change in quality of life with continuous positive airway pressure (CPAP) treatment was explored.

Methods: The OSA subjects (n = 822) were untreated newly diagnosed with moderate or severe OSA (665 males, 157 females). The control subjects (n = 742) were randomly selected Icelanders (394 males, 348 females) who participated in another epidemiological study (www.boldcopd.org). Quality of life was measured by the Short Form 12 (SF-12) which gives a physical component score (PCS) and mental component score (MCS). Scoring are transformed into a scale ranging from 0 (worst possible health) to 100 (best possible health). The change with CPAP treatment was assessed after two years and 90.1% (n = 741) of the OSA subjects finished the two-year follow up.

Results: OSA patients reported worse quality of life than controls from the general population [mean PCS 40.3 ± 10.9 versus 50.7 ± 8.0 for controls (P < 0.0001) and mean ± MCS 48.3 ± 10.9 versus 51.4 ± 4.7 for controls (P < 0.0001)]. Among OSA patients, both mental and physical health improved from baseline to follow up (mean change for PCS = 2.57 ± 9.4 and for MCS = 2.37 ± 11.12). Altogether, 64% of OSA patients were using CPAP at the two-year follow up and most of them were full users. Among CPAP users, there was an increase in MCS of 2.6 ± 11.1 versus 1.9 ± 11.3 among non-users and in PCS of 3.0 ± 9.0 versus 1.8 ± 10.2 among non-users. The difference between users and non-users was however non significant.

Conclusion: OSA patients report severely impaired quality of life compared to controls, especially in physical quality of life. Even though both physical and mental health improves from baseline to follow for OSA patients, the improvement is not significantly greater among CPAP users.

P489

Prevalence of sleep disorders in Ehlers-Danlos syndrome: a questionnaire study

A. METLAINE[1], C. HAMONET[1], M. ELBAZ[1], K. YAUY[1], D. FREDDY[2] and D. LÉGER[3]

[1]Université Paris Descartes, Paris, FR, [2]APHP Hotel Dieu, Paris, FR, [3]Hôpital Sainte Anne, Paris, FR

Context: The Ehlers-Danlos Syndrome (EDS) is a clinically group of connective tissue disorders characterized by joint hypermobility, skin hyperextensibility, and tissue fragility. Althought sleep complaints are very common, there are limited studies about sleep disorders according to international classifications in these patients.

Objectives: The aim of this study was to determine the prevalence of sleep complaints, insomnia, sleep related breathing disorders (SRBD), restless legs syndrome (RLS) and excessive daytime sleepiness in patients suffering from hypermobilty type of EDS.

Methods: Patients coming from the EDS center of our hospital were sytematically interwied on their sleep, using HD42 DMSIV criteria for insomnia, RLS, the Berlin questionnaire and the Epworth Sleepiness Scale (ESS and the Insomnia Severity Index (ISI). Psychological status was assessed by the Hospital Anxiety and Depression Scale including depression subscale and anxiety subscale.

Results: Forty patients (38 Females et two males) were included in this study. The mean age of the group is 37.6 ranged from 14 to 63 years. The mean of BMI is 23kg/m^2 (14.9–35.8 kg/m^2). Anxiety was found in 55% of the patient and depression in 35%. Insomnia was reported by 95% of the patients. Of the respondents with insomnia 75% had difficulties of initiating sleep, 88% had difficulties of maintaining sleep, and 55% reported early morning awakening. The mean ISI score was 18.1, 81% of the patients had moderate to severe insomnia (ISI score > 14). The prevalence of RLS and OSAS were 42.5% and 17.5%, respectively. Sixty three percent of the patients had excessive daytime sleepiness; the mean score of ESS was 13.7.

Conclusions: Insomnia may be considred as a criteria symptom amongst patients with hypermobility type EDS. The most frequent complaints are the difficulties of maintaining sleep. Pain and anxiety may influence those sleep disturbance. Restless leg syndrome seems to be more frequent than OSAS. Our study calls for greater attention to sleep complaints in these patients, and suggest that an optimal management of pain and anxiety may improve sleep quality of such patients.

P490

Leg thermal therapy could improve sleep structure without changing sleep-disturbed breathing in patients with chronic heart failure

M. NISHIZAKA, H. SAWATARI, E. EURA, A. YANAI, A. RAHAMAWATI, T. IDE, S. INOUE, M. TAKEMOTO, M. MIYAZONO, N. HASHIGUCHI, K. SUNAGAWA, A. SUYAMA-CHISHAKI and S.-I. ANDO

Kyushu University, Fukuoka, JP

Backgrounds: An increasing number of patients with CHF are suffering from refractory symptoms to the conventional pharmaceutical therapy and have problems of sleep related to pulmonary congestion or resultant Cheyne-Stokes respiration, which is also impairing their QOL and might induce depression. We have recently reported that leg thermal therapy (LTT) is effective in improving the hemodynamics, vascular endothelial function, and reducing oxidative stress in patients with CHF. We also found, through their questionnaire, improved quality of sleep such as sensation of deep sleep, less daytime sleepiness and fewer nightmare, which might be related to better QOL of the patients. However, no objective or quantitative analysis about the effect(s) of LTT on sleep quality has been investigated.

Objectives: The aim of this study was to determine whether the LTT has a positive impact on sleep quality in patients with CHF.

Methods and Results: Three patients with CHF (53 ± 5 y.o., left ventricular ejection fraction = 26 ± 12%) underwent LTT (45°C) for 20 min. Immediately after the treatment, the core temperature had barely increased (0.2 ± 0.2°C, P < 0.05) as we reported previously. The LTT improved endothelial function indexed by flow-mediated vasodilatation (%FMD) from 4.6 ± 2.1 to 5.9 ± 1.3%. Full polysomnography (PSG) which was performed to evaluate the efficacy on sleep before introduction and after 3 days protocol of LTT showed no improvement in apnea hypopnea index (34.8 ± 26.5 versus 40.6 ± 28.5/h) but marked increase in sleep stage 3 plus 4 (Stage 3 + 4: 9.8 ± 3.9 versus 22.7 ± 10.8%). No patients had any adverse effects associated with the LTT.

Conclusions: LTT acutely improved not only vascular endothelial function, but also sleep structure without changing the characteristics of sleep disturbed breathing in patients with CHF. Although these are tentative data and the long term effect of LTT on sleep disturbance or prognosis remains to be investigated, current result suggests that LTT could be used to improve not only vascular function but also QOL of the worst CHF patients through improvement of their sleep quality.

P491

The first report on Down's syndrome and sleep abnormalities in Saudi Arabia

M. G. JAMIL, H. BANJAR, S. AL-ZABIN, J. JECINTHA and H. KATTAN

King Faisal Hospital and Research Center, Riyadh, SA

Introduction: Children with DS are prone to develop obstructive sleep apnea syndrome because of chronic upper airway obstruction. Untreated OSA results in serious morbidities including failure to thrive, pulmonary hypertension (PHT), poor academic performance, and deterioration in mental function. The prevalence of OSA in children with DS has been reported to be between 45% and 50%.

Objective: The aim of our study is: To identify the prevalence of OSA in Pediatric patients with DS that are referred to Pediatric services, from the period 1st January 30 December 2011 for respiratory symptoms and regular check up.

Methods: Prospective Sleep study (Polysomnography) was carried out in the sleep laboratory. Demographic, clinical, diagnostic, morbidity, mortality data, sleep studies abnormalities, and type of medical or surgical interventions were reported.

Results: A total of 23 patients confirmed DS clinically and by Chromosomal studies. Fifteen male (65%), eight female (35%). The most presenting symptoms were: snoring 19 (82%), Shortness of Breath 16 (70%), cough 16 (70%), witness apnea 16 (70%), increase body movements in 18 (78%), Rhinorrhea in 14 (61%), Sweating 13 (56%), Mouth breathing in 16 (70%), frequent URI in 17 (73%), Difficulty in Swallowing in 5 (22%), difficulty in hearing in 4 (17%), EDS in 6 (26%), Enuresis in 5 (22%), Aggressive behaviors in 9 (39%), Asthma in 14 (60%), Recurrent pneumonia in 13 (57%), Home O2 requirement in 4 (17%), Hypothyroidism in 6 (26%), Gastro-esophageal reflux (GER) in 4 (17%). Sleep Study was done in all 23 patients. Nineteen patients (83%) showed sleep related disorder breathing (SRDB). Abnormal mean AHI of 12.3 (Normal <1.5%) in 19 patients (83%), mean OA index (OAI) of 4.7 in 11 patients (48%), abnormal hypopnea index of 5.6 ($N \leq 1$), abnormal PLM of mean 5.9 in 6 patients (26%). Sixteen of 23 patients (70%) have congenital heart disease (CHD). PHT was detected by Cardiac Cath in 10 patients (43%) with mean PAP 40 mmHg. Persistent PHT at follow up was detected in 8 (35%) of patients with mean PAP of 55 mmHg.

Conclusion: Sleep related disorder breathing (SRDB) is common in patients with Down syndrome (DS) and has been under estimated by many physicians for a long time. Such patients should be screened for sleep abnormalities especially with significant respiratory or sleep disturbance symptoms. Medical or surgical options should be offered to such patients without delay to prevent complications.

P492

Sleep curtailment is associated with altered autonomic tonus in eutrophic individuals

W. A. MORAES, D. POYARES, L. BITTENCOURT, M. MELLO and S. TUFIK

University Federal of Sao Paulo, Sao Paulo, BR

Introduction: Increased sympathetic tonus has been suggested as a mechanism linking short sleep duration to overweight and hypertension. The present study was proposed to assess autonomic tonus in relation to sleep duration in a representative sample of eutrophic individuals from the general adult population.

Methods: A representative sample of the city of Sao Paulo was selected (20–80 years), including 1024 individuals, from which 224 females and 193 males were eutrophic (body mass index ≤ 25). They underwent full polysomnography with ECG recording. Heart Rate Variability (HRV) was analyzed for the whole night using a polysomnography ECG lead (D2 modified). Time and Frequency domains variables were calculated for individuals who slept more (controls) and <5 h (experimental group) per night, assessed by objective measures. One-way ANOVA was performed considering insomnia syndrome and AHI > 5 as covariates.

Results: Sleep curtailment was significantly associated with reduced SDNN ($P = 0.02$) and SDNNINDEX ($P < 0.01$) which are related to a reduction in HRV. RMSS was also reduced ($P < 0.01$) indicating reduction in parasympathetic tonus, and LF/HF ratio increased suggesting high sympathetic tonus.

Conclusion: Sleep shortage was associated with reduced HRV and parasympathetic tonus, and increased sympathetic tonus in eutrophic individuals. These findings support the concept that altered autonomic tonus is associated to sleep curtailment independently from the presence of obesity. This alteration could mediate the link between short sleep, obesity and cardiovascular risk. Longitudinal studies are needed to support this hypothesis.

P493

Analysis of sleep disturbances related to falls in cirrhotic patients

S. GIMÉNEZ[1], S. ROMERO[2], S. CLOS[3], E. ROMÁN[3], G. SORIANO[3] and R. ANTONIJOAN[3]

[1]Institut de Recerca de l 'HSCSP, Barcelona, ES, [2]Universitat Politècnica de Catalunya, Barcelona, ES, [3]Hospital de Sant Pau. UAB, Barcelona, ES

Objectives: Sleep difficulties are very common reported in patients with cirrhosis, but objective polysomnographic (PSG) data evaluating these sleep disturbances are scarce. There is a growing interest to investigate the factors that could be involved in the increased risk of falls in patients with cirrhosis. The aim of this study was to evaluate nocturnal sleep in patients with cirrhosis assessing possible subjective and EEG sleep differences between patients with and without minimal hepatic encephalopathy (MHE) and between those who presented falls or not.

Methods: Twelve cirrhotic patients with and without MHE participated in the study, including five patients who reported falls in the previous year and seven without falls. Quantitative sleep variables were evaluated using visual analysis according to the American Academy of Sleep Medicine and all-night sleep electroencephalogram spectral analysis (slow wave activity – SWA, 0.5–4.0 Hz; and spindle frequency activity – SFA, 11.0–14.0 Hz). Subjective sleep features were evaluated by the Self-assessment Scale for Sleep and Awakening quality.

Results: Cirrhotic patients with MHE presented a longer REM sleep latency ($P < 0.077$), decreases in REM sleep stage duration ($P < 0.008$) with a statistical significant worsening in subjective sleep quality ($P < 0.030$) in comparison to those patients without MHE. Although not significant, the energy of SWA and SFA calculated in the first nonREM-REM cycle was much lower for patients with encephalopathy in comparison to those without. Significant decreases in total sleep period ($P < 0.062$), total sleep time ($P < 0.077$), stage 2 duration ($P < 0.069$) and sleep efficiency ($P < 0.090$) with an additional worsening of subjective sleep quality ($P < 0.085$) and sleep efficiency (0.062) in patients with falls compared to those patients without them. Spectral analysis did not show any significant difference between both groups.

There were no significant differences in the apnea-hiponea index neither periodic leg movement index among cirrhotic patients with MHE and falls.

Conclusions: Sleep differences were obtained among cirrhotic patients with disturbing effects on sleep in patients with MHE and those who suffered falls. These sleep disturbances could contribute to the increase of falls in patients with cirrhosis. Further studies with a large sample size are necessary to confirm these results.

P494

An exploratory study of dissociated states during sleep in patients with fibromyalgia

T. F. OLIVEIRA[1], L. FERREIRA[2], J. SANCHES[3] and T. PAIVA[4]
[1]FMUL/ISPA-IU/CENC, Lisbon, PT, [2]CENC, Lisbon, PT, [3]ISR-IST, UTL, Lisbon, PT, [4]FMUL/CENC, Lisbon, PT

Introduction: Fibromyalgia (FMS) is a chronic syndrome of widespread pain and fatigue. It has been suggested that it is a psychosomatic response to psychological distress, but several underlying organic factors exist and symptoms have intriguing and ambiguous characteristics. We hypothesize that this disorder is explained by the dissociated state (DS) concept. A DS is a state that gathers characteristics from two functional states that should not coexist. A clear example is the alpha-delta sleep pattern, somehow reflecting a 'sleeping-awake' state. Having in mind that FMS patients may suffer from 'dissociation', it is very important to characterize their awake and sleep brain microstates.

Objectives: Our main goal was to test the presence of DS during sleep, both in NREM and in REM, in patients with FMS and healthy controls.

Methods: Nine women (ages 30–57) with FMS and 9 age-matched healthy controls performed a polysomnography (PSG) at our sleep laboratory, using a 19 EEG channels. Participants completed several questionnaires: FIQ and PSQI. All FMS subjects had at least 11 tender points (TP). PSG exams were scored according to the AASM 2007 criteria; the DS were marked in each 30 s epoch. The dissociations observed were: alpha-delta sleep; presence of rapid eye movements or saw tooth like activity in N2; the presence of alpha and spindle like activity in REM; slow eye movements in N2. Sleep parameters were introduced in tables for statistical analysis.

Results: The percentage of epochs with DS was significantly higher in FMS than in controls, as well as sleep latency, REM latency and PSQI total score. On the contrary, sleep efficiency was higher in controls. PSQI total score was positively correlated with total percentage of epochs with DS as well as with sleep latency, and was negatively correlated with sleep efficiency.

Conclusion: The analysis of EEG activities in FMS seems to reveal a consistent reduction of delta during NREM2 and a persistent dominance of more rapid frequencies throughout the night, as well as a high predominance of abnormal events in stages where they shouldn't occur. This is in favour of a deficient homeostatic process for sleep. These DS in FMS revealing the difficult boundaries between stages are in line with other clinical symptoms of dissociation, namely in what concerns pain and disease severity evaluation.

Funded by: FCT PRAXISXXI/BD/36746/2007 & FCT PTDC/SAU-BEB/104948/2008.

P495

Polysomnography findings in patients with fibromyalgia and chronic pain

L. C. GUZMÁN[1], S. DE LA TORRE[1], M. J. JURADO[1], O. ROMERO[1], L. VIGIL[1], C. TURPIN[2], C. GALISTEO[2], M. LARROSA[2], M. JODAR[2] and M. J. MASDEU[2]
[1]Hospital Vall d'Hebron, Barcelona, ES, [2]Parc Tauli Sanitary Coorp, Barcelona, ES

Objectives: Patients with fibromyalgia (FMS) usually present sleep disorders and nonrestorative sleep as a prominent feature. Several studies have reported a correlation between this pathology and disturbances in sleep architecture, continuity, respiratory patterns and periodic limb movements (PLM) during sleep. Nowadays, comparative studies with other chronic pain processes are scarce. Our main objective is to evaluate the polysomnographic (PSG) findings in patients with FMS and compare them to healthy subjects and to chronic pain patients.

Methods: Observational study. We recruited 30 postmenopausal women with fibromyalgia, 17 with chronic pain (CP) and 25 healthy women, aged matched. They underwent one night PSG. None had any medical or psychiatric disorder. No subject was taking psychotropic medications. Sleep studies were scored, following the standard criteria. Data was summarized as mean ± standard deviation and compared using Student's T-test.

Results: Women with FMS in comparison to controls, showed longer sleep latency ($P = 0.02$), more stage shifts ($P = 0.02$), less sleep efficiency ($P = 0.02$) and more respiratory effort related to arousals (RERA) ($P = 0.001$). Patients with fibromyalgia and chronic pain also showed more PLM index, both compared to controls ($P = 0.02$ and $P = 0.01$).

Conclusions: Patients with fibromyalgia showed some disturbances in sleep microstructure (more stage shifts and less sleep efficiency), higher RERA index and more PLM; but no significant differences in sleep macrostructure compared to controls were found. These findings are similar to those reported in bibliography. There were no significant differences in sleep characteristics between patients with fibromyalgia compared to those with chronic pain. On the other hand, patients with chronic pain showed more PLM than healthy subjects, but no differences were found in any other PSG parameter also compared to controls.

P496

Fibromyalgia and gender differences in respiratory parameters during sleep

E. MIRÓ[1], G. PRADOS[1], P. MARTÍNEZ[2], A. SÁNCHEZ[2], S. LÓPEZ[3], G. SAÉZ[3], M. LAMI[1] and F. DIENER[1]
[1]University of Granada, Granada, ES, [2]Faculty of Psychology, Granada, ES, [3]Virgen de las Nieves University Hospital, Granada, ES

Objective: Several studies have hypothesized that sleep-disordered breathing might be involved in the aetiology of the non-refreshing sleep symptoms reported by fibromyalgia (FM) patients. However, the possible existence of gender differences in the relationship between fibromyalgia and sleep-disordered breathing remains ambiguous. The aim of the present study was to explore the differences in respiratory parameters during sleep between male and female FM patients and their relationship with non-restorative sleep patterns.

Methods: Two clinical groups (18 males and 22 females) of participants from 30 to 60 years old who met the diagnostic criteria

for FM as defined by the American College of Rheumatology underwent full-night polysomnography recording.

Results: The main explanatory variable was group (female versus male). Data were summarized as mean and standard deviation. Student's T test revealed significant group differences in respiratory patterns. Male patients had significantly greater alterations in respiratory and oxymetry variables than females. FM males had a greater number of desaturations per hour of sleep (mean ± SD, 20.1 ± 23.1 versus 7.1 ± 8.5; $P < 0.03$) and higher scores in the apnoea/hypopnoea index (mean ± SD, 27.1 ± 24.6 versus 12.7 ± 9.6; $P < 0.01$). Males also showed more transient arousal from sleep associated with respiratory events compared to females ($t = 15.5$, $P < 0.01$). Simple Pearson correlation coefficients confirmed significant associations between respiratory parameters and some sleep patterns in the male FM group. The desaturation index correlated positively with the stage shift index ($r = 0.595$, $P < 0.01$) and the apnoea/hypopnea index correlated negatively with the duration of the REM stage ($r = -0.514$, $P < 0.05$).

Conclusions: Our findings suggest that alterations in sleep respiratory patterns are more frequent in male FM patients than in female FM patients. The alterations in sleep patterns, non-refreshing sleep and other FM-related symptoms observed in this population might be part of a primary respiratory sleep problem.

This study is part of a broader research project financially supported by the Spanish Ministry of Science and Innovation (research project PSI2009-13765PSIC).

P497

Sleep disturbances and chronic fatigue – 1–10 years after haematopoietic stem-cell transplantation

D. SCHMID, G. DEURING, A. KISS and P. GROSSMAN
University Hospital, Basel, CH

Aims: Sleep disturbances and chronic fatigue are common, debilitating consequences among patients who have undergone hematopoietic stem-cell transplantation (HSCT) as therapy for malignant diseases of the blood-forming system. Fatigue is difficult to treat, and not well understood in terms of etiology or course. We present findings of a study to identify physiological and psychological parameters differentiating 71 HSCT recipients, 1–10 years post-transplantation (mean 4.2; SD 2.6 years) compared to 44 age-, gender- and BMI (mean 23.2., SD 2.4) matched healthy individuals, in terms of group differences and correlations of fatigue and disturbed sleep.

Methods: Cardiovascular, respiratory and activity parameters were recorded using the LifeShirt during a 24-h daily-life ambulatory assessment. 'Sleep' was defined by protocol as reported time going to bed combined with locomotor activity and heart rate. For the time-in-bed period respiratory symptoms (apnea/hypopnea) and out-of-bed events were scored. Retrospective self-report questionnaires assessed QoL, fatigue, anxiety, depression and HSCT-related complaints.

Results: HSCT survivors as compared to controls reported significantly higher levels of fatigue and sleep disturbances. On physiological measures, patients manifested lower respiratory sinus arrhythmia, higher heart rate and increased locomotor activity, longer wake periods and significantly increased apnea index during night time. Within the patient group, level of fatigue was strongly associated with subjective sleep quality and night time activity. Fatigue was weakly and inconsistently related to other physiological night time parameters and physical functioning.

Conclusions: Cardiac autonomic functioning may be impaired among HSCT survivors. HSCT fatigue appears to be related to extent of perceived symptoms, but inconsistently to physiological parameters.

P498

Sleep, pain and psychosocial variables in fibromyalgia: gender differences

E. MIRÓ[1], G. PRADOS[2], P. MARTÍNEZ[1], A. SÁNCHEZ[1], M. LAMI[1], F. DIENER[1], S. LÓPEZ[2] and G. SÁEZ[2]
[1]University of Granada, Granada, ES, [2]Virgen de las Nieves University Hospital, Granada, ES

Objective: The prevalence of fibromyalgia (FM) is much lower in men than women. Therefore, current knowledge about this chronic pain syndrome has been developed mainly from research with women. The aim of the present study was to compare sleep parameters and clinical symptoms between male and female FM patients and to analyze possible differences in the relationship between sleep and the main clinical manifestations of FM.

Methods: Forty FM patients (18 males and 22 females) from 30 to 60 years old who met the diagnostic criteria for FM of the American College of Rheumatology underwent nocturnal polysomnography. Several aspects of pain, sleep, fatigue, psychopathology, emotional distress and functional impact of FM were evaluated with questionnaires.

Results: Males had more microarousals per hour of sleep than females (mean ± SD, 23.2 ± 14.7 versus 10.8 ± 4.9; $P < 0.01$). Similarly, 61% of male FM patients had an apnoea/hypopnoea index (AHI) >15 compared to 31.8% of females; in addition, a desaturation index above five was twice more prevalent in men. No differences between both groups were found in parameters related to sleep architecture, level of pain, emotional distress or social dysfunction. Yet, relationships between duration of sleep stages and psychosocial variables were different depending on the sex. In the female group, the duration of stage 2 correlated positively with Fibromyalgia Impact Questionnaire scores ($r = 0.433$; $P < 0.05$) and anxiety seemed to be negatively associated with the duration of the REM stage ($r = -0.424$; $P < 0.05$). By contrast, males had greater pain perception when the duration of stage 2 was greater ($r = 0.487$; $P < 0.05$) and worse social functioning associated to shortened deep sleep ($r = -0.567$; $P < 0.05$).

Conclusions: Sleep fragmentation and alterations in the duration of sleep stages may be involved in the clinical and psychosocial problems of FM. Gender differences in the manifestations of these symptoms may be the expression of different physiopathological sleep processes in men and women.

This study is part of a broader research project financially supported by the Spanish Ministry of Science and Innovation (research project PSI2009-13765PSIC).

P499

Insomnia, mood and fatigue symptoms among newly diagnosed breast cancer patients

K. RANDELL, C. ESPIE, D. MORRISON, J. PAUL and L. FLEMING
University of Glasgow, Glasgow, UK

Objectives: Sleep disturbance is a common symptom affecting women undergoing treatments for breast cancer. Often occurring around diagnosis, symptoms regularly persist beyond completion of active treatment, causing significant disruption and distress. Insomnia symptoms tend to exist within a symptom cluster affecting sleep,

mood and fatigue. The aim of this study is to describe the natural history of insomnia in breast cancer patients; interplay between sleep and related symptoms; and potential 'critical' periods where intervention may be most effectively implemented.

Methods: This ongoing longitudinal study is measuring sleep and related symptoms among 250 newly diagnosed breast cancer patients. Participants provide a retrospective account of sleep quality using the Insomnia Severity Index (ISI); prior to diagnosis, and then monthly for the year following diagnosis. Using a modified version of the ISI (including frequency of symptoms and use of sleep medication) allows participants to be classified as 'Good Sleepers'; those with 'Insomnia Symptoms'; and those with 'Insomnia Syndrome'. The Hospital Anxiety and Depression Scale (HADS) and Fatigue Severity Scale (FSS) provide measures of mood and fatigue symptoms at 0, 3, 6, 9 and 12 month assessment points.

Results: Currently, 110 females are participating in the study. This interim analysis reports data from 24 participants who have completed measures up to 3 months. Exploration of sleep data reveals a pre-diagnosis median ISI score of 3.5, increasing to 10.0 at month 0 (shortly after diagnosis). Scores remain in the range of subclinical sleep disturbance at months 1 (10.5) and 2 (9.0), peaking at month 3 (13.0), during active treatment. Pre-diagnosis, 61.5% of participants were 'Good Sleepers', dropping to 26.9% by month 3. Conversely, only 7.7% of participants were experiencing 'Insomnia Syndrome' pre-diagnosis, rising to 30.8% at month 3. Exploring mood and fatigue variables at month 3 reveals moderate positive associations between ISI and HADS scores ($r = +0.43$, $P = 0.029$) and ISI and FSS scores ($r = +0.39$, $P = 0.056$).

Conclusion: These early findings provide information on the time course of disturbed sleep among breast cancer patients and associations between sleep, mood and fatigue symptoms during active cancer treatment. On completion, this study will provide important novel data on the natural history of sleep disturbance in this population, with implications for the implementation of evidence based treatments.

This study is funded by Breast Cancer Campaign.

P500

The relationship between depressive symptoms and restless legs syndrome in two independent prospective cohort studies

A. SZENTKIRÁLYI[1], H. VÖLZKE[2], W. HOFFMANN[2], B. T. BAUNE[3] and K. BERGER[4]

[1]University of Münster, Münster, DE, [2]University Medicine Greifswald, Greifswald, DE, [3]University of Adelaide, Adelaide, AU, [4]Institute for Epidemiology and Social Medicine, Münster, DE

Background: Cross-sectional studies suggest a strong association between depression and restless legs syndrome (RLS), however, the temporal relationship between the two disorders remains unknown.

Aim: We sought to prospectively examine the temporal relationship between depressive symptoms and RLS in the general population.

Methods: Two independently conducted prospective cohort studies, the Dortmund Health Study (DHS, $n = 1312$, follow-up time: 2.2 years) and the Study of Health in Pomerania (SHIP, $n = 4308$, follow-up time: 5.2 years) were used for the analyses. RLS was assessed in both studies according to the RLS minimal criteria, at baseline and at follow-up. Depressive symptoms were assessed by the Center for Epidemiologic Studies–Depression scale in DHS only at baseline and by the Munich-Composite International Diagnostic-Screener in SHIP both at baseline and at follow-up.

Results: Participants with depressed mood at baseline were more likely to report new-onset RLS in both studies (in DHS: OR = 1.94, 95% CI 1.09–3.44; in SHIP: OR = 2.37, 95% CI 1.65–3.40) after adjustment for sociodemographics, lifestyle factors and co-morbidities. RLS at baseline was an independent risk factor of incident depressive symptoms in SHIP (odds ratio: 1.82, 95% CI 1.10–3.00).

Conclusions: The presence of depressive symptoms may be a risk factor of RLS in the general population. The relationship between the two disorders seems bidirectional, however, as RLS also predicted the development of depressive symptoms.

B.B.: received travel support to RLS meeting from the U.S. Restless Legs Foundation; K.B.: received travel support to RLS and other meetings from NIH and the U.S. Restless Legs Foundation.

P501

Insulin resistance enhanced arterial stiffness in OSAHS with metabolic syndrome

H. MITSUBAYASHI, M. OHTSU, T. ISHII, A. SUZUKI, M. NAKAUMA, U. SATOSHI, Y. NAKAHARA, H. MITSUYASU, Y. YOSHIDA, Y. KAMEI and A. KOMORI

Nippon Dental University, Tokyo, JP

Purpose: The aim of this study was to evaluate the relationship between the effect of continuous positive airway pressure (CPAP) and the change of arterial stiffness in obstrucive sleep apnea hypopnea syndrome (OSAHS) with metabolic syndrome (MS).

Methods: Thirty five OSAHS males with MS as experimental groups and twenty five OSAHS males without MS as controls were enrolled and were evaluated by polysomnography (PSG) during sleep. Alll subjects were 30–70 years old in hospital from April 2005 to September 2011. Cardio-ankle vasucular index (CAVI) is superior to estimate the extent of atherosclerosis in large arteries. Therefore, We measured CAVI as arterial stiffness in all subjects before and after CPAP treatment.

Result: Apnea-hypopnea index (AHI) in OSAHS males with MS group higher than that in control group (39.7 versus 32.5 $P < 0.05$). CAVI in OSAHS males with MS group were similar to that in control group (8.58 versus 8.33). After CPAP treatment, AHI decreased in both groups (5.1 versus 4.8 n.s). CAVI in OSAHS males with MS group strongly decresed compare to control group (6.16 versus 7.15 $P < 0.01$).

Conclusion: To conclude, these findings suggest the improvements of CAVI in OSAHS males with MS group by CPAP that may contribute to improvements of insulin resistance

Poster Session – Sleep Disorders: Psychological and Social Factors

P502

Does keeping a sleep diary promote selective attention and sleep worry? A single-blind randomised controlled clinical trial

M. SERNEE and G. KERKHOF
MCH Hospital, The Hague, NL

Study objectives: To evaluate the impact of keeping a sleep diary upon sleep-related worry and anxiety in insomnia patients.
Design: Single-blind randomized controlled clinical trial.
Setting: Specialized sleep treatment centre.
Methods: participants consisted of 37 randomly selected consecutive patients (22 females and 15 males; mean overall age: 49 years), that were referred by the neurologist for psychological treatment. All participants met the ICSD-2 criteria for insomnia. Participants where randomly assigned to an experimental group (N = 19; mean age: 50 years) or a control group (N = 18; mean age: 49 years). Patients in the experimental group where asked to keep a sleep diary for six consecutive weeks. Participants in the control group where on a waiting list. Controls who (on their own initiative) did keep a sleep diary or underwent a treatment for there sleep problems during the six weeks of the trial, where as yet excluded. At baseline, and two and six weeks later, both groups where asked to fill in a number of sleep questionnaires. Questionnaires consists of Dutch translations of the Sleep Associated Monitoring Index (SAMI), the Dysfunctional Believes and Attitudes Scale (DBAS) and the State-Trait Anxiety Inventory (STAI).
Results: repeated-measures analysis of variance, with 'group' as between-subjects factor and 'time' as within-subjects factor, failed to show any significant main or interaction effects.
Conclusion: These results indicate that daily self-monitoring of sleep does not negatively impact upon sleep worry or anxiety, as suggested by Espie et al (Sleep Med Rev, 2006).

P503

Psychometric properties of the Insomnia Catastrophising Scale

M. JANSSON-FRÖJMARK[1], A. G. HARVEY[2] and I. FLINK[3]
[1]Stockholm University, Stockholm, SE, [2]Berkeley University, San Francisco, US, [3]Örebro University, Örebro, SE

Objectives: Few questionnaires have been developed and validated to specifically index insomnia-specific cognitive mechanisms. The purpose of this study was to investigate the psychometric properties of a newly developed instrument, the Insomnia Catastrophising Scale (ICS). We seek to examine the factorial validity and internal consistency, discriminative and convergent validity along with associations with anxiety, depression, sleep parameters, and daytime impairment.
Methods: Participants (n = 1803) from a randomly selected sample of the general population completed a survey that probed demographics, night-time symptoms, daytime impairment, anxiety and depression. The ICS was also administered. Excluding those with a sleep disorder other than insomnia, the study sample consisted of 1558 participants.
Results: Of the twenty original ICS items, three were removed due to low communality. Exploratory factor analysis of the eleven items indexing night-time catastrophising indicated a one-factor solution (59.1% variance), strong primary loadings, and high internal consistency (alpha = 0.92). Analysis of the six items indexing daytime catastrophising indicated a one-factor solution (70.1% variance), strong primary loadings, and high internal consistency (alpha = 0.91). The internal consistency for the total ICS was 0.95. At scale-, subscale-, and item-levels significant mean differences were noted between three groups which differed on insomnia symptomatology; the insomnia disorder group (n = 113) reported significantly higher scores than the poor sleep (n = 247) and normal sleep groups (n = 1157), and the poor sleep group exhibited significantly higher scores than the normal sleep group. Receiver operating characteristics analyses indicated that when using an optimal cut-off for the ICS, the sensitivity was 84.1% (detecting those with insomnia disorder) and specificity was 81.5% (detecting those with normal sleep). The ICS was significantly associated with anxiety and depression (P = 0.44–0.54), total wake time (beta = 0.38), total sleep time (beta = 0.29), sleep quality (P = 0.49), and daytime impairment (P = 0.57).
Conclusion: The ICS can be considered as a reliable and valid questionnaire for indexing insomnia-specific catastrophising. The use of the ICS is recommended in research and clinical settings for assessing insomnia-related catastrophising.

P504

Associations between psychological factors and night-time/daytime symptomatology in insomnia

M. JANSSON-FRÖJMARK[1], A. G. HARVEY[2], A. NORELL-CLARKE[3] and S. J. LINTON[3]
[1]Stockholm University, Stockholm, SE, [2]Berkeley University, San Francisco, US, [3]Örebro University, Örebro, SE

Objectives: Cognitive models of insomnia underscore cognitive mechanisms as important in the maintenance of insomnia. The aim of this study was to examine psychological factors in insomnia and the association between psychological mechanisms with night-time and daytime symptoms.
Methods: In a cross-sectional examination, participants (n = 2327) from a randomly selected sample of the general population completed a survey on demographic parameters, night-time symptoms, daytime impairment, health outcomes, and psychological factors intended to index five cognitive processes (Harvey, 2002). Excluding those with a sleep disorder other than insomnia, the study sample consisted of 1890 participants.
Results: Relative to poor and normal sleepers, the insomnia group scored higher on worry, beliefs, physiologic arousal, monitoring/attentional bias, and safety behaviours relative to the other two groups, and the poor sleepers exhibited a similar pattern relative to the normal sleepers. High total wake time was associated with more worry, physiologic arousal, and safety behaviours (26.3% variance), low sleep restoration with more worry, unhelpful beliefs, and monitoring/attentional bias (28.2% variance), and low sleep quality with higher scores on all the psychological mechanisms (35.8%

variance). Elevated daytime symptoms were related to more unhelpful beliefs and monitoring/attentional bias (44.3% variance).
Conclusion: The findings show that psychological factors discriminate those with insomnia from those with poor or normal sleep. The results also indicate that psychological factors are linked to insomnia-specific night-time and daytime symptomatology.

P505

Psychological factors and their association with persistent insomnia

A. NORELL-CLARKE[1], M. JANSSON-FRÖJMARK[2], M. TILLFORS[1], A. G. HARVEY[3] and S. J. LINTON[1]
[1]Örebro University, Örebro, SE, [2]Stockholm University, Stockholm, SE, [3]University of California, Berkeley, US

Objectives: Models of chronic insomnia suggest that cognitive and behavioural factors may maintain sleep problems. This study focused on five psychological factors outlined by Harvey (2002): unhelpful beliefs about sleep, monitoring for sleep-related threats, sleep-related safety behaviours, pre-sleep somatic arousal, and sleep-related worry. The aim was to investigate if the degree of psychological factors at baseline would differ between three groups of stable sleep classifications over 18 months, defined as having either 'insomnia disorder', or 'poor sleep' or 'normal sleep' at both times. Another aim was to investigate if people with persistent insomnia would differ from those with improved sleep (e.g. insomnia to normal sleep) regarding the same psychological factors.
Methods: A longitudinal design with two measurement points, 18 months apart, was used. Participants (n = 1561) from a randomly selected sample of the general population completed a survey that included the five factors outlined by Harvey (2002).
Results: The persistent insomnia group had higher scores on all factors, compared with the persistent poor sleep group (worry: d = 0.92; beliefs: d = 0.85; somatic arousal: d = 0.58; monitoring: d = 0.88; safety behaviours: d = 0.91) who in turn had higher scores than the persistent normal sleep group (worry: d = 0.72; beliefs: d = 0.46; somatic arousal: d = 0.79; monitoring: d = 0.67; safety behaviours: d = 0.84). Investigating insomniacs only, the persistent insomnia group displayed more worry (d = 0.47), safety behaviours (d = 0.45), and more monitoring (d = 0.40) at baseline, compared with the group of people whose insomnia remitted fully over time. Those with remitted insomnia had a larger change (lowering) of worry (d = 0.43), dysfunctional beliefs (d = 0.52), monitoring (d = 0.52) and safety behaviours (d = 0.67) between the two measure points compared with the persistent insomnia group.
Conclusion: Persistent insomnia was linked to a higher degree of psychological factors compared with those with persistent poor sleep or persistent normal sleep. Worry, dysfunctional beliefs, monitoring and safety behaviours may have maintaining effects, as lower scores at baseline and/or a lowering of them over time were associated with remittance from insomnia.

P506

Motivation to sleep and nap quality in good sleepers

I. RUSAKOVA[1], E. RASSKAZOVA[2] and V. DOROKHOV[3]
[1]Severtsov Institute Ecology/Evolution Russian Academy of Sciences, Moscow, RU, [2]Lomonosov Moscow State University, Moscow, RU, [3]Neurocenter of the Southern Switzerland, Lugano, CH

Objectives: Recently, a growing number of researches focused on the feature of psychological factors in sleep disturbances. Excessive attempts to fall asleep may be one of these factors. The aim of this work is to study the effect of motivation to sleep on the characteristics of nap in good sleepers.
Methods: Thirty-three young good sleepers (22 F, 11 M, 24.1 ± 8.4 years) visited laboratory twice at the same afternoon time (during consecutive weekends). They were randomly assigned to a sequence of instructions: either 'free (lie, as if during daytime you lay down to rest) – motivating (very important for you to fall asleep as soon as possible, and if you succeed, you will receive additional financial remuneration)' (N = 17) or 'motivating – free' (N = 16). The polysomnography was recorded for 1 h by a polygraph 'Sagura Medizintechnik GmbH' and then scored manually according to standard standard criteria of the American Association of Sleep Medicine:
The results were processed using analysis of variance with repeated measures.
Results: Regardless of the order of instructions, in motivational condition there were increases in the latent period of the delta-sleep (F = 4.4, P < 0.05), duration of wakefulness during sleep (F = 6.5, P < 0.05), the number of episodes of prolonged (more than 3 min) awakenings (F = 4.6, P < 0.05), and – as a tendency – the number of all awakenings, and their maximum duration (F = 3.5, P < 0.1 and F = 4.0, P < 0.06). The latent period of sleep depended largely on the order of instructions, but the interaction was observed (tendency F = 3.2, P < 0.1): the subjects fell asleep longer in motivation condition, but only in the 'motivational-free' instructions' sequence.
Conclusions: Regardless of the order of instructions motivation to sleep as fast as possible affects nap quality: it becomes more superficial and fragmented. It can be assumed that the instruction affects the latent period of sleep, but it is influenced by other factors as well (order of instructions), that requires further research. Thus, we have received confirmation of the negative impact of excessive attempts to fall asleep to nap quality in good sleepers, that allows to indirectly confirm the hypothesis about the same mechanism in insomniac patients.
The study is supported by a grant RFH project 11-36-00242a.

P507

Emotion regulation, negative affect and insomnia

C. VIOLANI, G. BATTAGLIESE, R. PISANTI and C. LOMBARDO
Sapienza University of Rome, Rome, IT

Objectives: In the present two-wave prospective study, we examined how and to what extent emotion regulation (reappraisal and suppression) and a measure of negative affect are associated with insomnia complaints.
Methods: Two hundred and forty-eight participants in apparent good health (mean age: 26.4 ± 7.7).
Data collected at T1 and after two months (T2) included: 1. Vital Exhaustion (VE; Appels et al, 1987) measures negative affect through questions concerning feelings of fatigue, scarce energy and demoralization;
2. Emotional Regulation Questionnaire (ERQ; Gross, John, 2003): this questionnaire contains items regarding reappraisal and suppression, the prevalent emotional strategy is defined on the basis of the difference between the two scales;
3. Life Events: based on a check list of 18 stressors. We calculated the difference at T2 and T1.
4. Sleep Disorder Questionnaire (SDQ, Violani et al., 2004): based on this brief questionnaire we evaluated the presence of insomnia according to DSM-IV criteria and its impact through the number of daytime consequences

Results: Through hierarchical regression analyses (HRAs) we have examined how life events, negative affect and the prevalent use of two emotion regulation strategies, reappraisal and suppression, predict across-time changes in the impact of insomnia measured at T2. In the first block we included the insomnia impact measured at T1, while in the second block we entered the two way interactions between the predictors. The first block ($F_{4,204} = 20.57$; $P < 0.001$) accounted for the 28.7% of the variance and insomnia measured at T1 was the only significant predictor beta = 0.48). The second block accounted for a significant portion of variance (R2change = 0.045, $P = 0.02$; $F_{9,199} = 11.00$; $P < 0.001$; 33% total variance); significant effects were: insomnia measured at T1 beta = 0.59), the two-way interaction between insomnia measured at T1 and life events beta = 0.16), and the two way interaction between insomnia and vital exhaustion (beta = -0.17).

Conclusion: At time 2 the impact of insomnia is mostly associated with the impact of insomnia at time 1; this association is exacerbated by stressing life events. Furthermore at T2 insomnia will get worse among subjects who at T1 have a low impact of insomnia and high Vital Exhaustion.

P508

Personality traits in epilepsy patients with and without insomnia

L. GHAHRAMANYAN[1], D. GEVORGYAN[1] and S. KHACHATRYAN[2]
[1]Yerevan State University, Yerevan, AM, [2]Somnus Sleep and Movement Disorders Clinic, Yerevan, AM

Objectives: To study the distribution of personality traits in patients with epilepsy depending on presence of insomnia

Methods: We studied patients with confirmed diagnosis of all-cause epilepsy. A short interview was performed with every patient on the current symptoms of insomnia, considering sleep-onset, sleep-maintenance and sleep fragmentation complaints. Patients with any type of insomnia were enrolled in Insomnia group (IG) and the rest were included in the Non-Insomnia Group (NIG). The personality traits were assessed by MMPI Mini-mult (a short form of Minnesota Multiphasic Personality Inventory) scales: 1 – hypochondriasis, 2 – depression, 3 – hysteria, 4 – psychopathic deviate, 6 – paranoia, 7 – psychasthenia, 8 – schizophrenia and 9 – hypomania. T-test was used for statistics.

Results: Thirty four patients with epilepsy aged 18–52 (mean age – 32.6) of which 11 were females (32.3%) were enrolled in the study. We found the following data on mean values for MMPI Mini-mult scales: Scale 1 – 54.5; 2 – 59.7; 3 – 58; 4 – 54.2; 6 – 61.1; 7 – 57.6; 8 – 57.4; 9 – 54.7. Of the studied sample 19 (55.9%) patients with epilepsy had a complaint of recent insomnia and comprised the IG. In IG the mean values for the MMPI Mini-mult scales were as follows: 1 – 58.3; 2 – 63.1; 3 – 62.3; 4 – 56; 6 – 64.3; 7 – 59.3; 8 – 59; 9 – 52.5. In NIG the mean values for the MMPI Mini-mult scales were: 1 – 49.7; 2 – 55.5; 3 – 52.5; 4 – 52; 6 – 57.1; 7 – 55.3; 8 – 55.3; 9 – 57.4. There were some differences according to the mean values. In IG the values were higher for scales 1 (hypochondriasis), 2 (depression) and 3 (hysteria) and this difference was statistically significant ($P < 0.05$). There were also higher values for scales 4, 6, 7, 8 in IG and value for scale 9 was higher in NIG. But none of the latter reached statistical significance ($P > 0.05$).

Conclusion: Our data show that more than half of the epilepsy patients had insomnia complaint. Hypochondriasis, depression and hysteria are significantly more pronounced in epilepsy patients with insomnia than in patients without insomnia.

P509

Perfectionism, repetitive thought and sleep quality in male students

T. CLEMÊNCIO, S. SÁ, A. PEREIRA and M. H. AZEVEDO
University of Coimbra, Coimbra, PT

Objective: We have shown that in young female university students the link between perfectionism and sleep quality was mediated by worry (see Poster Nordm;125). However, results might differ in male subjects. Thus, the present study aimed to examine the relationship between worry and rumination, perfectionism and sleep quality in male students.

Method: Two hundred forty-five males (mean age 19.34 ± 1.227 years) completed two Perfectionism Scales, a brief measure of Repetitive thought (tendency to worry and rumination) and a sleep-wake questionnaire including questions on sleep depth, subjective sleep quality, nighttime awakenings and sleep latency. These items were summed to form a sleep quality index (SQI).

Results: SQI significantly correlated with Social Prescribed Perfectionism/SPP (r = 0.18, $P < 0.01$), Concern over Mistakes/CM (r = 0.14, $P < 0.01$), Doubts about Actions/DA (r = 0.23, $P < 0.01$), Parental Criticism (r = 0.13, $P < 0.01$), Negative Perfectionism/NegP (Social Prescribed Perfectionism + DA + CM, r = 0.22, $P < 0.05$), Worry (r = 0.20, $P < 0.01$) and Rumination (r = 0.14, $P < 0.05$). For each of these variables, SQI total mean scores were compared in three groups, based on M ± SD (low = M-1SD; medium = M ± 1SD; high = M + 1SD). Boys with high DA, NegP and Worry presented significantly higher mean scores ($P < 0.05$) than the other groups. Linear multiple regression showed that the model composed by SPP, CM, DA, Worry and Rumination explained 7.5% of the SQI variance (R2 = 0.075, $P = 0.004$) and that only DA was a significant predictor of SQI beta = 0.163, $P = 0.064$). The model composed by NegP, Worry and Rumination explained 6.3% of the SQI variance (R2 = 0.063, $P = 0.001$) and NegP was the unique significant predictor of SQI beta =0.163, $P = 0.024$). Logistic regression was used to analyze which variables were significant predictors of high SQI (M + 1SD; $n = 178$, 72.7%) versus low SQI (M-1SD; $n = 29$, 11.8%). DA was the unique variable significantly correlating with this dichotomized variable (rS = 0.304; $P = 0.014$) and explained 9.0% (Cox e Snell R square) to 12.1% (Nagelkerke R square) of the variance ($P = 0.014$). The odds ratio (OR) was 1.184 of (ß = 0.169; Wald = 5.335; $P = 0.021$; IC 95% OR = 1.026–1.367).

Conclusion: In males, Negative Perfectionism, Worry and Rumination are associated to sleep quality. Only the dimension Doubts about Actions is a significant predictor of sleep quality.

P510

Emotional blunting in psychophysiological insomnia: preliminary results from a facial expression paradigm

S. D. KYLE, L. BEATTIE, C. MILLER, A. CLARK, Z. ROGERS and C. ESPIE
University of Glasgow, Glasgow, UK

Objectives: Experimental work suggests an important role for sleep in the processing of affective information. Psychophysiological Insomnia (PI), a disorder of persistent subjective sleep disturbance, is associated with heightened emotional arousal and the future development of psychopathology. It is currently unknown whether patients with PI exhibit alterations in the processing and/or interpretation of emotional information, relative to good sleeping controls.

Methods: In the present (ongoing) study we compared individuals with PI and good sleepers (GS) on a facial expression task, requiring participants to (i) categorize, and (ii) rate the intensity of four

emotional expression categories: angry, fearful, happy, and sad. All participants were tested at 6 pm.

Results: Eleven patients with well-defined PI (7F, Mean age = 47.4) and 8 GS (4F, Mean age = 51.4) have thus far completed the task. Preliminary results indicate no group differences with respect to categorization performance, across any of the four emotions (*P*'s > 0.34), with accuracy being high (>80%) for both groups. Intensity judgements of facial expressions were found to be significantly decreased in PI patients relative to GS for fearful ($P < 0.05$; Cohen's d = 1.20), happy ($P < 0.05$; Cohen's d = 1.00), and sad ($P < 0.05$; Cohen's d = 1.13) facial expressions, failing to meet statistical significance for Angry ($P = 0.17$; Cohen's d = 0.66).

Conclusions: Though clearly preliminary, the emerging pattern of results indicate that while overt facial expression categorization remains intact in PI, ratings of intensity appear blunted relative to GS. This intensity-blunting tends to be most pronounced for fearful, happy and sad facial expressions. Results share some similarities with recent findings from sleep-deprived healthy subjects (van der helm et al., 2010), and provide support for affective dysregulation in PI.

P511

'**Sleep well, our tough heroes!**' – Mental toughness, sleep and psychological functioning in adolescents

S. BRAND[1], S. LEMOLA[1], N. KALAK[1], M. GERBER[1], P. CLOUGH[2] and E. HOLSBOER-TRACHSLER[1]

[1]University of Basel, Basel, CH, [2]University of Hull, Hull, UK

Background: Mental toughness is an ability, which comprises the following four domains: control, confidence, challenge, and commitment. So far, nothing is known about the associations between mental toughness, sleep and psychological functioning during adolescence. The aim of the present study was therefore to explore the relation of these dimensions.

Method: A total of 284 adolescents (mean age: 18.4 years; 77% females) took part in the study. They completed a series of questionnaires related to mental toughness, sleep and psychological functioning. The questionnaire booklet was completed in about 20 min.

Results: Increased mental toughness was highly associated with favorable sleep, decreased perceived stress, favorable coping strategies, increased curiosity and optimism. Male participants reported statistically significantly increased scores of mental toughness.

Conclusions: Among a sample of late adolescents, mental toughness was positively associated with favorable sleep and favorable psychological functioning. Whereas the underlying mechanisms remained unclear, it is conceivable that improving both sleep and mental toughness might confer to increased well-being.

P512

Long-term impact of the 2009 L'Aquila earthquake on sleep quality

D. TEMPESTA[1], G. CURCIO[1], L. DE GENNARO[2] and M. FERRARA[1]

[1]Uiversity Of L`aquila, L`aquila, IT, [2]Uiversity Of Rome, Rome, IT

Objectives: Natural disasters like earthquakes are traumatic events that can manifest their long-term effects on subjective and objective sleep quality. In this study we investigated the impact of the 2009 L'Aquila earthquake on the quality of sleep of the population directly hit by the natural disaster, as well as of people living in the immediate surroundings, two years after the traumatic event.

Methods: A general community study was conducted, comparing subjective sleep assessment before and after the earthquake of people living within 110 km from the epicenter. From a population-based sample of 5200 participants balanced for gender and age, 4862 individuals were selected and asked to fill in the following questionnaires: the Pittsburgh Sleep Quality Index (PSQI) to evaluate subjective sleep quality, the PSQI Addendum to assess post-traumatic disruptive nocturnal behaviors (DNB), and the Beck Depression Inventory (BDI) to assess depressive symptoms.

Results: Sleep quality of people living in the city of L'Aquila significantly worsened after the earthquake with respect to before the traumatic event. This effects differed for specific age groups indicating a reduced quality after the earthquake mainly for adults and elderly compared to younger participants. When compared with people living in the surroundings, citizens living close to the epicenter showed the worst sleep quality. Sleep quality increased as a function of the distance from the epicenter. With respect to DNB incidence, disruptive nocturnal behaviours were more frequent in participants living close to the epicenter and in the immediate surroundings (within 40 km), and this relation was independent of age.

Conclusion: The present data show a long-lasting effect of traumatic experiences on subjective sleep measures. Even after a period of two years, people exposed to a severe stress like an earthquake continue to suffer from a reduced sleep quality and an increased frequency of disruptive nocturnal behaviours. These effects are larger around the epicenter and in the elderly.

P513

OSAS and co-morbidity of cronified (war) PTSD

R. BULJAN and A. M. SANTIC

Psychiatric Clinic Vrapce, Zagreb, HR

A number of patients with chronified (war) PTSD were addressed to our Center for resistant insomnia. By using PSG (overnight polysomnography) they were diagnosed with OSAS.

Aim of the study: To present the complexity of treatment of OSAS in comorbidity with chronified PTSD.

Materials and methods: all the participants were men with OSAS. There were 15 patients in the study group who had the comorbidity of PTSD and 20 patients in the control group without the comorbidity. In the first phase of the study we investigated differences between two groups by using the following variables: age, duration of disorder, utilization of psychopharmacologic therapy and response to the application of CPAP. After that the results were analyzed statistically.

Conclusion: in persons with the comorbidity of PTSD the results of treatment were inferior due to the rejection of a CPAP. However, in those patients from study group who had good response to CPAP there was a significant reduction of psychopharmacologic therapy.

P514

Occupational distress in a group of nurses: the moderator role of insomnia

R. PISANTI, C. LOMBARDO and C. VIOLANI

Sapienza University of Rome, Rome, IT

Objectives: The Job Strain theory proposed by Karasek and Theorell (1990) suggests that health risks are greater among people who experience high job demands (e.g., time pressure), coupled with low control (e.g., decision authority) over how their work is conducted. Demanding jobs, accompanied with low decision latitude, have been associated with various physical and psychological stress related disorders. The present cross sectional study examined in a group of nurses the possible moderator role of insomnia in the relationship between job strain (High Demands/Low Control) and emotional exhaustion and somatic complaints.

Methods.: Participants were 215 nurses (female = 84%; mean age: 44.8 ± 7.4); Predictor Variables were:
1. Measures of the occupation demands and control specific for the nursing profession (Leiden Quality of Work Life Questionaire for Nurses, Maes. et al., 1999).
2. Impact of the insomnia evaluated through the Sleep Disorder Questionnaire (Violani, et al., 2004), a brief questionnaire which evaluates the presence of insomnia according to DSM-IV criteria and its impact based on the number of daytime consequences.
Criterion Variables were: 1. Emotional Exhaustion measured through the Maslach Burnout Inventory (Maslach et al., 1996).
2. Somatic complaints measured through a scale from the Symptom Checklist (Derogatis, 1983).
Results: Results show that both levels of demands and insomnia are positively correlated with emotional exhaustion beta = 0.21; $P < 0.05$; beta = 0.33; $P < 0.005$), and with somatic complaints (beta;=0.39; $P < 0.000$; beta = 0.30; $P < 0.005$). For both criterion variables the three way interaction is significant, explaining respectively 4%; $P < 0.01$ and 6%; $P < 0.009$ of the variance. In both cases, the Slopes analyses show that the condition characterized by high demands-low control and insomnia was more detrimental for the well being of participants than the other conditions. The final model explained 45% of variance in the case of emotional exhaustion ($F_{7,83} = 9.73$; $P < 0.001$) and 37% of variance in the case of somatic complaints ($F_{7,88} = 6.69$; $P < 0.001$).
Conclusion: Insomnia seems to act as exacerbator of the effects of perceived job strain on psychological distress (emotional exhaustion and somatic complaints). These findings suggest to include sleep hygiene workshop in stress management programs for nurses.

P515

Prevalence, characteristics and response to CPAP therapy of nightmares

A. S. BAHAMMAM, S. AL-SHIMEMERI, M. SHARIF and R. SALAMA
King Saud University, Riyadh, SA

Objectives: Previous studies have reported conflicting results regarding the relationship between obstructive sleep apnoea (OSA) and dream recall and nightmares. We designed this study to assess the characteristics of OSA patients with nightmares and the effects of CPAP therapy on nightmares.
Methods: Consecutive patients (>18 years) referred to the sleep disorders center with a clinical suspicion of OSA were recruited. Patients with other sleep-related breathing disorders, psychiatric disorders and those on medications that may influence nightmares were excluded. Nightmares were diagnosed according to the International Classification of Sleep Disorders (ICSD 2005). CPAP titration was performed in accordance with the AASM guidelines and CPAP was provided to patients. Follow up was done 6–10 months later and patients with nightmares were divided into two groups; group 1, those who used CPAP with good compliance, and group 2, those who refused CPAP treatment and did not use other alternative treatments for OSA. Persistence of nightmares was assessed upon follow up.
Results: Ninety seven (49.7%) patients were diagnosed to have OSA with recurrent nightmares with a mean age of 47.0 ± 11.0 years, BMI of 36.4 ± 9.1 and apnea hypopnea index (AHI) of 42.2 ± 36.6/h. Ninety eight (50.3%) patients with OSA without nightmares had a mean age of 45.4 ± 14.2 years, BMI 35.1 ± 8.6 and AHI of 40.4 ± 34.5/h. Analysis of the presenting symptoms revealed that OSA-nightmares patients presented more frequently with witnessed apnea compared to OSA patients without nightmares (64% versus 42%, $P = 0.015$). Patients with nightmares had a significantly higher AHI during REM (52.8 ± 29.4/h versus 35.9 ± 30.8/h, $P < 0.001$). There was no relation between the severity of OSA based on AHI or time spent with O2 saturation <90% and the presence of nightmares. Thirty three patients with OSA and nightmares used CPAP regularly. Among those, nightmares disappeared in 90%. On the other hand 54 patients with nightmares refused to use CPAP and did not undergo alternative non-CPAP therapy. Among those nightmares disappeared in 68% ($P = 0.016$).
Conclusion: Nightmares is prevalent among OSA patients particularly among OSA patients in whom apnea occurs during REM sleep. CPAP therapy results in significant improvement in nightmares. Sleep disordered breathing should be considered as a possible cause in patients who present with nightmares.

P516

Dilemmas associated with having delayed sleep phase disorder

A. WILHELMSEN-LANGELAND[1], I. DUNDAS[1], I. WEST SAXVIG[1], S. PALLESEN[1], I. H. NORDHUS[1] and B. BJORVATN[2]
[1]University of Bergen, Bergen, NO, [2]Norwegian Competence Center for Sleep Disorders, Bergen, NO

Objective: Delayed sleep phase disorder (DSPD) is a sleep disorder where the circadian rhythm is significantly delayed according to the environmental demands. Existing research on DSPD has primarily focused on the sleep problems as well as the underlying circadian rhythm. Less is known about the consequences of DSPD in terms of daily life and how those with DSPD cope with their disorder. The present study aims to describe challenges concerning how to cope with DSPD in daily life.
Methods: We conducted a qualitative study using in-depth semi structured interviews focusing on the challenges associated with suffering from DSPD. A sample of 9 participants aged 16–23 years (six high school students and three university/college students; five women, four men) who all met the International Classification of Sleep Disorders (ICSD-2) criteria for DSPD were interviewed. We used systematic text condensation with four stages of analysis: review the whole text to identify themes, code units of meaning, abstract the meaning and finally summarize the content within the coded groups to generalized descriptions and concepts. The analysis was assisted by the NVivo 8 program.
Results: The analysis suggested that a core theme in the interviews was how to cope with certain specific dilemmas related to the disorder. Dilemmas were defined as a choice between equally undesirable alternatives. We labelled the specific dilemmas that emerged: (i) What shall I give up? (ii) Whom shall I blame? and (iii) Shall I regard my sleep pattern as a problem? Dilemma (i) involved deciding on one of two kinds of losses, each depending on how the subject chose to sleep: by following socially preferred sleep patterns, or one's own. Dilemma, (ii) involved losses and gains in blaming oneself, versus blaming others or biology for one's sleep patterns. Dilemma, and (iii) involved losses and gains regarding the sleep pattern as a problem, versus denying that the sleep pattern was problematic.
Conclusions: The study may increase our understanding of the perceived losses and gains of trying to adapt to socially accepted sleeping patterns and other dilemmas faced by youngsters suffering from DSPD. This understanding may assist clinicians in their work with DSPD as it points to several dilemmas where the patients feel they have to choose one of several approaches which can influence the emotional consequences of the disorder.

Poster Session – Neurological Disorders and Sleep

P517

Effect of lacosamide on sleep-wake cycle of adult patients with drug-resistant partial onset epilepsy

E. IACOPINI, L. CARNICELLI, E. DI COSCIO, M. MAESTRI, E. BARTOLINI, F. GIORGI, V. PELLICCIA, C. PIZZANELLI, A. IUDICE, U. BONUCCELLI and E. BONANNI
Neurological Clinic, Pisa, IT

Objectives: Many studies have investigated modifications of sleep structure and vigilance induced by antiepilectic drugs (AEDs) and very few data about Lacosamide (LCM) effects are present in literature. Aim of the study was to evaluate the modifications on nocturnal sleep and vigilance induced by LCM in a group of patients with drug resistant partial-onset epilepsy.

Methods: Ten consecutive adult patients, diagnosed with drug resistant focal or cryptogenic epilepsy, were enrolled in the study. All the subjects underwent psychometric evaluation with self-administered standardized scales, laboratory nocturnal polisomnography, waking video-EEG and Multiple Sleep Latency Test (MSLT) before and after 6 months of add-on 200–400 mg/die LCM therapy. Sleep microstructure was evaluated by cyclic alternating pattern (CAP) scoring. Ten healthy controls, age and sex matched, were selected for comparison.

Results: LCM improved sleep efficiency and wake after sleep onset time. CAP scoring showed decreased CAP-rate. A tendency towards improved diurnal vigilance and mood, with a reduction in the scores for depression and trait anxiety scales was observed.

Conclusions: LCM showed a positive effect on nocturnal sleep macro and microstructure, with no negative effects on diurnal vigilance when used as an add-on therapy in patients with drug resistant partial-onset epilepsy.

P518

Sleep features of the primary generalised epileptic patients and partial epileptic patients and scoring of the cyclic alternating pattern

D. TUNCEL and B. KAYA
Kahramanmaras Sutcu Imam University, Kahramanmaras, TR

Objectives: To analyze the microstructure and macrostructure of sleep and cyclic alternating pattern (CAP) ratios distribution in primary generalized and partial epileptic patients. Also to compare sleep features, distribution of cyclic alteranating pattern and effects of these on sleep structure in both of the epileptic groups.

Methods: Ten patients with primary generalized epilepsy and 10 patients with partial epilepsy diagnosed according to International League Aganist Epilepsy were admitted to study. Pittsburgh sleep quality index, Epworth sleepiness scale and sleep diary were applied to patients before recording of sleep EEG. Sleep EEG recording was done with bipolar derivations in eight channels (Fp1-F3, F3-C3, C3-P3, P3-O1 or Fp2-F4, F4-C4, C4-P4, P4-O2) at least 3 weeks before last attacks of seizures for each patient. Sleep scoring was performed using American Academy of Sleep Medicine criteria and cyclic alternating pattern was scored according to Terzano MG's consensus report and both of the groups were compared.

Results: The mean age of primary generalize epileptic patients was 27.5 and was 31.0 for partial epileptic patients. Epileptic activity was found in 50% of partial epileptic patients and 30% of primary generalized epileptic patients in sleep EEG. There was no statistically meaningful difference between two groups when sleep structure compared. The quality of sleep was low in partial epileptic patients and was found statistically meaningful. Moreover cyclic alternating pattern distribution ratios was high in partial epileptic patients and was found statistically meaningful (CAP distribution ratios 26.8% in the primary generalized epilepsy, 43.6% in the partial epilepsy). When sleep efficiency and cyclic alternating pattern ratios compared there was no statistically difference found between patients who had epileptic activity and who had not epileptic activity in sleep EEG.

Conclusion: Fragmented sleep, low quality of sleep, high ratio of cyclic alternating pattern and easily triggered epileptic activity in partial epileptic patients may be the reason of the refractory epilepsy. Therefore the true classification of seizures in refractory epileptic patients is benefical in the planning of effective treatment. Also analyzing the sleep features and distribution of cyclic alternating pattern may be benefical in the setting of treatment.

P519

Polysomnographic variables in patients with epilepsy: a preliminary evaluation in Armenia

S. KHACHATRYAN[1], Z. TAVADYAN[1], Z. KHECHUMYAN[2], N. YEGHIAZARYAN[2] and T. STEPANYAN[2]
[1]Yerevan State Medical University, Yerevan, AM, [2]Republic Epilepsy Center Erebouni, Yerevan, AM

Objectives: To assess the polysomnographic variables in patients with epilepsy in Armenia

Methods: Patients with a confirmed diagnosis of all-cause epilepsy were enrolled in the study regardless of sleep complaints. The patients had stable course of epilepsy, were on their anticonvulsant treatment for at least 3 months and they had no other serious comorbidities. They have passed a one-night polysomnography (PSG) at a sleep laboratory. It included standard PSG channels: EOG, chin EMG, ECG, airflow, respiratory effort, pulseoximetry, leg movements and body position alongside with full EEG. Scoring was performed by a trained technician supervised by a sleep clinician according to the recommended scoring rules (AASM 2007). Descriptive statistical analysis was performed.

Results: Twenty two patients with epilepsy aged 19–64 (mean age – 33 years), of which 7 were females (31.8%) were enrolled. Their mean BMI was 23.8. The following are mean variables from their PSG data. The mean apnea-hypopnea index (AHI) was 7.6/h (0.3–75.1). Of all patients 7 (31.8%) had AHI 5 and higher. Mean oxygen desaturation index (ODI) was 7.0/h (0–72.2). For periodic leg movement index (PLMI) mean was found at 3.2. Four patients (18.2%) had PLMI >5. The mean number of REM periods was 2.5 per night. The analysis of sleep stages showed the following mean percentages: NREM1 – 9.9%, NREM2 – 31.5%, NREM3 – 31.5%, REM – 7.9%, wake – 19.1%. The mean arousal index of this sample was 23/h. We also assessed the mean heart rate which was 67.2 beats per minute.

Conclusion: Our data show that sleep structure and PSG variables in patients with epilepsy are deviated from normal pattern. They have less REM duration and number of REM periods. In about a third of the patients a diagnosis of obstructive sleep apnea was confirmed. They had high degree of sleep disruption due to frequent sleep-disordered breathing events, periodic leg movements and possibly

intrinsic factors and anticonvulsants. PSG variable analysis is important to predict sleep quality in patients with epilepsy.

P520

Is sleep-onset ischaemic stroke more frequent in patients with obstructive sleep apnoea?

J. H. KIM[1], S. J. HAN[2], M. O. SHIN[1], C. M. LEE[1], Y. M. SONG[1], G.-H. LEE[1] and J. KIM[1]

[1]Dankook University College of Medicine, Cheonan, KR, [2]Wonkwang University Sanbon Hospital, Gunpo, KR

Objectives: The aim of this study is to evaluate the relationship of sleep-onset ischemic stroke and obstructive sleep apnea (OSA), and the characteristics of patients who had sleep-onset ischemic stroke.

Method: Consecutive patients with acute to subacute ischemic stroke were evaluated for the presence of OSA before stroke onset using Berlin Questionnaire (BQ). Sleep-onset ischemic stroke (SOIS) was defined as the patients who developed during sleep or detected the first neurologic symptoms immediately after sleep. Their medical history, demographic data, and neurologic examination were reviewed as well as lesion location.

Results: Four hundred and forty-seven patients with ischemic stroke have been enrolled (mean age 65.4 ± 11.4 years, 86 male). Mean body mass index (BMI) was 24.6 ± 2.94 kg/85.7% and 11.6% of 147 patients who answered BQ had a history of persistent snoring and witnessed apnea, respectively. High risk of OSA according to BQ was 41.5% (61/147). SIOS was reported in 26.7%. SOIS was insignificantly more frequent in patients with high risk OSA group. The history of witnessed apnea was more frequent in patients with SOIS than those with daytime onset stroke although statistically insignificant. The severity of neurologic deficit, prevalence of hypertension, diabetes mellitus, ischemic heart disease, age, BMI, gender and lesion location were not different between patients with SOIS and those with daytime onset.

Conclusion: Our study showed that clinical history of OSA is very prevalent in patients with ischemic stroke either with sleep-onset or daytime onset. Patients with sleep-onset ischemic stroke reported more frequent history of witnessed apnea, suggesting apneic event might be the triggering factor for the onset of ischemic stroke during sleep.

P521

Siesta-strokes: clinical characteristics and outcome of ischaemic strokes occurring during day-sleep

J. HABA-RUBIO, M. FAOUZI and P. MICHEL

Centre Hospitalier Uinversitaire Vaudois, Lausanne, CH

Objectives: In the occurrence of ischemic strokes circadian influences (blood pressure, cortisol levels and platelet aggregation circadian variations) and sleep-related cardiovascular particularities (hypotension, dysrrythmias, hypoxemia, sleep apnea) seem to play a significant role. Although some studies have examined the characteristics of strokes occurring during night-sleep none has addressed specifically the question of strokes occurring during day sleep (DS) or siesta-strokes.

Methods: We used data from the Acute STroke Registry and Analysis of Lausanne (ASTRAL), which is the prospective registry of all acute ischemic stroke patients admitted to the CHUV within 24 h after last-well time. ASTRAL includes demographic data, vascular risk factors and comorbidities, metabolic, hematological variables and vital signs on admission, stroke pathophysiology, clinical and radiological findings and outcomes.

Results: A total of 2471 consecutive patients with acute ischemic stroke were included in the study. DS was documented in 50 cases (2%). When compared with patients with known stroke onset while awake (KO) there were no significant differences with regard to demographic or clinical characteristics. Fewer DS patients were treated with a thrombolysis procedure (12% versus 28.7%, $P = 0.01$), due to late arrival at the hospital from 'last seen well' time (4.9 ± 6.4 h versus 2.2 ± 3.40, $P < 0.001$). Although differences does not reach statistical significance, patients with DS have more lacunar strokes (21.7% versus 13.8%, $P = 0.05$) and more of them were taking antihypertensive drugs at the moment of the stroke (60.4% versus 55.1% $P = 0.05$). With regard to short and long-term outcomes, there were no significant differences in the discharge NIH Stroke Scale score and the modified Rankin Scale scores at 3 and 12 months. One-year mortality rates were 30% in the DS group and 17.9% in the KO group ($P = 0.09$).

Conclusion: Within our population, 2% of ischemic strokes occurred during day-sleep (siesta strokes). They seem associated with more lacunar strokes, the use of antihypertensive drugs and higher mortality rates at one year. Few of them were treated with thrombolysis due to limitations of the current time-based therapy. Efforts are needed to develop methods to identify which of them could benefit from acute treatment minimizing risks.

P522

Impaired time perception in narcolepsy in comparison to patients with Parkinson's disease and healthy controls

R. PORYAZOVA[1], A. MENSEN[2], N. ZOLLINGER[1], F. BISLIMI[1], A. ZIOGAS[1], T. EBERLE[2], G. HUEGLI[2], L. BADEL[2], C. R. BAUMANN[1] and R. KHATAMI[2]

[1]University Hospital Zurich, Zurich, CH, [2]Klinik Barmelweid, Barmelweid, CH

Objectives: The striatum and the prefrontal cortex play an important role in cognitive time processing, and time perception depends on sustained attention. Narcolepsy-cataplexy (NC) patients are unable to maintain sustained attention, probably due to deficient hypocretin signaling. Impaired time perception has been found in Parkinson's disease (PD) and attributed to dysfunctional dopaminergic striatal pacemaker. We aimed at assessing time perception in patients with NC and PD and at comparing the outcome to that of healthy control subjects.

Methods: Seventeen HLA positive, hypocretin-deficient (13/13 tested) unmedicated (9/17) NC patients (mean age 42 years), 11 PD patients (mean age 66 years) on dopaminergic medication, and 18 healthy controls (mean age 36 years) performed a short time estimation task, where they had to estimate an interval of 1, 2 or 5 s. Accuracy of interval timing and its variability were analyzed using repeated measures ANOVA with group (NC, PD, controls) as a between subject factor and length of time to be estimated (1s, 2s, 5s) as within factor.

Results: Accuracy of time estimation for different time intervals was similar in patients and controls (main effect for length, $F = 0.14$, $P = 0.79$; main effect for group $F = 2.51$, $P = 0.095$), but variability of responses differed significantly between NC, PD and controls (main effect for group, $F = 6.02$, $P = 0.005$). *Post hoc* tests revealed that responses were significantly more variable in NC in comparison to PD and controls. In all groups response variability was higher for longer time intervals (main effect for length, $F = 18.06$, $P < 0.001$). There was no interaction between group and variability.

Conclusions: Short time perception is more variable in narcolepsy patients as compared to healthy controls and PD patients. These

preliminary data may point to a dysfunctional network that is critically involved in distinct stages of temporal processing including the prefrontal cortex and the basal ganglia.

Acknowledgements: The study is sponsored by a Swiss National Foundation (SNF) Grant.

P523

Differentiated treatment of sleep-disordered breathing in Parkinson's disease

A. HEIDBREDER, I. SUTTRUP, M. BOENTERT, A. OKEGWO, T. WARNECKE and P. YOUNG

Universiätsklinikum Münster, Münster, DE

Introduction: Sleep disorders are a common nonmotor symptom in Parkinson's disease (PD) significantly affecting quality of life. Up to now the clinical relevance and therapeutic implications of sleep disordered breathing other than obstructive sleep apnea remain unclear in PD.

Methods: Thirty-six consecutive PD patients (32 male, mean age 68.4 years, mean Hoehn and Yahr stage 2, 7) underwent cardiorespiratory polysomnography (PSG) Sleep disordered breathing was diagnosed according to criteria of ICSD-2. Treatment was started according to the following algorithm: In the first step, all PD patients with any form of sleep disordered breathing received continuous positive airway pressure (CPAP). In a consecutive night treatment efficiency was controlled by PSG. In subjects insufficiently treated apnoe hypopnea index (AHI) and oxygen desaturation index (ODI) >10/h with CPAP, ventilation therapy was escalated in a second step to Bilevel-positive airway pressure-ventilation (BiPAP) in predominant central sleep apnea syndrome (CSA) or auto-servo-ventilation (ASV) in predominat Cheyne-Stoke respiration (CSR). When patients did not tolerate CPAP and apnea occurred predominantly in supine positions they received a vest preventing supine position. Ventilation therapy was controlled after six month by PSG.

Results: We found sleep disordered breathing in 20 of the included PD patients. Thirteen patients suffered from OSA, 3 from CSA and 4 from CSR. Initial CPAP therapy was successful in 12 patients. BiPAP and ASV were initiated in two patients respectively. Two patients were provided with a vest preventing supine position. All of these 8 PD patients showed a significant reduction of AHI and ODI in the following PSG. Two patients did not tolerate any treatment strategy. None of the treated PD patients discontinued therapy during the follow-up period. Sufficient reduction of AHI and ODI was still detected by PSG after six month.

Conclusion: In our study population 35% of patients showed sleep disordered breathing other than OSA indicating CSA and CSR to be a relevant issue in PD patients. Furthermore these forms of sleep disordered breathing resulted in failure of CPAP therapy in more than half of the patients. The high frequency of CSA and CSR in our study population may reflect the widespread neurodegeneration causing of non motor symptoms in PD.

P524

Yawning in de novo Parkinson's patients

F. GIGANTI, S. GUIDI, I. ZILLI, S. RAMAT, M. RAGLIONE, S. SORBI and P. SALZARULO

University of Florence, Firenze, IT

Objectives: Yawning is a dopamine mediated behaviour [1] whose frequency correlates with sleepiness and its daily time course [2]. Moreover, in healthy subjects some studies reported that yawning is frequently followed by increased motor activity [3] and electroencephalographic activation [4], suggesting that this behaviour arises in order to counteract the increase of sleepiness [3]. Since Parkinson's Disease (PD) is a neurodegenerative pathology characterized by excessive daytime sleepiness [5,6] and by a dysfunction of the dopamine system [7], it could be suggested that alterations in yawning may occur in this disease. Therefore, the aim of this study was to evaluate the frequency and temporal distribution of yawning in de novo PD patients and in healthy subjects.

Methods: Eighteen PD patients who had never been treated with antiparkinsonian therapy and 18 healthy subjects underwent a three-day actigraphic monitoring and were required to signal each yawning occurrence (isolated yawning, IY) by using an event marker button placed on the top of the actiwatch, and to report the presence of a yawning burst (YB, i.e. the occurrence of more than one yawn within a minute) on a specific schedule.

Results: The frequency of YB was higher in de novo PD patients compared to healthy subjects, whereas there were no significant differences in the overall frequency of yawns, in the frequency of IY and in the number of yawns in each burst. The daytime course of overall yawning frequency varies similarly in both groups; however yawns at 2 pm, mainly YB type, are more frequent in PD than in healthy subjects.

Conclusions: The higher frequency of YB at 2 pm in PD patients parallels higher levels of sleepiness previously found in these patients [8]; possibly because they are trying to contrast increased sleepiness.

References:

1. Daquin G., Micallef J., Blin O. *Sleep Med Rev* 2001, 5: 299–312.
2. Giganti F., Zilli I., Aboudan S., Salzarulo P. The mystery of yawning in physiology and disease. Karger, Basel, 2010, pp 42–46.
3. Baenninger R., Binkley S., Baenninger M. *Physiol Behav* 1996, 59: 421–425.
4. Kasuya Y., Murakami T., Oshima T., Dohi S. *Anesth Analg* 2005, 101: 382–384.
5. Arnulf E. *Sleep Med Rev* 2005, 9: 185–200.
6. Poryazova R., Benninger D., Waldvogel D., Bassetti C. L. *Eur Neurol* 2009, 63:129–35.
7. Jankovic J. *Neurosurg Psychiatr* 2008, 79: 368–376.
8. Giganti F., Ramat S., Zilli I., Guidi S., Raglione L. M., Sorbi S., Salzarulo P. Submitted, 2012.

P525

Symptomatic narcolepsy in Parkinson's disease: is there a place for cataplexy?

D. MATACIUNIENE[1], R. MASAITIENE[2] and V. LIESIENE[3]

[1]Vilnius University Hospital Santariskiu Klinikos, Vilnius, LT, [2]Vilnius Clinical Hospital, Vilnius, LT, [3]Kaunas Medical Centre Neuromeda, Kaunas, LT

Objective: Narcolepsy is a chronic neurological condition classically characterised by a tetrad of symptoms: excessive daytime sleepiness (EDS), cataplexy, sleep paralysis and hypnagogic hallucinations. The symptoms of narcolepsy can be seen during the course of other neurological disease process – symptomatic narcolepsy. Inherited disorders, tumors, and head trauma are the three most frequent causes for symptomatic narcolepsy reported in the literature. Parkinson's disease (PD) is often associated with EDS and other REM sleep abnormalities (hallucinations, REM behaviour disorder). According to the literature, a narcolepsy-like phenotype (≥2 sleep-onset REM periods) can be found in 29–39% of PD

patients with EDS. Interestingly, there have been no reports, in which cataplexy or sleep paralysis would be present in PD with EDS.

Methods: We report a case of 64 years old man, who complained with brief unexpected episodes of bifacial 'paralysis', head drop and weakness of his hands, lasting 20 s–2 min. These attacks tended to appear repeatedly up to five times per day, could be provoked by emotions. Other complaints were excessive daytime sleepiness, trembling and clumsy right extremities, loss of memory and snoring. Tremor and rigidity of the right hand appeared 10 years ago together with excessive sleepiness which gadually increased over the time. Episodes of muscle atonia appeared 4 years ago and were initially misdiagnosed and treated as epilepsy. The patient was never treated for PD.

Results: Neurological examination showed right-sided parkinsonism and mild cognitive decline (Mini Mental State Examination score 23). Multiple sleep latency test was typical for narcolepsy (mean sleep latency of 2 min 15 s with four sleep onset REM in four tests). HLA typing proved he was HLA DQB1*0602 positive. Conventional polysomnography revealed moderate sleep apnea syndrome (apnea hypopnea index – 34.5). CPAP therapy was applied which improved patient's night sleep and slightly decreased daytime sleepiness. Treatment with imipramine resulted in significant reduction of cataplexy episodes.

Conclusion: As typical features of narcolepsy with cataplexy evolved together with signs and symptoms of neurodegenerative disorder (PD), we assume that we faced a case of symptomatic narcolepsy in PD with very unusual feature – cataplexy. Questions about possible pathophysiological mechanisms for the occurrence of cataplexy in symptomatic narcolepsy are still open.

P526

Parkinson's disease and turning in bed

M. LOUTER[1], D. PEVERNAGIE[1], J. B. A. M. ARENDS[1], P. J. M. CLUITMANS[1], B. R. BLOEM[2] and S. OVEREEM[1]

[1]Kempenhaeghe, Heeze, NL, [2]Radboud University Medical Centre, Nijmegen, NL

Objectives: Complaints of impaired bed mobility are reported by 45 to up to 80% of patients with Parkinson's Disease (PD). So far, there is only little objective data on difficulties turning in bed in PD, and the relation with sleep disturbances.

Methods: A total of 44 PD patients were included, who presented with problems initiating or maintaining sleep. The group was divided in patients with (PD+) and without (PD-) complaints of difficulties turning around in bed. All patients received a semi-structured clinical interview, and a nocturnal video-polysomnography (PSG). As a control group, 19 patients with psychophysiological insomnia were included (CO). The three groups were compared regarding actual body position movements, clinical characteristics and PSG outcomes.

Results: Twenty-one of the 44 PD patients (47.7%) had difficulties turning around in bed based on the clinical interview. PD patients with subjective bed mobility problems had significantly less turns per hour during sleep compared to PD- patients and controls (0.6 ± 0.5 (PD+, 1.3 ± 1.2 (PD-); 1.4 ± 1.4 (CO), $P = 0.038$). However, this was not the case for turns per hour during wake in bed (6.6 ± 3.6 (PD+); 7.7 ± 4.4 (PD-); 7.8 ± 3.9 (CO), $P = 0.578$). PD patients with and without turning difficulties differed significantly regarding overall dopaminergic dose [levodopa equivalent dose (LED) 1162.4 ± 527.1 (PD+); 772.2 ± 564.9 (PD-), $P < 0.001$] but not regarding night time dopaminergic therapy (LED 121.1 ± 39.3 (PD+); 121.9 ± 56.0 (PD–), $P = 0.967$). Polysomnography showed a significant difference between total sleep time and sleep efficiency between the three groups. Total sleep time (min): 278.6 ± 77.5 (PD+); 375.1 ± 64.0 (PD-); 386.6 ± 75.6 (CO), $P < 0.001$. Sleep efficiency (%): 60.8 ± 14.3 (PD+); 75.5 ± 10.0 (PD-); 77.8 ± 15.8 (CO), $P < 0.001$).

Conclusion: PD patients with subjective complaints of turning around in bed showed more than 2 times less body position changes during sleep. Interestingly, there were no difference regarding bed mobility during wake. Problems turning in bed were associated with a decreased total sleep time and sleep efficiency.

P527

Subjective and objective sleep quality related to pain thresholds in tension type headache and controls

M. ENGSTRØM[1], K. HAGEN[2], M. BJØRK[3], L. J. STOVNER[2], G. GRAVDAHL[2], M. STJERN[1] and T. SAND[1]

[1]Norwegian University of Science and Technology, Trondheim, NO, [2]Norwegian National Headache Centre, St. Ola versus Hospital, Trondheim, NO, [3]Haukeland University Hospital, Bergen, NO

Objective: To evaluate of sleep symptoms and objective sleep structure, including the correlation between sleep variables and pain thresholds, of healthy controls and tension type headache patients (TTH).

Methods: Twenty-two tension-type headache (TTH) patients diagnosed according to the ICHD-1 [1] by headache specialists, and 29 controls (mean 41 years, 26 women) were enrolled in the study. The participants were evaluated by questionnaires, sleep diary, headache diary for the TTH group, polysomnography, thermal- and pressure-pain threshold measurements. Sleep was analyzed according to the AASM manual [2] with few exceptions. AASM-arousals were defined as an abrupt shift of EEG frequency lasting 3–30 s. We also scored bursts of K-complexes and delta-waves. Thermal pain thresholds were measured on the hand and the forehead on both sides. Pressure pain thresholds (PPT) were measured at eight locations (bilateral in: m. temporalis, m. splenius, m. trapezius and over the distal middle finger). Groups were compared with Mann–Whitney *U*-test and *P*-values < 0.05 was regarded as significant. We used Spearman's rho for correlation calculations.

Results: The TTH group reported significantly more sleep-related problems including insomnia ($P < 0.01$), more long awakenings ($P = 0.01$) and more anxiety ($P < 0.01$) than controls. The TTH group had significant more slow-wave N3 sleep than controls, 107 versus 84 min ($P < 0.01$), and lower AASM arousal index for the overall night, 14.5 versus 19.2 per hour ($P < 0.01$). Among controls AASM-arousals were positively correlated to thermal pain thresholds while KD- bursts were negatively correlated to pressure pain thresholds. No such correlations were found for TTH.

Conclusion: The TTH group reported more sleep problems than controls, but revealed increased sleep quality, possibly caused by a relative sleep deprivation. Even though sleep diaries showed more awakenings among TTH than controls, no sleep time difference was found. It might be hypothesized that TTH need more sleep than healthy controls. No relationship between sleep variables and pain thresholds among TTH was found.

1. The International Classification of Headache Disorders: 2nd edition. Cephalalgia 2004, 24 (suppl 1).
2. American Academy of Sleep Medicine W, IL 60154, U.S.A. The AASM Manual for the Scoring of Sleep and Associated Events. Rules, Terminology and Technical Specifications. American Academy of Sleep Medicine, Westchester, IL, 2007.

P528

Subjective quality of sleep in chronic migraine patients with cerebral lateral ventricles asymmetry

V. VOVC[1], I. MOLDOVANU[2] and L. ROTARU[2]
[1]State University of Medicine and Pharmacy 'Nicolae Testemitanu', Chisinau, MD, [2]Institute of Neurology and Neurosurgery, Chisinau, MD

Objective: To explore the subjective quality of sleep in chronic migraine patients with cerebral lateral ventricles asymmetry.

Methods: A total of 114 patients with chronic migraine (CM) without (n = 52, the reference group) and with cerebral lateral ventricles asymmetry (CLVA) (62 patients) participated in the study. Patients with CM and CLVA were divided into three groups: with mild (n = 22), moderate (n = 20) and severe (n = 20) CLVA. The subjective quality of sleep was estimated by use of Pittsburgh Sleep Quality Index (PSQI). The term 'rate of sleep disorders' means the rate of patients with the total PSQI score ≥ 5.

Results: Rate of sleep disorders increased from 57.7% in reference group to 75% in group with severe CLVA, but without statistical significance. The highest scores were found for the following PSQI components: 'sleep latency', 'sleep disturbance' and 'subjective sleep quality'. But all of these scales values as well as increase of PSQI total score with 30% didn't achieve statistical significance.

Conclusion: Our results demonstrate that increasing grade of cerebral lateral ventricles asymmetry in patients with chronic migraine didn't change the subjective sleep quality.

P529

Subjective sleep complaints in traumatic brain injury patients are explained by the influences of depression, presence of pain and pain catastrophising

F. CHOUCHOU[1], S. KHOURY[1], I. ROY[2], C. MANZINI[1], R. DENIS[2], J.-F. GIGUÈRE[2] and G. LAVIGNE[1]
[1]Centre d'étude avancée en médecine du sommeil, Montreal, CA, [2]Hôpital du Sacré Coeur de Montréal, Montreal, CA

Objectives: Poor sleep quality complaints, pain, depression and anxiety are frequently reported in TBI patients. The relationship between the above remains unclear. In the present prospective study we aim to assess whether sleep complaints in mild TBI population could be explained by pain, depression, pain catastrophizing or anxiety.

Methods: We recruited 24 mild TBI patients (38.3 years of age ± 11.4; 15M/9F; mean ± SD) and compared them to 18 control subjects (29.1 years ± 7.5; 6M/12F). On an average of 48.7 ± 22.7 (19–117) days after trauma, they completed the Pittsburgh Sleep Quality Index (PSQI), a pain visual analog scale (100 mm VAS pain intensity), pain catastrophizing scale (PCS; rumination, magnification and helplessness), Beck Depression and Beck Anxiety inventories.

Results: Mild TBI patients, in comparison to controls, reported higher global score on the PSQI (9.3 ± 4.8 versus 2.8 ± 1.6; $P < 0.01$) and for each PSQI sub scores ($P < 0.05$). They also reported higher pain intensity (30.7 ± 26.9 versus 6.5 ± 14.7; $P < 0.01$), pain catastrophizing (19.7 ± 12.8 versus 9.1 ± 5.7; $P = 0.010$), depression (15.1 ± 10.0 versus 1.3 ± 2.1; $P < 0.01$), and anxiety (9.5 ± 9.4 versus 0.9 ± 1.4; $P < 0.01$). In this population, simple regression showed that pain ($r^2 = 0.31$, $P < 0.01$), pain catastrophizing ($r^2 = 0.41$, $P < 0.01$) and depression ($r^2 = 0.57$, $P < 0.01$) were related to the global PSQI score and sub scores ($r^2 = 0.14$–0.62, $P < 0.05$) but not anxiety ($r^2 = 0.07$, $P = 0.23$). At last, when multivariate stepwise regression was applied, only depression seems to be explain the global PSQI score ($P < 0.001$, $r^2 = 0.50$).

Conclusion: These results suggested that pain, depression and pain catastrophizing contribute to poor sleep quality in mild traumatic brain injury patients. Although pain, depression and pain catastrophizing seem to be related to each other to influence poor sleep quality, depression seems to play a major role in these sleep complaints.

P530

Presence of pain in acute mild traumatic brain injury patients blunts electroencephalographic differences: a controlled sleep lab-study

S. KHOURY[1], F. CHOUCHOU[1], F. AMZICA[2], S. PELLETIER[1], R. DENIS[3], J.-F. GIGUÈRE[3] and G. LAVIGNE[1]
[1]Centre d'études avancées en médecine du sommeil, Montreal, CA, [2]Université de Montréal, Montreal, CA, [3]Hôpital du Sacré-Coeur, Montreal, CA

Objectives: Pain is a highly prevalent post-concussion symptom occurring in majority of Mild Traumatic Brain Injury (MTBI) patients. About half of MTBI patients report sleep-wake disturbances following trauma. It is known that pain could alter sleep quality, but the interaction between the two is not fully understood in MTBI population. We aim at identifying how pain affects sleep architecture and brain activity following MTBI.

Methods: Twenty-four MTBI patients complaining of sleep-wake disturbances, with and without pain, were prospectively recruited on average 45 days post-trauma. Data were compared with 18 healthy control subjects (no sleep and pain complaints). Pain was assessed using questionnaires and a 100 mm visual analogue scale (VAS). Sleep quality, architecture and electroencephalographic (EEG) activity were analysed.

Results: Sleep macrostructure was not different between the MTBI and the control subjects. Global EEG spectral analysis did not reveal differences between the MTBI and the control groups for all frequency bands during sleep. However, after group separation according to pain status, MTBI patients with pain showed an increase in rapid EEG frequency bands (alpha, sigma and beta) during slow wave and REM sleep in comparison to MTBI patients without pain and controls subjects ($P < 0.001$).

Conclusion: Presence of pain in MTBI patients blunts differences in EEG spectral analysis. Such observation suggests that pain significantly contributes to sleep problems in post-MTBI period and may be a critical condition in the management of post-concussion symptoms.

P531

Sleep architecture and sleep-disordered breathing in patients with myotonic dystrophy type 1 and 2

L. LEONARDIS and L. DOLENC GROSELJ
University Medical Center, Ljubljana, SI

Objectives: Myotonic dystrophy types 1 (DM1) and 2 (DM2) are progressive multisystemic dominantly inherited disorders with predominant muscle weakness and myotonia. In DM1 sleep disorders with excessive daytime sleepiness (EDS) are common, while in myotonic DM2 the presence of sleep disturbances is less known. We were interested in differences of sleep architecture between patients with DM1–DM2 and their respiratory parameters during sleep.

Methods: Twenty-six patients with DM1 and 16 patients with DM2 (genetically proven) were recorded in sleep laboratory with full night polysomnography (PSG). Sleep was scored in 30-s epochs using

Rechtshaffen & Kales and AASM criteria. Chest wall and abdominal movement were monitored with piezoelectric strain gauges. Respiratory events and CO_2 were monitored using oro/nasal cannula flow signal, and oxygen saturation was monitored with a pulse oximeter. **Results:** Mean age of patients with DM1 and DM2 were 47 and 56 years, respectively. Sleep efficiency were similar in both groups (69% in patients with DM1 and 76% in patients with DM2). Stage 2 was longer in DM1 patients, while stage 3 was longer in patients with DM2 ($P < 0.001$). REM sleep and stage 1 were similar in both groups. Oxygen saturation was lower in patients with DM1 ($P = 0.04$). AHI was higher in DM1 (mean 17) than in DM2 (mean 6) ($P = 0.02$). DM1 had more central and mixed apnea and more central apneas with desaturation ($P < 0.05$). Oxygen saturation was lower in REM sleep than in wakefulness and other sleep stages. **Conclusion:** Breathing during sleep is more affected in patients with DM1 than in DM2. Greater oxygen desaturation in DM1 is present partly due to more apneas and due to abnormalities in REM that are most likely because of diaphragmal weakness.

P532

Analysis of polysomnographic findings in Agrypnia excitata

A. GARAY[1] and S. BLANCO[2]
[1]CEMIC, Buenos Aires, AR, [2]CONICET-Facultad de Ingeniería, Buenos Aires, AR

Objectives: 'Agrypnia Excitata' is a term coined originally by Lugaresi and Provini (Sleep Medicine Reviews 2001) to describe a syndrome caused by a dysfunction in thalamo-limbic circuits producing severe insomnia, mental confusion, dream enactment, motor and autonomic activation. Of conceptual importance for the understanding of the neurophysiopathology of mechanisms of wakefulness and sleep, this syndrome is observed in fatal familial insomnia (FFI), delirium tremens, limbic autoimmune encephalopaties (LAE) and the Mulvihill-Smith syndrome. We analized polysomnographic findings of a proven case of LAE associated with VGKC antibodies (LAE-VGKG) and performed its comparisons with findings previously reported in our case of FFI (Garay A. et al., Neurology 1996).

Methods: We analized polisomnograms of LAE-VGKC (PSGs, $n = 3$) using digital video-polysomnographic recordings. Sleep-wake patterns were scored in 30 s epochs and in 5 s epochs by time-frequency analysis thorough continuous wavelet transform (CWT). For the analysis of our results we performed simulations using a mathematical model of sleep and wake of Rempe et al. (J. Math. Biol. 2010).

Results: LAE-VGKC showed during epochs analysis of the motor segmental overactivity a cyclic alternating pattern (CAP) with cycles of rest and activity of 60–90 s. ($P < 0.05$, Kruskall-Wallis NP Test, Dunn′s NC Test). Previous data of IFF showed CAP during 'intra-atypical REM sleep' fragmentation near to 60–90 s. Using a multirresolution wavelet filter we split the band under 5 s activity. We then perform the Fourier spectrum of this extracted activity, detecting oscillations below <1 Hz. During modeling, modifications of circadian and homeostatic variables were able to produce a cyclic behaviour like LAE-VGKC and IFF.

Conclusions: This study demonstrates patterns of severe abnormality during cycles of wakefulness-sleep and activity-rest with CAP behavior during motor overactivity (LAE-VGKC) and during fragmentation of atypical REM sleep (IFF). These findings could be related to a lost of the inhibitory control of cortico-thalamic-limbic circuits upon the hypothalamic and reticular-activating-systems allowing the expression of cortical top-down oscillations.

P533

Symptomatic narcolepsy in anti-LGI1 autoimmune encephalitis

M. TODOSIJEVIC[1], B. ROJC[2], B. MEGLIC[3], G. GRANDA[3] and L. DOLENC GROSELJ[3]
[1]General Hospital Novo mesto, Novo mesto, SI, [2]General Hospital Izola, Izola, SI, [3]University medical center Ljubljana, Ljubljana, SI

A 59-year-old man with anti–LGI1 autoimmune encephalopathy was reffered to the sleep laboratory with history of excessive daytime sleepiness and unexplained falls. He became ill ten month prior with excessive daytime sleepiness, changes in mood, behaviour and speech, desorientation and generalized epileptic seizures. Head CT with contrast was performed and was unremarkable. He showed mental slowing and difficulty finding words on admission to neurological department. Brain MRI showed few small chronic ischemic lesions in deep white matter of frontal lobes and right cerebellum and mild cortical atrophy. While on ward his mental state deteriorated. He had generalized seizures and what were thought to be drop attacks. EEG was pathological and showed slow, low amplitude basic activity, slow intermittent waves of high amplitude, spikes and sharp waves and three paroxysms from right frontal and temporal lobes, during which the patient had automatic behaviour and did not respond to comands. Neuropsychological evaluation showed cognitive decline with severe impairment of attention, executive functions and mental slowing, memory was mostly preserved. Extensive diagnostic was done, which excluded other causes and he was put on methylprednisolon on suspicion of having autoimmune encephalopathy. Therapy led to significant improvement in cognition. He was treated with levetiracetam, clobazam and phenobarbiton, generalized seizures subsided but what were thought to be epileptic drop attacks remained and he was discharged with valproat as monotherapy. During his second stay on the ward anti-LGI1 antibodies were detected in cerebrospinal fluid and confirmed the diagnosis of autoimune encephalopathy. Despite the general improvement, he still suffered from unexplained falls during the day, which led to refferal to our PSG laboratory during his third stay. We performed 24-h portable polysomnography (PSG). Of 3 SOREM-s were detected (2 during the day and 1 during the night). The PSG recording also showed central sleep apneas with high apnea hypopnea index (AHI = 32). The night polygraphic recording confirmed symptomatic narcolepsy with cataplexy and discovered central apneas during sleep. We present a rare case of symptomatic narcolepsy with cataplexy, symptomatic epilepsy and central sleep apneas in anti-LGI1 autoimmune encephalopathy.

P534

Sleep-wake cycle in the Kennedy's disease: a controlled polysomnographic study and self-reported questionnaires

C. LIGUORI, F. PLACIDI, A. ROMIGI, F. IZZI, M. ALBANESE, C. TERRACCIANO, R. MASSA, N. B. MERCURI and M. G. MARCIANI
University of Rome Tor Vergata, Rome, IT

Objective: Kennedy's disease, also known as spinobulbar muscular atrophy (SBMA), is an adult-onset X-linked recessive trinucleotide polyglutamine disorder, caused by expansion of a polymorphic CAG tandem-repeat in exon 1 of the androgen-receptor (AR) gene on chromosome Xq11-12 (La Spada, 1991; Katsuno, 2004). Mutated AR accumulates in nuclei and cytoplasm of motor neurons, resulting in their degeneration and loss (Sobue, 1989). Immunohistochemical distribution of mutant AR is also localized in hypothalamus, locus coeruleus, reticular formation of pons and nucleus raphe pontis

(Adachi, 2005), who play a critical role in vigilance regulation. Sleep-disordered breathing and sleep disruption are common in neuromuscular disorders associated with respiratory muscle weakness (Bourke, 2002).

The aim of our study was to evaluate sleep-wake cycle in 9 consecutive unselected SBMA patients compared with 9 healthy control subjects, sex and age matched.

Methods: Nocturnal sleep and daytime somnolence were investigated using both subjective questionnaires (Pittsburgh Sleep Quality Index, PSQI; Epworth Sleepiness Scale, ESS) and objective data such as ambulatory polysomnography followed by the Multiple Sleep Latency Test (MSLT). Statistical analysis was performed by the Mann–Whitney *U* test; *P* level of <0.05 was considered significant.

Results: SBMA patients presented a significantly reduced total sleep time and an increased apnea-hypopnea index in respect to controls. Six out of nine patients (66.7%) presented Obstructive Sleep Apnea (OSA). SBMA patients showed a mean global PSQI score significantly higher than controls. Increased value was also evident in SMBA in four of the seven components of PSQI: 'Subjective Sleep Quality', 'Sleep Duration', 'Habitual Sleep Efficiency', 'Sleep Desturbances'. In addition SBMA patients showed a mean ESS score significantly higher than healthy subjects, but the mean sleep latency measured by MSLT was not significantly different between the two groups.

Conclusion: Our study demonstrates that SBMA patients show an alteration of both subjective and objective sleep quality. OSA may be frequent in these patients, probably caused by effects on oropharyngeal and respiratory muscles leading to obstructive sleep apnea and nocturnal hypoventilation, as reported in several neuromuscular disorders (Bourke, 2002). SBMA patients present subjective excessive daytime somnolence which was not confirmed by MSLT findings.

We suggest that sleep impairment could be also due to the neurodegenerative process involving cerebral structures regulating the sleep-wake cycle.

P535

The influence of periodic leg movements in sleep on clinical outcome following acute ischaemic stroke

D. KARADENIZ and G. BENBIR

Istanbul University, Istanbul, TR

Periodic leg movements in sleep (PLMS) are characterized by periodic episodes of repetitive and highly stereotyped limb movements as dorsiflexion of the ankle, toes and a partial flexion of knee and sometimes hip. Although the underlying pathophysiology is still not well-known, electrophysiological and functional magnetic resonance studies showed a strong association between dysfunction in brainstem level and PLMS. There is a growing body of the literature implicating PLMS in cardiovascular risks. These patients were reported to be more likely to suffer from coronary artery disease, hypertension, and stroke. We designed a prospective study to investigate the association of PLMS with clinical outcome in patients with acute ischemic stroke. A total of 24 patients with acute ischemic stroke and PLMS were enrolled into the study. The mean PLM index was 54.3 + 53.6/h (between 5 and 252/h). The arousal-associated PLMS index was 15.0 + 23.6 (ranging between 0 and 80/h). The NIH stroke scale and Barthel scales were performed at admission, at 3rd week and 3rd month. The delta change in mean NIH scales and Barthel scales were correlated with mean PLMS index, which were not significantly different at subacute or chronic phase. On the other hand, the delta change in mean NIH scales and Barthel scales were correlated with mean arousal-associated PLMS index at chronic phase ($P < 0.005$). Increased sympathetic activation secondary to arousal reactions following PLMS have been suggested as the underlying pathophysiology of cardiovascular complications. We observed that stroke patients with PLMS have a tendency to have a worse prognosis, if PLMS are associated with arousal reactions.

P536

Multiple sclerosis, restless legs syndrome and sleep

C. SORIA-BRETONES, M. GARCÍA-BELLÓN, L. GÓMEZ-ROMERO and M. A. GARCÍA-JIMÉNEZ

Hospital Virgen de la Luz, Cuenca, ES

Objectives: The association between Multiple Sclerosis (MS) and sleep disorders is known.

We present a case of MS with severe Sleep Apnea-Hypopnea Syndrome (SAHS), Restless Legs Syndrome (RLS) and Periodic Limb Movements (PLM) during sleep, whose severity evolves with that of MS.

Methods: Thirty four year-old male with Relapsing-Remitting MS (RRMS) for 8 years, with left hemiparesia and dysmetria as well as brainstem and optic nerves involvement. Followed by Neurology and other departments due to different symptoms (Urology, Psychiatry); RLS symptoms appear 5 years after MS onset, together with PLM during sleep that cause conciliation and intermediate insomnia. Magnetic Resonance Imaging (MRI), overnight Video-Polysomnography (VPSG), Multimodal Evoked Potentials (MMEPs), Electromiography (EMG) and Electroneurography (ENG) were performed several times.

Results: MRI: demyelination in left frontal cortex, cerebellum right hemisphere, bulbomedullar junction and medulla oblongata. MMEPs: left predominance involvement with left predominance in cortico-subcortical structures, brainstem and optic nerves. In repeated tests, progressive impairment. EMG and ENG: normal. First overnight VPSG: predominantly central SAHS (Apnea-Hipopnea Index (AHI) 80.2), PLM (19.2/h) with severe disruption of sleep architecture (long onset latency, low sleep efficiency (45.2%) and absence of N3 and REM phases). Two years later, after treatment with Continuous Positive Airway Pressure (CPAP) at a pressure of 7 cm H20, Ropinirole and Pregabalin: daytime VPSG shows worsening in PLM (174/h) and slight improvement in sleep efficiency (62%). One year later, bizarre symptoms appear in arms at rest and during sleep. Daytime VPSG without (CPAP): pure central SAHS (AHI 98.6), stable PLM (156/h) and very low sleep efficiency (28.1%); 4 months later, after adding Copaxone, an overnight VPSG for CPAP titration shows predominantly central SAHS, optimal CPAP pressure of 8 cm H20, as well as great improvement in PLM (2.3/h) and in sleep efficiency (91.1%).

Conclusion: This case is unusual due to an early onset of sleep disruption, male sex and several severe concomitant sleep disorders. There is a striking correlation between the severity and changes in MRI, neurophysiological tests and clinical signs and symptoms. This case raises the possibility to consider MS as a cause of Secondary RLS.

P537

Features of sleep structure in patients with multiple sclerosis associated fatigue

L. KHUCHUA[1], A. CHIKADZE[1], M. KIZIRIA[1], T. VASHADZE[1], D. GUGUTSIDZE[1], A. TSISKARIDZE[1], I. BURDULADZE[2], M. JIBLADZE[1] and R. SHAKARISHVILI[1]

[1]P.Sarajishvili Institute of Neurology, Tbilisi, GE, [2]Research Institute of Clinical Medicine, Tbilisi, GE

Objective: Fatigue is the most frequent symptom in multiple sclerosis (MS) patients and often is profoundly debilitating. It is poorly understood and difficult to treat. Patients with MS do not often distinguish between fatigue and sleepiness. Excessive somnolence, inappropriate daytime sleep and sleep disorders (restless legs syndrome, REM-sleep behavioral disorders, obstructive sleep apnea and others) are common in patients with MS. In one study there was a significant correlation between fatigue and disrupted sleep in patients with MS. To determine sleep disturbances associated with fatigue in patients with MS and correlation with the location of demyelinating lesions seen on magnetic resonance imaging (MRI).

Methods: Ten consecutive patients with relapsing-remitting (RR) MS (Mc Donald diagnostic criteria) who had fatigue based on fatigue questionnaire (Modified Fatigue Impact Scale – MFIS) undergo nocturnal polysomnography, utilizing standard technique with additional arm electromyography leads and time-synchronized digital video recording. There were three men and seven women aged between 20 and 32 with Expanded Disability Status Scale (EDSS) ranging between 2.0 and 4.5. Eight patients reported sleep-related problems. These included difficulties initiating sleep and/or frequent awakenings due to spasms in the legs (7), difficulties in initiating or maintaining sleep (4), snoring (2) and nocturia (3). All patients were screened for depression with Beck Depression Inventory (BDI) and no one had score more then 14. MRI scans were performed in all patients in the day of polysomnography.

Results: Of the 10 fatigued patients with MS all had REM-sleep without atonia, two had REM-sleep associated motor activity in legs, seven had frequent awakenings and significantly reduced sleep efficiency, five had hypopnea. One patient had sleep apnoea and fatigue was especially prominent in this case. Two had snoring. In patients with MS was reduced REM stages and REM defragmentation quality was significantly high. All patients had MRI brain stem lesions and two of them had demyelinating lesions in pons.

Conclusion: We have disclosed relationship between fatigue-associated sleep abnormalities in MS patients and MRI brain stem lesions. These abnormalities may play role in the pathophysiology of poorly understood MS fatigue. Large-scale studies are needed to confirm our findings.

P538

Restless legs syndrome in blood donors

R. PERAITA-ADRADOS[1], E. CALVO[1], L. LILLO[1], A. DEL CASTILLO[1], R. DEL RÍO VILLEGAS[2] and A. GUILLÉM[1]

[1]University Hospital Gregorio Marañón, Madrid, ES, [2]University Hospital La Paz, Madrid, ES

Aim: To report a series of patients referred for RLS associated with repeated blood donations.

Patients and method: The sample comprised 15 patients (nine male), mean age at diagnosis of 53.4 years (28–67 years). Selection involved asking consecutive patients with RLS from 2010 to 2011 whether they had donated blood. All patients underwent a physical and neurological examination, and video-PSG. We performed a complete blood count and determined serum iron, serum ferritin, transferrin saturation, and soluble transferrin receptors (STR).

Results: All patients fulfilled the International Restless Legs Syndrome Study Group criteria. RLS was familial in three cases, associated with OSA in four cases, and associated with insomnia in one case. V-PSG recordings showed disturbed sleep with a reduction in TST, increased WASO, low sleep efficiency, respiratory abnormalities with an AHI >10/h in three cases, and a PLM index >5/h in eight cases. Haemoglobin was normal and iron levels were within the normal range (61–150 μg/dl) in all cases, whereas ferritin levels were low except in one case (350 μg/l). Low transferrin levels were recorded in six cases and low STR in two cases.

Conclusions: Repeated blood donation was associated with an increased risk of having RLS. In a series of consecutive patients in whom iron studies were not performed at the time of the donation we recorded severe RLS syndromes. It is possible that RLS involves compromise of peripheral CNS iron regulation. Iron status must be checked prior to blood donation in order to avoid a potential risk of developing RLS.

P539

Sleep alterations in dementia with Lewy bodies: sleep patterns and clinical correlates. A descriptive video-PSG study

M. TERZAGHI[1], B. MINAFRA[1], D. ARNALDI[2], V. RUSTIONI[1], R. ZANGAGLIA[1], C. PASOTTI[1], R. CREMASCOLI[1], E. SINFORIANI[1], C. PACCHETTI[1] and R. MANNI[1]

[1]IRCCS C. Mondino National Institute of Neurology Foundation, Pavia, IT, [2]Universisty of Genoa, Genoa, IT

Objective: Sleep disorders are very common in dementia with Lewy bodies (DLB), but knowledge of sleep architecture and disorders of nocturnal sleep in DLB is limited by the absence of systematic video-polysomnographic investigations.

Methods: We describe the video-polysomnographic findings in twenty-three subjects diagnosed with probable DLB submitted to face-to-face clinical interview and overnight in-hospital video-polysomnography. A Spearman's Rank correlation was run to test the relationship between clinical and cognitive features and sleep-related measures.

Results: All the patients reported at least one sleep disturbance, which was the presenting symptom in eight subjects (34.7%). Video-polysomnography documented, within a pattern of reduced sleep continuity and REM sleep, sleep apnoea in 35%, periodic limb movements in 80% and disruptive motor behavioural manifestations in 75.0% of the subjects. Motor behavioural events consisted of REM Sleep Behaviour Disorder (RBD) in 53%, episodes mimicking RBD but related to arousal from NREM or REM sleep in 13% and confusional events in 34% of the cases, isolated or in the framework of parasomnia overlap disorder. No consistent correlations were found between analysed clinical, cognitive and sleep-related variables.

Conclusion: Clinicians should be aware of the complexity of sleep alterations in DLB, which encompass an overlap of impaired sleep structure, sleep comorbidities and various motor-behavioural abnormal events, and bear in mind the possibility of misleading symptoms and that of overlooking sleep comorbidities; they should consider the possibility of polysomnographic sleep investigations in order to obtain a correct diagnosis and optimize treatment of disrupted sleep.

P540

RLS in Parkinson's disease patients in Armenia

Z. TAVADYAN[1], H. BAKUNTS[1] and S. KHACHATRYAN[2]
[1]*Yerevan State Medical University, Yerevan, AM,* [2]*Somnus Sleep and Movement Disorders Clinic, Yerevan, AM*

Objectives: To reveal relationship between dopaminergic treatment and presence of restless legs syndrome (RLS) in patients with Parkinson's disease (PD).

Methods: PD was diagnosed according to UK BB PDS Diagnostic Criteria aged 42–85 (mean age – 64.9 years), with H&Y stage 1–4 were enrolled in the study: 30 of them were females (46.9%) and 34 were males (53.1%). Patients on dopaminergic therapy (levodopa, dopamine agonist or both) and those not on it were interviewed for having four essential RLS diagnostic criteria proposed by International RLS Study Group in 2003. Careful interview was performed to differentiate from akathisia and other mimics. According to confirmed clinical diagnosis of RLS the patients were divided into 2 groups – with RLS (Group 1) and without RLS (Group 2). Proportional analysis and T-test were used for statistical analysis.

Results: Sixty four patients with PD aged 42–85 (mean age – 64.9 years), were enrolled in the study: 30 of them were females (46.9%) and 34 were males (53.1%). Forty one (64%) of all patients in our study were on dopaminergic therapy. Of them 16 (39%) patients had RLS and were included in Group 1: F – 11 (68.8%), mean age 59.5 years (42–70). Twenty five patients (36%) were enrolled in Group 2: F – 9 (36%), mean age 63.8 years (52–78). In Group 1 mean duration of therapy was 9.1 years (0.5–28) and in Group 2 – 3.4 years (0.5–8) and this difference was statistically significant ($P < 0.05$). Among 23 patients without dopaminergic therapy only 2 (8.7%) had RLS.

Conclusion: RLS is very prevalent among Parkinson's disease patients on dopaminergic therapy, especially in females. Patients with RLS were younger and had longer duration of therapy. Prevalence of RLS in PD patients that are not treated with dopaminergic drugs was nearly the same as in general population (7.9%) in Yerevan, Armenia (Khachatryan et al. 2007 Sleep Med suppl. 1). RLS is a serious problem in management of PD patients and the risks of its development should carefully monitored and avoided.

P541

Sleep position in idiopathic Parkinson's disease

P. O. VALKO[1], S. HAUSER[1], M. SOMMERAUER[1], Y. V. GAVRILOV[2], E. WERTH[1] and C. R. BAUMANN[1]
[1]*University Hospital of Zurich, Zurich, CH,* [2]*Harvard Medical School, Boston, US*

Objectives: Although clinical experience suggests that patients with idiopathic Parkinson's disease (PD) sleep more on supine position than subjects without PD, this has not yet been confirmed by polysomnographic studies. Increased time in supine position might have detrimental effects, in particular on sleep-disordered breathing (SDB).

Methods: Retrospective assessment of polysomnographic and clinical variables in 107 consecutive PD patients and 107 age-, sex- and body mass index (BMI)-matched control subjects. SDB was diagnosed when the apnea-hypopnea index (AHI) was higher than 5/h.

Results: Compared to control subjects, PD patients spent almost twice as much time in supine sleep position (60.1 ± 32.9% versus 32.9 ± 55.3%, $P < 0.001$). We found an increased percentage of supine position in PD patients with longer disease duration (rho = 0.39, $P < 0.001$) and higher UPDRS III score (rho = 0.30, $P = 0.002$). In addition, percentage of supine position was increased in PD patients with dyskinesia (72.5 ± 35.5% versus 51.4 ± 30.6%, $P = 0.002$) and hallucinations (74.5 ± 31.0% versus 52.7 ± 33.1%, $P = 0.008$) compared to PD patients without these symptoms. The prevalence of SDB was similar in PD patients and controls subjects (51% versus 64%, $P = 0.07$). Despite the largely increased amount of time spent in supine position, the prevalence of positional SDB – diagnosed in all patients with an at least twofold increased apnea-hypopnea index (AHI) in supine compared to non-supine position – was similar in PD patients and control subjects (65% versus 57%, $P = 0.29$). Positional SDB was associated with milder SDB in both groups.

Conclusions: Our findings demonstrate that patients with idiopathic PD sleep a good deal more on supine position than carefully matched control subjects. As expected, the progression of the neurodegeneration – clinically assessed by disease duration, severity of motor symptoms and presence of dyskinesia and hallucinations – was associated with an increased time spent in supine sleep position. However, this preference of supine sleep position does not seem to have detrimental consequences in terms of positional SDB.

P542

Simultaneous OSLER test and EEG recording in sleepy Parkinson's disease patients

D. NEUTEL, A. R. PERALTA, C. BENTES and J. J. FERREIRA
Hospital de Santa Maria, Lisbon, PT

Objective: To evaluate the validity of the OSLER test to document sleep onset in Parkinson Disease patients.

Material and Methods: Exploratory study conducted in PD patients with excessive daytime sleepiness (EDS) [Epworth Sleepiness Scale (ESS) >9]. The OSLER test consists of a 40-min sleep-resistance challenge; patients were asked to press a switch button in response to the illumination of a LED, which was set to occur every 3 s. 'Sleep onset' was defined as missing seven presses or absence of response for 21 s. The session was terminated after sleep onset determined by the OSLER or after 40 min, whichever came first. There was a concomitant Electroencephalography (F3, F4, C3, C4, O1 and O2), EMG (mentalis), right and left Electroculogram and video monitoring. Neurophysiologic sleep onset was defined according to AASM criteria.

Results: Five PD patients with a mean age of 62.4 (56–72 years old) were included. Disease duration of 5.6 years (3–10 years) and a mean Hoehn & Yahr stage of 2. ESS with a mean of 14 (10–16). One patient had previously sudden sleep episodes. The mean duration of the OSLER test sessions was 0:20:39 (00:04:06–00:36:37). Only one patient had EEG criteria of sleep onset in his four sessions (NREM N1). Neurophysiologic monitoring showed signs of sleepiness in all patients, with microsleeps, slow eye movements, theta and delta bursts. Behaviorally some patients had increased blinking, one patient performed significant periods of the exam with the eyes closed.

Conclusion: In this exploratory study, the early termination of an OSLER test session did not correspond to a true sleep onset on EEG. However, all patients had neurophysiologic and behavioral sleepiness, which have been correlated to accidents in other populations. Further studies are needed to access the usefulness of the OSLER test as a simple test to evaluate the risk of sleep episodes in PD.

P543

Subjective and objective sleep in men and women after first-time brain stroke, in the acute phase and at 6-month follow-up

L. N. BAKKEN[1] and A. LERDAL[2]
[1]*Buskerud University College, Drammen, NO,* [2]*Lovisenberg Diaconal Hospital, Oslo, NO*

Objectives: In rehabilitation after a brain stroke the patients sleep may be essential for participating in recovering and thus independency in their daily functions (ADL-functions). We examined whether subjective and objective assessed sleep may change from the acute phase to six-month follow-up after first time stroke, whether subjective and objective sleep parameters correlated and if there are any gender differences in the subjective and objective sleep at the two time-points.

Methods: In a cross-sectional study with a correlation design 100 patients were interviewed and their sleep assessed in the acute phase to 6-month follow-up. Subjective sleep was measured by Pittsburgh's Sleep Quality Index (PSQI) and objective sleep was assessed by actigraphy (Motion Logger Actigraphs) for three consecutive nights and two intervening days at the two time-points.

Results: The men (n = 60) reported better subjective sleep quality (d = 0.37) after six months, but worse subjective sleep efficiency (d = 0.44) at 6 months compared to baseline. Their objective wake percentage during night had was lower at follow-up (d = 0.28). The women (n = 40) improved their subjective sleep quality (d = 0.41) from baseline to six months follow up. No other sleep variables showed significant difference for women between to two time-points. There were no correlations between subjective and objective sleep in the acute phase. At six-month follow-up longer subjective sleep duration were related to more objective total sleep time (r = -0.21, P = 0.04). Less subjective sleep disturbance was related to more objective total sleep time (r = -0.23, P = 0.02), the use of more sleep medication was related to more objective total sleep time (r = 0.24, P = 0.02), and more subjective daytime dysfunction was related to more objective nap time during day (r = 0.27, P = 0.01). Men reported better habitual sleep efficiency (d = 0.57) and better total sleep quality (PSQI) (d = 0.57) than women in the acute phase. Women slept objectively more than men in the course of a day (d = 0.57) in the acute phase. At 6-month follow-up there were no gender differences in neither subjective nor objective sleep measures.

P544

Prepulse inhibition is correlated with 123I-FP-CIT SPECT and cognition in Parkinson's disease

M. ZOETMULDER[1], H. BIERNAT[1], M. NIKOLIC[2], L. FRIBERG[1], L. KORBO[1], H. PFEIFFER[1] and P. JENNUM[3]
[1]*Bispebjerg Hospital, Copenhagen, DK,* [2]*Glostrup Hospital, Glostrup, DK,* [3]*Danish Center for Sleep Medicine, Glostrup, DK*

Objectives: Prepulse inhibition (PPI) is a measure for sensorimotor gating, which reflects the ability to filter out unnecessary information. PPI has been linked to Nurr1 and dopaminergic function in fronto-striatal circuits. This implies that prepulse inhibition could be related to cognitive function. Parkinson's disease (PD) is associated with dopamine-related dysfunction of movement and cognition associated with frontal-striatal circuits. We examined the possible relation between prepulse inhibition, cognitive function and the dopamine system measured by [(123)I]N-omega-fluoropropyl-2beta-carbomethoxy-3beta-{4-iodophenyl}nortropane (123I-FP-CIT) single photon emission computed tomography (SPECT) in PD.

Methods: Thirty-eight PD patients were assessed with prepulse inhibition, neuropsychological testing, and neurological testing. Twenty-three of these patients underwent 123I-FP-CIT-SPECT scanning.

Results: There were significant correlations between PPI at 60 ms 85dB and 123I-FP-CIT uptake in caudate, putamen and striatum. In addition, patients in the high-PPI group (N = 14) performed better on cognitive measures tapping processing speed and executive function than patients in the low-PPI group (N = 9). Moreover, we found an association between 123I-FP-CIT uptake in striatum and cognitive function.

Conclusion: The current study suggests that the level of PPI is related to density of the dopamine transporters in the striatum, and that PPI indexes the efficiency of information processing in PD.

P545

Prepulse inhibition in idiopathic REM sleep behaviour disorder, Parkinson's disease and multiple system atrophy

M. ZOETMULDER[1], H. BIERNAT[1], M. NIKOLIC[2], L. KORBO[1] and P. JENNUM[3]
[1]*Bispebjerg Hospital, Copenhagen, DK,* [2]*Glostrup Hospital, Glostrup, DK,* [3]*Danish Center for Sleep Medicine, Glostrup, DK*

Objectives: Prepulse inhibition (PPI) of the acoustic startle response is a measure of sensorimotor gating, in which a weaker prestimulus (prepulse) inhibits the reaction of an organism to a subsequent strong startling stimulus (pulse). The objective of this study was to determine whether patients with idiopathic REM sleep behaviour disorder (iRBD), Parkinson's disease (PD) and multiple system atrophy (MSA) have altered PPI.

Methods: Twenty-one PD patients with RBD, 20 PD patients without RBD, 12 with iRBD, 10 with MSA and 20 healthy and gender-matched controls entered and completed the study. A passive acoustic PPI paradigm was applied with prepulses 5 dB and 15 dB above background noise at 30-, 60-, 120- and 300-ms intervals.

Results: Startle-response characteristics (latency and habituation) did not differ between patients and controls ($P \geq 0.05$). Non-parametric analyses showed that MSA patients had a significantly lower PPI than the other groups for the 60 ms-85 dB and 120 ms-85 dB prepulses. No differences in PPI were found between the other groups.

Conclusion: The present study suggests that prepulse inhibition is markedly altered in MSA. Since striatal dopaminergic function and the pedunculopontine nucleus (PPN) play a major role in prepulse inhibition, these results are in line with the functional involvement of the striatum and PPN in the pathogenesis of multiple system atrophy. This work was supported by the Lundbeck Foundation; the National Foundation for Parkinson's Disease; Toyota Foundation; and UCB Nordic.

P546

High prevalence of restless legs syndrome among women with generalised pain – a population based study in Dalarna, Sweden

R. STEHLIK[1], J. ULFBERG[2], J. HEDNER[3] and L. GROTE[3]
[1]*Pain Center, Sater, SE,* [2]*Sleep Disorder Center, Orebro, SE,* [3]*Center for Sleep and Vigilance Disorders, Gothenburg, SE*

Background: In a recent pilot study we demonstrated a high prevalence (64%) of the Restless Legs Syndrome (RLS) in patients

with fibromyalgia. The current study extended the investigations to a population-based sample of middle-aged women. The study aimed to assess a possible association between RLS symptoms and the reported degree and localization of pain with a specific focus on females with reported widespread pain.

Method: Of 3084 out of 10 000 randomly selected women aged 18–64 years in Dalarna county, Sweden, responded to a questionnaire on life style items, mental illness, anthropometrics, co-morbidities, medication, and number of areas with bodily pain (five zones, grading 0–5). Subjects also answered four validated questions related to the occurrence of RLS symptoms.

Results: RLS prevalence increased linearly along with number of reported pain areas: No pain – 9.6%/1 zone – 23.9%/2 zones – 26.9%/3 zones – 39.7%/4 zones – 46.2%/and 5 zones – 56.1% prevalence of RLS, respectively. Women with widespread pain (five zones, no pain as a reference) experienced shorter total sleep time (385/424 min), longer sleep latency (42/18 min), increased daytime sleepiness (Epworth Sleepiness Scale 8/5) and reduced mental health (history of psychiatric diseases 54%/14%).

Conclusion: This study shows a significantly increased prevalence of RLS among women with generalized pain in the population. The degree of symptom burden generated by pain and RLS correlate with measures of disturbed sleep and impaired daytime function. Further studies are warranted to identify potential pathophysiological factors and improved treatment strategies.

P547

Rapid eye movement sleep behaviour disorder in the Korean elderly population; prevalence and clinical characteristics

S. H. KANG[1], I. Y. YOON[2], K. W. KIM[2] and S. D. LEE[2]
[1]Dankook university, Cheonan-si, KR, [2]Seoul National University Bundang Hospital, Gyeonggi-do, KR

Objectives: There have been just a few studies to explore the epidemiology of rapid eye movement (REM) sleep behavior disorder (RBD) which are known to cause injuries to patients themselves and bed partners. We examined the prevalence and clinical characteristics of RBD in the Korean elderly population.

Methods: We conducted a cross-sectional and community-based study in Youngin-si, South Korea, from November 2010 to January 2012. Among 6959 individuals aged 60 years or older, 696 subjects were selected using systemic random sampling. All the subjects were invited to visit Seoul National University Bundang Hospital for overnight polysomnographic study. In total, 696 elderly were surveyed and 354 completed overnight polysomnographic studies with video recording. Of the 354 subject, 348 who had a total sleep time more than 3 h and at least 2 episodes of REM sleep were included in this study. Finally, diagnosis of RBD was made according to the criteria of the International classification of sleep disorders (ICSD).

Results: Of 348 subjects, 18 (5.17%, 14 male, four female) were diagnosed as subclinical RBD based on the finding of REM sleep without atonia according to 2007 America Academy of Sleep Medicine (AASM) Manual on polysomnographic data and telephone interview. A total of 7 subjects (2.01%, two female, five male) were confirmed to have RBD, and 4 male subjects were idiopathic RBD and three subjects (one male, two female) were secondary to Parkinson's disease. Mean duration of RBD symptoms was 7.2 years. Dream enacting behaviors (DEB) included talking, shouting, arm flailing and kicking. DEBs were reported at least once a month in RBD patients and one patient had a serious sleep-related injury.

Conclusion: We found that RBD and subclinical RBD were not rare in the elderly but were frequently missed to diagnose. In this study, RBD was more frequently observed in men than women, which is consistent with previous reports. The clinical characteristics and long-term progression of subclinical RBD subjects need to be explored.

P548

Rapid eye movement sleep without atonia and rapid eye movements in narcolepsy with cataplexy

R. IMAI, M. OKURA, H. SUGITA, M. TANIGUCHI and M. OHI
Osaka Kaisei Hospital, Osaka, JP

Objectives: The loss of the skeletal muscle atonia during rapid eye movement (REM) sleep (REM sleep without atonia; RWA) is known as the polysomnographical hallmarks of REM sleep behavior disorder (RBD). However, RWA is also caused by other disorders and medications. An increased chin electromyographic (EMG) activity during REM sleep has frequently been observed in narcolepsy with cataplexy (NC), whereas reports of the patterns and the quantity are fewer in NC than in RBD. We will analyze an increased chin EMG and REMs during REM sleep and will discuss some features of RWA.

Methods: The subjects were 15 consecutive NC (7 male and 8 female, mean age: 40.3 ± 17.7 years old) who underwent video-polysomnography and multiple sleep latency tests at Osaka Kaisei Hospital from January to December 2008. In our RWA scoring based on'The American Academy of Sleep Medicine Manual for Scoring 2007', increased EMG activity was counted separately according to the EMG activity patterns; tonic EMG, the phasic pattern, and combined EMG activities. If chin EMG activity was present for more than 50% of each 30-second epoch, that epoch was scored as tonic. Phasic EMG density was scored from the chin EMG and represented the percentage of 3-second mini-epochs containing EMG activity lasting 0.1–5 s. We calculated the RWA% of total sleep time (TST), the tonic REM%, the phasic REM% and the REMs% during REM sleep.

Results: RWA epochs were seen in 10 (five male and five female, mean age: 46.6 ± 17.2 years old) of the 15 NC. None of the subjects showed any signs of nocturnal behaviors either at home or in the sleep laboratory. The mean values of RWA% of TST were 0.4 ± 0.4% among 10 NC having RWA epochs. The mean values of the tonic REM%, the phasic REM% and the REMs% during REM sleep were 0.04 ± 0.1%, 5.3 ± 2.0% and 37.1 ± 10.6%. Most were occupied by the phasic pattern.

Conclusion: RWA was observed in a high rate of our NC. Some groups have reported mean values of RWA in NC. Compared to that data, our tonic REM% was quite low. Differences in characteristics of the patients and/or methods of RWA scoring might have caused the discordant results. Moreover, compared to RBD, atonia is maintained comparatively, RWA was mainly occupied by the phasic pattern. It was suggested that the mechanism which causes RWA in NC might differ from RBD. Further investigation may be important to clarify the anatomically-distinct pathway of motor control during REM sleep between NC and RBD.

Poster Session – Emotional Processing and Dreaming

P549

Sleep-related attentional bias in poor versus good sleepers is independent of affective valence

N. L. BARCLAY, M. P. STEWART and J. G. ELLIS
Northumbria University, Newcastle, UK

Objectives: There is contradictory evidence related to the presence of an attentional bias to sleep-related stimuli in poor sleepers/insomnia using the Emotional Stroop (ES) paradigm. These inconsistencies may be due to methodological flaws related to the affective valence of the sleep-related stimuli used. Thus, participants may attend differentially to sleep-related stimuli not because of the 'sleep' properties of the words, but their negativity. The current study addresses this by controlling the affective valence of the sleep-related words, compared to neutral and negatively valenced words.

Methods: One hundred and thirty-four participants (mean age = 33.66; SD = 12.61; 63.4% female) were recruited during an evening event at the Newcastle Science Festival. Participants completed the Pittsburgh Sleep Quality Index and an ES task containing 20 purely sleep-related, 20 neutral and 20 negatively valenced words.

Results: Poor sleepers ($n = 63$) were categorised as individuals scoring >5 on the PSQI. There was a significant interaction between good versus poor sleepers and word type on reaction time (RT) in the ES ($F_{1,132} = 4.85$, $P < 0.05$). Poor sleepers took significantly longer than good sleepers to respond to the sleep-related words. Furthermore, for both good and poor sleepers, there was a significantly faster RT to respond to negatively valenced words compared to sleep-related and neutral words ($F_{2,264} = 272.87$, $P < 0.05$).

Conclusion: The results demonstrate the presence of an attentional bias towards sleep-related stimuli in poor versus good sleepers. Furthermore, regardless of one's sleep quality, individuals were faster to respond to negatively valenced words than sleep-related or neutral words. This pattern of results is in accordance with the theory of biological preparedness, i.e. that we inherently respond faster to natural threats (negative words). Thus, speed of response is facilitated by the negative content of the stimuli presented. These patterns of results may account for the inconsistency in the literature. Because previous research has used negatively valenced sleep-related words the slower response to the sleep content may be confounded by the faster response to the negative content. Using emotionally neutral sleep-related words has enabled us to tease apart these effects. Accordingly, the present research suggests there may be two opposing threat-related forces at play: one that is biologically driven (facilitating performance) and the other cognitively driven (hindering performance).

P550

Perfectionism, repetitive thought and sleep quality in female students

S. SÁ, T. CLEMÊNCIO, M. MARQUES, A. PEREIRA and M. H. AZEVEDO
University of Coimbra, Coimbra, PT

To examine the relationship between worry and rumination, perfectionism and sleep quality in female students. Of 468 females (mean age = 19.34 years) completed two Perfectionism Scales, a brief measure of Repetitive thought (tendency to worry and rumination) and a sleep-wake questionnaire including questions on sleep depth, subjective sleep quality, nighttime awakenings and sleep latency. These items were summed to form a sleep quality index (SQI). SQI significantly correlated with Concern over Mistakes/CM ($r = 0.12$, $P < 0.01$), Doubts about Actions/DA ($r = 0.10$, $P < 0.01$), Negative Perfectionism/NegP (Social Prescribed Perfectionism/SPP + DA + CM, $r = 0.12$, $P < 0.05$), Worry ($r = 0.18$, $P < 0.01$) and Rumination ($r = 0.13$, $P < 0.01$). For each of these variables, SQI total mean scores were compared in three groups, based on M ± SD (low = M-1SD; medium = M ± 1SD; high = M + 1SD). Girls with high DA and Worry presented significantly higher mean scores ($P < 0.05$) than the other groups. Linear multiple regression showed that the model composed by CM, DA, Worry and Rumination explained 3.5% of the SQI variance (R2 = 0.035, $P = 0.004$) and that Worry was a significant predictor of SQI (beta = 0.144, $P = 0.018$). The model composed by NegP, Worry and Rumination explained 4.1% of the SQI variance ($R^2 = 0.041$, $P = 0.001$) and Worry was the unique significant predictor of SQI (beta = 0.167, $P = 0.007$). Logistic regression was used to analyze which variables were significant predictors of high SQI (M + 1SD; $n = 32$, 6.8%) versus low SQI (M-1SD; $n = 86$, 18.6%). Variables significantly correlated with this dichotomized variable were: SPP, $rS = 0.285$, $P = 0.003$; NegP, $rS = 0.301$, $P = 0.001$; Worry, $rS = 0.209$, $P = 0.027$; Rumination, $rS = 0.213$; $P = 0.022$. In the model composed by SPP, Worry and Rumination [explained variance = 13.4% (Cox e Snell R square) to19.7% (Nagelkerke R square), $P = 0.002$], only SPP (OR = 1.060, $P = 0.019$) and Worry (OR = 1.473, $P = 0.039$) were significant predictors. The mediation analysis, conducted using the bootstrapping methodology (Preacher & Hayes, 2004), revealed that Worry mediated the relationship between SPP and IQS (high versus low) (IC 95% 0.003–0.016). In the model composed by NegP, Worry and Rumination [explained variance = 17.7% to 26.6%, $P < 0.001$], it was NegP (OR = 1.067, $P = 0.019$) and Worry (OR = 1.412, $P = 0.039$) that were significant predictors. The mediation analysis revealed that Worry mediated the relationship between NegP and IQS (high versus low) (IC 95% 0.003-0.016). Worry mediated the link between perfectionism and sleep quality.

P551

Individual differences in the sleep architectural response to a negative emotional experience: implications for affective disorders

W. F. HOFMAN, L. F. BRINGMANN and L. M. TALAMINI
University of Amsterdam, Amsterdam, NL

Objectives: Sleep problems are strongly related to emotional trauma and affective psychopathology. Furthermore, recent findings show that (emotional) memories may be reprocessed and reorganised during sleep. These observations suggest that sleep-related processes might serve a role in emotional coping. However, direct evidence is scarce. Moreover, there is some evidence for a relation between emotional distress and subjective sleep quality, but the underlying sleep physiology is largely unknown.

Methods: Healthy subjects (23F/9M) spent two nights at the sleep laboratory, separated by at least a week. In a cross-over design sleep was preceded by watching an emotionally distressing film fragment from 'The Passion of the Christ' or a neutral film fragment from' March of the Penguins'. During sleep EEG, EOG and EMG were recorded. Subjective sleep quality was also assessed. The next evening six stills were presented from the pertaining film fragment to cue

subject's memory of the film. Emotional responses to film fragments and stills were assessed with the Dutch version of the Profile of Mood States and a VAS scale. Sleep variables derived from the manually scored sleep stages were: percentage light sleep, deep sleep and REM sleep (over the night and during 1st and 2nd half of the night), sleep latency, latency to deep sleep and REM sleep, number of REM episodes, REM sleep fragmentation, number of awakenings, WASO and sleep efficiency.

Results: Percentage SWS increased after the emotional film ($F_{1,29} = 4.2$, $P = 0.05$). The natural REM increase from the 1st to the 2nd half of the night was reduced ($F_{1,30} = 4.62$, $P = 0.04$). Two subgroups were found who differed in subjective sleep quality after watching the emotional film, but not after the neutral film. The High Sleep Quality Responders (HSQR) had a higher sleep quality [$t(13) = 2.65$, $P = 0.02$] and an increase in%SWS [$t(12) = 2.19$, $P = 0.048$] in the emotional compared to the neutral condition. Conversely, the Low Sleep Quality Responders (LSQR) had a lower sleep quality [$t(17) = -3.43$, $P = 0.003$] in the emotional compared to the neutral condition, but no difference in %SWS. Instead, LSQR showed a lower REM% in the second night half in the emotional compared to the neutral condition [$t(17) = -2.19$, $P = 0.043$).

Conclusion: The combined results provide evidence for a reciprocal relation between sleep physiology and emotional processing and suggest there may be a coupling of certain emotion and sleep traits into distinct emotional sleep types.

P552

Dynamic representations of facial expressions of emotion are affected by time since waking

L. BEATTIE, O. G. B. GARROD, R. E. JACK, P. G. SCHYNS and S. M. BIELLO

University of Glasgow, Glasgow, UK

Objectives: Time of day is known to affect mood, and this may also affect the emotional representations of normal sleepers. Six basic emotions – 'Happy,' 'Surprise,' 'Fear,' 'Disgust,' 'Anger,' and 'Sadness' – are defined by specific, static patterns of facial muscle activation as measured by the Facial Action Coding System codes (FACS). Emotional reactivity seems to change over the day (Gujar et al., 2010; Hot et al., 2005), and there may be systematic differences in the recognition of these six facial expressions at different times since wakening. This raises the question: How variable are the representations of facial expressions over the waking period?

Methods: We derived models of facial expressions using state-of-the-art 4D imaging (dynamics of 3D face shape and texture) combined with a reverse correlation technique. Specifically, we modeled 41 core Action Units (AUs, groups of facial muscles) from certified FACS coders and parameterized each using six temporal parameters (peak amplitude; peak latency; onset latency; offset latency; acceleration; deceleration). On each trial, we pseudo-randomly selected parametric values for each AU, producing an expressive facial animation. Normal sleepers each categorized 1, 200 such animations according to the six emotion categories listed above and rated the perceived intensity of the emotion on a scale of 1–5. We scheduled test times over the test week for 3 or 12 h since habitual weekday waketimes, with eight subjects (four male, four female) in each of the two groups, and all subjects were Western Caucasian (Jack et al. 2009).

Results: A 3-way ANOVA performed on the temporal parameters of each facial expression model [Expression (6) X AU(41) X $Group^2$] revealed a main effect of group (early versus late) on AU peak amplitude, offset latency, and deceleration – specifically, the early group was more sensitive to these three temporal parameters than the late group.

Conclusion: We reveal variability in the dynamic signals representing each basic emotion which are affected by time since wake, demonstrating the complexities of emotion representations within normal sleepers. This adds to the existing literature on the effects of sleep, sleep deprivation, and circadian processes on emotional responding (e.g. Boivin et al., 1997; Golder & Macy, 2011; Gujar et al., 2011; Hot et al., 2005; van der Helm et al., 2010; Vandewalle et al., 2010; Yoo et al., 2007), and could have implications for the etiology of insomnia (Espie, 2002).

This research was supported by an ESRC studentship to L. Beattie.

P553

Sleep develops resistance to emotional interference in memory consolidation

G. DELIENS, M. GILSON, R. SCHMITZ and P. PEIGNEUX

University Libre, Brussels, BE

Objectives: Sleep protects declarative memories from lexical retroactive interference, but little is known about emotional retroactive interference. We investigated the effect of sleep on mood-dependent memory by inducing a similar or different mood at learning and recall sessions.

Methods: Participants ($N = 22$) learned a list of neutral word pairs after a mood induction procedure (combined imagery vignettes and music) then slept (SH) or stayed awake (SD) during the post-learning night in a within-subjects counterbalanced design. After two recovery nights, half of the list was recalled after a similar mood induction than at the encoding session (NIC; non interference condition), the other half after a different mood induction (IC; interference condition).

Results: Pre- and post-mood induction assessment revealed efficacious induction in 13 out of 22 participants only, in whom the same desired mood was present at encoding and retrieval in the NIC condition, and different desired moods were present in the IC condition. Consequently, mood induction efficacy was introduced as a between-groups factor [efficacious (E) or not (NE)] in the ANOVA conducted on number of correctly recalled pairs, with sleep and interference as within-subject factors. Results disclosed main effects of Sleep ($P < 0.02$; higher recall in SD than SH) and Interference ($P < 0.005$; higher recall in NIC than IC), and a Sleep $\times$ Interference $\times$ Mood induction interaction effect ($P < 0.05$). Statistical decomposition revealed that after efficient mood induction (E group), emotional interference was present after SD ($P < 0.001$) with lower recall of IC than NIC word pairs, but not after SH ($P > 0.9$). In the NE group (unsuccessful induction), recall of IC and NIC was lower after SH than SD ($P < 0.05$), but there was no interference effect both after SH and SD (all ps > 0.1).

Conclusion: Results support the hypothesis of a demodulation between memories (i.e. word pairs) and their 'affective blanket' tone (i.e. the emotional mood context) across post-learning sleep, eventually protecting memories against emotional retroactive interference, in line with the 'Sleep to Forget and Sleep to Remember' model (Walker & van der Helm, 2009). We surmise that sleep deprivation after learning prevents this demodulation process to occur, with the consequence that induction of a different mood during retrieval can interfere with the retrieval of word pairs still linked to their learning-related affective context.

This study was supported by a FNRS (Fonds National Belge de la Recherche Scientifique) grant CC 1.5.184.10F. GD and RS are supported by FNRS

P554

Emotional evaluation for decision-making and REM sleep

K. OGAWA, N. UMEMOTO and M. HAYASHI
Hiroshima University, Higashi-Hiroshima, JP

Objectives: Recently, the relationship between sleep and decision-making has been investigated. However, little is known about the relationship between REM sleep and emotional processing on decision-making. In this study, we focused emotion elicited by decision-making, and investigated the relationship between REM sleep and emotional evaluation for decision-making.

Methods: Healthy seven students (mean 21.6 years old) participated in the study for three days. Two days were nap condition and the other was no-nap condition. The order of the conditions was randomized among the participants. In the nap condition, they engaged in either of the decision-making or non decision-making task at 1 pm. They were required alternative judgment on the scenario of everyday life in the decision-making task. After the task, they immediately evaluated their emotion elicited by their decision (satisfaction, possibility of re-judgment, unhappiness, ambivalence, and validness). At 1:30 pm, they took a nap and were awakened after 90 min elapsed from the onset of sleep stage 2. After awakening from the nap, they re-evaluated their emotion. In the wake condition, they also engaged in the decision-making task and evaluated their decision. After 2-h waking, they re-evaluated their emotion as the nap condition.

Results: Total nap time was 101.2 ± 3.4 min after decision making task, while 102.1 ± 7.4 min after non-decision making task. No significant difference between the tasks was observed for total sleep time, NREM and SREM duration, SREM latency and rapid eye movements (REMs) density. However, unhappiness evaluated before the nap negatively correlated with SREM latency ($r = -0.83$, $P < 0.05$) and positively correlated with REMs density during REM sleep ($r = 0.77$, $P < 0.05$). Ambivalence significantly decreased after taking the nap, and negatively correlated with SREM duration ($r = -0.77$, $P < 0.05$).

Conclusion: These results suggest that negative emotion elicited by decision making before sleep affects REM sleep (SREM latency and REMs density), and that REM sleep itself associated with the inhibition of the negative emotion after sleep.

P555

Sleep preferentially advantages important memories

D. OUDIETTE, J. W. ANTONY, J. D. CREERY and K. A. PALLER
Northwestern University, Evanston, US

Objectives: After learning, some memories fade while others endure for a longer time. We hypothesize that sleep has a role in the seemingly arbitrary nature of memory preservation. Accordingly, we set out to determine whether, during sleep, stored information undergoes memory consolidation in accordance with the importance of that information.

Methods: Sixteen young subjects learned 72 object-place locations. A number in the middle of each object indicated its value in relation to subsequent reward (1 or 2 for a low value, 8 or 9 for a high value, equally distributed). Subjects earned the corresponding point value for correctly remembering an object's location, and they were instructed to plan their learning in order to maximize their score at the end of the session (which resulted in a corresponding monetary reward). Subjects were tested 40 min after the learning period, which was followed by a 90-min afternoon nap period and then a final test.

Results: Subjects slept 67 ± 21 min, and 32% of sleep time was spent in slow-wave sleep. Before sleep, recall was better for high-value items than for low-value items (81% versus 64% correct, respectively, $P = 0.008$; recall error 1.66 ± 0.25 cm versus 1.93 ± 0.3 cm, $P = 0.004$). After sleep, recall was less accurate than before, but this decline was not as great for high-value items compared to low-value items (change in error 0.59 ± 0.75 cm versus 1.26 ± 0.83, respectively, interaction, $P = 0.013$).

Conclusion: Our data indicate that sleep provides a particular advantage for items that are tagged as important to remember during learning. Presumably, sleep entails the preferential reactivation of high-value items over low-value items. Spectral analyses will be conducted to determine whether delta power or spindle activity is associated the differential memory advantage as a function of item value.

P556

Visual creativity and sleep structure and quality among visual arts and psychology students

T. SHOCHAT[1], N. RAM[1], A. GREEN[2] and O. TZISCHINSKY[3]
[1]University of Haifa, Haifa, IL, [2]Assuta Medical Center, Tel Aviv, IL, [3]Emek Yezreel College, Emek Yezreel, IL

Objectives: Several studies have suggested that sleep facilitates creativity. Conversely, little is known regarding the possible effects of creativity as an individual trait or profession on sleep structure and quality. There are some indications that creativity may be related to specific sleep stages and may predispose individuals to poor sleep quality. This study explores relationships between visual creativity and the structure and quality of sleep in visual arts students and psychology students. It was hypothesized that visual creativity and the practice of visual arts may predispose to alterations in sleep structure and to poor sleep quality. Specifically, it was predicted that: (i) among all students, increased visual creativity is related to altered sleep structure and reduced sleep quality, (ii) visual arts students exhibit altered sleep structure and reduced sleep quality compared to psychology students.

Methods: Fourteen visual arts and 16 psychology students participated in the study. Visual creativity was measured using the Torrance Tests of Creative Thinking (TTCT). Sleep was assessed by overnight polysomnography (PSG) and the self-report Pittsburgh Sleep Quality Index (PSQI). Relationships between measures of creativity and sleep for the entire sample were computed by Pearson correlations, and group comparisons of sleep measures were performed by MANOVA.

Results: Increased visual creativity was related to poor subjective sleep quality ($r = 0.37$, $P = 0.045$). In particular, visual elaboration was related to sleep disturbances ($r = 0.39$, $P = 0.035$), daytime dysfunction ($r = 0.39$, $P = 0.033$) and overall sleep quality ($r = 0.39$, $P = 0.036$). Significant relationships were not found between measures of creativity and stages of sleep. Compared to psychology students, visual arts students reported more sleep disturbances ($P = 0.006$), more daytime dysfunction ($P = 0.050$), tended to report poorer overall sleep quality ($P = 0.088$) and tended to have shorter stage 3 sleep percentage (8.50 ± 2.44 versus 6.68 ± 2.86, $P = 0.07$).

Conclusions: This study suggests that visual creativity and the practice of visual arts may constitute predispositions for poor sleep

quality among young adults. Future investigations may characterize specific cognitive, emotional and behavioral mechanisms underlying the relationships between the creative process and the structure and quality of sleep.

P557

Experiential versus analytical emotion regulation and sleep: breaking the link between negative events and sleep disturbance

M. VANDEKERCKHOVE[1], J. KESTEMONT[1], J. GROSS[2], R. WEISS[3], E. DE VALCK[1], J. WUYTS[1], N. MARCOEN[1], C. SCHOTTE[1], V. EXADAKTYLOS[4], V. VERHAERT[4], B. HAEX[4], J. VERBRAECKEN[5] and R. CLUYDTS[1]

[1]Vrije Universiteit Brussel, Brussels, BE, [2]Stanford University, Stanford, US, [3]University of Cologne, Cologne, DE, [4]Catholique University of Louvain, Louvain, BE, [5]University of Antwerp, Antwerp, BE

Objectives: Despite a history of interest in emotion regulation as well as in the mechanisms that regulate sleep, the relationship between emotion regulation and sleep is not well understood yet.

Methods: The present study investigated whether an 'experiential' compared to a' cognitive analytical approach' would buffer the impact of an emotional failure experience on (i) emotion, and (ii) sleep structure assessed by EEG polysomnography. The 'experiential approach' (EA) is defined as affectively acknowledging, understanding, and the preparedness to express actual emotional experience and affective feeling about a situation, while the cognitive analytical approach (AA) is defined by the cognitive analysis of the causes, meanings and implications of the situation for the own self. Twenty-eight healthy volunteers (15 male, 13 female) were enrolled (mean age = 22.43 years, SD = 5.79) participated in this study.

Results: A direct comparison of the two emotion regulation strategies revealed that participants who were instructed to apply an EA felt significantly less 'distressed' (MExper. = 1.46-MAnal. = 2.00) ($F_{1,15} = 5.22$, $P = 0.037$), 'hostile' (MExper. = 1.15-MAnal. = 1.50) ($F_{1,15} = 29.77$, $P < 0.001$) and less 'irritable' (MExper. = 1.69-MAnal. = 2.30). On the level of sleep physiology, participants instructed to use an EA compared to those instructed to apply an AA showed less fragmentation of sleep. They were found to have more -total sleep time (MExper. = 425.05, SD = ±16.26) than participants in the analytical condition (Anal. M = 408.48, SD = 13.55) ($F_{1,14} = 4.31$, $P = 0.057$), -a slightly shorter sleep onset latency (MExper = 11.05, SD = ± 6-MAnal. = 29.86, SD = ±4.47), ($F_{1,14} = 5.26$, $P = 0.038$), -less awake after sleep onset (WASO) (MExper. = 16.63, SD = ±10.72 – MAnal. = 48.05, SD = 9.17), ($F_{1,14} = 4.57$, $P = 0.051$), -less awakenings (MExper. = 5.21, SD = ±1.49 – MAnal. = 10.96, SD = 1.26), ($F_{1,14} = 8.44$, $P = 0.012$), and higher sleep efficiency (MExper. = 96, 63, SD = ±2.36 – MAnal. = 89.36, SD = ±2.03), ($F_{1,14} = 5.07$, $P = 0.041$).

Conclusion: The present study suggests an adaptive regulatory effect of an EA in the recovery from a painful experience with effects even extending into sleep physiology.

This study was part of a research project funded by the agency for Innovation by Science and Technology (IWT).

P558

Neuronal correlates of emotional olfactory processing during sleep

J. S. RIHM, O. BOSCH, P. STÄMPFLI, E. SEIFRITZ and B. RASCH

University of Zurich, Zurich, CH

Objectives: Odours are actively processed during sleep. For example, odours administered during sleep are incorporated into dreams (Trotter et al., 1988) and influence the emotional valence of dream reports (Schredl et al., 2007). However, the underlying brain activation of emotional olfactory processing during sleep is unknown.

Methods: In this study, we specified the neural correlates of emotional olfactory processing during sleep using combined electroencephalography (EEG) – functional magnetic resonance imaging (fMRI) recordings. In a within-subject design, healthy young women either slept or stayed awake in the magnetic resonance imaging (MRI) scanner. During sleep and wakefulness, the participants repeatedly received a negative, a positive and a neutral odour as well as an odourless vehicle in a randomized order. EEG and skin conductance responses were measured during fMRI recording.

Results: Preliminary analyses show that administration of emotional odours results in valence-specific activation in similar brain regions during sleep and wakefulness, including for example the primary olfactory cortex as well as orbitofrontal brain regions.

Conclusion: Our results suggest that subcortical as well as cortical brain areas participate in the valence-specific evaluation of emotional stimuli in the absence of conscious awareness during sleep.

P559

Sleep loss and night-time impair the recognition of emotional facial expressions but not the perception of emotional verbal stimuli

L. MACCARI[1], D. MARTELLA[2], A. MAROTTA[1], M. SEBASTIANI[1], N. BANJAI[1], A. SPAGNA[1], L. J. FUENTES[3] and M. CASAGRANDE[1]

[1]University of Rome 'Sapienza', Rome, IT, [2]Basque Center on Cognition, Brain and Language, San Sebastian, ES, [3]Universidad de Murcia, Murcia, ES

Objectives: It is well known that reduced vigilance due to both night-time work and Sleep Deprivation (SD) cause a general slowing of reaction times (RTs) but it is not yet clear how emotions can modulate such effect. Recently, it has been observed an amplified hyper-limbic response by the human amygdala to negative emotional stimuli and amplified human mesolimbic reward brain networks in response to pleasure-evoking stimuli under conditions of SD. Furthermore SD selectively impairs the subjective judgment of human facial emotions. This study aims to evaluate the effect of partial SD and nighttime on the recognition of emotional faces (EF) and words (EW).

Methods: Eighteen healthy volunteers (3M/15F; mean age: 24.3 ± 2.3) had to discriminate the emotional valence (negative NG, positive PS, neutral NU) of the stimuli (EF, EW) presented laterally to a central fixation by pressing a key on the clipboard. The experiments were run on two consecutive days. In the morning of the first day, participants performed the training task. On the second day, after participants slept their usual 8 h, they were kept awake for 24 h and were required to perform the EF test at about 12.00a.m. (Baseline: BSL) and at 3.00 am. (SD) and the EW test at about 6.00 p.m. (BSL) and at 7.00a.m. (SD). The order of BSL and SD conditions were balanced across subjects.

Results: The ANOVA performed on RTs showed a significant effect for Session in both experiments (EF: $F_{1,17} = 14.3$; $P < 0.001$; partial eta2 = 0.46; EW: $F_{1,17} = 20.1$; $P < 0.0001$; partial eta2 = 0.54), with slower RTs in the SD (Mean EF RT: 881.6 ms; Mean EW RT: 829.2 ms) than in BSL (Mean EF RT: 843.2 ms; Mean EW RT: 912.9 ms). The main effect of Valence (EF: $F_{2,34} = 21.3$; $P < 0.0001$; partial eta2 = 0.56; EW: $F_{2,34} = 26.3$; $P < 0.0001$; partial eta2 =

0.61) was also significant in both experiments. The Session × Valence interaction ($F_{2,34} = 3.9$; $P < 0.005$) was significant only in the EF experiment, showing a stronger effect of the SD for the NU facial expressions (871.3 ms versus 936.4 ms; $P < 0.0001$), a weaker effect for the NG ones (854.1 ms versus 888.2 ms; $P < 0.05$) and no effect for the PS expressions (804.1 ms versus 820.3 ms; $P = 0.2$).

Conclusion: The emotional valence modules the SD effect only during the face recognition, while emotional valence does not interact with SD effect when EW are used. These findings suggest that SD affects the processing of emotional stimuli only when the latter have an important biological value (e.g. they are faces).

P560

Sleeping on it: the role of sleep in affective decision-making

C. J. SEELEY[1], C. T. SMITH[2] and R. J. BENINGER[1]

[1]Queens University, Kingston, CA, [2]Trent University, Peterborough, CA

Objectives: The Iowa Gambling Task (IGT) was developed to measure implicit cognitive-emotional reasoning ability – that is, the ability to use past experience with rewards and penalties to make advantageous decisions. A criticism of the original 100-trial task is that learning behaviour is a result of a preference for decks with low-frequency penalties (LFP) rather than an understanding of the strategy involved in gaining money. We conducted two studies to investigate: (i) how decisions improve with extended trials and across multiple sessions, and (ii) whether intervening sleep improves performance.

Methods: Study 1: participants ($n = 11$) underwent two, 200-trial sessions spaced 24 h apart. Results suggested a strong preference for the LFP decks at time 1, and a shift towards an advantageous strategy within the first 50 trials at time 2. Study 2: the same 200-trial task was tested and retested after 12 h of wakefulness ($n = 25$) or 12 h with intervening sleep ($n = 25$). Participants were categorized into: 1) learners ($n = 19$) and 2) non-learners ($n = 31$) based on initial performance at time 1. Improvement from time 1 to time 2 for all decks was combined for a total improvement score. All participants were healthy young adults (aged 18–24; 38 females).

Results: Study 1: Across 400 trials, deck choice began to shift towards the 'good' decks with positive net gain and away from the 'bad' decks with negative net gain. At 250 trials, preference for the LFP 'bad' deck (Deck 2) decreased from 40 to 30% ($P < 0.05$) and increased from 20 to 30% ($P < 0.05$) for the high-frequency penalty 'good' deck (Deck 3). Study 2: Learners in session 1 reached the criteria reported above (<30% on Deck 2 and >20% of Deck 3). Non-learners were above and below the respective values, or chose bad decks 40–70% of the time. At time 1 the learning 'wake' and 'sleep' groups chose equally from all decks ($P = 0.70$). However, at time 2 those with intervening sleep improved more than those that remained awake [$F_{1,17} = 4.90$, $P = 0.04$]. The non-learning 'sleep' and 'wake' groups improved equally [$F_{1,29} = 0.06$, $P = 0.80$].

Conclusion: Over time choices decreased in the LFP 'bad deck' and towards the high-frequency penalty 'good' deck. Individuals that showed evidence of this shift and had intervening sleep, improved 32%, while those that remained awake improved only 15%. These results imply 'sleeping on it' may be effective in processing affective information and help when making complex decisions.

P561

The Effects of sleep restriction or fragmentation on attention, mood and emotion recognition

A. SADEH, Y. BAR HAIM, S. FRIDENZON and R. LERER

Tel Aviv University, Tel Aviv, IL

Objectives: To compare the effects of sleep restriction (SR) versus sleep fragmentation (SF) on attention, mood and emotion recognition in young adults.

Methods: Sleep, attention, mood and emotion recognition were assessed in 42 students (26 females; mean age = 24.3) using a home-based experimental design of SR/SF. Participants were randomly divided into SR or SF groups. In the SR group participants were tested twice: following a night of normal sleep (>7 h) and following restricted sleep (<4 h), in random order. In the SF group the participants were tested twice: following normal sleep and following sleep fragmented night during which they were awakened four times for at least 10 min. Compliance with the sleep protocol was monitored using actigraphy, scheduled phone calls and online Internet tasks. Attention was tested using an online continuous performance test (OCPT). Mood was tested using the POMS and emotion recognition was tested using the Eyes Test requiring recognition of emotional expressions from pictures of the eyes area reflecting different emotions. All these tools have been validated in previous research and were administered online.

Results: Actigraphic measures verified the effects of the manipulations. In the SR group true sleep time during the SR night was significantly shorter in comparison to the control night (Mean = 202 versus 417 min). In the SF group, the number of night-wakings was significantly higher during the SF night in comparison to normal night (Mean = 5.6 versus 2.4). A significant increase in omission errors was found on the OCPT following SR and SF nights in comparison to normal sleep. Mood scales reflected significant increase in fatigue and negative mood following SF/SR. On the emotion recognition task the accuracy of the recognition was similar following normal versus SF/SR nights, however, following SR/SF, performance was significantly faster in comparison to performance following normal sleep. There were no significant differences in outcomes between SR and SF on all tasks and both sleep manipulations led to similar effects.

Conclusions: Very similar effects were found for SR and SF. The effects included compromised vigilance/attention and increase in reported fatigue and negative mood. SR and SF did not influence the accuracy of emotion recognition. However, the emotion recognition was much faster following SF/SR, which may be linked to reduced involvement of higher regulatory cognitive processes and self-criticism.

P562

Dreaming while asleep; a cognitive simulation of wakefulness -the neuroscience perspective

M. TORABI NAMI[1], A. A. SAREMI[1], H.-R. CHEGINI[1], Y. BAGHER-ZADEH[1] and G. MADADI[2]

[1]Institute for Cognitive Sciences Studies, Tehran, IR, [2]Shiraz Medical University, Shiraz, IR

Recent neuroscience research on mind wandering, daydreaming and simulation has offered interesting insights about the common mechanisms which govern dreaming, its content and relation with regard to wakeful cognition. Based on cognitive neuroscience theories of sleep, distinct brain regions including association cortices, limbic and para- limbic structures are considered as neuro-anatomical underpinnings for dreaming. These areas are also involved in

integration of sensory inputs, memory processing and regulation of emotions. There are commonalities in neural circuitries of wakeful cognitive processing and dreaming while asleep. The theories supporting the interface of the systems regulating wakeful cognition and dreaming continue to gain strength. The default mode network is involved in regulation of brain calm wakefulness state. This network also plays a role during mind wandering, daydreaming and simulation. Given this, it is hypothesized that dreaming occurrs due to partial activation of default network during sleep. This communication tries to put these ideas together, so that to conceptualize a framework in understanding the relationship between wakeful cognition and dreaming.

P563

Biases in the relationship between dream threats and level of anxiety upon awakening

I. SAEZ-URIBARRI
Fundación Hobetuz, Vitoria-Gasteiz, ES

Objectives: Controlling report length in dream content analysis comprises a significant methodological problem. Individual differences occur in report length which can influence category coding and rating scales. Differences are also found in dream content by sex and age. The aim of this study is to determine the bias of certain variables in dream content analysis when using rating scales, coding systems and questionnaires. As such, an evaluation was performed of the bias of these variables on the relationship between anxiety upon awakening, social threats (ST) and terrifying threats (TT) established in a previous study.

Methods: The sample consisted of 215 dreams collected in dreamers' homes (63 belonged to men and 152 to women). The dreamer's level of anxiety upon awakening was assessed with the CEAD. The level of social and terrifying threats in the content of the dreams was also assessed. Other variables entered into the analysis were sex, age, dream length, number of hours before answering the questionnaire, number of hours' sleep and the frequency with which the dreamer suffers nightmares.

Results: Use of the Mann Whitney U found significant differences by sex in the dreamer's nightmare frequency ($z = -2.53$ $P = 0.011$), in terrifying threats in the dream ($z = -2.03$ $P = 0.042$) and by dream time ($z = -2.51$ $P = 0.012$). The Spearman Rho correlation coefficient indicated a positive relationship between anxiety upon awakening and nightmare frequency ($Rho = 0.26$ $P < 0.001$). Social and terrifying threats were also positively correlated with word count and the number of dream characters ($Rho = 0.37$ $P < 0.001$, $Rho = 0.17$ $P = 0.010$). Both anxiety upon awakening and social and terrifying threats were negatively correlated with the age of the dreamer [$Rho(CEAD\text{-}AGE) = -0.20$ $P = 0.006$, $Rho(ST\text{-}AGE) = -0.30$ $P < 0.001$, $Rho(TT\text{-}AGE) = -0.37$ $P < 0.001$]. Possible biases due to sex, age, word count and the number of characters were statistically controlled by means of partial correlation. Through the use of partial correlations, the significance between anxiety upon awakening, social threats and terrifying threats in the dream was observed to be maintained [$r(CEAD\text{-}TS) = 0.17$ $P = 0.025$, $r(CEAD\text{-}TT) = 0.19$ $P = 0.011$].

Conclusion: The sex, age of the dreamer, the report word count and the number of dream characters must be controlled in research into dream content. In addition, after eliminating these biases, a significant relationship was confirmed between threats which appear in the dream and the dreamer's level of anxiety upon awakening.

P564

Changing perspectives in rapid eye movement behaviour disorder

A. DAGOSTINO[1], R. MANNI[2], G. FARACI[3], M. TERZAGHI[2], S. CAVALLOTTI[1], A. CASTELNOVO[4], R. RANIERI[4], M. MARCATILI[4] and S. SCARONE[1]
[1]Università degli Studi di Milano, Milan, IT, [2]National Institute of Neurology C. Mondino, Pavia, IT, [3]National Institute of Mental Health, Bethesda, US, [4]San Paolo Hospital, Milan, IT

Objectives: Early descriptions of violent and aggressive behaviors during REM sleep are now thought to only partially reflect the complex variety of motor enactments observed in patients diagnosed with REM sleep behavior disorder (RBD). Dreams in this population are also anecdotally described as violent, threatening and aggressive as opposed to a generally 'mild' waking temperament. This finding led to the development of several hypotheses of dream generation related to disinhibition of archaic cerebral regions in the context of a neurodegenerative disturbance. The main objective of this presentation is to review recent advances with detailed reference to emerging laboratory findings in both dream and behavioral sleep research.

Methods: We will thoroughly review literature on abnormal movements and correlated dream mentation in patients affected by RBD. We will describe current controversies in the field and develop plausible explanations to direct future research.

Results: Several recent studies, including some of our group, seem to suggest a discrepancy between clinically described phenomena and experimental findings in both dream and behavioral sleep research. Indeed, the typically depicted aggressive and violent nature of the disorder appears to depend upon a comprehensible episode recall biases in terms of both behavioral enactment and dreams.

Conclusion: Recent findings do not support the anecdotal view that dreams of RBD patients contain more aggressive elements than those of the general population. This observation appears to be in line with findings on a vast array of enactments ranging from simple limb movements to complex behavior such as smoking or eating besides the well-known punching and kicking episodes. Absence of a clear differentiation between symptomatic and idipathic RBD could also contribute to previous misleading findings. Patients' passive, reluctant personality trait could be interpreted as an early subtle sign of the apathy that is commonly described in the context of neurodegenerative disorders.

P565

Event-related potentials via non-painful tactile stimuli in sleep

A. ONIZ, G. INANC and M. OZGOREN
Dokuz Eylul University, Izmir, TR

Objective: There are no studies in literature related to research on non painful tactile stimuli during sleep in the adult population; Therefore the aim of this study was to investigate brain responses to non-painful tactile stimuli in oddball paradigm via electrophysiological during different (light and deep) stages of sleep.

Methods: In the study, 10 healthy volunteers (21–26 years old, mean age: 23; five females) slept at Sleep Dynamics Research Laboratories of Dokuz Eylul University Department of Biophysics (SDRL-DEU). All subjects were right-handed. No one reported a history of psychiatric or neurological disorder. The subjects spent a full night in a dimly illuminated, isolated room. Electroencephalography (EEG, 40 channels, ref as linked earlobes), electrooculography

(EOG) and electromyography (EMG) activities were recorded. Non-painful pneumatic (4-D Neuroimaging) tactile stimuli were applied to the two (index and middle) fingers on the right hand. The target (%20–25) stimuli were presented on index finger and non-target stimuli (%75–80) were presented on middle finger, randomly. Inter-stimulus interval was selected as 3–3.5 s. Scoring was made in accordance with American Academy of Sleep Medicine (AASM). In this study only light and deep sleep stages are reported. SPSS 16.0 was used for the statistical analysis. Wilcoxon test was used to compare two stimuli (target and non-target, T and NT) within groups (light and deep sleep).

Results: Primarily 12 electrodes (FZ, CZ, PZ, OZ, F3, F4, C3, C4, P3, P4, T3, T4) were analyzed. N100, P200, N300, P450, N550 and P900 waveforms were clearly observed in light and deep sleep for both T and NT. There was no significant difference between target and non-target responses for right hand.

Conclusion: During wakefulness, event related potentials (ERPs) are related to attention and information processing; P300 is the best known of such potentials. This component is often studied using an oddball task for investigating cognitive functions. The amplitudes of the responses to T are known to be larger than to NT stimuli during wakefulness. The current study shows that, with the use of oddball paradigm, the standard P300 component disappears in sleep and replaced by sleep specific waveforms (N300, P450, N550, P900) during NREM sleep.

P566

Types of dream incorporations of language learning and learning efficiency

J. DE KONINCK, C. WONG and G. HÉBERT
University of Ottawa, Ottawa, CA

Objective: It has been observed that incorporations of a new language into dreams appears earlier in more efficient language learners. It has more recently been proposed that dream content itself is involved in the learning process. However, we have recently reported that incorporations related to the learning experience were often expressions of frustration/anxiety with the task rather than actual rehearsal exercises. We attempted to determine if language learning performance is related to the type of incorporations and hypothesized that incorporations of learning with frustration/anxiety (FA) would be associated with poorer performance while incorporations without anxiety would be associated with better performance.

Methods: Sixteen young adult Anglophones recorded their morning recalled dreams during a six- week total French immersion program: classes, social activities in French and sharing a room in residence with a French-speaking student. Participants took a French competency test before and after the program. The dreams were scored for incorporations involving French and divided into those who were expressions of frustration/anxiety and those who were not.

Results: There was a positive correlation between the total number of incorporations and improvements in language proficiency but it did not reach significance ($r = 0.35$). As predicted, there was a significant negative correlation between the number of incorporations associated with FA and language proficiency ($r = -0.45$, $P < 0.04$, directional). More specifically, there was a significant negative correlation between the proportion of incorporations with FA and language proficiency ($r = -0.54$, $P < 0.02$, directional). Finally, incorporations of learning tasks without FA were positively correlated with performance but did not reach significance ($r = 0.40$).

Conclusion: While it is recognized that these correlations do not explain a lot of the variance, these results support the notion that incorporations of learning experiences into dreams that contain frustration and anxiety do not appear to be associated with the learning process but instead may be a reflection of obstacles encountered. To the extent that the dreams studied here arose from REM sleep, it can be speculated that the intense activation of the amygdala in this stage may prevent the dream content from engaging in actual rehearsal of learning while other centres may be responsible for the documented contribution of this stage to learning.

Poster Session – Neurophysiology: Cholinergic, Forebrain Systems

P567

Changes in M2/M4 muscarinic cholinoreceptors density and sleep disturbances against a background of hypo- and hyper-functioning of brain muscarinic cholinergic system

N. MAGLAKELIDZE, E. CHKHARTISHVILI, O. MCHEDLIDZE, S. DZADZAMIA, M. BABILODZE, E. CHIJAVADZE, T. ONIANI and N. NACHKEBIA

I.Beritashvili Center of Experimental Biomedicine, Tbilisi, GE

Objectives: Functional modification of muscarinic cholinergic system (MChS) is producible by different methods. Multiple administrations of muscarinic antagonists and their withdrawal are considered as one of the most appropriate tools. Against a background of these conditions it is topical to clarify whether withdrawal of muscarinic antagonists can lead to sleep changes opposite to those developed during its hypo-functional state and to changes in density of M2/M4 muscarinic cholinoreceptors supposed to be involved in REM sleep basic mechanisms and pathophysiology of depressive disease.

Methods: In cats (n = 3) systemic administration of atropine and/or scopolamine was made once daily at 10:00 am and immediately was started EEG registration of sleep cycles (SAGURA EEG/PSG system) lasting for 10 h daily. Each animal received anti-muscarinic drugs for 12 times. Thereafter drugs administrations were ceased but 10 h EEG registration of sleep cycles was continued during 10 consecutive days. Sleep changes were analyzed during the periods of drug delivery (MChS hypo-functional state) and withdrawal period (MChS hyper-functional state). Measurement of the density M2/M4 muscarinic cholinoreceptors in synaptic membranes of hippocampus and neocortex was made by Western Blotting by means of specific antibodies. Statistical processing was made by Students' t-test.

Results: MChS hypo-functioning produced sharp increase of sleep latency and distinct dissociations between EEG and behavioral patterns of sleep-wakefulness cycle behavioral states. REM sleep was wholly deprived during all the periods of occupation of muscarinic cholinoreceptors by antagonists. The first REM episode appeared after partial recovery of hippocampal theta rhythm i.e. after partial removal of muscarinic antagonists from cholinoreceptors and partial normalization of their functional state. For the period of MChS hyper-functioning REM latency appeared sharply shortened, REM incidence and total time was increased significantly. Slow wave sleep was fragmented and more superficial then during MChS hypo-functioning. Density of M2 and M4 muscarinic cholinoreceptors in post-synaptic membranes of hippocampus and neocortical areas was significantly increased in drug withdrawal period.

Conclusion: MChS hypo- and hyper-functioning leads to opposite sleep disturbances and significant increase in density of M2/M4 subtypes of muscarinic cholinoreceptors in drug withdrawal period.

P568

Disturbances of sleep-wakefulness cycle and changes in density of M2/M4 muscarinic receptors in animal model of depression with super-sensitivity of brain muscarinic cholinergic system

N. NACHKEBIA, E. CHKHARTISHVILI, O. MCHEDLIDZE, S. DZADZAMIA, N. MAGLAKELIDZE, M. BABILODZE, E. CHIJAVADZE and T. ONIANI

I.Beritashvili Center of Experimental Biomedicine, Tbilisi, GE

Objectives: Work was intended to develop animal model of depression by means of methodical approach inducing malfunctioning of muscarinic cholinergic system (MChS) in rat pups during early postnatal period. We believed that experimentally induced deficiency in MChS functioning would produce lasting super-sensitivity of MChS in adult age. We have studied character of sleep disturbances and changes in the rate of M2/M4 muscarinic cholinoreceptors in neocortex and hippocampus of adult rats exposed postnatally to Atropine (Atr) and/or Scopolamine (Scop).

Methods: Rat pups received subcutaneously Atr and/or Scop (15 mg/kg) daily during two weeks as follows: Atr injection starting at postnatal day 7 (P7) and/or at P14; Scop injection starting at P7 and/or at P14. Adult control non-depressive rats were selected by Porsolt's test. After drugs discontinuation rat pups were maintained in home cages under special care. EEG registration of sleep-wakefulness cycle was started 8–12 weeks after the end of treatment and continued for 10 h daily during 7 consecutive days. Density of M2/M4 muscarinic cholinoreceptors in synaptic membranes of hippocampus and neocortex was measured by Western Blotting by means of specific antibodies. Statistical processing was made by Students' t-test.

Results: In all experimental groups slow wave sleep became fragmented and superficial. REM latency appeared four times shorter than in control rats. Sleep was frequently started by REM episodes. REM incidence was three times frequent comparing with the same indices of control rats. REM total time was increased for three times. Mean time of REM episodes was sharply reduced. Minimal duration of REM fragments was in the range of 10–15 s. Such fragments appeared frequently during 10 h EEG registration. The rate of M2/M4 sub-types of muscarinic cholinoreceptors appeared significantly higher in hippocampal and neocortical postsynaptic membranes in rats with postnatal exposure to muscarinic antagonists.

Conclusion: Rat pups exposed postnatally to muscarinic antagonists exhibit in adult age MChS super-sensitivity and face and construct validity with human depressive disease, considering character of sleep disturbances and significant up-regulation of M2 and M4 cholinoreceptors. Results support the significant role of MChS super-sensitivity in pathogenesis of depression.

Supported by Science and Technology Center in Ukraine and Shota Rustaveli National Science Foundation, Grants # 545 and 6–465

P569

Enhanced REM sleep and cholinergic hyperactivity in forebrain-specific CRH-overexpressing mice

M. L. CURZI, C. FLACHSKAMM, J. M. DEUSSING and M. KIMURA
Max Planck Institute of Psychiatry, Munich, DE

Objectives: Sleep disorders have been considered as a cardinal symptom of depression. Furthermore, increased hypothalamic–pituitary–adrenal (HPA) axis activity appears to be related to impaired sleep, in particular reduced slow-wave sleep and disinhibition of rapid eye movement (REM) sleep. Recently, we demonstrated upregulated REM sleep in two types of different conditional CRH-overexpressing mouse models, i.e., CNS-specific (CRH-COE-Nes) and forebrain-specific (CRH-COE-Cam). These results suggest that overexpressed CRH in the forebrain including limbic structures contributes to enhanced REM sleep, which may apply similarly to the case of depressed patients. The present study examined a possible involvement of altered cholinergic activity by limbic CRH in REM sleep regulation.

Methods: CRH-COE-Cam mice were implanted with a guide cannula for *in vivo* microdialysis probe targeting the right central nucleus of amygdala (CeA). Extracellular levels of acethylcholine (ACh) and spontaneous locomotor activity were determined across 2 days. In another experiment, mice of the same line were bilaterally implanted with cannulae in the CeA for microinjection of a muscarinic receptor antagonist, atropine, and EEG/EMG recording electrodes. After baseline recordings, all animals were bilaterally injected either with 10 ng of atropine or with saline at ZT 6 from the onset of the light period (ZT 0). Recovery sleep was compared between control and homozygous CRH-COE-Cam mice.

Results: Compared with controls, homozygous CRH-COE-Cam mice showed constantly elevated ACh levels throughout 48 h, whereas spontaneous locomotor activity was similarly observed in both genotypes. All animals showed correlative increases in the concentration of ACh and spontaneous locomotor activity. Atropine injection in the CeA reduced REM sleep but not NREM sleep in homozygous CRH-COE-Cam mice, compared with saline injection. However, atropine did not exert any significant effects on either NREM or REM sleep in control animals.

Conclusion: The results here suggest that cholinergic activity is higher in the limbic system of CRH-COE-Cam mice than that of controls. In this model, overexpressed CRH in the amygdala may contribute to intensifying the cholinergic system, which may lead to upregulated REM sleep. As seen in depressed patients, CRH-COE mice would possess hyper-cholinergic sensitivity.

P570

Interleukin-1 microinjection into the perifornical area selectively inhibits REM sleep and increases brain cortical temperature

L. IMERI[1], S. BIANCHI[1] and R. OPP[2]
[1]University of Milan Medical School, Milan, IT, [2]University of Washington, Seattle, US

Objectives: Sleep and fever are hallmarks of infection. During immune activation NREM sleep is enhanced and fragmented, and REM sleep is suppressed. Whereas brain mechanisms mediating alterations in NREM sleep induced by immune activation have been investigated at length, few, if any, studies have been conducted to determine mechanisms and brain regions whereby REM sleep is suppressed. The perifornical region (PeF), containing hypocretin/orexin neurons and melanin-concentrating hormone neurons, is implicated in the regulation of the sleep-wake cycle and body temperature. The objective of this study was to determine a role for the PeF as a potential site whereby interleukin-1 (IL-1) inhibits REM sleep and induces fever.

Methods: Adult male rats ($n = 12$; 280 g; Charles River) were implanted with standard recording electrodes for polygraphic determination of sleep-wake behavior and of brain cortical temperature. A guide cannula aimed to the PeF was also implanted. Rats were kept on a 12:12 h light:dark cycle, at 24 ± 1°C. Rats were injected intracerebroventricularly, at light onset, on separate days, with 100 nl saline, and 1 and 4 ng IL-1, and recorded for 24 h. Injections were randomly scheduled.

Results: IL-1 administration significantly increased brain cortical temperature: maximal increases (in comparison to saline) were 0.7 ± 0.2 and 1.5 ± 0.1 degree C after 1 and 4 ng IL-1, respectively. During the first 6 post-injection hours, REM sleep was reduced by about 14% and 30% following IL-1 1 and 4 ng, respectively. REM sleep amount changed from 10.8 ± 0.8% of recording time following saline to 9.2 ± 0.7 and 7.5 ± 0.6 following IL-1 1 and 4 ng, respectively. NREM sleep was not altered.

Conclusions: Results of this study support the hypothesis that the PeF is one brain region where IL-1 can act to inhibit REM sleep and generate fever.

Aknowledgments: NIH MH064843–09 (MRO, LI).

P571

Effects on sleep of the inhibition of the lateral hypothalamus in the rat

F. DEL VECCHIO[1], A. AL-JAHMANY[1], R. AMICI[1], M. CERRI[1], M. LUPPI[1], D. MARTELLI[2], M. MASTROTTO[1], E. PEREZ[1], D. TUPONE[3] and G. ZAMBONI[1]
[1]University of Bologna, Bologna, IT, [2]Florey Neuroscience Institute, Melbourne, AU, [3]Oregon Health & Science University, Portland, US

Introduction: The antagonism of hypocretins (HCRT) has been proposed as a new approach to the treatment of insomnia. Since HCRT is exclusively synthesized by neurons located within the lateral hypothalamus (LH) [1], in the present study, we have evaluated the effects on sleep induced by a prolonged pharmacological inhibition of the LH at both normal laboratory (25°C) and low (10°C) ambient temperature (T_a), a condition which is known to dysfacilitate sleep ocurrence [2].

Methods: Twelve male Sprague-Dawley rats (300–350 g) were surgically implanted, under general anaesthesia (Diazepam, 5mg/kg, i.m., ketamine, 100 mg/kg, i.p.), with electrodes for chronic EEG recording, a thermistor for the detection of the hypothalamic temperature, a catheter for arterial blood presssure recording and two microcannulas for drug delivery within the LH. Two groups of animals were studied under a 6-day (D1–D6) protocol. Animals from group 1 ($n = 5$) were injected with either the GABAA agonist Muscimol (100 nl, 1 mM, 1 injection/h for 6 h, from 11:00 h to 16:00 h) or vehicle (saline, 0.9%; according to the former protocol) during D2 and D5, respecitvely. In group 2 ($n = 7$), the same experimental protocol was carried out, but Ta was lowered to 10°C in both D2 and D5, from 9:00 h to 17:00 h.

Results: In the six experimental hours, muscimol injection induced a significant increase in NREM sleep amount at both T_a 25°C (+6099 ± 574 s) and T_a 10°C (+4896 ± 408 s) compared to what observed after vehicle ($P < 0.01$, for both comparisons). In both groups, a concomitant suppression of REM sleep was obsereved after muscimol injection

Conclusion: The acute inhibition of LH neurons in free behaving rats produces a long bout of NREM sleep, even in environmental condition unfavourable to sleep occurence. This effect can be explained by the inhibition of the activity of HCRT neurons, which would favor the activation of the circuits promoting NREM sleep occurrence. The suppression of REM sleep may be due to the concomitant inhibithion of a group of melanin concentrating hormone (MCH) neurons located in the LH, which have been shown to be involved in REM sleep regulation [3].

1. Sakurai T, Mieda M, Tsujino N. *Ann N Y Acad Sci* 2010, 1200: 149–61.
2. Cerri, M. Ocampo-Garces, A. Amici R, Baracchi F, Capitani P, Jones CA, Luppi M, Perez E, Parmeggiani PL, and Zamboni G. *Sleep* 2005, 28: 694:705.
3. Sapin E, Bérod A, Léger L, Herman PA, Luppi PH, Peyron C. *PLoS One* 2010, 5: e11766.

P572

Evidence that the lateral hypothalamic area controls paradoxical (REM) sleep by means of descending projections to brainstem GABAergic neurons

O. CLÉMENT[1], E. SAPIN[2], P.-A. LIBOUREL[1], S. ARTHAUD[1], P. FORT[1] and P.-H. LUPPI[1]

[1]INSERM U1028, CNRS UMR5292, Lyon, FR, [2]INSERM U1042, Grenoble, FR

Objectives: It is well accepted that the pontine sublaterodorsal tegmental nucleus (SLD) is responsible for muscle atonia and cortical activation characterizing paradoxical sleep (PS). We further demonstrated that SLD activation, and thus PS onset, is due to the removal of a tonic GABAergic input from the ventrolateral periaqueductal gray (VLPAG) and the dorsal deep mesencephalic reticular nucleus (dDpMe) just ventral to it. However, despite their essential role in PS genesis, the mechanisms controlling the cessation of activity of these GABAergic neurons at the onset and during PS are not fully understood. To determine which structure(s) could inhibit(s) VLPAG/dDpMe GABAergic neurons during PS, and thus control(s) this state, we combined tract-tracing, functional neuroanatomical and local pharmacological experiments.

Methods: To exhaustively map all afferents to the VLPAG/dDpMe activated during PS, we combined the immunodetection of c-FOS, a marker of neuronal activation, with cholera-toxin b subunit (CTb) retrograde tracing from VLPAG/dDpMe in three groups of rats (control, PS deprived and PS hypersomniac, $n = 4$ in each group). Eight additional rats were bilaterally implanted with guide cannula targeting the lateral hypothalamic area (LH). The sleep-waking cycle of these animals was analyzed during 16 h following injection in the LH of NaCl, clonidine (an alpha2 adrenergic agonist) or muscimol (a GABAa agonist). Combining c-FOS, CTb (injected in the SLD) and glutamate decarboxylase 67 (GABA synthesizing enzyme) staining, we also determined whether VLPAG/dDpMe GABAergic neurons projecting to the SLD are activated after the inhibition of the LH by muscimol.

Results: The LH was the only brain structure containing a very large number of neurons activated (c-FOS positive) during PS hypersomnia and projecting to the VLPAG/dDpMe. Moreover, 44% of these neurons expressed the neuropeptide melanin concentrating hormone (MCH) in triple labelled sections (MCH, CTb, c-FOS). We additionally showed that bilateral inhibition of LH neurons by clonidine or muscimol injection induced an inhibition of PS compared to saline. Furthermore, VLPAG/dDpMe GABAergic neurons projecting to the SLD were strongly activated by muscimol application in the LH.

Conclusion: Altogether, our data strongly suggest that LH PS-on neurons, in part MCH positive, control PS onset by means of their inhibitory projections to PS-off GABAergic neurons of the VLPAG/dDpMe.

P573

Preferential role of brain adrenergic system in REM sleep permissive mechanisms

E. CHKHARTISHVILI, O. MCHEDLIDZE, S. DZADZAMIA, T. ONIANI and N. NACHKEBIA

I.Beritashvili Center of Experimental Biomedicine, Tbilisi, GE

Objectives: According with current models of sleep regulation whole depression of activity of nor-adrenergic and serotonergic neuronal populations is considered as the main part of REM sleep permissive mechanisms. Moreover experimentally induced excess of these monoamines prevents REM sleep appearance for a long time. In this work we were interested in clarifying of individual role of brain nor-adrenergic system and in determining which of these two monoamine systems are more essential in REM sleep permissive mechanisms.

Methods: Experiments were conducted on cats ($n = 5$) with implanted electrodes for EEG registration (SAGURA EEG/PSG system) lasting for 12 h daily in both baseline and experiments. Sleep latency, sleep quality, REM latency, REM incidence and total time, REM cycles were assessed after systemic injection of: Obzidane (7–10 mg/kg), blocker of beta adrenoreceptors; Amitriptyline (6–10 mg/kg), tricyclic antidepressant; concomitant administration of Obzidane and Amitriptyline and in control condition. Statistical processing was made by Students' t-test.

Results: Systemic administration of Obzidane produced significant dose-dependent shortening of REM sleep latency and increase of its incidence and total time. Therefore when brain serotonergic system functions normally, but nor-adrenergic system is antagonized, REM sleep permissive mechanisms work intensively and trigger REM sleep earlier than in baseline. Against a background of Amitriptyline isolated injection REM latency was sharply increased, REM sleep was entirely deprived for 25 ± 3 post-injection hours, that is excess of nor-adrenaline and serotonin makes REM sleep appearance impossible for a long time. During concomitant administration of Obzidane and Amitriptyline REM latency was not changed significantly in comparison to baseline, but with regard to effects of Amitriptyline isolated injection it was sharply shortened. REM incidence and total time appeared also significantly increased in comparison to the effects of amitriptyline isolated influence. In the case, when the increase of nor-adrenaline and serotonin content was preceded by blocking of beta adrenoreceptors, REM sleep developed normally, despite the excess of serotonin content in the brain and despite of the fact that nothing have been impede to its action.

Conclusions: Brain nor-adrenergic system can have the preferential role in REM sleep permissive mechanisms.

P574

Hypothalamic dopamine neurons are important for coupling arousal and motor activity

J. FRAIGNE, N. YEE and J. PEEVER

University of Toronto, Toronto, CA

Objectives: Dopaminergic abnormalities have been linked to problems in arousal maintenance as well as motor disturbances during sleep. Previously, we showed that there is an excitatory dopamine drive onto skeletal motoneurons during waking, which is lost during

sleep. Here, we aimed to identify the dopaminergic circuitry involved in regulating motoneuron activity during waking.

Methods: Study #1: 14 Sprague-Dawley rats were sleep deprived for 6 h and 7 rats were allowed to recover sleep for 2 h. Double immunohistochemical staining for c-fos and tyrosine hydroxylase (TH) of brain tissue was performed to determine sleep/wake specificity of dopaminergic structures.

Study #2: To determine dopaminergic projections to the trigeminal motor pool (Mo5), we perfused Fluorogold via microdialysis into Mo5 of 6 rats, and immunostained for TH. Study #3: To determine the effect of A11 (caudal hypothalamic dopamine group) neuron stimulation on cranial motor pool activity, we implanted 11 rats with electrodes to record electromyogram (EMG) of the masseter muscle and perfused 10mM NMDA into the dopaminergic A11 region. In 5 of these animals, we also perfused a D1 dopamine receptor antagonist into the Mo5 prior and during A11 stimulation.

Results: A11, ventral tegmental area (VTA) and ventral periaqueductal gray (vPAG) neurons were significantly more active during waking. We found that 64% of A11, 21% of VTA and 61% of vPAG neurons were c-fos/TH positive in awake animals. However, during sleep most A11, VTA and vPAG neurons were inactive, i.e., c-fos negative but TH positive. Nevertheless, only A11, and to a smaller extent, A13 (zona incerta) neurons project to the trigeminal motor pool. Direct stimulation of A11 neurons significantly increased masseteric (by 522%) muscle tone in anesthetized rats. This increase in activity was partially reversed by blocking D1 receptors of the Mo5 motoneurons.

Conclusion: These results indicate that hypothalamic dopamine neurons project to and activate cranial motoneurons during wakefulness. This waking drive is withdrawn during sleep. We conclude that this dopamine circuit is important for coupling arousal and motor activity.

P575

Role of the sublaterodorsal tegmental nucleus in cortical activation and muscle atonia during paradoxical (REM) sleep: a functional neuroanatomical study

S. VALENCIA GARCIA, L. RENOUARD, P.-H. LUPPI and P. FORT
Centre de Recherche Neurosciences de Lyon, Lyon, FR

Objectives: Paradoxical Sleep (PS) is characterized by a cortical activation and muscle atonia. We recently proposed that glutamatergic neurons of the pontine sublaterodorsal tegmental nucleus (SLD) are responsible for these events as well as the induction and maintenance of PS *per se*. Our previous tract-tracing study showed that the SLD provides descending projections to the glycinergic neurons of the ventral gigantocellular medullary nucleus (GiV) likely involved in muscle atonia and ascending ones to the intralaminar thalamic nucleus (ITha) possibly responsible for cortical activation. The aim of this work was to directly demonstrate combining Fos staining and retrograde tracing whether muscle atonia and cortical activation during PS are controlled by the same SLD neurons.

Methods: Under anesthesia, eight rats received an iontophoretic microinjection of two retrograde tracers, Fluorogold (FG) and Cholera-Toxin B subunit (CTb) within the ITha and GiV, respectively. The rats were then implanted with EEG and EMG electrodes for polysomnographic recordings. Fifteen days later, they were segregated in two groups either deprived of PS during 72 h (PSD) or allowed to recover for 150 min of such deprivation during which they experienced 40% of PS (PSR). SLD sections were then submitted to FG/CTb, Fos/CTb and Fos/FG double immunostaining.

Results: As expected, large populations of FG+ and CTb+ neurons were intermingled within the SLD. However, only occasional double-labeled neurons were found. In addition, we observed numerous Fos+/CTb+ cells in the SLD of PSR rats while a few were detected in PSD rats. On the contrary, occasional Fos+/FG+ neurons were counted in the SLD both in PSD and PSR rats.

Conclusion: The fact that SLD neurons projecting to the GiV are Fos-positive in PSR rats strongly suggest that they are selectively activated during PS (PS-on) and induce muscle atonia via their projections to GiV glycine premotoneurons. In contrast, SLD neurons projecting to the ITha are distinct from the descending ones and are not Fos-labeled during PSR. These results cast a doubt on their PS-on nature and role in cortical activation although it is accepted that all active neurons do not express Fos. In summary, our results indicate that ascending and descending SLD neurons form two distinct intermingled populations of neurons. Additional electrophysiological experiments are needed to determine whether the SLD-ITha pathway indeed plays a role in cortical activation during PS.

P576

Sn-2-docosahexaenoyl posphatidycholine (PC-DHA) increases REM sleep in human subjects

T. OHKUBO[1], H. HIBINO[1], S. TSUSHIMA[1] and T. KOBAYASHI[2]
[1]Functional foods research laboratory, Kawasaki, JP, [2]Ashikaga Institute of Technology, Ashikaga, JP

Objectives: It is known that REM sleep is manipulated by the cholinergic system. Because, it has been pointed out that the choline antagonist suppressed REM sleep, and that the choline agonist facilitated REM sleep in animal study. However, effects of acetylcholine (ACH) upon REM sleep have not yet studied in human study. We have a hypothesis that Sn2-PC-DHA has a positive effect upon REM sleep mechanism. Sn2-PC-DHA is DHA combined with PC. PC has been expected to interact with cholinergic system, and DHA has been indicated to affect the cognitive function of the central nervous system. Effects of the long term oral administration of PC-DHA upon REM sleep was examined for human subjects by the use of salmon roe's oil with much PC-DHA

Method: The nine healthy male adult paid volunteers (aged: 38.9 ± 11.5 years) participated the experiment as subjects. The experiment is organized three different kinds of sessions, the base line session of one week, the administration session of 3 months, and the wash out session of one week. The wash out session was placed at more than 3 months from the end of the administration session. They intake a capsule consisting of 1000 mg Salmon roe's oil per day during the administration session. Salmon roe's oil contained 5.37% of PC-DHA. Their night sleep was recorded by PSG.

Results: It was found that% REM sleep, the relative amount of REM sleep to the total sleep time, was significantly increased to 25–35% at the 3rd month of the administration session in compared with the base line nights. This increment of% REM sleep disappeared in the wash out session. By ingestion of the salmon roe oil containing PC-DHA for a long period, the rate of the REM sleep in the total sleep hours increased. And REM cycle became gradually regular in proportion to the length of PC-DHA administration period. It was suggested that a continuous ingestion of PC-DHA had affected with REM cycle especially in the first half of a night sleep.

Conclusion: These results suggest that a continuous ingestion of the salmon roe oil containing PC-DHA had influenced the quality and quantity of REM sleep.

P577

Chronic application of a CRH receptor type 1 antagonist decreases rapid-eye movement sleep in a mouse model of brain-specific CRH excess

C. P. N. ROMANOWSKI, C. FLACHSKAMM, F. HOLSBOER, J. M. DEUSSING and M. KIMURA
Max Planck Institute of Psychiatry, Munich, DE

Objectives: Corticotropin-releasing hormone (CRH) receptor type 1 (CRH-R1) antagonists have been discarded as antidepressants (AD), disregarding patients in whom overexpression of CRH is causal for the disease. Those patients display changes in rapid-eye movement sleep (REMS) such as increased REM density, and shortened REMS latency turning REMS into a possible predictability marker for positive AD treatment effects. Therefore, CRH-R1 antagonists could serve as effective ADs, and their application should restore normal sleeping patterns, especially REMS. In this regard we tested the highly specific CRH-R1 antagonist DMP696 in mice overexpressing CRH in the brain which show increased REMS.
Methods: Twenty six male CNS-specific CRH overexpressing (Nes-Cre) mice and control littermates (CL) were implanted with EEG and EMG electrodes. After two weeks of recovery, animals were chronically treated for one week with vehicle or 20mg/kg BW DMP696 dissolved in drinking water. During a baseline day and the first five treatment days EEG and EMG signals were recorded. Following the last treatment day animals were subjected to forced swimming (FST) for 6 min. Ten minutes after swimming animals were killed, and blood samples were collected to asses plasma corticosterone (CORT) levels.
Results: Nes-Cre mice displayed increased baseline REMS during the light period as compared to CL animals, whereas wake and non-REMS (NREMS) did not differ. In contrast to vehicle treatment which did not affect sleep, DMP696 in Nes-Cre mice decreased REMS to baseline levels of CL mice on treatment day two. Concerning the FST under vehicle conditions, CL animals spent the same amount of time active (swimming) as inactive (floating), while Nes-Cre mice were significantly longer active than inactive. Only in CL mice DMP696 increased time active. Baseline CORT levels did not differ between the two genotypes. Although significantly increased after the FST, CORT levels (independent of treatment) were similar in both genotypes.
Conclusion: According to the results DMP696 seems to be capable of reducing REMS in CRH-overexpressing mice. Thus CRH-R1 antagonists might turn out effective ADs in the patient group with CRH hyperactivity. Since significant effects could be obtained on treatment day two only, a higher DMP696 dosage might be mandatory. Further, the FST was incapable of retrieving the putative AD effect of DMP696 and might be inadequate to screen for compounds based on CRH-R1 antagonism.

P578

Amygdala neurons drive phasic fluctuation of autonomic nervous system during REM sleep

Y. KOYAMA, T. AOYAGI, S. TOYOMAKI and K. TAKAHASHI
Fukushima University, Fukushima, JP

Objectives: Amygdala is closely related with regulation of emotion and with regulation of autonomic nervous systems associated with emotion. During REM sleep, large fluctuation of autonomic signs such as blood pressure, heart rate or body temperature occur and such fluctuations of autonomic nervous systems are considered to reflect the emotional changes during REM sleep. It has been reported that, in human, activity of amygdale increases during REM sleep. However, little is known about the single neuronal activity in the amygdale during REM sleep.
Methods: Single neuronal activity during sleep-waking cycles was recorded from the amygdala in non-anesthetized, head restrained rats.
Results: More than half of the neurons (21/39) in the amygdala displayed active firing during REM sleep (highest firing during REM sleep, higher during REM sleep and waking, or higher during slow wave sleep (SWS) and REM sleep. About 10% (4/39) were most active during waking, and 28% (11/39) were most active during SWS. Even they were most active, the highest firing of more than 90% (36/39) of the recorded neurons was <10 Hz. Of 21 REM sleep-active neurons, four (20%) increased the firing in advance of the onset of REM sleep, while rest of them started to fire after the onset of REM sleep. Most of the amygdala neurons displayed phasic firing during REM sleep. More than 80% of them showed the phasic firing temporally at the limited period of REM sleep, while others showed the firing continuously all through the REM sleep period. The phasic firing in some neurons was in close correlation with blood pressure fluctuation during REM sleep. The changes of firing rate in these neurons preceded to the onset of blood pressure fluctuation.
Conclusion: These results suggest that amygdala is deeply involved in some physiological events during REM sleep, especially in phasic changes in the autonomic nervous systems including blood pressure fluctuation.

P579

Automatic detection of rapid-eye movements in REM sleep

M. ADAMCZYK[1], S. FULDA[2], M. PAWLOWSKI[1], A. STEIGER[1], F. HOLSBOER[1] and E. FRIESS[1]
[1]Max Planck Institute of Psychiatry, Munich, DE, [2]Neurocenter of Southern Switzerland, Lugano, DE

Sleep characteristics are candidates for predictive biomarkers in depressed patients. In particular, increased amount of rapid eye movements (REMs) was demonstrated in depressed patients and in individuals at high familial risk to develop this disorder. Elevated REM density is a candidate for an endophenotype of depressive disorders. Efficient and reliable identification of REMs is crucial for assessing REM density in large samples. This study presents and validates a new and automatic algorithm for scoring REM density from standard electrooculographic recordings during polysomnography. Sleep recordings of 59 healthy subjects were used for method development after REM density was scored by one expert scorer. Further, two recordings from healthy subjects scored by two expert scorers were used for threshold settings and method evaluation. The automatic algorithm was then validated in twelve polysomnographic recordings from seven healthy subjects which were scored by two expert scorers. For the validation set, mean correlation between the experts was 0.91 (epoch-wise Pearson's correlation averaged across nights) and mean kappa coefficient was 0.77. Comparison of automatic scoring with each of the scorers revealed mean correlations of 0.94 and 0.90, and mean kappa coefficients of 0.86 and 0.76, respectively. Agreement between automatic scoring and each visual scoring was within the range or superior to agreement between the two visual scorers for each night. Validation of the automatic REM density algorithm presented here showed satisfactory or excellent agreement with visual scorings. The algorithm is an objective method that avoids human scorer biases and intra-rater variability and is suited to score REM density in larger patient samples.

P580

Sleep deprivation prior to stroke increases sleep and attenuates brain lesion in the rat

E. CAM[1], B. GAO[1], L. IMBACH[1], A. HODOR[2] and C. BASSETTI[1]
[1]University Hospital Zurich, Zurich, CH, [2]Neurocenter of Southern Switzerland, Lugano, CH

Objectives: Sleep-wake disturbances are frequent in stroke patients and linked with a poorer functional outcome. We have provided direct evidence in a rat model of focal cerebral ischemia that sleep disruption shortly after stroke onset aggravates brain damage and impairs long-term stroke recovery. However, sleep deprivation (SD) prior to stroke in rodents is recently reported to be neuroprotective and beneficial for functional recovery. The aim of this study was to test the hypotheses that (i) SD prior to stroke may be neuroprotective, and (ii) this effect may be related to an increase in sleep after SD/during the acute phase of stroke.

Methods: Adult Sprague Dawly rats were subjected to continuous polygraphic recordings for baseline, during SD, and 24 h after ischemia. SD for 6 h was performed by gentle handling before ischemia. Focal cerebral ischemia was induced by permanent occlusion of distal branches of the middle cerebral artery, which induces an injury in the somatosensory cortex. Brains were collected 3 or 7 days after surgery. Control experiments included ischemia without SD (nSD), sham surgery with SD or nSD (n = 6/group). Cresyl violet staining was used for assessing the infarct volume.

Results: During the first 12 h after stroke onset (dark phase), the amount of slow wave sleep (SWS) and paradoxical sleep (PS) increased significantly ($P < 0.05$) in both SD groups (ischemia and sham control), resulting in an increase in the total sleep time by 30% compared to baseline (paired t-test), or by 20% compared with the nSD/ischemia group (One way ANOVA: $F_{2,15} = 10.4$, $P = 0.001$, followed by *post hoc* comparison). However, the delta power (1–4 Hz) in SWS did not change significantly from baseline in the SD/ischemia group, whereas increased at early hours in the SD/sham control group as expected. The infarct volume reduced significantly by 50% in the SD/ischemia compared to nSD/ischemia group [(SD 28.8 + 10.4 (median 26.5) versus nSD 57.4 + 16.2 (median 51.3) mm^3; U = 1.0, $P = 0.006$] on poststroke day 7. Removal of sleep rebound by allowing SD-rats sleep for 24 hrs before ischemia eliminated the reduction in the infarct volume [48.5 + 1.8 (48.2) mm^3 versus nSD 57.4 + 16.2 (51.3) mm^3, $P = 0.211$].

Conclusion: These results confirm that prestroke SD is neuroprotective and suggest that sleep rebound during the acute phase of stroke may be responsible for this effect. The molecular mechanisms involved are currently investigated.

P581

Experimental model of Parkinson′s disease: sleep in MPTP-treated mice

V. KOVALZON[1], A. MANOLOV[1], V. DOLGIKH[2], T. PRONINA[1] and V. DOROKHOV[1]
[1]Russian Academy Sciences, Moscow, RU, [2]Lomonosov Moscow State University, Moscow, RU

The search of early markers of Parkinson disease (PD) is one of the most important problems in the struggle against neurodegenerative illnesses. It is well known that a complete set of sleep-wake disorders is essential to PD, including RBD, daytime somnolence, nighttime insomnia etc., which nature is generally unknown. Not infrequently such disorders appear several years before motor symptoms of PD. Recently, a new murine model of PD has been developed which for the first time gives an opportunity to searching early markers of this illness including sleep disorders [Khaindrava et al., Zh Nevrol Psikhiatr 2010; 110(7): 41–47]. In accordance to this model, two successive subcutaneous injections (with 2-h interval) of 12 mg/kg MPTP (specific neurotoxin of dopamine neurons) imitate preclinical, and four injections – early clinical forms of PD 2 weeks later in C57 black mice. We tried to study possible changes in sleep-wake states in this model. A group of mice with preliminary implanted (under general anesthesia) electrodes for cortical EEG and nuchal EMG after a period of postoperative rest and adaptation to recording cables was subjected to continuous 24-h video and digital polygraphy recordings in individual experimental chambers with 12/12 LD schedule, constant temperature (24–260C) and food and water *ad libitum*. After stabilization of the baseline sleep-wake ratio, mice were divided into three groups. The 1st group had received two MPTP injections, the 2nd – four, the 3rd – 2 or 4 injections of saline (control) and recordings were continued for 2 weeks more. It was found a significant decrease in SWS during the dark period (-25%) at the expense of increased waking as compared to baseline and control recording (100%). The effect was seen just at the 7th day following MPTP administration and became significant by the 14th day. The effect was more pronounced after four injections than after two. There was no change in PS. Also, there were no changes either in SWS or PS during the light period. No signs of increase in PS 'pressure' were found [Monaca et al., *Eur J Neurosci* 2004; 20(9): 2474–2478]. The reason for this diminished SWS level during the dark period in MPTP-treated mice is under study now.

P582

Dynamics of sleep self-limiting factors assessed by state-transition timing in the rat

E. A. VIVALDI, A. BASSI and J. DIAZ
Universidad de Chile, Santiago de Chile, CL

Objectives: To ascertain whether there are sleep self-limiting factors in the dynamics of episodes of NREM sleep (N) and REM sleep (R) cycling and to differentially determine its time course within episodes of either state.

Methods: Fully automated state scoring in 5-s epochs was performed on recordings from 60 days of six rats under a 12:12 L:D schedule. Only 9 h per day, from L03 to L12 were considered for analysis. Wake (W), N and R episodes were detected and 1-epoch episodes were smoothed out. There were 5835 sleep/wake cycles, 7930 N episodes and 3131 R episodes. As N and R episodes cycled within sleep periods, they were designated Ne1 (first N episode), Re1, Ne2, etc. As episodes evolve, the fraction of cases that stays in the same state and that transit to each of the other two states are calculated in 30 s bins.

Results: Only 31% of Ne1 actually transit to R. Once in Re1, 60% of cases transit to Ne2. Afterward, the probability of transiting to the other sleep state rather than waking up actually increases, being 74% in Ne4 and 78% in Re4. Through Ne1 the consolidation of the sleep episode is expressed by a decrease of N to W transitions and the priming effect on R by an increase of N to R transitions. Both effects are dependent on the length of the preceding W. For the following N episodes (Ne^{2+}) as episodes evolves there is a marked decrease of N to R transition rate (from 0.17 to 0.07 at min 4.0) and a marked increase of N to W transition rate (from 0.02 to 0.06 at min 4.0). Within R episodes the fraction staying in R follows an inverted-U shape curve with a zenith at 1.75 min, mirrored by the fraction that

transits from R to N. The fraction that transits from R to W increases steadily through the episode. After 2.5 min within an R episode the fraction that transits to W is 0.20, whereas, after 2.5 min within an N episode the fraction that transits to W is 0.06.

Conclusion: N goes through and initial stabilization phase after it transits from W, not as it alternates with R. A self-limitation effect is not apparent for N. R goes through an initial stabilization phase as it transits from N, opposing N inertia; afterwards it is self-limited. As an R episode evolves, it becomes more likely that it will end, whereas N does not seem to tire out. Probability of waking up increases as an episode of N or R evolves, but it does so much more drastically in R than in N.

Grants by Fondecyt and Fundación Puelma.

P583

Quantifying brain states and their transitions

R. G. ABEYSURIYA, S. POSTNOVA, P. A. ROBINSON and C. J. RENNIE

University of Sydney, Sydney, AU

Objectives: The aim of this study is to use EEG data in sleep and wake to infer properties of the mechanisms responsible for the sleep-wake transition using physiologically-based modeling. Understanding the large-scale dynamical changes in the brain that occur when falling asleep provides a way to integrate current knowledge of wake-active and sleep-active neuronal populations and their projections into a wider picture of sleep-wake dynamics.

Methods: An established mean-field model of the brain is used, which models population activity in the cortex, thalamic reticular nucleus and thalamic relay nuclei to predict EEG time series and power spectra in terms of the connectivity between each of the populations. By comparing predicted EEG to experimental data from nine healthy control subjects, the regimes of connection strengths that give rise to wake and sleep EEG power spectra are quantitatively identified and mapped. Comparing the connection strengths between the wake and sleep states indicates which parts of the system undergo the most significant changes during the sleep-wake transition. In this pilot study, the transition from wake to sleep is modeled by linearly varying the connection strengths, which also predicts EEG spectra for intermediate states.

Results: The connection strengths associated with wake and sleep EEG spectra are identified, and the most significant differences observed when transitioning to sleep are an increase in self-excitation of the cortex, and in excitatory feedback to the thalamic reticular nucleus. The increase in intracortical feedback maintains a similar cortical firing rate for wake and sleep states despite a reduction in thalamic stimulation in sleep, as well as enhancing delta power in the spectrum. Intermediate states between sleep and wake predicted by the model correspond to Stage 1 sleep. Brain states in the model are mapped in a 3-dimensional space, which generalizes traditional sleep state classification into a continuum of states whose differences are represented in terms of physiology.

Conclusion: Understanding the large scale changes that take place in the brain when falling asleep is central to understanding the relative importance of changes in the neuronal populations involved in the wake-sleep transition. This study predicts that an increase in the self-excitation of the cortex and in excitation of the thalamic reticular nucleus are two of the most significant processes occuring during the transition.

P584

Defining rat and human sleep bout parameters using distribution fit statistics

A. MCCARTHY[1], D. M. EDGAR[2] and D.-J. DIJK[1]

[1]University of Surrey, Guildford, UK, [2]Eli Lilly and Company, Windlesham, UK

Objectives: Survival analysis has been used to quantify sleep continuity and better distinguish variation in sleep architecture than standard PSG measures. Lo et al. previously showed that sleep bouts follow an exponential distribution (Lo et al. 2004). This finding translated across species with sleep bouts showing time-scale dependant values that are proportional to brain mass. They also showed that the epoch length chosen to define a sleep bout had a significant impact on the time-scale. We aim to show how NREM, REM and combined Total Sleep (TS) bout distributions differ between rats and humans and how the definitions impact the appropriate choice of distribution.

Methods: Data were captured from healthy adult male human volunteers (manually scored in 10 h PSG, 30 s epochs), and adult male Wistar rats (automatically scored 60 h EEG/EMG, using SCORE-2004, 10 s epochs). Threshold criteria used to define a TS, NREM or REM bout was systematically increased to calculate bout lengths. Using this approach we optimized the bout definition in both humans and rats across a range of distributions.

Results: Increasing the number of consecutive epochs that defines a human bout to 2 optimized the fits for TS and NREM bouts across all classes of distribution. However, REM did not benefit from an increased number of epochs for defining a bout. Across each state the consistently best fit was obtained using the Weibull distribution with shape and scale parameters of 0.75 and 38.83 for TS; 0.75 and 17.39 for NREM; and 1.16 and 8.17 for REM bouts respectively. In rats six consecutive epochs to define a TS or NREM bout provides the best fit, whilst REM sleep was best defined by three epochs. The best distribution for rat sleep bouts was lognormal with shape and scale parameters of 0.92 and 1.81 for TS, 0.71 and 1.45 for NREM and 0.53 and 0.21 for REM bouts respectively.

Conclusion: We show that alternatives to the exponential distribution provide a better fit to sleep bout distributions. The Weibull distribution was the most appropriate for human sleep bouts and for rat bouts the lognormal gave the best fit. The number of epochs for obtaining the optimum fit gives equivalent times of 1 min to define a TS or NREM bout and 30 s to define a REM bout. It is clear that rodent and human sleep operates on different time-scales but translatable patterns exist that will aid future work into sleep fragmentation.

1. Lo, C.C. et al. Proc.Natl.Acad.Sci. U.S.A 101, 17545–17548 (2004); This work was supported by the Lilly Centre for Cognitive Neuroscience, Eli Lilly and Company, UK

Poster Session – Instrumentation and Methodology

P585

Sleep estimation using BodyMedia's SenseWear™ armband in patients with obstructive sleep Apnoea

A. S. BAHAMMAM and M. SHARIF
King Saud University, Riyadh, SA

Objectives: The BodyMedia's SenseWear™ Armband (BSA) is a portable device that measures skin temperature, galvanic skin response, heat flux, and body acceleration (accelerometry). Accelerometry is measured using a two-axis micro-electronic mechanical sensor and the device has a built in algorithm that can identify sleep and wakefulness based on arm movement. We aimed to evaluate the validity of the BSA device in detecting sleep-wake pattern and sleep efficiency in patients with obstructive sleep apnoea (OSA).

Material and Methods: Simultaneous overnight recordings of in-laboratory polysomnography (PSG) and BSA were performed on (i) 107 OSA (mean age of 45.2 ± 14.3 years, BMI 34.6 ± 8.5, mean apnea hypopnea index of 43 ± 35.7/h and (ii) 30 controls matched with OSA patients for age and body mass index (BMI). The BSA device was placed over the triceps during the overnight sleep studies. The collected data were analyzed using a special algorithm. Bedtime and wake-up time were adjusted/synchronized for both recordings. Paired sample correlation was used to assess the strength of the relationship between sleep duration, wake duration and sleep efficiency using PSG and BSA. An agreement analysis between the PSG and BSA scoring results was performed using the Bland and Altman method.

Results: There was no significant difference in OSA patients between BSA and PSG with regard to total sleep time (186.9 ± 98.5 min versus 184.9 ± 99.5 min; $P = 0.71$), total wake up time (70.9 ± 62.4 min versus 72.9 ± 62.5 min; $P = 0.71$) and sleep efficiency (72.6 ± 19 min, 71.3 ± 22.7 min; $P = 0.52$). There were strong correlations between BSA and PSG with regard to total sleep time ($r = 0.84$; $P < 0.001$), total wake up time ($r = 0.61$; $P < 0.001$) and sleep efficiency ($r = 0.52$; $P < 0.001$). There was also no significant difference in the controls between BSA and PSG with regard to total sleep time (290.4 ± 105.5 min versus 301.1 ± 96.5 min; $P = 0.32$), total wake up time (74 ± 71.1 min versus 63.2 ± 61.5 min; $P = 0.32$) and sleep efficiency (79.8 ± 17.63 min, 83.3 ± 14.6 min; $P = 0.23$). Bland Altman plots showed strong agreement between total sleep time, wake up time and sleep efficiency for both OSA and the controls.

Conclusion: Results suggest that BSA is a reliable method for determining sleep in patients with OSA when compared against the gold standard test (PSG). BSA can be a useful tool in determining sleep in patients with OSA and can be combined with portable sleep studies to determine total sleep time.

P586

Piezoelectric system as an alternative for electroencephalography in animal sleep experiments

G. M. MANG[1], J. NICOD[2], K. D. DONOHUE[3], B. F. OHARA[3], J. FLINT[2] and P. FRANKEN[1]
[1]University of Lausanne, Lausanne, CH, [2]University of Oxford, Oxford, UK, [3]University of Kentucky, Lexington, US

Background: Non-invasive methods to record sleep in animals are being developed as an alternative to electroencephalography (EEG) and electromyography (EMG). The 'piezo' system uses piezoelectric films placed on the bottom of a cage to detect animal's movements with high sensitivity. The resulting signal can be used to automatically distinguish sleep from wakefulness. During wakefulness, locomotor activity and even small movements result in a high frequency, erratic, and irregular signal while during Non Rapid Eye Movement Sleep (NREMS) the principal movements are respiration-related chest-wall movements, producing a ca. 2 Hz rhythmic signal. We are currently validating this technique in a cohort of CFW outbred mice by comparing EEG/EMG-determined sleep to piezo-determined sleep within individual mice. The piezo-system is part of a phenotyping pipeline in CFW mice for an ongoing Genome-Wide-Association study at MRC Harwell run by Jérome Nicod.

Methods: Eleven male and ten female Swiss Webster CFW mice (Charles River, USA), 18–20 weeks old were used. Mice were maintained under standard housing condition, with food and water *ad libitum*, in a temperature controlled room (25°C) and a 12 h:12 h light/dark cycle. Mice were implanted with EEG/EMG electrodes under deep anesthesia. After surgery, mice were singly housed and connected to recording cables. A minimum of 13 days for recovery and habituation were allowed prior to the experiments. For the EEG/EMG-piezo comparison mice were transferred to recording cages each of which contained a piezoelectric film, covered with some litter. EEG/EMG (EMBLA and Somnologica, ResMed) and piezo (MouseRec, Signal Solutions LLC) signals were recorded continuously for 3 consecutive days.

Results: Comparison from EEG/EMG recordings and piezoelectric data showed that the sleep/wake distribution over the day as well as the amount of sleep and wake is consistent with both techniques. Although the piezo system detected slightly more sleep during the light period than EEG/EMG, the results of the two recording techniques were highly correlated and the global sleep/wake pattern was similar.

Conclusion: Although EEG activity cannot be measured and Rapid Eye Movement Sleep cannot be distinguished yet, piezoelectric system is an interesting alternative to EEG/EMG experiments in mice that can be used for large-scale sleep studies and rapid screening of sleep/wake promoting drugs.

P587

Using accelerometers as actigraphs

J. VIRKKALA
Finnish Institute of Occupational Health, Helsinki, FI

Objectives: Actigraphy is an accepted measure of sleep wake cycles. Typically actigraphs quantify uniaxial movement into proprietary epoch based activity counts which are then used for sleep wake classification. With recent technical advances standard accelerometers can record raw three dimensional acceleration values for 3–4 weeks comparable to traditional actigraphs. Currently it is unknown how these raw accelerometer values correspond to standard actigraph activity counts.

Methods: In this study we studied how new GENEActiv (Activinsights Ltd) raw 100 Hz accelerometer values could be transformed into values comparable to common actigraph (Actiwatch 7, CamNtech Ltd). Total of 372 h of 24 h activity data was collected from four participants with two devices fixed together. After temporal alignment of data the three dimensional raw GENEActiv accelerometer values were converted into epoch values (G) by filtering one axes values and calculating maximum absolute values inside 1 s epochs. These

maximum values were then summed over 30 s epochs. Epoch values were used for sleep stage classification using the Actiwatch algorithm.

Results: With 1st order butterworth IIR filter with bandwidth 3–11 Hz cross correlation between calculated epoch values between two devices was 0.96. Equation to obtain Actiwatch 30 s epoch data (A) was A = 49G-23, where G was calculated as earlier described. Agreement of wake/sleep classification of 24 h data between devices was 94%. With 2nd order filter results were 0.95, A = 53G-20, and 93%.

Conclusion: New three dimensional accelerometers can be used to obtain activity counts comparable to traditional actigraphs. However new algorithms should be developed and validated against polysomnography to take advantage of additional recorded data. New algorithms could lead to better agreement with polysomnography. While this development is undertaken results comparable to standard actigraphs can be obtained by simple filtering.

P588

Developing an architectural dosimetry protocol for residential properties in circadian sleep research

L. L. A. PRICE[1], M. KHAZOVA[1], J. B. OHAGAN[1], N. SANTHI[2] and D.-J. DIJK[2]

[1]Health Protection Agency, Didcot, UK, [2]University of Surrey, Guildford, UK

Objectives: To support meaningful associations between lighting parameters and health outcomes, data relating to lighting must be closely related to personal exposure of experimental subjects. Dosimetry devices worn close to the eye are generally agreed to provide the closest match, but represent an intrusive protocol. Consequently behaviour patterns may be affected and compliance impaired. Wrist based devices are less intrusive, but may depart significantly from eye exposures and light sensors may be obscured by long-sleeved clothing. The objective was to develop an architectural dosimetry protocol for circadian studies in residential properties.

Methods: A three location protocol for measuring light levels and broadband spectral data in two main rooms, those primarily used for day and night-time occupation, using actigraphy based dosimetry devices was designed. The criteria considered most important in determining the placement of the devices were, firstly, expectations for typical eye-level and location during room occupancy and, secondly, quantifying the contribution of daylight and artificial light, and room dimensions. Retinal irradiances and spectra determine the effectiveness of light exposures for circadian entrainment, arousal and melatonin suppression. Calibrated measurements were taken with a portable spectroradiometer, to supplement the broadband actigraphy data, and capture data relating to lights, blinds and curtains. Actigraphy devices were individually calibrated, as previously presented.

Results: Examples are given of baseline data for architectural dosimetry including UK care homes and houses of UK retired Class I and II workers. Building on this, comparisons are shown between the protocol data and data from wrist worn actigraphy light measurements collected from the non-intervention stage of a study based at a UK retirement development of houses and flats. The hypothesised differences in light exposures and architectural dosimetry data for the intervention are considered. If available, advance data from the UK retirement home study may be briefly presented.

Conclusions: As the architecture and lighting of residential properties are heterogeneous, home-based studies related to light exposure, including sleep research, should ideally be controlled for the impact on personal light exposures. Protocols for light measurement in architectural spaces also support lighting design using computer software.

P589

Psychometric properties of a subjective sleep quality index to be used with the elderly: an exploratory study

M. MARQUES, H. ESPÍRITO SANTO, J. MATRENO, S. FERMINO, V. ALVES, V. VIGÁRIO, T. NASCIMENTO, S. MOITINHO, R. ALMEIDA, M. COSTA, M. TOMAZ, L. CALDAS, L. TESTAS and L. FERREIRA

Instituto Superior Miguel Torga, Coimbra, PT

Explore the psychometric properties of a sleep quality index to be used with the elderly population. Ninety-nine elderly (mean age, M = 78.65; SD = 6.92; range = 60–95) under social responses in institutions from Coimbra Council accepted to fill in voluntarily a test battery (or whose relatives/caregivers gave consent), including socio-demographic questions, neuropsychological tests and a sleep questionnaire, composed of a sleep quality index (adapted from a sleep index used with undergraduate students) and questions assessing sleep correlates, as sleep hygiene, practice of physical exercise, among others. The sleep index is composed by seven items assessing sleep latency, difficulty in falling asleep, number of night awakenings, waking up spontaneously too early, subjective perception that waking up too early constitutes a problem for the person and two items that evaluate general subjective sleep quality and sleep depth. We slightly rephrased the items from the original index so it could be used with this population (e.g. While having classes, how many times do you awake during the night? ' versus 'How many time do you awake during the night?). The Kaiser-Meyer-Olkin Measure of Sampling Adequacy (should be ≥ 0.6; was of 0.830) and the Bartlett's Test of Sphericity value (should be ≤ 05; was of ≤ 001) allowed us to verify data suitability for factor analysis. A principal components analysis and the scree plot inspection revealed a meaningful one-factor solution (eigenvalue > 1), explaining 48.8% of the total variance. The Component Matrix, presenting each item unrotated loading, showed that all items loaded quite strongly (>0.4). The index revealed a very good internal consistency (Cronbach alpha coefficient; alpha = 0.812). The corrected item-total correlations, which present a degree of correlation of each item with the total score, showed that all presented higher values than 0.3, with the exception of the item assessing sleep depth, indicating that, in general, they are similar as whole. Analyzing Cronbach's alphas when each item was removed, none of them led to a higher alpha value. We decided not to exclude any item. This sleep quality index, adapted for the elderly population, presents good psychometric properties. Since, in terms of assessment, it is important not to overload this population, this very short instrument constitutes a good option to assess sleep quality, filling up a gap regarding instruments in this area.

P590

Wearable wireless physiological monitoring for chronobiology and sleep

A. KUMAR, W. F. HOFMAN, C. LIJZENGA and W. VAN ECKE

Personal Health Institute international, Amsterdam, NL

Objectives: The study of circadian rhythms, continuous monitoring of vital signs or home sleep testing demand continuous non-invasive monitoring of physiological signals. The device has to be ubiquitous

to make interference by the device in daily life as minimal as possible. We developed a wearable monitor and studied the reliability for measuring 24-h physiological rhythms in everyday life (FP6 EU-CLOCK project).

Methods: We chose a three-tier architecture. The first tier is formed by a wearable and wireless sensor-unit, using minimal power. We used ultra-low power micro-electronics, based on patented Sensium technology, designed for medical wireless transmission. The first tier also has a Bluetooth Oximeter. Storage and analysis of the signals were implemented in a PDA (2nd tier). The third tier is a wireless connection to a server with Galaxy software for database management, analysis and reporting. The following signals can be measured: ECG, 2 channel RIP respiration, 3-axis body position and actigraphy, nasal pressure, temperature, light, sound, oximetry and pulse wave. Wireless transmission is prone to errors of data loss and synchronization. Proprietary algorithms were developed to synchronize data and detect transmission loss. Reliability and validity of the system was assessed in a field experiment with 9 subjects who performed simulated shiftwork. In addition the signals were analyzed to explore the possibility of detecting circadian phase and to verify the synchronization.

Results: Data from a total of 49 recordings were analyzed (up to 128 h duration). The number of transmission errors ranged from 2% to 10%. Longer transmission errors were due to movements. However, during movements the physiological and sensor artefacts were more dominant than the transmission errors.

Core body temperature, heart rate and respiratory rate simultaneously showed a decrease during the night and an increase in the early morning. Interestingly, heart rate and respiratory rate also showed an ultradian pattern, which may coincide with the REM/NREM cycle. During the day, however, respiratory effort was more sensitive for external influences.

Conclusion: Neptune is an ultra-low power, wireless, wearable device capable of continuous recording of physiological signals longer than 72 h. Core body temperature and heart rate seem to be good candidates for the determination of circadian phase. The variety of sensors in Neptune allows it's usage for many sleep applications.

P591

Slow and rapid eye-movements during REM sleep: effects of ageing and REM period

G. GRUBER[1], P. ANDERER[1], H. DANKER-HOPFE[2], D. GUGO-NATU[1], S. PARAPATICS[1] and G. DORFFNER[3]

[1]The Siesta Group, Vienna, AT, [2]FU-Berlin, Berlin, DE, [3]Medical University of Vienna, Vienna, AT

Objective: Rapid eye movements (REMs) are a cardinal feature of REM sleep and their rate ('density' – REMD) is an indicator of the intensity of a hypothetical 'REM process' (analogous to spectral power in the delta range in NREM sleep). The generation of REMs is assumed to be controlled by cholinergic and/or glutamatergic systems and REMD correlates with cognitive functions in elderly subjects. Thus, REMD might be a biomarker of successful aging. REMD was reduced in healthy elderly subjects as compared to young controls (Darchia et al. 2011), while slow eye movements (SEMs) did not show any trend across REM periods (Pizza et al. 2011). However, those studies were limited due to the small number of subjects and need confirmation in larger samples allowing establishing age curves for REMD. The aim of the present study was to confirm these findings in a larger database, using an automatic detection algorithm.

Methods: REM density (time of REMs/time in stage REM) and REM intensity (sum of eye movement amplitudes/min REM sleep) were evaluated automaticlly. Moreover, the Atonia Index (ATI, Ferri et al. 2008) was quantified as a measure of REM sleep atonia. One hundred and sixty healthy subjects from the SIESTA database (86 females, 74 males aged between 20 and 95 years) participated in the study. REM periods were defined according to the standard criteria and visually checked for apparently missing periods. The effects of REM period and age on the obtained measures were investigated by means non parametric tests (Spearman rank correlations, Friedman test for dependent samples).

Results: There are significant differences in REMD between REM periods 1–4 ($P < 0.001$), which was reduced in REM period 1 [no significant differences between periods 2 and 4 ($P = 0.803$)]. Age did not correlate significantly with REMD (R = -0.102, $P = 0.199$), but with REM intensity (R = -0.272, $P < 0.001$). Neither SEM density ($P = 0.446$), nor SEM intensity ($P = 0.688$) differed significantly between REM periods, or correlated significantly with age. There is a significant difference in ATI between REM periods (declining over the night), but no significant correlation with age (R = 0.081).

Discussion: As expected, we could confirm a reduced REMD during the 1st REM period and a significant aging effect in REM intensity but not REMD. Likewise, REM ATI increases during the night, but was not significantly affected by aging.

Conclusion: Computerized analysis of REMs and SEMs is a sensitive marker ofREM sleep intensity.

P592

An innovative auto-programme to investigate sleepiness of drivers at the wheel

R. J. HUANG[1], H. TING[1], S. D. LEE[2], S. Y. CHANG[1], T. S. SHIH[3], Y. HSIAO[1], C.H. LAI[1] and Y.X. WANG[1]

[1]CSMU, Taichung, TW, [2]CMU, Taichung, TW, [3]Institute of Occupational Safety Council of Labor Affairs of Executive Yuan, Taipei, TW

Objectives: Bus drivers' sleepiness on wheels would seriously threaten public safety. Oxford sleep resistance (OSLER) test is a gold standard to evaluate subject's ability to keep alert in twilight situation. The wakefulness catalog of OSLER test includes awake, lose attention, micro-sleep and sleep onset. However, this test is not eligible to be applied to drivers at driving to avoid risk ahead. Therefore, for crucial and practical sakes, we tried to develop an auto-program, analyzing electrooculogram (EOG) and electroencephalographic (EEG) signals in a quasi-real-time manner, to warn immediate working individuals when sense ongoing of sleep onset. Doubtlessly the computed sleep onset latency by this program, using indices of blink movements (BM) and of slow eye movements (SEM) to EOG and using indices of beta, of theta, and of delta band to EEG, should agree to sleep latency and errors (nonresponses to stimulations) by OSLER.

Methods: Accordingly, 117 bus drivers were recruited in present study to test this hypothesis. No matter at first and third or second and fourth bouts, had each volunteer randomly received two bouts of OSLER testing with simultaneous EEG and EOG measures. For EOG records blink signals were characterized by pulse-type, high amplitude and high frequency (0.6–1.3 Hz), corresponding to fast eye jumping, SEM appeared low frequency (0.2–0.6 Hz), corresponding to rolling, horizontal, bidirectional and conjugate eye movements. Sleep onset and error profiles would be determined by the Blink index lower than a certain arbitrary threshold concomitant

with the SEM index higher than another one, both threshold-settings fulfilling the situations of OSLER-determined sleep-onset. For EEG records signals 3 frequency bands, include beta (14–20 Hz), theta (2.5–7.5 Hz), and delta (0.5–2.5) were used by auto program.
Results: (i) sleep onset: comparing observed group with sleep onset and control group without sleep onset, we found SEM, Blink, beta, theta, and delta have statistical significance with *P* value equal to 0.018, 0.020, 0.034, 0.003 and 0.039, respectively, (ii) Error profiles: after tuning the thresholds for indices of SEM, BM, beta, theta, and delta we get a good match to OSLER wakefulness catalog.
Conclusion: Our innovated EOG/EEG-based program might be eligible to apply drivers at work for detect sleep onset and error profiles in an almost real time manner.

P593

The influence of time of the day and napping in between test sessions on performance on the sustained attention to response task in healthy controls

M. K. M. VAN SCHIE, E. E. ALBLAS, R. D. THIJS, R. FRONCZEK, H. A. M. MIDDELKOOP, G. J. LAMMERS and J. G. VAN DIJK
Leiden University Medical Centre, Leiden, NL

Objectives: The Sustained Attention to Response Task (SART) is a go/no-go task in which the no-go target appears unpredictably and rarely, and in which both accuracy, i.e. omission and commission errors, and response speed, i.e. reaction time (RT) are important. The SART proved to be a useful tool to investigate sustained attention in disorders of excessive daytime sleepiness, including narcolepsy. Our previous studies (Fronczek et al. 2006, Van Schie et al. 2011) showed an improvement of performance from the first to the second of five SART sessions that were administered prior to a Multiple Sleep Latency Test (MSLT) session. Before implementing the SART in clinical settings other than a 5/day administration on fixed times, possible causes of this improvement need to be assessed. This study aims to investigate the influence of two variables on performance of the SART in healthy controls, (i) time of day and (ii) the possibility to sleep between two SART sessions.
Methods: A total of 80 healthy participants performed the SART twice with a 1.5-h break in between. Half of the participants were assigned to one of the two morning groups, half to one of the two afternoon groups. Participants from one morning group and one afternoon group were offered a 20-min nap directly following the first SART session; the others had to stay awake for 90 min. Participants were assigned to one of the four conditions matched for age, sex and level of education. Midline EEG recordings controlled for the presence or absence of sleep in all participants during the protocol
Results: SART results are available for 43 patients. Mean SART error scores were 9.8 for the morning-sleep group, 10.1 for the morning-wake group, 9.5 for the afternoon-sleep group, and 12.4 for the afternoon-wake group. All groups performed better on the second SART session compared to the first. Preliminary analysis showed a tendency towards greater improvement in the sleep groups, which was more pronounced in the afternoon sleep group. However, an overall performance difference between the morning and afternoon groups was not (yet) observed.
Conclusion: The preliminary results suggest a positive influence of a 20-min rest period on SART performance, which is additional to a persistent learning effect between the first and second SART session.

P594

Quantification of sleep fragmentationl in intensive care patients

J. W. KIM[1], R. ELLIOTT[2], A. L. DENOTTI[3], P. A. CISTULLI[2], S. MCKINLEY[2], D. BARTLETT[3], P. A. ROBINSON[1] and R. R. GRUNSTEIN[3]
[1]University of Sydney, Sydney, AU, [2]Royal North Shore Hospital, Sydney, AU, [3]Woolcock Institute of Medical Research, Sydney, AU

Objectives: Patients in the Intensive Care Unit (ICU) often experience sleep disruption and fragmentation, which may worsen their health condition. In order to design appropriate interventions for improving ICU patients' sleep quality, objective quantification of fragmented sleep is important. Therefore the main objective was to characterise sleep in ICU patients.
Methods: To monitor sleep, full polysomnography (PSG) was performed on 22 ICU patients (24 h recording) and 9 healthy controls (9 h recording from lights out at 10 pm to lights on at 6 am). Each 30 s epoch of the PSG recordings were scored by an experienced technologist using Rechtschaffen and Kales criteria. The resulting hypnograms of both groups were compared. In particular, we assessed group differences in nocturnal sleep efficiency (11pm-7 am for ICU and Controls) and sleep fragmentation index (24 h for ICU and 8 h for Controls) using the t-test. We also investigated the effect of daytime sleep on nocturnal sleep efficiency and sleep fragmentation index using Pearson's correlation.
Results: Total sleep time (TST) did not differ between the two groups (ICU 24 h: 5.6 ± 4.6 h versus Controls 8 h: 6.5 ± 1.1 h, $P = 0.59$). However, nocturnal sleep efficiency was reduced in ICU patients compared to controls (ICU: 31 ± 26% versus Controls: 81 ± 13%, $P < 0.01$). The sleep fragmentation index was also higher in ICU patients than controls (ICU 24 h: 14.7 ± 12.0/h versus Controls 8 h: 4.9 ± 1.5/h, $P < 0.05$). The proportion of daytime sleep was correlated with nocturnal sleep efficiency ($r = -0.42$, $P = 0.05$) in ICU patients, but was not correlated with the sleep fragmentation index ($r = 0.01$, $P = 0.97$).
Conclusion: Intensive care patients' sleep was characterized by reduced nocturnal sleep efficiency and a higher fragmentation index compared to healthy controls. The reduced sleep efficiency may in part be explained by the increased amount of daytime sleep which may suggest a need for interventions to improve the quality of nocturnal sleep in ICU patients. The measures of sleep efficiency and sleep fragmentation could be used to monitor the effectiveness of interventions to improve sleep in this population.

P595

A practical method of identifying artefact in electroencephalograms via a computer-based automated algorithm

J. W. KIM[1], G. DUNGAN[2], A. L. DENOTTI[2], K. WONG[2], S. BANKS[3], P. LIU[2], P. A. ROBINSON[1] and R. R. GRUNSTEIN[2]
[1]University of Sydney, Sydney, AU, [2]Woolcock Institute of Medical Research, Sydney, AU, [3]University of South Astralia, Adelaide, AU

Objectives: Electroencephalography (EEG) is commonly used to monitor brain activity during sleep. However, EEG signals are often heavily contaminated by various non-neurogenic artefact such as muscle, eye and breathing movements, sweating, equipment interference and electrode popping. We developed an automated, practical method to identify the non-neurogenic artefact in EEG recorded during polysomnography to allow for quantitative analysis of the 'noise-free' signals.

Methods: Nocturnal polysomnography of 39 patients were sleep staged by an experienced technologist according to standard criteria. The EEG was systematically examined for the presence of non-neurogenic artefact. Experienced technologists manually reviewed each 5 s epoch of EEG and scored epochs contaminated by artefact. A computer-based automated algorithm also identified 5 s epochs of EEG contaminated by artefact. We compared the manual and automated artefact scores and assessed differences in accuracy, sensitivity, specificity, and Cohen's kappa of the two artefact identification methods. We also compared the absolute spectral power of the EEG from the raw recording (no artefact removal), and following manual and automated artefact removal.

Results: The proportion of 5 s epochs identified as contaminated by artefact were 5.3 ± 3.3% and 6.8 ± 1.2% with the manual and automated methods, respectively ($P < 0.05$). Compared to the gold-standard manual method, the accuracy of the automated algorithm was 93.3 ± 3.9%, sensitivity 71.9 ± 20.6% and specificity 94.6 ± 4.7%. Cohen's kappa showed moderate agreement between the two methods (0.47 ± 0.24). Power spectral analysis of the EEG during rapid-eye-movement sleep demonstrated a reduction of delta power (0.5–4.5 Hz) following the exclusion of artefactual epochs (raw: 103.3 ± 60.4 uV2; manual: 71.8 ± 34.8 uV2; automated: 68.6 ± 30.0 uV2; $P < 0.05$ for raw versus manual and raw versus automated; $P = 0.11$ for manual versus automated).

Conclusion: The high accuracy, sensitivity and specificity demonstrate the ability of the computer-based automated algorithm to successfully identify non-neurogenic artefact in sleep EEG. The statistical comparison of spectral power between the raw, manual, and automated artefact removal methods further support the importance and practical use of the automated algorithm to identify EEG artefact in sleep studies prior to quantitative analysis.

P596

Subjective sleep evaluation by laypersons

R. DE BRUIJN[1], E. I. S. MOST[2], R. J. E. M. RAYMANN[2], R. HAAKMA[2] and P. MARKOPOULOS[1]

[1]Eindhoven University of Technology, Eindhoven, NL, [2]Philips Group Innovation per cent Research, Eindhoven, NL

Objectives: Although many questionnaires to measure sleep quality are available, there is no clear definition of what aspects of perceived sleep contribute to the overall subjective evaluation of sleep quality. Most sleep quality measures take a scientific and/or clinical perspective, targeting quantification of sleep related behaviour and/or clinically relevant sleep anomalies. However, it is not known to what extent such inventories help characterize lay concepts of sleep quality. The aim of this study is to identify how laymen describe their sleep quality intuitively, using a sentence stem completion methodology.

Method: A 30 item sentence stem completion questionnaire was constructed to capture lay concepts of sleep experience and sleep quality. This is a method in which sentence stems, e.g. 'What influences my sleep the most...', need to be completed by participants own concepts and in their own wording. Included topics were sleep habits, experience of sleep itself and after awakening, and elements that influence sleep.

For the initial analysis of the item 'my ideal sleep…' 64 participants were included, equally distributed over the variables sex (male/female), age (18–50/≥51 years old), education level (< Bachelor/≥Bachelor) and sleep quality using the Pittsburgh Sleep Quality Index (< 5/≥6). Stem completions were examined with conventional content analysis in which unique descriptive codes (keywords) were assigned to cluster text with similar semantics.

Results: Preliminary results covering the initial coding of the single item 'my ideal sleep...' showed that six descriptive codes arose most frequently: Having a desired sleep duration (37.5%), not waking up during the night (34.4%), feeling refreshed after waking (14.1%), waking up on their own effort (12.5%), falling asleep fast (12.5%) and to be able to wake up at their desired time (12.5%).

Conclusion: The outcome shows that people's own description of their ideal sleep does not necessarily match the subscales mentioned in standard sleep questionnaires. Sleep questionnaires often inquire about exact values like sleep duration and leave the interpretation of this number to the scoring manual. However, the personal interpretation of sleep (e.g. whether the sleep duration matched the desired sleep duration) is very likely to be a key factor in a valid sleep quality construct. To gain a complete description of people's own subjective sleep perspective, analysis of all items still needs to be performed.

P597

Screening of obstructive sleep apnoea in awake subjects

P. CASEIRO[1], R. FONSECA-PINTO[2] and A. ANDRADE[3]

[1]Escola Superior de Tecnologia da Saúde de Coimbra, Coimbra, PT, [2]Instituto Politécnico de Leiria, Leiria, PT, [3]Instituto de Biofísica e Engenharia Biomédica, Lisbon, PT

Background: Polysomnographic signals are usually recorded from patients exhibiting symptoms related to sleep disorders such as Obstructive Sleep Apnea (OSA). OSA has a relatively high prevalence, occurring in 5% of the adult population, but the majority of these cases remain undiagnosed. The usual procedure entails an overnight recording several hours long. Our goal is to present a fast screening method to identify OSA during the awake period, in order to simplify the diagnosis and reduce costs and waiting time for diagnosis and treatment.

Methods: This study presents a methodology to help with the screening of OSA using a 5-min oronasal airway pressure signal emanating from a polysomnographic recording during the awake period, eschewing the need for an overnight recording. The Hilbert-Huang Transform (a recent time-frequency analysis method) was used to extract intrinsic oscillatory modes from the signals. The frequency distribution of both the first mode and the second mode and their sum was shown to differ significantly between non OSA subjects and OSA patients.

Results: The clinical sample consisted of a total of 41 subjects, 20 non OSA individuals and 21 individuals with OSA. An index measure based on the distribution frequencies of the oscillatory modes yielded a sensitivity of 81.0% (for 95% specificity) for the detection of OSA. Two other index measures based on the relation between the area and the maximum of the 1st and 2nd halves of the frequency histogram both yielded a sensitivity of 76.2% (for 95% specificity). The data was mostly composed of severe OSA patients (12), however it also included 4 patients with mild OSA and four patients with moderate OSA. Efficiency of detection was not dependent on disease severity. No significant correlations were found between age, sex and the best correlated indexes.

Conclusions: Although further studies will be needed to test the reproducibility of these results, the proposed measures seem to provide a fast method to screen OSA patients, in awake period, thus reducing the costs and the waiting time for diagnosis. The physio-

logical mechanisms that underlie the differences between OSA patients and non OSA subjects highlighted in the present study can be due to differences in upper airway anatomy and could be associated with an increase in airway resistance that is a feature of the disease.

P598

Long-term monitoring of genioglossus muscle tone during natural sleep and wake states in Wistar rats

S. SHAHABI[1], A. MCCARTHY[1], K. GRACE[2], R. HORNER[2], E. SHANKS[1], K. A. WAFFORD[1], W. F. SEIDEL[1], D. M. EDGAR[1] and S. HUGHES[1]

[1]Eli Lilly, Windlesham, UK, [2]University of Toronto, Toronto, CA

Objectives: The genioglossus (GG) muscle of the tongue, in conjunction with other pharyngeal muscles, plays an important role in maintaining a patent airway and thus ensuring efficient respiration. However, during sleep, and particularly in rapid eye movement (REM) sleep, the activity of this muscle is subject to periods of major suppression. In susceptible human subjects such suppression plays an important role in sleep-related breathing disorders. In order to study the mechanisms which underlie this phenomenon and provide the capacity to assess pharmacological agents that might influence suppression we obtained long-term chronic recordings of genioglossus (GG) muscle tone in natural sleep/wakes states in rats.

Methods: Briefly, adult male Wistar rats were surgically implanted with electrodes for recording the electroencephalogram (EEG), the trapezius electromyogram (EMG) and the GG EMG. Body temperature (Tb) and locomotor activity (LMA) were monitored using biotelemetry and arousal states were scored as either wake, theta-dominated wake, non-REM sleep or REM sleep using the automated EEG scoring system, SCORE 2004TM (Van Gelder et al., Sleep 14: 48).

Results: GG muscle activity was stable over several weeks and exhibited a collection of state-dependent characteristics that were both consistent with previous studies (e.g. Steenland et al. *J Neurosci* 28: 6826) and were shared between different animals. Such characteristics included, (i) a high level of GG tone in wakefulness compared to all other states, (ii) an unambiguous respiratory modulation of the GG muscle activity during non-REM sleep, (iii) a full suppression (i.e. atonia) of the GG muscle tone following the onset of REM sleep, and (iv) the appearance of prominent phasic 'twitches' toward the end of REM sleep epochs. Interestingly, we observed an approximately sigmoidal relationship between the GG EMG and trapezius EMG signals such that as the trapezius EMG signal increases the GG EMG signal initially remains at a relatively low level, then steeply increases when the trapezius EMG is at around 50% of its maximum, before stabilising again at higher level. Finally, we show that several pharmacological agents which affect trapezius EMG tone are also able to influence GG activity.

Conclusion: Overall we suggest that chronic long-term recording of GG muscle tone may be a useful way for investigating state-dependent changes in a muscle group that has a central importance to sleep-disordered breathing.

P599

Sleep stage scoring using EMD and neural networks

P. CASEIRO[1], L. FREIRE[2] and A. ANDRADE[3]

[1]Escola Superior de Tecnologia da Saúde de Coimbra, Coimbra, PT, [2]Escola Superior de Tecnologia da Saúde de Lisboa, Lisbon, PT, [3]Instituto de Biofísica e Engenharia Biomédica, Lisbon, PT

Polysomnographic signals are recorded from patients exhibiting symptoms related to sleep disorders. This paper presents a methodology to automatically detect sleep stages, in accordance to AASM Visual Scoring rules, using 30-s epochs taken from EEG and EMG signals. A signal analysis technique based on the extraction of intrinsic oscillatory modes (Empirical Mode Decomposition, EMD) was used, and a neural network analysis was implemented to rate EEG epochs based on the intensity and frequency spectrum of the intrinsic modes. Information from the EMG channel was added to the neural network as an additional feature. The clinical sample consisted of a total of 5464 epochs from six normal subjects. The average sensitivity of sleep stage classification without EMG was 89.17%, and the average specificity was 93.63%. Most errors involved N1 classified as REM and N3 classified as N2. In order to improve the performance of the neural network analysis, information about EMG average amplitude was added. The average sensitivity and specificity rose to 90.72% and 94.79%, respectively. Further tests will be needed to reproduce these results and optimize the procedure, but the proposed method seems to allow for fast sleep stage scoring, and thereby has the potential to reduce the costs and waiting times associated with the diagnosis of sleep pathologies.

P600

Assessment of an automatic analysis method of the Karolinska drowsiness test

C. BERTHOMIER[1], P. BERTHOMIER[1], M. BRANDEWINDER[1], J. MATTOUT[2], P. PHILIP[3] and J. TAILLARD[3]

[1]PHYSIP, Paris, FR, [2]INSERM U 1028, Lyon, FR, [3]CNRS USR 3413, Bordeaux, FR

Objectives: The Karolinska Drowsiness Test (KDT) is an alternative approach to the assessment of sleepiness. Its analysis is based on the spectral power calculation in the alpha-theta band of the artifact-free electroencephalogram (EEG). The visual artefact rejection (eye blinks, eye and body movements) is performed by a trained technician. This procedure is long, often tedious and can be an obstacle to the implementation of this test. The purpose of this study was to develop an algorithm for the automatic rejection of artefacts in the wake-EEG signal and subsequent power spectrum calculation.

Methods: Twenty-five volunteers (aged 20–75 years) were enrolled in a study including two 40-h constant routines. Each of those included 11 KDT of 4 min duration, one every 3h45. Recorded channels included EEGs (Fz, Cz, Oz referenced to A2), EOG, EMG and ECG.

The fully automated algorithm is based on EEG only and even further restricts the analysis to a single channel (Fz) for artefact rejection. It was tuned using all KDT data from three subjects (two young, one elderly) for a total of 66 tests. The algorithm was then evaluated using data from 20 other KDT (12 elderly and eight young subjects). The artefact rejection was performed 3 times independently: once automatically (A) and twice manually by an EEG expert (M1 and M2, with a 2 month interval). The spectral power of Fz signal was computed in the 6–9 Hz band for every 4-s epoch that was artifact-free. The obtained power values were then averaged to yield global spectral power values for each KDT, for A, M1, M2 and consensus manual rejection (M1-M2), respectively. The evaluation was assessed by both comparing the number of rejected epochs for each artefact rejection procedure and comparing the results of the subsequent spectral analysis.

Results: The percentages (mean ± SD) of rejected epochs were 33% ± 14% (A) 45% ± 20 (M1) and 44% ± 21 (M2), yielding an

epoch-wise rejection agreement of 83.1% ± 9.6 between A and M1-M2. An ANOVA on the log-power values showed no significant scorer effect.

Conclusion: There is no significant difference between power values in the theta-alpha band obtained by automatic and visual artefact rejections. Despite a lower quantity of rejected epochs, the algorithm yields results comparable to those of a trained expert, with a significant gain in time. This study suggests that the information contained in a single EEG channel is sufficient to both reject artefact and process the subsequent spectral power calculation.

P601

Long-lasting changes in sleep architecture in the cage exchange model of stress insomnia

P. J. KINSLEY, C. HOLTON, D. O. KELLETT, W. F. SEIDEL, D. M. EDGAR, K. A. WAFFORD and E. SHANKS

Eli Lilly, Windlesham, UK

Objectives: A recent model of interest is the technique of stress-induced insomnia induced by cage exchange (Cano et al, 2008): rats placed in a dirty cage previously occupied by another rat exhibited neuronal activation in arousal-related areas, and sleep disturbances (delayed onset and fragmentation). The objective of the present experiments was to investigate this model as a potential predictive and translational paradigm to screen novel compounds for hypnotic efficacy.

Methods: Male Wistar rats were instrumented for recording of electroencephalogram (EEG), electromyogram (EMG), locomotor activity (LMA) and body temperature (Tb), and raw signals were captured, automatically scored, and analyzed using SCORE-2004™, as previously described (Van Gelder et al, 1991, Seidel et al, 1995). Animals were housed individually in polycarbonate cages under LD 12:12 light schedule. After at least 48 hr undisturbed baseline, animals were cage exchanged at circadian time (CT) 3, and left undisturbed for at least 48 hr thereafter. Controls were placed in a clean cage. Data were analyzed by 2-way repeated measures analysis of variance (ANOVA), looking at time periods 0–20 h and 21–48 h respectively (as Day 1 and Day 2). Sleep latency was analyzed by Student's t-test. In all cases $P < 0.05$ was considered significant.

Results: Cage change significantly delayed sleep latency (by 14 ± 5 min versus control, $P = 0.01$). Non-rapid eye movement (NREM) sleep was significantly lower on Day 2 (F = 8.9), sleep continuity was lower on both days (F = 5.9, 5.4 respectively), NREM delta power was lower on Day 1 and lower still on Day 2 (F = 14.9, 92.0), Tb was raised on day 1 and higher still on Day 2 (F = 12.7, 20.4), LMA was higher on Day 1 only (F = 20.8, 0.6).

Conclusion: The present findings are similar to those of Cano et al (2008), but furthermore demonstrate, for the first time, that there are both immediate and long-lasting changes in sleep architecture and other physiological parameters in the cage exchange model. This suggests the technique may be an interesting model of sleep fragmentation, useful for the investigation of mechanisms and treatments for this form of insomnia.

References:

1. Cano G et al. *J Neurosci* 2008, 28(40): 10167–10184.
2. Seidel WF et al. *J Pharmacol Exp Ther* 1995, 275(1): 263–73.
3. Van Gelder RN et al. *Sleep* 1991, 14(1):48–55.

P602

First step in the Portuguese validation of Cleveland Adolescent Sleepiness Questionnaire

T. REBELO-PINTO[1], C. AMARAL[2], V. NEVES DA SILVA[2], H. REBELO-PINTO[1] and T. PAIVA[1]

[1]CENC, Lisbon, PT, [2]ISPA, Lisbon, PT

Objectives: One of the goals of the Sleep-Schools Project is to develop or adapt instruments to evaluate sleep. After a pre-validation of the Cleveland Adolescent Sleepiness Questionnaire – CASQ for Portuguese adolescents [1], this work presents the first results from a national validation of this instrument.

Methods: After authorization by the original author, we structured a representative sample of Portuguese adolescents and applied CASQ to circa 6000 students. We used external data to correlate with sleepiness results, such as age, gender, school grades, body mass index, extra-curricular activities, sleep habits and medical diseases.

Results: Data has just started to be collected. Here we present results from 807 participants, with ages between 12 and 22 (mean = 14.3 standard deviation = 2.02) from 7th to 12th grade; 53.1% of the participants were female. The mean scores of CASQ were similar to other works (29.06) and there was a significant correlation with age (R = 2.0). The frequency distribution curve is skewed to the right (skewness = 0.657). Sleepiness scores were related with some sleep habits like watching tv or using the computer at bedtime, and with sleep problems. High body mass index was significantly correlated with sleepiness ($P = 0.023$) and better grades were also associated with lower sleepiness ($P = 0.000$). The Cronbach alpha was 0.803.

Conclusions: These preliminary data shows that the Portuguese version of CASQ is a valid instrument to assess sleepiness in adolescents. Furthermore, these data reinforce already known correlations between age, body mass index, school grades, sleep habits and sleepiness. All together, these results corroborate the validity of the Portuguese version of CASQ.

1. T. Rebelo Pinto, H. Rebelo Pinto & T. Paiva (2011). Verbal and Pictorial Approach in Evaluating Excessive Daytime Sleepiness in Schools. Poster presented in the Annual Pediatric Sleep Medicine Meeting. Amelia Island, Florida.

P603

Night-to-night variability in home polysomnography parameters

N. TOBBACK, D. ANDRIES, M. TAFTI, J. HABA-RUBIO and R. HEINZER

University Hospital Lausanne, Lausanne, CH

Objectives: There are limited data on the night-to-night variability in home polysomnographic parameters. The aim of this study was to assess the presence of a first-night effect (FNE) and to examine whether a single-night sleep study is adequate for the assessment of sleep disorders in home settings.

Methods: Twenty-one subjects (76% males, 63.6 ± 11.4 years old, BMI 26.3 ± 2.8 kg/m^2) participating in an ongoing population-based cohort study (HypnoLaus, Lausanne, Switzerland), underwent two consecutive full polysomnographic recordings at home. The equipment was well tolerated and adequate sleep recordings were obtained on each test.

Results: To evaluate the presence of a FNE, we compared the electroencephalogram, electromyogram and respiratory parameters between the two nights using paired t tests. There were no significant statistical differences between the two night in regards to total sleep

time (413.5 ± 79.1 min versus 402.4 ± 73.8 min, $P = 0.49$), sleep efficiency (80 ± 0.09% versus 79 ± 0.11%, $P = 0.65$), wake after sleep onset, (106.3 ± 58.4 min versus 107.7 ± 65.6 min, $P = 0.92$), percentage of slow wave sleep (17.6 ± 7.5% versus 16.4 ± 7.9%, $P = 0.17$, apnea hypopnea index (12.1 ± 8.5/h versus 14.4 ± 12.7/h, P = 0.21), oxygen desaturation index (ODI ≥ 4% 10.7 ± 7/h versus 13 ± 11.5/h, $P = 0.47$) and arousal index (21.2 ± 8.5/h versus 20.1 ± 6.4/h, $P = 0.36$) between the two nights. Our results showed only a slight increase in the percentage of rapid eye movement sleep during the second night (21.4 ± 6.7% versus 24 ± 5, $P = 0.04$).

Conclusion: There was no major first night effect in home polysomnographic results except for a slight increase in the percentage of REM sleep during the second night.

P604

Sleep state continuity varies by time in sleep episode

N. SAZUKA[1], W. WANG[2], J. WYATT[2], C. GRONFIER[2] and E. KLERMAN[2]

[1]Sony Corporation, Tokyo, JP, [2]Harvard Medical School, Boston, US

Objectives: To investigate sleep state continuity associated with time in bed and prior wake duration using transition-based analyses.

Methods: Data are from inpatient experiments in which healthy participants were scheduled to a 20-hr, 28-h or 42.85-h 'day', causing a forced desynchrony (FD) of their sleep/wake schedule from their endogenous circadian rhythms. There were eight participants for 20-h 'day' (2006 Wyatt et al. Sleep), 12 for 28-h 'day' (2007 Gronfier et al. PNAS) and 8 (2004 Wyatt et al. Sleep) + 9 (2010 Grady et al. Neuropsychopharm) for 42.85-h 'day'. Sleep during the FD was recorded and scored using standard criteria in 30 s epochs. Two-state transition probabilities for Sleep-Sleep (remaining asleep), Sleep-Wake (awakening), Wake-Wake (remaining awake) and Wake-Sleep (falling asleep) were calculated between consecutive epochs for each individual across all sleep episodes. Similarly, three-state transition probabilities among NREM Sleep, REM Sleep and Wake were calculated. Data were analyzed in 2-h bins starting at scheduled sleep onset time and analyzed within an individual and then across individuals within each study.

Results: The overall patterns of the mean and variability of transition probabilities were the same among the four studies that included different lengths of scheduled wake and sleep. Mean transition probabilities decreased for remaining asleep (S-S) and increased for remaining awake (W-W) transitions as the sleep episode progressed. When three-state analyses were done, REM-REM Sleep (R-R) transitions remained constant while the NREM-NREM Sleep (N–N) transitions decreased as the sleep episode progressed, similar to the S-S results. The variability of S-S and W-W transitions across participants increased for the first 10 h of sleep episode. For the three-state analyses, variability of R-R transition remained constant across the sleep episode, while that of N-N transition increased, similar to the S-S results.

Conclusions: The results suggest that (i) transition state analysis is a novel method for assessing changes in sleep continuity within and across sleep episodes, (ii) at the start of sleep episodes there is little inter-participant variability in the ability to remain asleep or awake, and (iii) inter-participant variability increases across the first ~10 h of a sleep episode. The dissipation of high sleep homeostatic pressure may account for the latter two observations.

Support: AFOSR EUCLOCK NASA NIH NSBRI.

P605

In flight automatic detection of pilot drowsiness using a single EEG channel. The French naval aviation experience

M. COROENNE[1], L. LELY[2], P. VAN BEERS[3], M. ELBAZ[4], M. GUILLARD[3], D. LÉGER[4], M. CHENNAOUI[3] and F. SAUVET[3]

[1]Ecole du Val-de-Grâce, Paris, FR, [2]CMA Base aéronavale, Lann Bihoué, FR, [3]Institut de recherche biomédicale des armées, Brétigny sur Orge, FR, [4]Hôpital Hotel Dieu, APHP, Paris, FR

Objectives: Drowsiness is the transition state between awake and sleep during which one's abilities to observe and to analyse are strongly reduced. Preventing accidents in aviation caused by drowsiness has become a major focus of safety. The aim of this work is to assess the performance of an automatic drowsiness detection system using a single EEG channel recorded during real flights.

Methods: Polysomnograms (EOG, EEG, EMG and ECG) from 15 healthy pilots were recorded during long haul flights (Breguet Atlantic 2 and Dassault Falcon 50 M aircrafts from the French naval aviation). All signals were captured using ultra miniaturized recorders (Actiwave®) adapted to perform measurements in ecological situation. Automatic classification (awake per cent drowsy) was made for each 10 s epoch using a dedicated algorithm from one EEG channel (O1-M2 or C3-M2). This algorithm is based on a means comparison test to detect changes of the theta (4–8 Hz), alpha (4–8 Hz) and beta (12–26 Hz) expressed in relative power, of the ratio [(alpha + beta)/theta] and of the fuzzy (alpha and theta) fusion. The two first stable min of the recorded EEG channel were considered as reference. Finally, we assessed the performance of the algorithm in comparison with the results of a 2 experts consensual sleep stage scoring using conventional American academy of sleep medicine (AASM) rules.

Results: No subject was disturbed by the recording equipment to pilot. Algorithm was tested on a dataset of 14 long haul flights (10 ± 2.0 h) representing 168 h of flight. Nine pilots experienced at least a period of voluntary (short nap average duration: 26.8 ± 8.0 min, $n = 4$) or involuntary sleep (more than 10 s of N1 sleep stage; average duration: 26.6 ± 18.7 s, $n = 7$) during flight. With the O1-M2 channel, best concordance between automatic detection and the expert-scoring were observed using the ratio [(alpha + theta)/beta]: 97.5% of good detection and 4% of false alarms. The correct classification rate (92%) was lower using the C3-M2 channel.

Conclusion: Our results establish the validity of this method to detect automatically drowsiness periods during real flights using a single EEG (O1) channel. The detection threshold is completely independent of pilots and doesn't need to be tuned for each subject. Our work is a first step for online detection of drowsiness in flight.

P606

A user-friendly approach to sleep stage classification using heart rate, breathing rate and movement

T. WILLEMEN[1], D. VAN DEUN[1], V. VERHAERT[1], J. WUYTS[2], V. EXADAKTYLOS[1], J. VERBRAECKEN[3], S. VAN HUFFEL[4], B. HAEX[1] and J. VANDER SLOTEN[1]

[1]KU Leuven, Heverlee, BE, [2]Vrije Universiteit Brussel, Brussels, BE, [3]Antwerp University Hospital, Antwerp, BE, [4]KU Leuven, Leuven, BE

Objectives: Polysomnography allows to asses all aspects of sleep accurately, but can be costly, time-consuming and unpleasant, specifically in long-term studies. Actigraphy on the other hand is both cheap and user-friendly, but for many studies lacks detailed information and accuracy. Over the years, however, extensive

research has been done on changes in heart and breathing rate across sleep stages and during different sleep disorder related events. Our aim was to evaluate the use of heart rate, breathing rate and movement in discriminating between REM and NREM sleep.

Methods: The dataset comprised 85 nights from a healthy population (age 22.1 ± 3.2 years); 57 nights were taken as training set, 28 nights as test set. No nights from the same person were present in both training and test set to ensure that there was no person-specific training. Heart rate was extracted from ECG, breathing rate from Respiratory Inductance Plethysmography and movement from a changing mattress indentation measured by sensors integrated in the bed. In a first test series, signals where split in parts of five epochs (150 s) belonging to the same class (REM and NREM), excluding shorter intervals. In a second test series, signals where split in parts of two epochs (60 s), where if at least one epoch belonged to class REM, the entire interval was labelled as REM. From a broad set of 4094 predefined features, a subset was forwardly selected (test series-specific) on the training set using a minimum Redundancy Maximum Relevance criterion, based on mutual information calculation via kernel density estimation. The final classification of REM versus NREM was performed using Weka (data mining software), more specifically using Random Forests with 25 decision trees of 15 features each.

Results: For the first test series, a classification accuracy of 84.2% was reached on the test set, corresponding to a Cohen's kappa of 0.69 and a Receiver Operating Characteristic (ROC) of 0.91. True positive rate for class REM and NREM were respectively 0.87 and 0.81. The second test series gave a classification accuracy of 81.0%, a Cohen's kappa of 0.62 and a ROC of 0.88. True positive rate for class REM and NREM were respectively 0.77 and 0.85.

Conclusion: The results show the significant correlation of heart rate, breathing rate and movement towards the distinction between REM and NREM sleep. Further research will assess the effect of subject-specific training and add a primary sleep versus wake classification.

This research was carried out thanks to the financial support of the Institute for the Promotion of Innovation through Science and Technology in Flanders (IWT).

P607

About a data bank on sleep in Fine-Arts

L. CURZI-DASCALOVA

INSERM, Paris, FR

Objectives: As stressed by the German poet and philosopher Goethe at the beginning of the 19th century, we see only what we know. Having done research on sleep development for decades and being interested by the history of fine-arts, has inevitably compelled me to study the place of sleep as a subject of art. It was interesting to give the possibility to understand: (i) why a particular work of art has been done, what does the artist want to imply? (ii) Is the artist aware of what we presently know about sleep (state of sleep, pathology of sleep etc.)? (iii) What are the methods of representation used in relation to the personality of artistic school, in different periods in history? It was imperative to have a large data bank of examples of art-works dedicated to sleep.

Methods: (A) Sources, in decreasing order of number: art books (scanned), personal photos, Internet, and pictures given by contemporary artists. (B) Presentation of images using Power point2010. (C) Classification using Excel2010, giving information on: (a) artist (name, country, epoch); (b) present location of the art work (museum, collections, town, country); (c) techniques used (painting, sculpture, drawing, ceramic, textile …); (d) title and the main theme of the work as: holy tells (mythology, Old Testament, New Testament, Buddhism), legends and literature, sleep pathology…; (e) Type of 'sleep situation' (sleep, dream, siesta, awakening); (f) Population depicted (infant, child, animal, abstraction art-work).

Results: Our data bank includes 6134 art works, with 1358 on infant and child sleep, 424 on various animals sleep and 87 on awakening. The oldest sculpture found is about 5400 years old, and many works are done in the 21st century. The artist listed were born in 91 countries and works of art located in different places in 58 countries. Many of the images (we are expecting to present some of them) give information on sleep behavior and states, as well as on various sleep pathologies.

Conclusion: Our investigation shows that, throughout the different periods of the progress of human civilization, sleep has been and continues to be a permanent theme of artistic creativity. Our data bank gives the possibility to investigate the place of sleep representation in relation to important philosophical, religious, psychological and sleep research issues. It will be available for non-commercial consultation in a national public library in Paris.

Poster Session – Individual Differences in Sleep Deprivation

P609

Trait-like characteristics of the non-REM sleep EEG spectrum following total sleep deprivation

L. TAROKH[1], H. P. A. VAN DONGEN[2], T. RUSTERHOLZ[1] and P. ACHERMANN[1]

[1]University of Zurichc, Zurich, CH, [2]Washington State University, Spokane, US

Objectives: The sleep EEG spectrum is unique to an individual and stable across multiple recordings, leading some to suggest that the sleep EEG spectrum is a trait. Previous studies assessing trait-like characteristics of the sleep EEG typically examined baseline sleep after approximately 16 h of wakefulness. The aim of the current study was to assess whether the sleep EEG spectrum after 36 h of wakefulness also represents a trait.

Methods: As part of an 11-day in-laboratory study, polysomnography was recorded in sixteen healthy subjects between the ages of 22 and 40 years on six consecutive nights. Three nights of baseline sleep (12 h time in bed, 22:00–11:00, following 12 h of wakefulness) were interleaved with three nights of recovery sleep (12 h time in bed, 22:00–10:00, following 36 h of sustained wakefulness). Sleep was scored visually according to the criteria of Rechtschaffen and Kales, and spectral analysis of the NREM sleep EEG (derivation C3/A2) was performed. Interclass correlation coefficients (ICCs) were calculated for 0.25 Hz frequency bins between 0.75 and 16 Hz, for the baseline and recovery night spectra separately.

Results: As expected, ICCs were high (ranging between 0.50 and 0.87) and significant ($P < 0.05$) across the entire frequency range for the NREM sleep EEG spectra of the baseline nights. ICCs were also high (ranging between 0.48 and 0.91) and significant ($P < 0.05$) across all frequencies for the NREM sleep EEG spectra of the recovery nights.

Conclusions: Our results indicate that the spectrum of the NREM sleep EEG following sleep deprivation is trait-like. The stability of the spectra may be a reflection of individual neuroanatomy.

Supported by: This work was supported by Swiss National Science Foundation Grant 320030–130766 (to PA), NIH grant HL70154 (to HVD) and ONR grant N00014–11-C-0592.

P610

Tonic and rhythmic individual differences in baseline alertness profiles predict vigilance decrements after consecutive sleep restriction

O. MAIRESSE[1], A. CORTOOS[1], P. STENUIT[2], N. PATTYN[1] and M. KERKHOFS[2]

[1]Royal Military Academy, Brussels, BE, [2]CHU Vésale, Montigny le Tilleul, BE

Objectives: The purpose of this study is to assess if individual differences in baseline subjective alertness profiles are predictive of vigilance decrements during consecutive sleep restriction.

Methods: Twenty-nine healthy women (age = 43.4 ± 15.9; BMI = 22.7 ± 2.2; ESS = 6.66 ± 3.2; PQSI = 3.69 ± 1.8) underwent a full PSG before three consecutive nights of sleep restriction (4 h TIB). Baseline subjective alertness was assessed day 1 at 7:30 AM and from 9 AM 2-hourly until 1 AM by means of the Stanford Sleepiness Scale (SSS). SSS data were smoothed using 4th order B-splines with five equidistant interior knots. Smoothed profiles were subjected to a functional principal component analysis in order to assess the composite nature of the individual variability of alertness profiles. Psychomotor vigilance was assessed by means of the PVT every day at 9 AM and 1 PM and at 5 PM at baseline and after 3 days of sleep restriction.

Results: Of 96.1% of the individual variance in baseline subjective alertness profiles is accounted for by three functional components. The first functional component explains 78.3% of the variance and lowers or increases the mean function without altering its form. Component 1 scores were significantly related to perceived sleep quality (PSQI; r = 0.39, $P < 0.05$) and the average number of attentional lapses during sleep restriction (r = 0.36, $P < 0.05$), but not with any baseline objective sleep variable. The second functional component explains 9.1% of the variance and reflects circasemidian rhythmicity. Increased SWS latency is significantly associated with stronger circasemidan rhythmicity in alertness profiles the subsequent day (r = 0.34, $P < 0.05$), but is unrelated to PVT outcome variables. A third functional component explains 8.7% of the variance and reflects the timing of peak alertness (around 11 AM or 9PM). Vesperal peak alertness is associated with higher proportions of N2 (r = 0.43, $P < 0.01$) and lesser of N3 at baseline (r = -0.38, $P < 0.05$) and with a faster increase of attentional lapses (r = 0.34, $P < 0.05$) and a more rapid decline of fastest response speed (r = -0.46, $P < 0.01$) during sleep restriction.

Conclusion: Although most of the variance in individual profiles is accounted for by tonic differences, subtle rhythmic differences in baseline alertness related to the proportion of SWS predict the speed of vigilance decline during consecutive sleep restriction.

P611

Individual differences in sleep revisited: stability across sleep restriction, extension and total sleep loss

E. L. ARBON, A. S. LAZAR, J. C. LO, A. SLAK, P. J. MCCABE, J. BOYLE, S. N. ARCHER and D.-J. DIJK

University of Surrey, Guildford, UK

Objectives: There are prominent individual differences in sleep structure and it has been reported that these individual differences are robust against the effects of total sleep deprivation (TSD). We investigated the robustness and stability of individual differences across sleep extension (SE), sleep restriction (SR), and TSD. We also examined the contribution of a variable number tandem repeat polymorphism in PER3 (rs57875989) to individual differences in sleep-wake regulation.

Methods: The sample consisted of 12 PER34/4, 10 PER34/5 and 14 PER35/5 individuals (mean age 27.6 ± 4.0; 18 men). In this two-way cross-over study, polysomnography was recorded in a baseline night [8 h time in bed (TIB)], seven condition nights (SR: 6 h TIB, or SE: 10 h TIB), and a recovery sleep episode (12 h TIB) following a ~40 h TSD. Mixed model ANOVA was used to assess effects of condition, genotype and night. Stability and robustness of individual differences was assessed by computing the intraclass correlation coefficient (ICC) by calculating the ratio of between-subject variance to total variance.

Results: Sleep parameters were affected by the protocol, e.g. shorter total sleep time (TST) during SR than SE, and enhanced slow-wave sleep (SWS) after TSD. Even so, individual differences remained and were stable across these conditions. ICC's across baseline and condition nights were: TST, 0.29; sleep latency, 0.45; latency to persistent sleep, 0.48; wake after sleep onset, 0.22; sleep efficiency, 0.34; and 0.56, 0.50, 0.75, 0.36, 0.34 for% of stage 1, 2, SWS, REM sleep, and wake respectively. ICC values increased for almost all sleep parameters when only recovery nights were considered. Main effects of genotype were observed for% of REM sleep ($F_{2,33}$.1 = 4.27, P = 0.02) and SWS ($F_{2,33}$.1 = 4.42, P = 0.02).
Conclusion: We observed prominent inter-individual differences in many sleep parameters and these individual differences were robust against manipulations of sleep-wake history. SWS showed the most trait-like characteristic. The notion that these inter-individual differences to some extent represent genetic differences was supported by the observation that PER3 genotype differentially affected some sleep parameters. The data provide further evidence for the robustness and stability of sleep parameters across conditions which activate sleep homeostatic mechanism processes.
This research was supported by grants from the AFOSR (FA-9550–08–1–0080).

P612

Acute restriction of sleep duration and type D personality: haemodynamic and salivary alpha-amylase response to social stress in women

É. O LEARY[1], S. HOWARD[2] and J. JAMES[3]
[1]National University of Ireland, Galway, IE, [2]University of Limerick, Limerick, IE, [3]Reykjavík University, Reykjavík, IS

Objectives: The Type D (distressed) personality is defined as a combination of negative affectivity and social inhibition with proposed pathogenetic mechanisms including blood pressure (BP) hyper-reactivity. Previous research has indicated that the effects of sleep restriction on the psychophysiological functioning of an individual may depend on factors such as individual differences in personality characteristics.
Methods: To examine the effects of sleep restriction and Type D on reactivity to social stress, 70 normotensive female university students completed a laboratory based social stressor, following acute sleep restriction, receiving just 40% of their usual sleep (monitored using wrist actigraphy) or following a full night's rest.
Results: Analysis using the Multidimensional Fatigue Inventory (MFI) indicated significantly increased (all ps < 0.001) multifocal fatigue (i.e., general/physical fatigue and reduced activity/motivation) as a result of sleep restriction. Mixed factorial ANOVA indicated a significant Phase × Sleep interaction for salivary alpha-amylase (sAA) activity, $F_{1,67}$ = 8.18, P = 0.006, partial eta ^2 = 0.109, with significantly higher baseline levels of sAA under sleep restriction compared to rested conditions. Between-subjects ANCOVA analysis also revealed a Sleep × Type D interaction for systolic BP $F_{1,65}$ = 5.03, P = 0.028, partial eta^2 = 0.072, with buffered reactivity under rested conditions in individuals with Type D personality. A comparable pattern of buffered reactivity under rested conditions in those with Type D also approached significance for diastolic BP (P = 0.067). Further, data also indicate that Type D individuals report worse sleep quality (P = 0.034), in addition to reporting greater fatigue (P = 0.023) when rested, compared to non-Type D.
Conclusions: Such findings suggest that the acute restriction of sleep duration can result in greater behavioural report of fatigue, as well as increased baseline stress-related sympathetic activity (sAA). Furthermore, reactivity to social stress, when rested but not sleep restricted, may be moderated by individual trait differences in negative affectivity and social inhibition, resulting in attenuated BP reactivity for individuals classified as Type D, in addition to distinct fatigue and sleep quality subjective reports.

P614

Personality and sensitivity to sleep deprivation

M. MARQUES, M. H. AZEVEDO and A. PEREIRA
University of Coimbra, Coimbra, PT

Introduction: Studies have shown that healthy subjects differ markedly in their response to total or partial sleep deprivation. Although the causes of these differences are unknown, it is likely that biological, psychological and social factors are involved.
Aim: To explore the relationship between the personality traits of neuroticism, extraversion and perfectionism and self-reported sensitivity to sleep loss.
Methods: Seven hundred and thirteen medical students (65.6% females) participated. Two items were used to evaluate sensitivity to sleep deprivation (SSD): 'Do you feel that you function well after one night without sleep? ' and 'Are you able to go with only a few hours sleep per night for several days in a row? ' (response options from 'Very well' = 1 to 'Very badly' = 5). The scores of these two items were summed to form the sensitivity to sleep deprivation index (SSDI). Perceived sleep needs (Hours) and Habitual sleep duration (Hours) were evaluated with two items: 'How many hours you need of sleep to feel good and function well during the day?' and 'How many hours do you usually sleep per night?' (Both with 9 alternative replies from 5 h or less to 11 h or more). To evaluate personality traits the following questionnaires were used: Eysenck Personality Inventory (Extraversion and Neuroticism/EPI, NEO-PI-R Neuroticism and its facets; Hewitt & Flett and Frost Multi-Dimensional Perfectionism Scales.
Results: The SSD1/2 and the SSDI positively correlated with Sleep Duration and Sleep Needs (P < 0.01). SOP negatively correlated with SSDI (P < 0.05). Extraversion negatively correlated with SSD1/2 (P < 0.01 and SSDI (P < 0.01). Neuroticism/EPI positively correlated with SSD (P < 0.05). Neuroticism/NEO-PI-R positively correlated with SSD1/2 and SSDI (P < 0.01). There were not significant differences between any SSD groups in Perfectionism variables. Neuroticism mean scores significantly differ between SSD1 groups and Extraversion mean scores did not differ between SSD1 groups; the contrary was found for SSD2 (P < 0.05). In general, the higher the Neuroticism/NEO-PI-R and its facets the higher the SSD. Perceived Sleep Needs, Self Oriented Perfectionism, Anxiety and Vulnerability were significant predictors of SSD.
Conclusion: Neuroticism was found to be positively associated with self-reported sensitivity to sleep deprivation whereas the association with extraversion was negative. Our findings suggest that Self Oriented Perfectionism may be a predictor of sensitivity to sleep deprivation.

Poster Session – Light

P615

Influence of domestic light at Night on melatonin concentration and circadian phase in Japanese children

S. HIGUCHI[1], Y. NAGAFUCHI[1], T. HARADA[2], I. TANAKA[1] and K. HARADA[1]

[1]Kyushu University, Fukuoka, JP, [2]Kochi University, Kochi, JP

It has been pointed out that children in some country have a late bedtime and short sleeping time. Exposure to artificial light at night may be a cause of delayed bedtime and delayed circadian rhythm in children since light at night has the potential to delay circadian rhythm. Since pupil size and light transmission rate of the crystal lens in children are larger than those in adults, children might be more sensitive to light at night. We have already found that light-induced melatonin suppression in children is greater than that in adults. It has been reported that melatonin secretion is suppressed by several hundred luces of light at home. In this study, effects of domestic light on melatonin suppression and circadian phase in children were examined. Seventeen adults (41.7 ± 5.0 years old) and twenty children (9.2 ± 1.9 years old) volunteered to participate in this study. First, salivary samples were collected every 30 min from 19:00 to habitual bedtime under dim light (<15 lx) to measure salivary melatonin concentration before bedtime and timing of dim light melatonin onset (DLMO) as a marker of circadian phase. Next, the subjects were asked to collect saliva samples every hour at home under domestic light. They were also asked to measure illuminance level and color temperature of light at home. This study was approved by the Ethics Research Committee of Kyushu University. In children, the melatonin concentration under domestic light was significantly suppressed compared with that under dim light. No significant suppression by domestic light was found in adults. The average and standard deviation values of vertical illuminance level at eye level and color temperature of domestic light were 140.0 ± 82.7 lx and 3862.0 ± 965.6 K, respectively. There were significant positive correlations between DLMO and color temperature in adults and children. No significant correlation between DLMO and illuminance level was found. The results suggest that light-induced melatonin suppression in children is larger than that in adults even in the case of domestic light with a low illuminance level and that high color temperature of domestic light might be a cause of delay in circadian phase.

P616

Effects of evening blue-spectrum light on sleepiness and sleep quality

E. MARQUEZE[1], A. THOMPSON[2], G. ATKINSON[3] and C. MORENO[1]

[1]University of São Paulo, São Paulo, BR, [2]Liverpool John Moores University, Liverpool, UK, [3]Teesside University, Middlesbroug, UK

Objectives: To evaluate the effects of evening blue light on sleepiness and sleep quality. It has been postulated that, besides the intensity of light being important, but also light wavelength can affect levels of alertness and performance. Blue light has been shown to attenuate sleepiness and improve performance.

Methods: We recruited eight healthy participants to compare three conditions: no light (baseline); bright light (2500 lux), and bright light (2500 lux) with blue light filtered (<520 nm) using specialised glasses (Solar3, Eschenbach optik, Ridgefield, Connecticut). Participants were physically active, normotensive, males, aged 22 ± 2 years and BMI 24.19 ± 2.17 kg/m^2. Each subject attended the laboratory on three separate occasions, with 7-day washout period. Following each condition, participants were administered dim light for a further 75 min before retiring to bed at 23:45 h. Actigraphy data (Actiwatch, Cambridge Neurotechnology Ltd), visual analog scale and the Karolinska Sleepiness Scale were used to obtain sleep quality data. Prior to attending the laboratory participants were issued with silicon coated thermometric pill (CorTemp, Human Technologies Int.). Data was recorded at 30-s intervals throughout the protocol and during sleep. Saliva samples were collected throughout the protocol. A one-factor (condition) linear mixed model analysis and Pearson's correlation were performed.

Results: Means of actual sleep duration were 359.12 min, 358.33 min and 356.50 min during no light, bright light and blue light conditions, respectively. We have not observed a significant difference in core body temperature nadir, 36.34, 36.26 and 36.37°C (no light, bright light and blue light condition). Levels of alertness decreased significantly prior to sleep compared to daytime levels (09:30 h, 12:30 h and 15:30 h, $P < 0.05$). Pearson correlation between sleep parameters and melatonin post-light exposure (22:15 h) was not significant in any condition (15.3 pg/ml no light, 12.8 pg/ml bright light and 18.2 pg/ml blue light condition). However, wake time after sleep onset showed a positive correlation with melatonin post-exposure during baseline (no light) ($P < 0.01$).

Conclusion: No effects on sleep and sleepiness were observed, neither after bright light nor blue light exposure. Light exposure at this time of the day might not affect a subsequent sleep and the sleepiness on the following day.

Support: CNPq and Lumie.

P617

Blue-enriched room light in the morning enhances daytime alertness and night-time sleep

D. KUNZ, C. STOLL, S. HAEDEL and A. RODENBECK

Charité University Hospitals, Berlin, DE

Objectives: Basic research on the effects of blue wavelength light on wakefulness suggests that there are two distinct pathways of activating effects of bright light. One is an immediate pathway, causing cortical activation during task performance (Vandewalle et al, 2006). Another pathway is thought to act indirectly via the suprachiasmatic nucleus, controlling evening melatonin release and affecting the circadian pacemaker (Gordijn & Beersma; 1999; Hébert et al., 2002). However, it is unknown whether these two mechanisms can be influenced in a real life environment by bright morning light. The current study aims to compare biologically optimized room lighting to light bulb room lighting in the morning regarding subjective alertness, reaction times and night time sleep.

Methods: In a randomized cross-over design ten healthy participants were exposed to an optimized lighting condition (637 lux;3400 Kelvin) and 7 days later to a light bulb lighting condition (20 lux; 2400 Kelvin) or vice versa. Light exposure took place on three consecutive days from 8 to 11 am. During light exposure subjective alertness and reaction times on the psychomotor vigilance task were measured every hour. In the evening light conditions were controlled and sleep was polysomnographically recorded.

Results: During hours of optimized room lighting reaction times on the psychomotor vigilance task were significantly than in the light bulb condition (two-tailed paired t-test; $P < 0.05$). Similarly, subjective alertness in the optimized light condition was increased compared to the light bulb condition at all three of the hourly measurements (two tailed paired t-test; $P < 0.05$ at 9 am; $P < 0.1$ at 10 am and $P < 0.05$ at 11 am). Subjective alertness in the optimized light condition increased with every consecutive day, this effect was absent in the light bulb condition (repeated measures ANOVA; interaction light condition*day*time: $P < 0.05$). Polysomnography revealed that after optimized light participants experienced a mean of 29.4 min more total sleep time (two-tailed paired t-test; $P < 0.05$). Increased sleep was due to significantly more slow wave sleep ($P < 0.05$) and a trend towards more REM sleep ($P < 0.1$).

Conclusion: The current data show that optimized lighting in the morning is of great importance not only for immediate alertness, but also for sleep quality at night. Furthermore, results suggest that the immediate benefits of optimized room light increase with every consecutive day of light exposure.

P618

Salivary melatonin concentration and sleep patterns before and after pinealectomy in patients with pineocytoma WHO°I

H. C. SLAWIK, M. STOFFEL, Z. VESELÝ, J. LEHMBERG, C. POHL, B. MEYER, M. H. WIEGAND and S. M. KRIEG

Technical University Munich, Munich, DE

Objectives: The pineal gland as a melatonin-producing organ is suggested to be involved in the regulation of sleep and circadian rhythm. However, according to published data only 25–54% of patients suffer from sleep disturbances after pinealectomy (Macchi, 2004). Moreover, previous studies have not controlled for confounding factors such as chronotype, preexisting sleep disturbances, insomnia related to comorbid depression or preexisting changes in salivary melatonin concentration that might have been caused by tumour growth.

Methods: Eight consecutive patients with pineocytoma WHO°I that were considered for pinealectomy were prospectively assigned to the study. Before and 3 months after pinealectomy we performed a clinical interview by a sleep expert, two consecutive nights of polysomnography as well as 2 weeks of actimetry and sleep log. Moreover, subjects completed the Pittsburgh Sleep Quality Index (PSQI), the Epworth Sleepiness Scale (ESS), the Beck Depression Inventory and the Morningness-Eveningness Questionnaire (D-MEQ). At the evenings before polysomnography we assessed salivary dim-light melatonin onset (>3 pg/ml) within a time frame that was approximated by the individual D-MEQ score.

Results: In all subjects assessed to date preoperative salivary dim-light melatonin onset was within the expected physiological range but postoperative salivary melatonin was below detection levels. However, sleep patterns did not appear to be changed in relation to pinealectomy.

Conclusions: Although pinealectomy causes a lack of detectable salivary melatonin this is not related to changes in sleep patterns three months post surgery. Melatonin secretion in other organs that is undetectable in salivary samples might compensate for the lack of pineal melatonin secretion or the exclusive elimination of circadian pineal melatonin release does not destroy the complex regulation of sleep within the relatively short time of three months post pinealectomy.

Reference:

1. Human pineal physiology and functional significance of melatonin. Macchi MM, Bruce JN. *Front Neuroendocrinol* 2004, 25(3–4): 177–95.

P619

Melanopic lux in people's homes – logarithmic relation between melanopic lux and melatonin suppression after short-term evening light exposures in healthy subjects

C. STOLL, A. WAHNSCHAFFE, S. HAEDEL, A. RODENBECK and D. KUNZ

Charité University Hospitals, Berlin, DE

Objectives: Based on recent animal laboratory studies a melanopic spectral efficiency function (melanopic lux or mlux) has been developed to predict the activation of melanopsin containing ganglion cells in the retina by polychromatic light. Adapted to the human eye this function integrates brightness and sensitivity to blue wavelength light. Still it remains unknown whether this function can predict melatonin suppression (i) in humans, (ii) after short-term light exposure, and (iii) in a naturalistic setting. In this context the aim of the current study was to investigate whether the melanopic efficiency function is associated with melatonin suppression.

Methods: Thirteen light conditions were tested in 31 healthy men and women (18–35 years of age) in four sessions; every session included 9–11 participants and lasted 12–14 days. Dim light was applied four to 1 h before individual bedtime, followed by a 30 min light exposure and again 30 min dim light. Light conditions during light exposure varied between 79 and 2955 mlux (80–600 lux, 1500–12000 Kelvin). Experimental light condition plus a control condition were presented in a randomized order. Experimental light conditions plus a control dim light condition in each session were presented in a randomized order. Saliva was sampled in 10 and 30 min intervals.

Results: Repeated measures ANOVA revealed that five out of 12 light conditions suppressed melatonin significantly ($P < 0.05$), some already after 20 min. Subjective alertness was not associated with melanopic lux. Multiple regression analysis included factors melanopic lux, number of blue photons, lux and Kelvin. Melanopic lux was the best predictor for melatonin suppression (beta = -0.41; $P < 0.01$). The relationship between mlux and melatonin suppression was fitted into a logarithmic curve, revealing a significant relationship ($P < 0.01$) that explains 61% of the variance.

Conclusion: The current data demonstrates that mlux is a suitable measure of predicting melatonin suppression, after short-term light exposures and in a naturalistic setting. This confirms results of a recent study that reported changes in melatonin and sleep after 4 h of evening light. However, current data emphasizes the strength of the effect even after short-term light exposures. The logarithmic relationship clearly underlines a strong dependency even in rather low mlux values indicating that the specific mlux value of commercially available lamps should be labeled.

The study was financed by the German Ministry for Education and Research (BMBF FKZ: 13N8973).

P620

Evidence for a circalunar rhythm in human sleep structure, melatonin and cortisol levels

C. CAJOCHEN[1], M. MÜNCH[2], S. ALTANAY-EKICI[1], A. WIRZ-JUSTICE[1] and S. FREY[1]

[1]Centre for Chronobiology, Basel, CH, [2]EPFL, Lausanne, CH

Background: Endogenous circalunar rhythms have been demonstrated in a number of species under constant laboratory settings. Despite overwhelming evidence of the importance of lunar rhythms in various marine organisms and insects, in humans there is no consistent association with the moon and human pathology, phys-

iology or behaviour. Thus, we a posteriori tested whether lunar phase impacts on sleep and hormonal rhythms.

Methods: To exclude confounders such as the increase of light at night and a potential bias in perception regarding the lunar influence on sleep, we retrospectively analysed sleep structure, NREMS-EEG activity, melatonin and cortisol secretion under stringently controlled constant laboratory conditions in 32 healthy volunteers (16 men and 16 women; age: 19–35 years and 55–75 years). For each volunteer two baseline-nights timed at the individual's usual bedtimes entered statistical analysis. For each night, the distance from the nearest full moon date (Dfull) was determined and assigned to three different lunar classes: 0–4, 5–9 and 10–14 days of Dfull. Comparisons were made with mixed-model analyses of variance, with factors lunar class, gender and age. Sleep stages were scored according to conventional criteria, and the EEG subjected to spectral analysis.

Results: As expected we found significant effects for the factors age and gender in the following sleep variables: total sleep time (TST), sleep latency (SL), slow wave sleep (SWS) and delta EEG activity and REMS latency (RL) and SWS respectively. Unexpectedly, the factor lunar class yielded also significance for all the above mentioned sleep variables and melatonin (F at least 3.1; $P < 0.05$), with lower TST (figure), less SWS and delta EEG activity, longer SL, RL and lower melatonin levels 0–4 days around full moon compared to the other lunar classes, while cortisol levels did not significantly change.

Conclusion: We have surprising evidence that the distance to the nearest full moon phase significantly influences sleep and melatonin levels. Factors such as light and personal moon perception can be excluded, since the study was performed in windowless rooms and in retrospect. Although the finding needs prospective evidence in a larger subject sample, we have preliminary evidence that a circalunar rhythm modulates sleep structure in humans under the demasking conditions of a circadian laboratory study protocol.

Funding: This work was supported by the Swiss National Science Foundation.

P621

The effect of environmental light levels on chronotype

K. PORCHERET, K. WULFF, T. ROENNEBERG and R. G. FOSTER
University of Oxford, Oxford, UK

Objectives: To investigate the effect of environmental light levels divided up according to geographical location and season, on diurnal preference.

Methods: Students, aged 18–25 years old, completed the online version of the Munich Chronotype Questionnaire (MCTQ) in six different universities around the world (University of Oxford, UK; Ludwig Maximilians University, Munich, Germany; Groningen University, Netherlands; University of Western Australia, Perth, Australia; Monash University, Melbourne, Australia; University of Auckland, New Zealand). Data were collected twice over a period of three to four weeks in May and October 2010. Light levels were assessed by light exposure (hours spent outside) and light dose (light intensity experienced for hours spent outside: (daily irradiance/hours of daylight*light exposure). Mid-sleep on free days corrected for over sleep on free days due to sleep debt of work days (MSFsc) served as phase reference point and a correlate for chronotype.

Results: 13 299 students filled out the questionnaire online and of those 6443 had fully completed information and were included in the data analysis. MSFsc relative to local clock time was found to be earlier in the southern hemisphere cities (local time: 4.69 SD1.4) than in the northern hemisphere cities (local time: 5.20 SD1.26). Two way ANOVA analysis of city and season revealed a significant effect of city ($F = 25.664$, $P = 0.0001$) but no effect of season ($F = 0.574$, $P = 0.449$) or city/season interaction on MSFsc ($F = 1.878$, $P = 0.095$). *Post hoc* group analysis revealed that apart from Munich and Melbourne, a significant difference was found between the Northern (Oxford, Groningen) and Southern hemisphere (Perth, Auckland) cities. An effect of city was found for both, light exposure ($F = 7.112$, $P = 0.000$) and light dose ($F = 123.921$, $P < 0.0001$) but an effect of season was only found for light dose ($F = 428.371$, $P < 0.0001$). ANCOVA analysis found an effect of light exposure on MSFsc ($F = 4.386$, $P = 0.036$), but no effect of light dose on MSFsc ($F = 1.553$, $P = 0.213$).

Conclusions: Diurnal preference is significantly later in the Northern hemisphere cities compared to the Southern hemisphere cites, which can partly be explained by the amount of light individuals exposure themselves.

P622

The non-circadian effects of light influence depression-like behaviour in mice via melanopsin-based pathways

L. CALVEL, J. HUBBARD, L. CHOTEAU, C.-M. GROPP, E. RUPPERT and P. BOURGIN
Strasbourg University hospital, Strasbourg, FR

Objectives: The relationship between light, depression, sleep, and circadian rhythms has been strongly documented but still remains poorly understood. Sleep and mood are known to be strongly influenced by a circadian component. Light can impact mood through a phase advance of the circadian rhythm, however, the effect on the biological clock does not explain all of its antidepressive effects. Light is also known to exert direct effects, independent of a circadian rhythm. Based on our recent work, our goal was to determine whether the direct effects of light via melanopsinergic retinal ganglion cells (conveying this information to the brain) can also affect mood-related behavior in mice.

Methods: We examined behavioural responses under various light intensities in mice lacking melanopsin (KO- Opn4-/-) (C57BL/6, male) using several confirmed models of anxiety and depression-like behavior. The behavioral test battery consisted of the sucrose preference test, the forced swim test, the tail suspension test, and the elevated plus maze. Each lighting condition was applied for 12 h in order to not disrupt the normal 12:12 LD cycle of the circadian phase. Sleep and wake were previously phenotyped in these mice. All tests were performed under dim light (<10 Lux), between ZT 14 and ZT 22.

Results: Wild type (WT-Opn4+/+) animals exposed for 7 days to dim light ($n = 8$) during the light phase developed anxiety and depression-like behaviors (resignation, anhedonia, anxiety), as opposed to those exposed to high light intensities (550 lux; $n = 7$). WT mice that were subjected to standard light intensity (200 lux; $n = 9$) showed results ($P = 0.06$) between those exposed to the two extreme light intensities (dim light and 550 lux). A dose response between positive light intensity and depression-like responses was observed only in WT whereas KO mice were indifferent to variations in light intensity (genotype effect).

Conclusion: Mice are nocturnal and photophobic, yet the results show an improvement of their mood-related behavior under high light intensity. Our findings suggest that light exerts antidepressive effects through a direct influence on mood states via mechanisms mediated by melanopsin-based pathways. Further experiments are needed in order to determine whether light therapy can influence mood disorders and associated sleep disturbances through non-circadian direct effects.

Poster Session – Plasticity (Conditioning) Animals

P623

Effects of active-avoidance task training on REM sleep microstructure in the rat

I. BULLER, M. AYLWIN and A. OCAMPO
University of Chile, Santiago, CL

Consolidation of long-term memory formation includes an enhancement mechanism occurring primarily during sleep. It has been thoroughly studied and related to different sleep stages. Since pontine (P) wave expression is positively correlated to performance improvement in an active-avoidance task (Datta, 2000), a relationship has been suggested between rapid eye movement (REM) sleep expression and emotionally influenced learning. REM sleep can be categorized in two alternating sub-states, where the typical muscular atonia and sustained hyppocampal theta activity during tonic REM sleep are briefly interrupted by phasic EEG, muscular and autonomic phenomena. If phasic REM sleep is positively involved in an active-avoidance task consolidation, it should be manifested in an increased phasic muscular and EEG manifestations in REM sleep. Adult male Sprague-Dawley rats were chronically implanted for cortical electroencephalogram, nuchal electromyogram, electro-oculogram and whisker electromyogram recording. Sleep data was acquired under 12:12 light-dark cycle (lights on at zeitgeber time, ZT = 0). At ZT 1, three groups of rats were exposed to either: an avoidance task training session (AA group, $n = 5$), a random unpaired foot-shock session for stress control ($n = 5$), or a free exploration session ($n = 5$) at the conditioning box. Post-training sleep was recorded during ZT 2–7, visually scored and compared to baseline data acquired for 2 days before experiment. AA group was re-exposed to the avoidance task at ZT 8 for post-sleep performance improvements evaluation. The microstructure and the expression of phasic events densities (theta bursts, nuchal twitches and whisker movements) were evaluated. Total amount of wakefulness, non-REM and REM sleep where not affected after the avoidance training. Microstructure of REM sleep was studied analyzing episodes and sleep cycles duration, to determine single, sequential and clusters of REM sleep (Amici et al., 1998). Single REM sleep episodes tend to be selectively affected by the training session. The treatment do not affect short-term homeostasis of REM sleep (Ocampo-Garcés & Vivaldi, 2002), nevertheless REM episode duration is correlated to preceding ultradian interval in the AA group. Preliminary evaluation indicate that phasic nuchal and whisker events increase specifically in the AA group. Our results suggest that REM sleep is involved in consolidation process of emotionally influenced learning (Grant FONDECYT 1100245).

P624

Sleep architecture, behaviour, corticosterone and acoustic startle response after double exposure to social defeat in rats

A. M. KINN RØD, J. MRDALJ, A. M. MILDE, F. K. JELLESTAD, R. MURISON, L. A. ØVERNES and J. GRØNLI
University of Bergen, Bergen, NO

Objectives: The study aimed to investigate short- and long-term effects of social defeat (SD) on sleep architecture, anxiety-like behaviour, acoustic startle response and corticosterone.

Methods: Twenty adult male rats were implanted subcutaneously with telemetric devices for electroencephalogram (EEG) and electromyogram (EMG) recording and randomly divided into SD or control group (n's = 10). SD rats were exposed to and defeated by an aggressive dominant rat for 1 h on two consecutive days. Control animals were left undisturbed. Analysis of sleep stages and EEG power were performed for 8 h before and after SD (day 1, 14, and 21). The emergence test (open field with start-box) was used to test anxiety-like behaviour once a week for three weeks after the SD confrontations. Plasma corticosterone was measured before implantation of the transmitter and after the last emergence test. Acoustic startle responses were tested on day 23 after SD.

Results: SD rats as a group were not affected by the social conflict with regard to sleep architecture, behaviour, corticosterone response to the emergence test, or acoustic startle responses. Time spent outside the start-box increased over days in control rats ($P < 0.01$), while SD rats did not show this effect. Effects of social defeat seemed, however, to vary according to the behaviours that the intruder displayed during the social confrontation with the resident. Rats with an 'active coping' strategy (fighting back during the social confrontation; SDF) showed more fragmented slow wave sleep, both in SWS1 ($P < 0.05$) and SWS2 ($P < 0.01$) on day 1 compared to those showing quick submission and passivity, an effect more robust after 14 and 21 days. Also, SDF rats showed longer latency to leave the start-box, spent less time in the arena and failed to show habituation to a 95 dB stimuli in the acoustic startle test ($P < 0.01$, all).

Conclusion: SD *per se* did not affect sleep architecture, anxiety-like behaviour, acoustic startle response, or corticosterone response. Sleep-EEG and other behavioural traits for 'active or proactive coping' prior to and after a social conflict may be important in studies of SD to include an evaluation of subgroups based on how the rats actually behave in the confrontation with the resident.

P625

Short-term memory and plasticity are impaired in mice lacking melanin concentrating hormone neurons

L. LE BARILLIER, L. LÉGER, P. FORT, P.-H. LUPPI, G. MALLERET and P.-A. SALIN
UCBL, Lyon, FR

Objectives: Although it is well known that paradoxical sleep (PS) facilitates memory, the underlying cellular mechanisms are still unknown. Previous works demonstrated that PS deprivation modulates synaptic plasticity in the hippocampus, a structure which plays a key role in learning. Since it has been recently shown that Melanin Concentrating Hormone (MCH) neurons are selectively activated during PS, we hypothesize that MCH could be a molecular effector of PS-dependant memory function. The aim of this work was to determine whether MCH neurons are required for hippocampal synaptic plasticity and hippocampus dependent forms of memory by combining behavioral experiments and electrophysiological recordings in mice genetically lacking MCH neurons (MCH/ataxin3 mice). The characteristic of these mice is that MCH neurons are present during development and absent at adult age (three months).

Methods: We characterized synaptic plasticity at the Schaffer collaterals to CA1 pyramidal cells synapses (SC-CA1) in brain slices from MCH/ataxin3 mice ($n = 8$) and their matched controls ($n = 7$).

We performed protocols of long-term and short-term synaptic plasticity at SC-CA1 synapses. We also carried out two hippocampal dependent memory tasks (15 MCH/ataxin3 mice and 15 controls). Mice were first tested in a Morris water maze (MWM) to assess long-term memory and then tested in an open field to examine habituation and short-term memory.

Results: We found that the early phase of long-term potentiation at SC-CA1 synapses was impaired in MCH/ataxin3 mice. This suggests that short term synaptic plasticity was altered as this deficit was due to a blockade of post-tetanic potentiation. MCH/ataxin3 mice were also slower to learn the MWM task as compared to the controls, and presented a habituation deficit during the Open Field task. These behavioral results suggest an alteration of short term memory in MCH/ataxin3 mice.

Conclusion: Our results suggest that PS-dependant activation of MCH neuron enhances short term memory and short term plasticity in the hippocampus. Thus, MCH released during PS could induce a reset of hippocampal synapses which might facilitate short term memory after sleep.

P626

Tolerance or sensitisation to the impairing effects of total sleep deprivation in mice

K. ZANIN, C. PATTI, L. FERNANDES-SANTOS, L. OLIVEIRA, F. TALHATI, S. TUFIK, D. POYARES and R. FRUSSA-FILHO
Universidade Federal de São Paulo, São Paulo, BR

Objectives: Although the consequences of paradoxical sleep deprivation have been studied for many years, the effects of total sleep deprivation (TSD) on cognition remained overlooked. Recently, we demonstrated that acute TSD for 6 h induced performance impairments in mice subjected to the plus-maze discriminative avoidance task (PM-DAT). The aim of this study was to investigate whether 3 h of acute or repeated TSD (3 h or 6 h) for 10 days could induce memory impairments in mice subjected to the PM-DAT.

Methods: Three-month-old Swiss male mice were kept in home cage (CTRL – control condition) or subjected to TSD by the gentle handling method. In the 1st experiment, animals were acutely sleep-deprived for 3 h (TSD3h) or 6 h (TSD6h). The same regimen of TSD was applied for 10 consecutive days in the 2nd experiment. In both experiments, at the ending of TSD period, animals were trained in the PM-DAT. In all experiments, a 10-min training session on the PM-DAT was performed and 10 days after, animals were subjected to a 3-min test session.

Results: During the training of the 1st experiment, animals displayed no difference in the percent time spent in the aversive enclosed arm, showing learning of the task. TSD for 3 h induced anxiolytic and hyperlocomotor effects, which were tolerated by the 6 h of TSD. In the test session, the TSD6h group presented amnesia, corroborating our previous study. Opposite, acute TSD for 3 h did not induce memory impairments. In the training of the 2nd experiment, the repeated TSD for 3 h – but not for 6 h – induced higher exploration of the aversive enclosed arm, suggesting learning impairment. No alterations on anxiety-like behavior or locomotion were observed. In the test session, TSD3h group showed amnesia, which was tolerated by the repeated TSD for 6 h.

Conclusion: TSD-induced memory deficits are critically influenced by duration and frequency of the sleep deprivation. In this vein, the memory deficits induced by acute TSD for 6 h can be tolerated when the sleep deprivation was repeated for 10 consecutive days. Conversely, for the 3 h-TSD period, the acute memory impairing effects seem to be sensitized when the procedure was repeated for 10 days. Collectively, these data suggest that the amount of sleep loss is an important factor affecting performance.

Financial Support: FAPESP, AFIP, CNPq, CAPES.

P627

Short modulation of REM sleep quantity bidirectionally regulates hippocampal synaptic plasticity and memory

A. M. HAMIEH, P. RAVASSARD, N. FRAIZE, L. LE BARILLIER, P.-H. LUPPI, M. TOURET, G. MALLERET and P.-A. SALIN
Centre de recherche en neurosciences de Lyon, Lyon, FR

Study Objectives: Growing evidence supports that rapid eye movement sleep (REMS) plays a crucial role in memory. Previous studies have shown that long-term REM sleep deprivation (RSD) impairs synaptic plasticity, encoding and memory consolidation in rats. However, long-term RSD induces stress which is known to alter memory. Thus, we performed a mild-non stressful- RSD in order to assess a potential role of REMS in synaptic plasticity and memory. Then, we examined whether this RSD or REMS rebound (RSR) obtained 4 h after RSD affects CA1 hippocampal synaptic plasticity, encoding and memory consolidation of contextual fear conditioning (CFC).

Methods: RSD was induced using a dedicated protocol to induce short (4 h) and selective deprivation in order to avoid any stress. RSD was carried out before and after CFC encoding. Animals were examined 1 h later to test the effect on encoding or 24 h later to test the effect on consolidation.

Results: The results demonstrated that RSD decreases synaptic LTP selectively in dorsal CA1 and RSR rescues these deficits. RSD performed immediately following encoding impaired consolidation of CFC at test. In contrast, animals subjected to RSR before encoding showed an increase in the amount of freezing response during training. Moreover, increase in REMS quantity (RSR) after encoding facilitated consolidation of CFC at test. Our results suggest that an increase in the amount of REMS facilitates LTP, memory consolidation and encoding, while a decrease in REMS impairs LTP and memory consolidation.

Conclusion: These results suggest that REMS quantity may regulate synaptic plasticity, encoding and consolidation of memory in a bidirectional way.

P628

Total sleep deprivation impairs spatial memory consolidation in rats after one-day learning in the Morris water maze test

V. DOROKHOV, R. G. KOZHEDUB, G. N. ARSENYEV, O. I. BUKHGOLTS and V. KOVALZON
Russian Academy of Sciences, Moscow, RU

Objectives: There is now substantial evidence for the involvement of sleep in memory processing. Loss of sleep may result in memory impairment. Escape from water is relatively independent from physical activity or body mass differences, making it ideal for many experimental models. Role of posttraining sleep in memory in a Morris water test was typically studied after training for 3 days to 2 weeks. Less attention was paid to the effects of sleep deprivation on memory consolidation after one day learning. Our previous studies [Dorokhov et al., 2011; Kozhedub et al., in press] have indicated that 24-h sleep deprivation produce memory impairment which had depended on duration and presentation structure of trials during learning. The aim of the present study was to determine the

effects of total sleep deprivation on spatial memory after 1 day learning in accordance to Feldman et al. (2010) protocol.

Methods: The effect of 24-h total sleep deprivation using stressless 'carousel' method [Lan et al., 2001] on spatial memory consolidation was studied in rats. Rats were trained in a Morris water maze to find a hidden platform (a spatial task) after 24 h total sleep deprivation or spontaneous sleep. Spatial learning was assessed across repeated trials and reference memory was determined by preference for the platform area when the platform was absent. Experimental design included 15 trials to find the hidden platform using pseudo-random set of start locations. Trials 1–5, 7, 9, 11, 13, 15 were carried out with platform marked with flag. Trials 6, 8, 10, 12, 14 were carried out with the hidden platform.

Results: A tests trial given 24 h after training confirmed that long-term memory was generated. We found that 24-h sleep deprivation a violation of the consolidation of spatial memory. Statistically significant difference in the number of crossings of platform area between sleep deprived and control rats was found. Sleep deprivation decreased this parameter and increased dispersion of first platform area crossing latency period. There was no statistically significant difference in the average speed between these groups.

Conclusions: These results support a specific role for sleep in spatial learning after one day learning in the Morris water maze.

Poster Session – Diagnosis Methods

P629

Can the Sommeil Vigilance et Santé questionnaire be used to identify psychosocial risks? Validation based on a representative sample of 720 employees

A. DUBOIS[1], F. DUFOREZ[1], S. CAUVIN[2], S. SAMEUR[2] and D. LÉGER[3]

[1]European Sleep Center, Paris, FR, [2]REUNICA, Paris, FR, [3]Hôtel-Dieu, Paris, FR

Objectives: Psychosocial risks reflect the problems that employees have adapting to the rapidly changing organisation and management of companies in a difficult economic climate, and as such they have become a major concern.

Methods: In order to assess psychosocial risks, we used a simple survey-type questionnaire on sleep and alertness (SVS), set up by health insurer Reunica's sleep-alertness-health programme. The SVS (a questionnaire of 31 questions) was completed at the same time as the KARASEK occupational stress assessment and the HAD anxiety and depression evaluation, by 720 active adults aged over 18 and working in companies of over ten employees. The survey was carried out by TNS-SOFRES and the statistics compared the dimensions of the SVS to those of reference questionnaires.

Results: 1. The Total SVS score was very low among employees who scored high for work-related stress on the KARASEK.

2. The Total SVS score identified subjects suffering from anxiety (HAD anxiety > 12) and depression (HAD depression > 8), since the Total score, Sleep Quality score (S1) and Alertness score (S2) were significantly lower among anxious and depressed subjects than in the group overall.

3. A Total SVS score below 70 seems to be a significant indicator of anxiety, depression and stress.

Conclusion: For easier identification of psychosocial risks among working people, a sleep survey such as the SVS seems more appropriate to us than the use of stress or anxiety scales that employees find difficult to respond to out of context.

P630

Can the senior Sommeil Vigilance et Santé (SVS) questionnaire be used to identify marginalisation and memory disorders suggesting dependency? Validation based on a representative sample of 700 people aged over 50

A. DUBOIS[1], F. DUFOREZ[1], S. CAUVIN[2], S. SAMEUR[2] and D. LÉGER[3]

[1]European Sleep Center, Paris, FR, [2]REUNICA, Paris, FR, [3]Hôtel-Dieu, Paris, FR

Objectives: The risk of elderly people becoming dependent has become a priority focus of public health. Memory and marginalisation tests are hard to fill in. Given the links between sleep-alertness, cognition and marginalisation, we assessed dependency using the Reunica senior SVS, a questionnaire that was both easy to complete and comparable from one period to another.

Method: The senior SVS (a questionnaire of 28 questions) was completed at the same time as the MacNair memory test, the EPICES marginalisation assessment and the HAD anxiety and depression evaluation by 700 adults aged over 50 and representative of their age group in France. The survey was carried out by TNS-SOFRES and the statistics compared the dimensions of the SVS to those of reference questionnaires.

Results: 1. The Total senior SVS score identified subjects suffering from anxiety (HAD anxiety >12) and depression (HAD depression > 8), since the Home Environment score (S1), the Sleep Quality score (S3), the Alertness score (S2) and Total score were significantly higher among anxious and depressed subjects than in the group overall.

2. The Total SVS score and the three subscores also identified memory problems corresponding to a MacNair score over 15 and marginalisation corresponding to an EPICES score over 40.2.

3. A Total senior SVS score below 50 seems to be a significant indicator of anxiety, depression, memory problems and marginalisation among old people.

Conclusion: For easier identification of the risk of dependency among old people, a sleep survey such as the senior SVS seems more appropriate to us than a battery of memory, anxiety, depression and marginalisation tests that people are often reluctant or unable to complete.

P631

The HSDQ: a new sleep disorders questionnaire based on the ICSD-2

G. A. KERKHOF[1], M. E. H. GEUKE[1], A. BROUWER[1], R. M. RIJSMAN[2], R. J. SCHIMSHEIMER[2] and V. VAN KASTEEL[2]

[1]University of Amsterdam, Amsterdam, NL, [2]MCH Sleep Center, The Hague, NL

Objectives: There is a need for a self-assessment general diagnostic questionnaire for sleep disorders based on the International Classification of Sleep Disorders (ICSD). The primary objectives of this study were: (i) to construct a self-assessment questionnaire for sleep disorders (named Holland Sleep Disorders Questionnaire – HSDQ) based on the ICSD-2, (ii) to evaluate the questionnaire's psychometric properties with respect to a. it's total score, and b. the individual scores for each of the six sleep disorders, and (iii) to develop optimal criteria for identifying the presence of a sleep disorder and, if present, specifying which of the six ICSD-based sleep disorders applied.

Methods: In total, 1269 patients clinically diagnosed with a sleep disorder, and 412 subjects without sleep complaints were enrolled into this study. Principal Components Analysis confirmed that the HSDQ differentially represented the six symptom clusters associated with ICSD-2 classifications.

Results: The HSDQ's total score distinguished patients with a clinically diagnosed sleep disorder from individuals without sleep complaints, with area under the Receiver Operating Curve (P(A), a measure of classification accuracy insensitive to disorder prevalence) of 0.95. The internal reliability coefficient alpha was 0.90 and, applying the Youden criterion as cut-off score, the overall accuracy was 88% (kappa: 0.75). Subsequently, the six diagnostic groups of sleep disordered patients could be differentiated reliably, with P(A) values ranging between 0.65 and 0.95, alpha coefficients ranging between 0.73 and 0.91 and an overall percentage of 82% correctly classified patients (kappa = 0.77), indicating a substantial to excellent agreement between the primary diagnoses and the HSDQ classifications.

Conclusion: The HSDQ is a valid and accurate questionnaire, reliably reflecting the predominant symptoms and diagnostic criteria formulated in the ICSD-2.

P632

The impact of night-to-night variability as a trait on polysomnography

T. UNBEHAUN, B. FEIGE, K. SPIEGELHALDER, C. NISSEN, V. HIRSCHER and D. RIEMANN

University Medical Center Freiburg, Freiburg im Breisgau, DE

Objective: Studying sleep by polysomnography in a sleep laboratory is affected by previous sleep behaviour at home and therefore the preceding sleep-wake behaviour should be controlled. A regular or irregular sleep-wake pattern over a period of time prior to or after a sleep laboratory measurement might be considered a trait, though it can be influenced by transient external events. We analysed sleep diaries of good sleepers in comparison to polysomnography data in order to find out whether sleep-wake regularity has an impact on the outcome of PSG studies.

Methods: Our database for sleep diaries and PSG studies of good sleepers contained 151 subjects under control conditions. To obtain equal age and sex group sizes the sample was reduced to 80 subjects aged 18–24, 25–34, 35–44, 45–65 (10 m, 10f each group) as a normative sample. Partial correlations of RI14 values with sleep variables from the diaries (bedtime, sleep onset time, TST, time in bed (tib), wake-up, rise time, sleep global, bed global) and PSG data (adaptation and baseline nights) were conducted in order to remove the age effect. The RI14 is defined as a regularity measure over a period of 14 days using a hyperbolic tangent function for night-to-night shifts in time.

Outcome: Subjects with a more irregular pattern on RI14-bedtime and -sleep onset seem to fall asleep faster and have a longer SPT (1st night). The more irregular the diary pattern on bedtime, sleep onset, TST, tib, bed global and sleep global, the more leg movements were observed. There was also a positive partial correlation between SWA (% of SPT) and bed global and sleep global, respectively. During the second night there were negative correlations between REM3min latency and RI14-tib as well as the amount of S2 (% of SPT) and RI14-wake-up, -rise, -bed global, and -sleep global. All correlation coefficients were small to medium in size.

Discussion: Including participants with irregular sleep-wake behaviour could have an impact on target outcomes in studies/trials looking at sleep quality. During the first night in the sleep laboratory, these subjects fall asleep faster, possibly due to a higher sleep pressure or a higher flexibility in their sleep-wake behaviour. Insofar, controlling for regularity in sleep-wake behaviour for at least two weeks prior to study begin seems mandatory to exclude this source of variance.

P633

Assessment of polysomnography: first-night effect and night-to-night variability: relationships to diagnosis and intra-individual differences

J. NEWELL[1], O. MAIRESSE[2], P. VERBANCK[1] and D. NEU[1]

[1]Université Libre, Brussels, BE, [2]Royal Military Academy – VIPER research group, Brussels, BE

Objective: While polysomnography remains the current gold standard in sleep investigation, guidelines for single night versus consecutive recordings in a sleep laboratory have been disputed mainly because of two phenomena: the first-night effect and night-to-night variability.

Methods: One hundred and twenty-nine subjects, that underwent two consecutive nights of polysomnographic recording in a general University Hospital's sleep lab, were divided into four groups: (i) sleep-related breathing disorders (SRBD), (ii) insomnia, (iii) movement and behavioral disorders and (iv) a healthy control (HC) group based on their complaints at admission and sleep study results. Sleep parameters of both consecutive two nights were compared and analyzed.

Results: All groups showed a significant first-night effect. However the latter seemed more pronounced in the insomnia group and in HCs. Furthermore, a clinically significant intra-patient night-to-night variability was found for the apnea-hypopnea index in the SRBD-group and for the micro-arousal index in the movement and behavioral disorder group.

Conclusions: Due to the observed first-night effect among any subject group and the potential impact of night-to-night variability, we conclude that the clinical assessment of sleep disorders should be similar in every patient. Hence, the present study underlines the importance of two consecutive nights of polysomnographic recording as a potential reference standard for the execution of sleep investigations.

P634

How much silence is needed? – Influence of active sound isolation on sleep

M. GLOS, C. BARTHE, M. HOELZL, T. PENZEL, A. BLAU, C. GARCIA, D. BUCK and I. FIETZE

Charité University Hospitals, Berlin, DE

Introduction: It is well known that noise pollution during the night is one major environmental factor for a disrupted sleep micro and macro structure. As a consequence affected individuals report about non-restorative sleep and reduced daytime functioning. However, a great inter-individual variability in the vulnerability regarding noise is known. Therefore in our study we investigated whether active sound isolation could alter sleep structure and sleep quality in a population of young healthy individuals.

Methods: Twenty-four (M = 15, F = 9) students (age = 24.9 ± 4.1 years; BMI = 21.9 ± 1.6 kg/m^2) without any kind of sleep disorders slept consecutive single nights on three different locations in random order: (i) at home (HOME), (ii) in a research sleep lab (SLAB), and (iii) in a sound isolated room (ISOL). The sound isolated room was an audio box located in the audiology department of our hospital. During each night a full polysomnography was performed and sleep was scored afterwards according to AASM guidelines. Sound pressure was measured continuously throughout each night by an audio per cent acoustic analyser and the mean moving time-average sound level (LAeq) throughout the night was determined.

Results: Noise was lowest while sleeping in the audio box with a mean LAeq of 33.9 ± 3.8 dB (range 31–46 dB). In comparison to ISOL sleeping at home as well as in the sleep lab was accompanied by increased noise pollution (HOME: 40.6 ± 7.9 dB; range 21–51 dB, $P < 0.004$, SLAB: 39.8 ± 7.2 dB; range 30–56 dB, $P < 0.004$). In ISOL amount of slow wave sleep (35.4 ± 8.4%-TST) was increased in comparison to HOME (31.5 ± 8.4%-TST, $P < 0.02$) as well as to SLAB (27.9 ± 6.9%-TST, $P < 0.0001$). In contrast amount of REM sleep was highest in SLAB (12.5 ± 4.8%-TST) and lower in ISOL (12.5 ± 4.8%-TST, $P < 0.0001$) as well as at HOME (14.0 ± 5.7%-TST, $P < 0.01$). Sleep in ISOL was not different to HOME nor to SLAB in terms of sleep latency, sleep efficiency, and arousal index.

Discussion: By sleeping in a sound isolated room an active noise reduction could be applied to sleep. In the group of individuals investigated this lasts to some changes in the distribution of sleep stages whereas parameters of sleep quality were not affected. It seems that young individuals without any sleep problems still have a high capacity to cope with short-term environmental changes to sleep. Stronger effects might be seen in older people – a task for future research.

P635

Scoring sleep bruxism in absence of audio-video recording: risk of moderate overestimation

M. C. CARRA, N. HUYNH, P. ROMPRÈ and G. LAVIGNE
University of Montreal, Montreal, CA

Objectives: Based on the most recent available polysomnographic (PSG) research diagnostic criteria, sleep bruxism (SB) is diagnosed when more than two events of rhythmic masticatory muscle activity (RMMA)/h of sleep are scored on the electromyography (EMG) of the masseter and/or temporalis muscles. RMMA is characterized by at least 3 rhythmic EMG burst of 0.25–2 s or at least 1 tonic contraction lasting more than 2 s. These criteria have been formulated based on full in lab PSG with audio-video, that remains the gold standard technique. Nowadays, the use of portable PSG systems has been remarkably increased in both clinical and research setting. However, the diagnostic criteria for SB have not yet been validated for ambulatory PSG. The study aimed to examine the validity of SB scoring in absence of audio-video recordings.

Methods: Ten subjects (mean age 24.7 ± 2.2) with a clinical diagnosis of SB spent 1 night in the sleep lab. PSG were performed with an ambulatory system associated with audio-video recordings. All nights were scored by the same examiner three times (in a random order separated by 1 month interval): (i) without video, (ii) with video, (iii) without video; in order to test the intra-night and intra-examiner reliability. RMMA and other muscular activities (OMA) involving the masticatory muscles, which do not meet the RMMA scoring criteria were analyzed. Concordance tests between nights were performed.

Results: The RMMA event-by-event concordance rate between scoring without video and with video was 68.3%. Overall, the RMMA index was overestimated by approximately 20% while scoring without video. However, the intra class correlation coefficient (ICC) between RMMA scoring without video and with video was good (ICC = 0.91; $P < 0.001$). The intra-examiner reliability was good (ICC = 0.97; $P < 0.001$). The ICC between OMA scoring without video and with video was low (ICC = 0.18; $P = 0.1$). The clinical diagnosis of SB was confirmed in 9/10 subjects.

Conclusion: The audio-video recordings enable distinguishing between actual RMMA from other muscular activities involving the masticatory muscles during sleep (e.g., swallowing). Scoring RMMA in absence of audio-video recording is associated with a moderate over-scoring due to a lack of specificity in the EMG signals. This should be considered when using portable system to study SB.

P636

A telemedicine solution based on a piezoelectric movement sensor for the long-term monitoring of sleep disorder patients

J. PAALASMAA[1] and M. PARTINEN[2]
[1]Beddit.com Ltd, Espoo, FI, [2]Vitalmed Research Center, Helsinki, FI

Objectives: Actigraphy is commonly used in the screening of sleep disorders and gives useful information in the diagnosis and follow-up of patients with insomnia. The objective was to develop alternatives to actigraphy for long-term monitoring of sleep disorder patients. We set out to create a movement sensor based telemedicine solution to meet the following requirements: (i) the system must allow follow-up of sleep continuously for weeks and months, (ii) the measurement should happen automatically without attached sensors and without causing discomfort, (iii) compared to actigraphy, sleep staging should be more precise.

Methods: The vibrations caused by the heart, respiration and movements are measured with a flexible piezoelectric sensor. The sensor measures 70 by 4 cm, is 0.4 mm thick and is placed under the mattress topper (or mattress). Respiratory and heart rate variation as well as actigraphic data is measured from the vibration signal. Sleep/wake classification is done based on these parameters. The sleeping environment is measured with ambient noise, temperature and luminosity sensors. Sleep reports are given so that sleep patterns can be evaluated up to three months at a time. A report consists of 24-h or 7-day 'hypnograms' with stages 'not in bed', 'awake' and 'asleep', as well as sleeping environment measurements. Respiration waveforms from the vibration signal are automatically analyzed for potential apnea events. The raw data can be used for a preliminary analysis of sleep-related breathing disorders (SRBD).

Results: The system has been used for measuring patients for one to six months. The severity of the sleep disorder is evaluated based on the sleep/wake classification and the preliminary SRDB analysis. The long measurement period has been particularly suitable for diagnosing problematic hypersomnias. In one case, visualizing the circadian information three months at a time helped clarify the cause of hypersomnia, which was related to the weekly rhythm.

Conclusions: The presented sleep measurement method gives more information than actigraphy without causing discomfort to the patient. The drawback compared to actigraphy is that daytime activity is not measured. We believe that the method can be used in addition to actigraphy especially in the diagnosis of problematic (periodic) hypersomnias and in preliminary evaluation of SRBD. The telemedicine aspect of the method is beneficial, as the data can be monitored continuously via the Internet.

Research was supported by Beddit.com Ltd

P637

Validation of two new activity monitors: motionwatch 8 and pro-diary motion

P. L. MORGAN, S. HAMPTON, A. KARATZIOTOU, J. ZASLONA and B. MIDDLETON
University of Surrey, Guildford, UK

Objectives: The aim of the study was to validate the Motionwatch 8 (MW8) and PRODiaryMotion (P-DM) (CamNtech Ltd) for activity derived sleep parameters with the Actiwatch 4 (AW4). Participants' activity derived sleep parameters throughout the study are presented here with the hypothesis that no differences will be found between

the sleep parameters measured between the three types of activity monitors.

Methods: The 2-week field trial was initiated at the University of Surrey and was carried out early this year. Participants (n = 25, 10 males 15 females; 33 ± 12 years mean ± SD) completed a paper sleep diary and wore continuously, either a P-DM or MW8 alongside an AW4 on their non-dominant wrist. Half of each group wore the new devices nearest the hand and the other half visa versa. Actigraphically derived sleep parameters were determined using Actiwatch sleep analysis 7.43 software. Differences in the four sleep parameters (sleep fragmentation, sleep efficiency, sleep percentage, total sleep activity) between the MW8, P-DM and AW4 were compared using a two way mixed ANOVA followed by a *post hoc* Bonferroni multiple comparison test.

Results: In the group that wore the MW8 and AW4, there were no significant differences (Mean ± SD) in the fragmentation index (MW8 35 ± 27, AW4 36 ± 18), sleep efficiency (MW8 80 ± 13, AW4 77 ± 9), sleep percentage (MW8 86 ± 14, AW4 84 ± 9) or total activity scores (MW8 9599 ± 16072, AW4 11793 ± 10334). There were also no significant differences between the P-DM and AW4 for the parameters of fragmentation index (P-DM 31 ± 13, AW4 37 ± 18), sleep efficiency (P-DM 82 ± 8, AW4 79 ± 9), sleep percentage (P-DM 90 ± 5, AW4 86 ± 7) and total activity scores (P-DM 7014 ± 8486, AW4 10206 ± 9942).

Conclusions: The findings indicate that in all four activity derived sleep parameters, there were no difference between the AW4 and the new MW8 and P-DM. This is a preliminary analysis and more participants are in the process of completing the study and a full analysis of the data will then be carried out.

Supported by CamNtech Ltd, Cambridge

P638

Validation of a new actigraph motion watch versus polysomnography on 70 healthy and suspected sleep-disordered subjects

M. ELBAZ[1], K. YAUY[1], A. METLAINE[1], M. MARTONI[2] and D. LÉGER[1]

[1]Sorbonne Paris Cité, Paris, FR, [2]University of Bologna, Bologna, IT

Study objectives: Comparison of sleep parameters values (Total Sleep Time-TST, Sleep Latency-SL, Sleep efficiency-SE, Wake after sleep onset-WASO) obtained by all-night polysomnography (PSG) and actigraphy (ACT) MotionWatch (MW8, CamNtech Ltd) and subjective questionnaires.

Background: Actigraphy is commonly used to assist sleep specialists in the diagnosis of sleep disorders. This new actigraph is a MotionWatch including new digital accelerometer is lower power and allows tri-axial recording. The MotionWatch is small, light-weight, waterproof device and direct USB connected.

Patients: Clinical 50 consecutive adults with suspected sleep disorders (30 women, 20 men, mean age of 50 ± 2 years) and 20 consecutive healthy control subjects (10 men, 10 women, mean age of 35 ± 2 years).

Measurements and Results: For now only 14 sleep-disordered patients were analyzed by two scorers working independently. Sensitivity, specificity, and accuracy measures were obtained from epoch-by-epoch comparison of PSG and ACT data. Objective and subjective sleep parameters data were derived from PSG, ACT and questionnaires given to subjects in the morning following their recording night. In this preliminary results, according to the Bland and Altman method and Pearson correlation, there is no significative differences between ACT Low threshold-TST and PSG-TST ($r = 0.63$, $P < 0.02$); as the same for the ACT Low threshold-SE versus PSG-SE ($r = 0.56$, $P < 0.04$).

Study sponsored by CamNtech, Cambridge, UK

P639

Limitations on the clinical use of wrist actigraphy for evaluating insomnia

M. MARTONI[1], D. LÉGER[2], A. ERBACCI[1], V. BAYON[2], M. ELBAZ[2] and V. NATALE[1]

[1]University of Bologna, Bologna, IT, [2]Université Paris Descartes, Paris, FR

Objectives: The lack of standard solutions regarding accelerometer and algorithm employed to evaluate sleep using actigraph represents a limit for the clinical use of actigraphy. The current study aimed to compare quantitative actigraphic criteria (QAC) to evaluate insomnia of two different actigraph brands.

Methods: Performing a retrospective study we recovered 215 actigraphic (Actiwatch AW64, Cambridge Neurotechnology) records belonging to insomnia patients (n = 107) and to normal sleepers (n = 108). We compared the two samples analyzing the following actigraphic sleep parameters: time in bed (TIB), sleep onset latency (SOL), total sleep time (TST), wake after sleep onset (WASO), sleep efficiency (SE), number of awakenings (NWAK), terminal wakefulness (TWAK), fragmentation index (FI) and mean motor activity (MA). Moreover, we also consider two actigraphic circadian indexes: interdaily stability (IS) and intradaily variability (IV). Using Youden index we calculated the best performing QAC for each actigraphic sleep parameter. Finally, we performed Receiver Operator Characteristic (ROC) curves for testing the accuracy of QAC.

Results: Together with a previous research employing Basic Ambulatory Monitoring Motionlogger, SOL, MA, FI, NWAK, WASO and SE significantly differentiated insomnia patients from normal sleepers. However QAC obtained in the present study were significantly different compared to QAC obtained in the previous study.

Conclusion: The results confirmed actigraphy as a satisfactory tool for assessing sleep quality in insomnia patients objectively. As for QAC, we recommend companies to achieve an agreement about a standard solution concerning hardware and software actigraphic features.

P640

Activity-based accelerometry for identification of infant sleep-wake states: trial of a new algorithm and investigation of performance and accuracy

B. GALLAND[1], G. KENNEDY[1], E. MITCHELL[2] and B. TAYLOR[1]

[1]University of Otago, Dunedin, NZ, [2]University of Auckland, Dunedin, NZ

Objective: To determine the accuracy of the Actical accelerometer, a device normally used to measure physical activity, to distinguish sleep from wake states. We sought the best performing algorithm and sampling epoch from algorithms commonly used with wrist devices, and from a new algorithm developed for this study.

Methods: Thirty-one infants aged 10–22 weeks wore the accelerometer on the shin for a nap fragmentation study recorded in tandem with PSG. Sleep-wake epochs were identified using the zero-count threshold, Sadeh and Cole algorithms, and our new algorithm (Count-scaled) performed using count-scaled data. Each epoch in a trial (entire recording period of each participant) is scaled relative to the mean value of all trial epochs that have non-zero counts. i.e. an

epoch with an original count of 30 would be scaled to 1; if the mean value of all non-zero epochs was 30, an original value of 15 would be scaled to 0.5, 60 would be scaled to 2 etc. This makes the algorithm able to cope with different devices with different count thresholds, or placements etc with different sensitivities. Accuracy was examined in direct epoch comparison with PSG in 15, 30 and 60-s epochs.

Results: Overall agreements (accuracy) for sleep-wake states were above 80% for all computations. The Count-scaled algorithm sampling 15-s epochs gave the highest accuracy with sensitivity (sleep agreement) at 85.7%, and specificity (wake agreement) at 84.7%. Other computations yielded higher sensitivity at the expense of specificity. Another way to assess accuracy was to compare sleep parameter outputs. All computations and sampling epochs significantly correlated with total sleep time sleep (r = 0.76–0.88), sleep latency (r = 0.70–0.93), sleep efficiency (r = 0.76–0.87), and the duration of waking (r = 0.41–0.53). The number of wakings after sleep onset was overestimated by accelerometry.

Conclusions: This is a first step in identifying the utility of the activity-based accelerometer for infant sleep with implications for wider application of the algorithm for use with other devices. The count-scaled algorithm showed some advantage over existing algorithms in respect of balancing sleep and wake agreement. Further development or adjustment is needed for waking after sleep onset. The ability to use this one device for activity and sleep has many advantages for epidemiological and clinical research, and the algorithm could be used for Actical archival dataset analysis.

P641

Are you just a snorer or apnoeic? A new tool for detecting moderate or severe apnoea

G. CHAUMET[1], T. COLLEONY[2], A. COURSON[2] and O. COSTE[2]
[1]Université de la Méditerranée, Marseille, FR, [2]HIA Desgenettes, Lyon, FR

Introduction: Obstructive sleep apnea syndrome (OSAS) is highly associated to other syndromes: hypertension, T2 diabetes, and low tension glaucoma with negative interactions. It would be therefore crucial for non-sleep practitioners to identify patients with severe OSAS faster and accurately. Any appropriate diagnosis help could be interesting and the RU SLEEPING (PHILIPS) is one of the potential candidates.

Methods: One hundred and fifty patients (54 women; Age: 56.5 ± 15.4 years) were recruited from endocrinology and general medicine (ambulatory) services. Our sample was divided in two groups ($n = 75$) according to STARD guidelines: a development group and validation group. All patients underwent a polysomnography (PSG) and were equipped during a different night with RU SLEEPING device. This system gives us mean Respiratory Event Index (m-REI) the main criterion and maximum per hour Respiratory Event Index (max h-REI) the second criterion. These criteria were compared to the gold standard, i.e. the Apnea-Hypopnea Index (AHI) determined by PSG using a linear correlation method. The detection performances of the RU SLEEPING against OSAS (AHI ≥ 10) and severe form of OSAS (AHI ≥ 30) were then studied thanks receiver operating characteristic (ROC) curves. Area under curve (AUC) was calculated from ROC curve. Best kappa method for the determination of best cut-off values in the development group was computed. Contingency tables were built for the validation group. Sensitivity (Se) and specificity (Sp) were finally calculated from these tables.

Results: Patients have AHI = 32 ± 22.5, m-REI = 18.7 ± 13.6 and max h-RE = 37.4 ± 21.8. We found a strong association between AHI and m-REI [r = 0.67 (0.57;0.75), $P < 0.001$] and max h-REI [r = 0.68 (0.58;0.76), $P < 0.001$]. According to kappa criterion, best cutoff on the development group data for m-REI with AHI ≥ 10 is m-REI ≥ 7 and with AHI ≥ 30 is m-REI ≥ 19. Best cut-off for max h-REI with AHI ≥ 10 is max h-REI ≥ 24 and with AHI ≥ 30 is max h-REI ≥ 32. Now we use RU sleeping outputs against AHI on validation group and we found:

1. AHI ≥ 10 versus m-REI ≥ 7 (Se = 95.5%, Sp = 58.8%, AUC = 0.81)
2. AHI ≥ 30 versus m-REI ≥ 19 (Se = 75.5%, Sp = 76.8%, AUC = 0.76)
3. AHI ≥ 10 versus max h-REI ≥ 24 (Se = 98%, Sp = 52%, AUC = 0.75)
4. AHI ≥ 30 versus max h-REI ≥ 32 (Se = 71.4%, Sp = 85%, AUC = 0.78)

Conclusion: Results show that best detection was obtained for severe apnea, particularly with the second criterion. Therefore, this device seems to be useful to send patients with supposed severe OSAS to sleep specialist more quickly.

Thanks to Philips-Respironics for technical support

P642

Mandibular movement automated analysis in a screening monitoring device: gender effect

G. MAURY[1], L. CAMBRON[2], J. JAMART[1], E. MARCHAND[1], F. SENNY[3] and R. POIRRIER[2]
[1]CHU Mont Godinne, Yvoir, BE, [2]Neurology B 35 CHU Sart Tilman, Liège, BE, [3]Electronic department B 28 Sart Tilman, Liège, BE

We aimed at assessing the influence of gender on the accuracy of a novel portable screening device. We prospectively compared in-laboratory polysomnography (PSG) to simultaneous recording with a portable device in 570 patients referred for diagnostic PSG. The portable device included three signals: oxymetry (SpO2), nasal airflow (NAF) and mandible movement (MM). The three signals were automatically analysed and the method called mandible respiratory disorder index (MRDI). To argue on the added value of MM study, another automatic method, called RDI, was applied such that only SpO_2 and NAF were analysed. In order to avoid divergences of sensors, NAF and SpO_2 signals were common. The number of respiratory events (apneas and hypopneas) per hour was calculated using as denominator the time between lights out and lights on (called the total dark time (TDT) for RDI and MRDI and the total sleep time (TST) for PSG, providing an apnea hypopnea index (AHI) for PSG. The population studied was divided in two groups according to gender (male: 382; age: 50 ± 13; BMI: 30 ± 6 kg/m^2) and (female: 188; age: 49 ± 13; BMI: 27 ± 6 kg/m^2). Male had a higher mean AHI (29 ± 24) compared to female (16 ± 19) ($P < 0.001$). More male had severe AHI ≥ 30/h ($n = 145$; 38%) than female ($n = 24$; 13%) ($P < 0.001$). Male had a higher mean MRDI 23 ± 19 compared to female MRDI 12 ± 14 ($P < 0.001$). TST and TDT were respectively 416 ± 94 and 549 ± 87 min in male and 426 ± 107 and 563 ± 94 min in female. Correlations between PSG and MRDI were excellent both in male (r: 0.95) and female group (r: 0.94) and better ($P < 0.001$ between correlations for both genders) than RDI with respectively r: 0.93 and r: 0.91. For MRDI, mean difference was significantly smaller ($P < 0.001$) in female than in male with respectively 3.4 ± 7.4 and 6 ± 8. Compared to MRDI, mean difference RDI was significantly higher ($P < 0.001$) (8 ± 9 in female and 11 ± 9 in male). In severe patients, sensitivity and specificity improved by

adding MM study reaching 68 and 99.6% in male and 71 and 99% in female.

Conclusion: 1. In the field of apneas and hypopneas screening devices, data concerning women are often scarce.

2. In our cohort, MRDI correlations were excellent in both genders despite a lower severity index in female group.

3. The addition of MM automated analysis to NAF and oxymetry significantly improves the accuracy for the detection of respiratory events with similar sensitivity and specificity in male and female patients.

P643

Oxyholter – good screening tool in high-risk OSA patients

M. TOMASZEWSKA-KIECANA, M. ROSTEK, J. RAWDANOWICZ, I. ZALESKA-ZYDLEWSKA, M. GALECKA-NOWAK and M. DLUZNIEWSKI

Medical University of Warsaw, Warsaw, PL

Background: Obstructive sleep apnea is a common problem in about 2–4% of all population. The Golden standard in diagnosing OSA is polisomnography. The method is very expensive and rarely available. The aim of this study was to assess the predictive role of an oxyholter in high risk OSA patients.

Patients and Methods: We had 56 participating patients who exhibited high risk of OSA (history of heavy snoring, overweight – BMI ≥ 28, neck circumference >44 cm), mean age 54.26 years, 88.6% men. Concurrently all patients were also monitored using the scale of sleepiness Epworth (>15 points). We performed an oxyholter registration. Mean AHI was 20.32, (SD 13.79, mediana 17.65). OSA defined as AHI >5 was diagnosed in 92.85% of patients AHI >15 was diagnosed in 30 cases 53.57%. We decided to perform a polygraphy in this group to compare the oxyholter results using the recommended method for OSA diagnosis. The mean AHI using polygraphy was 25.44, estimated AHI >15 was 57.14%. Downfalls in saturation seems to correlated with bradyarrhythmias throughout the night hours and tachyarrhythmias during the early morning hours but there was no statistical significance.

Results: AHI obtained using the oxyholter correlated with AHI obtained using polygraphy ($R = 0.9225$ $P < 0.0001$). The oxyholter seems to be a good affordable screening tool of OSA for patients in the high risk group.

Conclusion: We concluded that the oxyholter is an effective and not expensive screening tool in high risk OSA patients.

P644

Pulse propagation time assessed by overnight pulse oximetry is associated with daytime blood pressure in patients with sleep apnoea

L. GROTE, D. SOMMERMEYER, D. ZOU, D. N. EDER, J. FICKER, W. RANDERATH, I. FIETZE, B. SANNER and J. HEDNER on behalf of the ASIC study group

Introduction: The state of sleep is characterized by reduced sensory input and relative unloading of the autonomic nervous system. Therefore, sleep may represent an opportunity to investigate the properties of the cardiovascular (CV) system in a unique manner. In fact, several sleep associated conditions have been established as risk factors for CV disease. The current study investigated the association between pulse propagation time (PPT) as an indirect measure of vascular stiffness during sleep and daytime blood pressure.

Methods: The digital pulse wave, assessed by a novel finger oximetry probe, was recorded through the entire sleep period in 495 subjects (169 females, age 54 ± 12 years, BMI 30 ± 6 kg/m^2, AHI19 ± 23 n/h) suspected for sleep disordered breathing and referred to five sleep centers in Germany and Sweden. Daytime blood pressure and established cardiovascular risk factors were carefully assessed. PPT was calculated as the time between the top and the subsequent dichotic notch of the digital pulse wave. Mean PPT across the entire sleep period was calculated. Univariate and multivariate statistical analyses were performed to determine factors associated with PPT.

Results: PPT was significantly and linearly associated with age, systolic and diastolic blood pressure, as well as the number of apneic and hypoxic events during sleep (r = -0.54, -0.19, -0.21, -0.13, and -0.11, respectively, all $P < 0.01$). Additionally, PPT was reduced in patients with systemic hypertension (160 ± 34 ms versus 178 ± 47 ms, $P < 0.001$). In multivariate analysis, PPT was independently associated with age, height, waist, and modifiable CV risk factors including smoking, hypertension, and diabetes mellitus. After control for anthropometrics and comorbidities sleep apnea indices were no longer independently associated with PPT.

Conclusions: PPT determined by overnight oximetry reflects daytime blood pressure and presence of hypertension. This type of assessment during sleep may be a useful tool for classification of overall CV function and risk.

The study was supported by Weinmann GMBH, the Swedish Heart and Lung Foundation and the University of Gothenburg.

P645

Pulse wave photo-plethysmogram analysis, calculation and distribution of a reactivity index over 1837 polysomnographics recordings

D. CUGY

CHU, Bordeaux, FR

Pulse Wave photoplethysmography uses light absorbance technology to detect waves produced by heart pulsation. This technique associated with absoprtion spectrophotometry is at origin of SpO2 measure. Photoplethysmogram is frequently a part of signals recorded during polysomnography. For Brosh and al this signal can be considered as good indicator of coronary pathology. For Kirichenko and al normalization of the pulse photoplethysmogram amplitude can be used as indicator of anti-hypertensive efficiency. Clinical observation allows easy individualization of the photoplethysmography signal amplitude in touch with events arising during sleep. We attempted to develop an algorithm to analyse amplitude variations of pulse photoplethysmogram, we apply it to the database of our polysomnography recordings dantabase and analyse distribution according to sleep parameters parameters and subjective scales (Epworth, ADA PICHOT, Q2DA Pichot).

Material and Methods: Amplitude variations of the photopléthysmogram are calculated from a baseline elabored on slippery average of signal amplitude and filtered. Amplitude variations superior to 50% of basic line are deducted and associated with the current period. This allow to calculate an index of reactivity of pulse wave (Pulse Wave Reactivity:PWR). This algorithm was applied to our database of 1837 polysomnography recordings made between 2002 and 2011. Results were visually validated.

Results: Average of PWR index reported to the total sleep time is 53/h ± 29/h. There are significant differences of index reported to sleep stage (SS: 54/h ± 33/h, SW: 44/h ± 32/h, REM: 67/h ± 35/h;

$P < 0.001$), sex ($P < 0.001$), age ($P < 0.001$). There is significant correlations ($P < 0.05$) between the index and Epworth Sleepiness Score (ESS), Pichot asthenia scale (ADA) and Pichot depression scale (Q2DA).

Conclusion: Because of relations between Pulse Wave Eeactivity and others sleep elements it seems necessary to introduce this new parameter in polygraphy and polysomnography analysis.

An analysis of the reference distribution in normal population must be made.

P646

Mandatory assessment of structured peer reviewed of process quality in sleep laboratories in Germany: a 2-year experience

A. RODENBECK, A. BLAU and L. UTTE on behalf of the Task Force for Quality Control and the Board of the German Sleep Society

The 'Task Force for Quality Control' of the German Sleep Society (DGSM) established an external structured peer-review quality rating program ten years ago, which has become mandatory for DGSM accredited sleep labs. Data on predictive parameters for overall outcome quality are still missing as well as data on the impact of different manners of choosing case reports for reviewing. All labs provided three case reports based on a forgone diagnostic stay. One half of the labs has been requested to send consecutive reports based on a retrospective cut-off day in 2009, the other half has have sampled cases over 14 days and reports were chosen out of this list by lot in 2010. The ratings for each lab were done by three different reviewers out of 30 highly experienced sleep specialists. The requested details for the night protocol and sleep parameters, and criteria for assessing quality through graded levels on anamnesis, diagnostical and therapeutical procedures, comorbitities, and physicians report were announced previously. Global quality was assessed on a visual analogue scale. Reviewers may give comments to be forwarded to the labs and request an audit in cases of serious concerns. An audit was scheduled, when it was requested by at least 2 of 3 reviewers.

In the cut-off round 149 sleep labs with 446 cases participated, in the lot round 128 labs with 382 cases. Although in the latter round items on anamnesis, diagnostical and therapeutical procedures, as well as sleep parameters were rated more often as fully done, neither global quality nor the percentage of labs with a subsequent audit (9 versus 8%) differed between the two ways of selecting case reports. Case reports with a requested audit showed significantly more often missing or inadequate data in nearly all items. Due to the increased number of completely fulfilled items in 2010 no predictive parameters could be stated over all cases, but comorbidities, coherence of diagnosis and therapy, and the summarised assessments of sleep parameters seem to be crucial points. Mandatory assessment of process quality by a structured peer-reviewed program revealed sufficient to high quality in most of the tested German sleep labs independent of the way of selecting case reports. The increased number of fulfilled items in 2010 clearly indicates the improving impact of publishing the general outcomes of the peer-review assessment to all sleep laboratories.

P647

Novel thermovascular changes in restless legs syndrome using thermal imaging and laser Doppler flowmetry

C. DIMARIA, J. ALLEN and K. N. ANDERSON

Newcastle upon Tyne Hospitals, Newcastle upon Tyne, UK

Objectives: Many patients with Restless Leg Syndrome (RLS) complain of burning sensations in their feet associated with the desire to move, such that they seek a cooler environment. This study aimed to characterise the microvascular skin changes in patients with RLS compared to age and sex matched controls.

Methods: Twelve patients with moderate or severe RLS and 12 age- and sex-matched controls (53.3 ± 14.5 years versus 51.7 ± 14.6 years; 4M:8F) underwent detailed thermovascular assessment in a controlled temperature room at three different settings (normothermic phase 23°C, hot phase 30°C, cold phase 18°C). Microvascular activity was recorded during all phases by bilateral laser-Doppler flowmetry (LDF) at the great toe sites and also by whole-body thermography. Patient and control measurements were compared by considering both the absolute values at each phase and between-phase changes.

Results: The study protocol was well tolerated by all subjects. Parameters extracted from the LDF measurements were used to model a logistic function by Binary Logistic Regression. This logistic function provided a statistically significant difference between RLS patients and controls ($P < 0.001$), indicating that only a multivariate combination of LDF parameters was able to differentiate the two groups. Clinical performance was optimised with a cut-off value of 0.4 to obtain sensitivity and specificity of 100% and 92%. Visual inspection of whole body thermography image sequences showed increased leg movement in RLS patients compared to controls most marked during the hot phase. Thermography analysis showed a significant difference between foot temperatures in RLS patients compared to controls during the hot phase ($P = 0.011$). RLS patients had more uniform feet temperatures than controls. An optimum linear discrimination provided sensitivity and specificity of 92% and 83%.

Conclusions: This novel study provides evidence for an impaired microvascular circulation in RLS patients in comparison to controls and a potential mechanism for the sensation of burning in the feet. Core body temperature and feet temperature have a clear circadian rhythm so this provides a mechanism whereby RLS patients may be more symptomatic both in warmer temperatures and at sleep onset. The well tolerated protocol also provides an experimental paradigm to test therapeutic interventions for the future.

This research was funded by an unrestricted educational grant from Phillips – Research and Development.

P648

The relationships between the Pittsburgh Sleep Quality Index, Epworth Sleepiness Scale, and health-related quality of life measures in extremely obese patients

M. HOSSEINI ARAGHI, A. CARTWRIGHT, I. NEIRA, S. TAHERI and N. THOMAS

University of Birmingham, Birmingham, UK

Objectives: The prevalence of obesity (body mass index, BMI ≥ 30 kg/m^2) has increased simultaneously with decreasing average sleeping duration. Several risk factors for obesity including alter diet and physical activity have already been identified, but the impact of others such as sleep are increasingly appreciated. The objective of the present study was to examine the associations between sleep (measured through Pittsburgh Sleep Quality Index (PSQI) and

Epworth Sleepiness Scale (ESS) scores) and components of Quality of Life (EuroQol-5D) and the Hospital Anxiety and Depression Scale (HADS) in a population with extreme obesity.

Methods: Two hundred and seventy one consecutively recruited patients with a mean BMI of 47.0 kg/m^2 enrolled in a specialist weight management service from January 2009 to October 2011 were studied. The PSQI, ESS, EQ-5D and HADS were collected from the patients as part of a baseline assessment of their health status. Correlation and regression analyses were used to characterize the relationships between the PSQI, ESS, and EQ-5D and HADS.

Results: Mean PSQI score was 8.24 (5.28), and mean ESS score was 8.84 (5.79). After controlling for covariates, poor sleep quality and excessive daytime sleepiness were found to be a significant predictors of lower health-related quality of life as indicated by lower scores on usual activities, pain/discomfort and anxiety/depression component scores of EQ-5D ($P < 0.05$). Poor sleep quality and daytime sleepiness were also associated with worse HADS scores. Patients with lower sleep quality had 58% higher risk of being in the depressed category (OR = 1.58, 95% CI: 1.20, 2.09).

Conclusion: The results suggest that poor sleep is an important problem in extremely obese patients and is associated with poorer quality of life and depression. Although the direction of these relationships is not clear, attention to sleep hygiene could be beneficial as part of a holistic weight management clinic programme.

P649

Malingering daytime sleepiness – symptom validity of multidimensional sleepiness parameters

M. STIGLOHER, P. GEISLER, G. HAJAK and R. POPP
Sleep Disorders and Research Center, Regensburg, DE

Objectives: Experts' reports on daytime sleepiness become more and more necessary in the context of a person's fitness to drive. Aim of the study was to assess, whether experimentally induced daytime sleepi-ness can be faked and if symptom validity tests (which have been successfully established for other neurological diseases) can detect malingering.

Methods: Twenty-three healthy probands were tested (i) after one night of partial sleep deprivation (PSD; four hours of sleep), (ii) after multiple nights with sufficient sleep (RESTED), (iii) same as (iii) with the instruction to fake sleepiness (FAKE). Sub-jective sleepiness was measured by the Karolinska Sleepiness Scale (KSS), physiological sleepiness by the Pupillographic Sleepiness Test (PST). Sus-tained attention was assessed by the Psychomotor Vigilance Test (PVT) and the Mackworth Clock (MC). For cognitive attention aspects, Reaction Test (RT), Determination Test (DT), Cognitrone (COG) and Peripheral Perception Test (PP) (sub-tests of the Expert System Traffic), were used. Symptom validity (SV) was tested by the Dot Counting Test (DCT) and the Reliable Digit Span (RDS).

Results: PSD significantly increased subjective sleepiness (KSS) and reaction times in PVT, MC, COG and decreased the field of vision in PP compared to RESTED. All these differences were also present in FAKE compared to RESTED. Addi-tionally, we found higher numbers of missed reactions in PVT and MC, and a higher eye-tracking score in PP. The most prominent difference between PSD and FAKE was the disproportionally higher number of missed reactions in the FAKE condition (PVT: RESTED 0.4 per cent PSD 0.6 per cent FAKE 7.6; MC: 1.6% 3.5% 13.3, $P < 0.001$) Reaction times in PVT and MC, and eye-tracking in PP, were also sig-nificantly higher in FAKE, compared to PSD.

The SV assessment tests were not sensitive to detect malingering of daytime sleepiness.

Conclusion: Even if probands had previous experience with PSD, they most prominently showed exaggerated numbers of missed reactions in MC and PVT when trying to fake sleepiness. Therefore, extremely high rates of missed reactions in these tests should alert clinicians to possible malingering.

Poster Session – SDB, Epidemiology and Diagnosis Part I

P650

Clinical characteristics of central sleep apnoea within young male population

A. TERRAY-HORVATH, I. BERNATH, Z. SZAKACS
State Health Centre, Budapest, HU

Intoduction: Under emerging network-centric warfighting human error attributed to failures of cognitive performance becomes a critical issue. Abundant studies are dealing with sleep deficiency underlying the cognitive deficits, sporadic works dealing with obstructive sleep apnea are also available, but the prevalence of central sleep apnea has not yet been brought to the focus of interest.

Patients and method: Data of the last 8 years –gained between 2002 and 2010-came into consideration. During this period 1963 young and middle aged (18–35 years) male patients were referred to our sleep laboratory and had polysomnography testing. Having filled our questionnaries (ESS Fatigue Berlin) all patients underwent polysomnography testing. Complete over-night polysomnography was performed.

Results: Out of 1963 studies 60 remained negative except for benign snoring. In 312 cases sleep fragmentation due to respiratory effort related arousals was the salient finding characteristic for upper airway resistance syndrome (UARS). Severe obstructive apnea (AHI over 30/h) was encountered in 1319 cases. Moderate obstructive apnea (AHI between 5 and 30/h) was found in 100 cases. Central sleep apnea was diagnosed in 72 cases. In 100 cases sleep related movement disorder – periodic leg movement during sleep- was recorded. Further details of central sleep apnea group were the follows. In all cases AHI was over 30/h. Impaired respiratory motor control was responsible for 12 cases. Myasthenia gravis, post encephalitis syndrome, myopathies and severe kyphoscoliosis were the underlying pathologies. Cheyne-Stoke periodic breathing along with congestive heart failure or left ventricular systolic dysfunction was established in eight cases. In the remaining 52 cases central sleep apnea fell into the idiopathic or primary subgroup.

Conclusion: In the present work we have reviewed our sleep data bank to retrospectively estimate the prevalence and the clinical characteristics of central sleep apnea (CSA) within young male population comparable with he sample of military population.

P651

Sleep-disordered breathing in Chiari malformation

A. LOSURDO, S. DITTONI, E. TESTANI, S. COLICCHIO, V. GNONI, C. DI BLASI, C. VOLLONO, P. MARIOTTI, G. PATERNOSTER, C. DI ROCCO, L. MASSIMI and G. DELLA MARCA
Catholic University, Rome, IT

Objectives: Chiari Malformation (CM) is defined as a downward herniation of the caudal part of the cerebellum and/or medulla oblongata into the spinal canal. CM is classified into distinct types according to the degree of herniation. CM type II is associated with severe malformations, particularly with Myelomeningocele. An association has been reported between CM and sleep disordered breathing (SDB), either central or obstructive. The aim of this study was to evaluate the prevalence of SDB in CM, and its clinical correlates.

Methods: Fifty-three consecutive patients (26 girls and 27 boys, mean age: mean age 10.3 ± 4.4, range: 6 months–18 years) affected by CM underwent a full neurological examination, neuroimaging (brain MRI) and polysomnography (PSG).

Results: Fifty patients were classified as CM type I, three patients had CM type II. Mean size of the herniation was 10.6 ± 6.5 mm. Sixteen patients had synringomyelia and eight had hydrocephalus. PSG revealed SDB in 15 subjects (12 out of 50 with CM-I, all the three patients with CM-II). Within the CM-II patients, two had Obstructive-SDB (O-SDB) and one had both obstructive and central SDB (CO-SDB). Within the CM-I group, 6 patients had O-SDB (12%), four patients had Central-SDB (8%) and two patients had CO-SDB (4%). Patients with SDB, compared to those without SDB, had a higher prevalence hydrocephalus, syringomyelia, subjective sleep disturbances and neurological symptoms. No significant difference was observed in age, gender, prevalence of epilepsy and in the size of the herniation.

Conclusion: Our data show a prevalence of SDB in CM of 28%, lower when compared to that reported in literature. Moreover, our findings suggest that abnormalities in cerebro-spinal fluid dynamics, in particular syringomyelia and hydrocephalus, may play a major role in the pathogenesis of SDB in CM.

P652

Validation of polygraphy versus polysomnography in the diagnosis of sleep disordered breathing, with special emphasis on heart failure patients

L. MARGARIT[1], X. DROUOT[2], A. BOKAR-THIRÉ[2], M. STOÏCA[1], T. DAMY[2], L. HITTINGER[2], F. ROUDOT-THOROVAL[2] and M.-P. DORTHO[1]
[1]Hôpital Bichat – Claude Bernard, Paris, FR, [2]Hôpital Henri Mondor, Créteil, FR

Background: The increasing demand for sleep recordings leads to longer waiting lists to access the gold standard method, polysomnography. More simplistic methods are needed for the detection and the assessment of sleep apnea syndrom. One possible approach is polygraphy, with, however, possible pitfalls.

Objective: This study aims at comparing respiratory nocturnal polygraphy to full polysomnography in diagnosing sleep disordered breathing, in patients addressed to the sleep laboratory for suspected sleep apnea syndrome, in a general population and in heart failure patients.

Methods: One hundred and ten patients were included: 95 for possible sleep apnea syndrome, and 15 for other suspected sleep pathologies. The mean age was 56.6 ± 14.1 years, mean body mass index was 28.5 ± 8.6 kg/m^2, sex ratio was 75/110 men. In the suspected sleep apnea syndrome group, 20 patients had heart failure. They all had polysomnography. The same night recording was analysed conventionnally according to the international criteria, then also analysed blindly using only the respiratory parameters to mimic the polygraphy. Order of analysis was randomized, and recordings anonymized. Correlation and regression between polysomnographic and polygraphic apnea hypopnea indexes were calculated, together with sensitivity, specificty, predictive positive and negative values, together with receiving operating characteristic curves. Bland and Altman curves were plotted.

Results: The correlation coefficient between polysomnographic and polygraphic apnea hypopnea indexes was r = 0.972 ($P < 0.001$) in the whole population. It was as good in the heart failure group. The sensitivity and the specificity were high. The receiver operating curves showed a high area under the curve.

Conclusion: Polygraphy is a robust alternative to polysomnography to diagnose sleep disordered breathing and sleep apnea syndrome in a general population and in heart failure patients.
The study was sponsored by ResMed

P653

What strategies do drivers use to counteract sleepiness?

M. GONÇALVES[1], A. R. PERALTA[2], J. MONTEIRO FERREIRA[3] and C. GUILEMINAULT[4]
[1]Instituto do Sono, Porto, PT, [2]Santa Maria Hospital, Centro Hospitalar Lisboa Norte, EEG/Sleep Lab, Lisbon, PT, [3]Centro de Estudos de Doenças Respiratórias e Alérgicas, Coimbra, PT, [4]Stanford University Sleep Disorders Clinic, Stanford, US

Objectives: The purpose of this study was to determine the prevalence of sleepy drivers choosing efficacious measures to counteracting sleepiness while driving and to note the differences between this drivers and those using other measures.

Methods: A subsample of 215 sleepy drivers among a representative population of Portuguese drivers ($n = 900$) responded to a questionnaire administered through phone interview. Subjects reporting experience sleepiness while driving were asked about their prefered methods to counteract sleepiness. Demographic variables, Pittsburg Sleep Quality Index PSQI, Berlin questionnaire, Epworth Sleepiness Scale (ESS) were collected. Comparison of percentages were performed with Chi-square statistics ($P = 0.05$).

Results: in response to sleepiness at the wheel 44.0% responded stopping for a rest, 1.9% stopping and taking a nap, 26.1% opened the window, 9.3% increased the loudness of the radio, 6.1% drank caffeinated beverages, 1.1% turned on air conditioner and 4.8% did other things included (eat, drink water, wash face, talk to someone else, etc) 6.7% did nothing.

Young adults (18–24 years) had a different set of measures. Only 27% stopped and took a rest, 2.5% stopped and slept, 40.0% opened the window, 10% increased the loudness of the radio, 5% drank caffeinated beverages, 5% turned on the air conditioner, 2.5% talked to someone else and 2.5% performed other actions and 5% did nothing. In the 18–25 age subjects that preferentially performed the most recommended measures (either stopping, drinking caffeinated or sleeping) reported less frequently sleep related accidents or near misses ($P = 0.050$), men ($P = 0.004$), older subjects ($P = 0.050$) and subjects with more years with a driving license ($P = 0.026$) were more likely to perform these appropriated measures to counteract sleepiness.

Conclusion: Drivers using appropriate countermeasures had less accidents or near miss accidents. An important percentage of drivers still rely on un-efficacious measures. This is particularly true in young drivers. This is in similar to the previously found risk for sleep related car accidents in young drivers. Educational campaigns specifically addressing these risk- factors are urgent.

This Study was performed with the help of Portuguese Sleep Association and suported by educational grant from Colunex, Praxair and Volkswagen.

P654

The evaluation of risk for obstructive sleep apnoea in patients with type 2 diabetes

R. PECOTIC, V. ZEMUNIK, I. PAVLINAC DODIG, M. VALIC, T. TICINOVIC KURIR and Z. DOGAS
University of Split, Split, HR

Objective: The aim of this study was to evaluate risk for obstructive sleep apnea (OSA) in patients with type 2 diabetes using STOP questionnaire (Snoring, Tiredness, Observed, Pressure, STOP). Excessive daytime sleepiness was evaluated with Epworth sleepiness scale (ESS). Previous studies support the idea that glucose intolerance and type 2 diabetes might represent risk factors for OSA.

Methods: A total of 252 patients with type 2 diabetes were surveyed during regular visits in Centre for diabetes, endocrinology and metabolic diseases of University Hospital Split. All patients completed the Croatian version of ESS and STOP questionnaire.

Results: Our study indicates that 156 patients (61.9%) have increased risk for OSA according to STOP questionnaire results. In addition, those at high risk for OSA were older (65 versus 61 years of age, $P < 0.05$), had higher body mass index (BMI, 28.6 ± 5.1 versus 26.5 ± 4.1, $P < 0.001$), higher neck circumference (41.5 ± 4.7 versus 39.6 ± 6.2, $P < 0.009$), and had excessive daytime sleepiness according to ESS score (5.3 ± 3.1 versus 3.9 ± 2.5, $P < 0.001$). Individuals with type 2 diabetes reported to have conditions that usually correlate with OSA, mainly hypertension (46%), gastroesophageal reflux disease (28%), depression (10%), and asthma (8%).

Conclusion: Based on current evidence from literature, OSA could be related to clinical conditions such as diabetes and essential hypertension. More epidemiological data are needed regarding prevalence of obstructive sleep apnea in Croatian patients with type 2 diabetes. Our findings indicate relevance of STOP questionnaire as an useful screening tool for obstructive sleep apnea in Croatian patients with type 2 diabetes.

P655

Occurrence of psychiatric diseases in patients with obstructive sleep apnoea – results from the multinational ESADA cohort

M. PRETL, T. SIEGER, K. ŠONKA, L. GROTE and J. HEDNER on behalf of the ESADA study group

Objectives: Obstructive sleep apnea (OSA) is a common disorder with considerable comorbidity including cardiovascular and metabolic disorders. Increased prevalence of psychiatric diseases (PD) has also been reported in OSA but the association is less well established. The impact of PD on OSA treatment and outcome has not been addressed. We have explored the occurrence of PD in the ESADA multicentric sleep apnea cohort and investigated coinciding risk factors for PD in these patients.

Methods: The European Sleep Apnea Database (ESADA) is a joint multicentric study of patients referred to 24 laboratories in 15 Europaean countries and Israel with a suspected sleep apnea diagnosis. Study data includes information on anthropometrics, medical history, medication, daytime symptoms and sleep. All information is collected via a structured web-based format. The current report is based on data collected between 2007 and 2010 and comprises 8205 patients [5876 males with a mean (SD) age of 52 (13) years]. The current analysis used logistic regression to address various factors hypothesized to influence the association between OSA and PD.

Results: OSA (AHI > 5) was identified in 67% of patients and a comorbid PD diagnosis was present in 8% of OSA compared with 10% in non-OSA subjects. Prevalence was higher in females (15%) than in males (6%). Shortening of sleep length influenced the odds of PD which increased along with deviation from a mean subjective sleep length of 7 hrs (odds increase 21% per each hour, $P < 0.001$). In addition prolongation of sleep latency was associated with a PD

diagnosis (odds increase 7% per 10 min, $P < 0.001$). Several other factors were associated with increased risk for PD. The odds of PD diagnosis increased linearly up to the age of 50 years (on average 23% per 10 years, $P < 0.05$) and decreased in older patients (on average 35% per 10 years, $P < 0.001$). The odds of PD was higher (44%, $P < 0.01$) in smokers, increased with heart rate (13% per 10 beats, $P < 0.05$) but decreased with lower systolic pressure (9% per 10mmHg, $P < 0.01$). Elevated cholesterol increased the odds in females only (11% per 1 mM, $P < 0.05$). All influences were independent of OSA activity.

Conclusion: PD was common in a large cohort of patients with OSA. Prevalence was an even higher in females. Several sleep related, cardiovascular and metabolic factors were associated with PD independent of OSA severity. Future research will assess if comorbid PD influences long-term outcome in OSA patients.

The ESADA study is supported by enabling grants from RESMED and PHILIPS RESPIRONICS. The ESADA network has been supported by the EU COST Action B 26.

P656

Assessment of screening tests for obstructive sleep apnoea syndrome in pre-operative surgical patients

Z. DOGAS[1], R. PECOTIC[1], M. CAREV[1], N. KARANOVIC[1], M. VALIC[1], I. PAVLINAC DODIG[1], L. BRISKY[1], T. BRISKY[2] and G. RACIC[1]

[1]University of Split, Split, HR, [2]University Hospital Split, Split, HR

Objective: To determine excessive daytime sleepiness (EDS), as a major symptom of obstructive sleep apnea (OSA), in preoperative surgical patients by applying Croatian version of Epworth Sleepiness Scale (ESS), and to test their risk for OSA using STOP and STOP-BANG questionnaires.

Methods: The observational cross-sectional study included 1.348 consecutive patients (737 females) in Pre-anesthesia Evaluation Clinic aged 18 years or older without, previously diagnosed OSA.

Results: STOP positive patients were older [62 (20–88) versus 50 (18–89) yrs, $P < 0.001$], had greater BMI (28.5 ± 4.2 versus 25.7 ± 4.3 kg/m, $P < 0.001$), neck circumference (40.8 ± 4.1 versus 39.2 ± 4.2 cm, $P < 0.001$), and greater ASA physical status (chi2 = 33.03, $P < 0.001$) compared to STOP negative patients. Also, STOP positive patients had greater ESS scores compared with STOP negative patients (5.25 ± 3.8 versus 3.91 ± 3.1, $P < 0.001$). STOP-BANG positive patients had greater ASA physical status than STOP-BANG negative patients (chi2 = 37.96, $P < 0.001$). Also, STOP-BANG positive patients had greater ESS scores compared with STOP-BANG negative patients (4.55 ± 3.5 versus 3.97 ± 3.1, $P = 0.003$). The average ESS score in all subjects was 4.2 ± 3.3. In male subjects it was 3.97 ± 3.1, and in females 4.46 ± 3.5 ($P = 0.012$). More male patients reported snoring ($P < 0.001$), and that someone had observed them to have stopped breathing during sleep ($P = 0.017$), whereas more female patients reported being tired ($P < 0.001$).

Conclusion: EDS measured using the ESS score was significantly greater in the STOP and the STOP-BANG positive patients compared with no-risk patients. The Croatian version of the ESS seems to be better correlated with the STOP than with the STOP-BANG questionnaire. All tested screening tools may be useful in testing risk for OSA in preoperative surgical patients.

P657

Excessive sleepiness and the risk of obstructive sleep apnoea syndrome in professional taxi drivers

M. POPEVIC, A. MILOVANOVIC and D. BABIC

University of Belgrade, Belgrade, RS

Objectives: Excessive sleepiness and obstructive sleep apnoea syndrome (OSAS) are important causes of traffic accidents, but their prevalence in taxi drivers has rarely been reported. The aim of the study was to explore the association of excessive sleepiness and risk of OSAS with self-reported drowsy driving and traffic accidents in a sample of professional taxi drivers in Belgrade, Serbia.

Methods: A questionnaire was distributed to taxi drivers on three random taxi stops. A total of 54 drivers (response rate 67.5%) answered the questions on demographics, driving and sleep habits, sleepiness or falling asleep while driving and traffic accidents in the last year. Excessive sleepiness was measured with Epworth sleepiness scale (ESS ≥ 10 was considered indicative). Risk of OSAS was measured by Berlin questionnaire.

Results: All taxi drivers were male; mean age was 43 years, mean body mass index (BMI) was 26.91 and 66.7% of participants were overweight. Average driving experience was 19.3 years, with 59 working hours per week. Average sleep duration was 7 h. Habitual snoring was reported by 48% of drivers. Almost 80% of drivers reported drowsy driving and 33.3% had fallen asleep while driving. Traffic accidents had 19.6% of drivers in the last year. Mean ESS score was 7, and ESS ≥ 10 was found in 24.1% of drivers. High risk of OSAS was found in 34.1% of the participants. Excessive sleepiness was associated with habitual snoring (ro = 0.324, $P = 0.017$), drowsy driving (ro = 0.285, $P = 0.037$) and number of traffic accidents (ro = 0.301, $P = 0.027$). Risk of OSAS was associated with habitual snoring (ro = 0.464, $P = 0.000$), falling asleep while driving (ro = 0.282, $P = 0.039$) and BMI (ro = 0.320, $P = 0.018$). There was a significant relationship between ESS ≥ 10 and risk of OSAS (ro = 0.271, $P = 0.0471$). Logistic regression model showed a significant predictive association of excessive sleepiness and the number of traffic accidents (Wald coefficient 3.973, $P = 0.046$). Second model showed a significant correlation between risk of OSAS and BMI (Wald 5.297, $P = 0.021$) and habitual snoring (Wald 9.796, $P = 0.002$).

Conclusion: Prevalence of excessive sleepiness and high risk of OSAS in this sample of taxi drivers are similar to findings in other commercial drivers' studies. Excessive sleepiness is significantly associated with traffic accidents. High risk of OSAS is associated with falling asleep while driving. None of the participants had ever been screened for excessive sleepiness or OSAS before.

Research project ON 175081 for 2011–2014 funded by Ministry of Education and Science, Government of the Republic of Serbia

P658

Excessive daytime somnolence is not an independent predictor for sleep apnoea syndrome

S. D. MIHAICUTA[1], C. L. ARDELEAN[1], S. M. FRENT[1] and O. C. DELEANU[2]

[1]University of Medicine and Pharmacy, Timisoara, RO, [2]University of Medicine and Pharmacy, Bucharest, RO

Introduction: Excessive daytime somnolence (EDS) is one of the most significant symptoms of obstructive sleep apnea syndrome (OSAS).

Aims and Objectives: Evaluation of EDS and Epworth Sleepiness Score (ESS) at patients with OSAS.

Material and Methods: Of 1135 consecutive patients with suspected OSAS were evaluated with sleep questionnaires, anthropometric measurements, polisomnography or somnography for AHI (apnea-hypopnea index normal 0–4, mild 5–14, moderate 15–29, severe over 30). We evaluated the Odds Ratio (OR) together with 95% confidence interval (CI) in a univariate analysis and the independent variables were used in order to identify the most important predictors.

Results: Eight hundred and twenty-four males (72.59%), 311 females (27.41%), age 55 ± 10.89 years (6–84), BMI 33.18 ± 6.29 kg/m^2 (17–56), AHI 34.10/h ± 27.41. EDS is not an independent predictor for OSAS in univariate analysis (OR 1.205, $P < 0.001$). In linear regression EDS-AHI relation is direct proportional, almost medium correlation (r = 0.435, $P < 0.001$). ESS has a powerfull correlation with OSAS in multiple regression analysis (r = 0.79, $P < 0.001$) and it has higher and significant values at patients with OSAS (10.88 versus 7.49, $P < 0.001$), COPD (11.38 versus 9.82, $P < 0.01$), hypertension (10.77 versus 9.09 $P = 0.007$).

Conclusion: EDS is multifactorial and significant higher at patients with co morbidities. In the presence of other risk factors but without EDS, patients with suspicion of OSAS need a polysomnography.

P659

Validation of the STOP and STOP BANG questionnaire in primary health care

C. CRUCES-ARTERO[1], M. V. MARTIN-MIGUEL[1], C. HERVES-BELOSO[1], F. LAGO-DEIBE[1], S. HERNAIZ-VALERO[1], A. CLAVERIA-FONTAN[1] and O. GUGLIELMI[2]

[1]Primary Health Care Service, Vigo, ES, [2]Faculty of Psychology, Granada, ES

Objective: To validate the spanish version of STOP and STOP-Bang Questionnaires to apply to patients in primary health care (PHC) and to provide a quick tool for family physicians to optimize the referral of patients with suspected Obstructive Sleep Apnea Syndrome (OSAS) to secondary care.

Method: The questionnaires were validated by comparing scores obtained with information of polysomnography as gold-standard. We included 178 people who attended to PHC and accepted to participate in the study. After signing the informed consent, all participants answered a general interview and STOP and STOP-Bang questionnaires, and underwent a full night polysomnography.

Results: Of the people who constitute the whole sample, 39.8% had a Apnea Hipopnea Index (AHI) <5, 19.3% had a mild OSAS (AHI between 5 and 15), 10.2% moderate (AHI between 15 and 30) and 30.7% severe (AHI > 30). For the STOP questionnaire with a cutoff of AHI ≥ 5, this results were found: sensitivity (S) = 91.89%, specificity (E) = 28.16%, positive predictive value (PPV) = 66.66%, negative predictive value (NPV) = 68.96%, positive likelihood ratio (L+) = 1.28, negative likelihood ratio (L-) = 0.29. For the STOP-Bang questionnaire and an IHA cutoff of ≥5, the results were: S = 96.39%, E = 23.94%, PPV = 66.45%, NPV = 80.95%, L+ = 1.27 and L- = 0.15. By adding one point to STOP Bang in patients with a time spent below 90% oxygen saturation (T90) >0, results were: S = 95.45%, E = 45.71%, PPV = 73.43%, NPV = 86.49%, L+ = 1.75 and L- = 0.10. The ROC curve analysis indicated that this is a test with high diagnostic value.

Conclusion: The preliminary validation of the STOP and STOP Bang questionnaires in primary care shows good sensitivity of the instruments to detect the risk of OSAS, but low specificity. However, when T90 was added, a data obtainable with a night of pulse oximetry, STOP Bang questionnaire would adequately discriminate patients to be referred for polysomnography.

P660

Association of obstructive sleep apnoea syndrome with other non-communicable diseases in young adults

L. ROSCA[1], D. TODEA[2], A. HERESCU[1] and A. COMAN[1]

[1]Clinical Hospital of Pneumology Leon Daniello, Cluj-Napoca, RO, [2]University of Medicine and Pharmacy Iuliu Hatieganu Cluj Napoca, Cluj-Napoca, RO

Obstructive sleep apnea syndrome (OSAS) is a highly prevalent disorder affecting 2–4% of the adult population. The signs, symptoms (the most important excessive daytime sleepiness) and consequences of OSAS are a direct result of the derangements that occur due to repetitive collapse of the upper airway during sleep, leading to markedly reduced (hypopnea) or absent (apnea) airflow. The high medical and economic burden of OSAS and its comorbidities underlines the importance for maximizing the recognition and diagnosis of this disorder. Non-communicable diseases (NCDs), principally cardiovascular diseases, diabetes, cancers and chronic respiratory diseases, are the leading global causes of death, causing more deaths than all other causes combined, and they strike hardest at the world's low- and middle-income populations. These diseases have reached epidemic proportions, yet they could be significantly reduced, with millions of lives saved and untold suffering avoided, through reduction of their risk factors, early detection and timely treatments. The aim of the study was to show what proportion from the young adults diagnosed with OSAS is affected by more than 1 non-communicable disease.

Material and Methods: We performed cardiorespiratory poligraphy and polysomnography to 325 patients in 3 years. We assessed the presence of non-communicable diseases in these patients (diabetes, cardiovascular diseases, chronic respiratory diseases, cancer).

Results: From 325 patients 256 were males (72; 28.12% with age between 20 and 40), 69 females (6; 8.69% with age between 20 and 40). In the group of males- young adults the mean age was 33.98, the mean of the apnea hypopnea index was 44.98, and 3 of them were with diabetes, 27.77% with hypertension. In the group of females the mean age was 38.6, the mean of the apnea hypopnea index was 17.86, and 1 of them was with diabetes, 1 with hypertension.

Conclusion: The group of males- young adults is more affected by non-communicable disease. Even if the prevalence of OSAS is increasing with age, also young adults are affected by this disease and they can develop severe forms associated with other important comorbidities. Prevention and effective treatment will help this category of people to improve their quality of life.

P661

Mortality and morbidity in patients with sleep disordered breathing: a national controlled prospective study

P. JENNUM, R. IBSEN and J. KJELLBERG

Danish Center for Sleep Medicine, Glostrup, DK

Objectives: The long-term prognosis of obstructive sleep apnea (OSA) and obesity hypoventilation syndrome (OHS), as compared to age, gender and social controls, are incompletely described.

Methods: Using data from the Danish National Patient Registry (NPR) (1998–2010), 30278 individuals with a diagnosis of OSA (23208 men and 7070 women) and 1562 with a diagnosis OHS (1092 men and 470 women) were identified. For every patient, four ages-,

sex- and social matched citizens were randomly selected from the Danish Civil Registration System, a total of 120506 OSA and 6241 HS controls. Morbidity and all-cause mortality was extracted from the NPR.

Results: The 10 years survival of treated and untreated OSA patients was 90.7% compared to 92.4% (controls) and of OHS patients 63.9% compared to 85.5% (controls) (both: $P < 0.0001$). CPAP reduced all-cause mortality in OSA patients, but not in OHS patients. Commonly significant ($P < 0.01$) observed morbidities in OSA patients OSA were related to respiratory (1.91 (1.82–2.01), nervous (1.65 (1.55–1.75), endocrine, metabolic, nutrietal (1.53 (1.54–1.75), ENT:1.39 (1.30–1.49), circulatory: 1.20 (1.16–1.27), musculoskeletal: 1.25 (1.20–1.30), digestive illnesses (1.09 (1.03–0.14), and injuries 1.12 (10.8–1.16). Mental disease and neoplasm showed a lower occurrence: 0.90 (0.81–0.99) and 0.85 (0.80–0.95), respectively. OHS showed higher morbidities to respiratory: 4.03 (3.21–5.07), nervous: 3.17 (2.43–4.15), endocrine, metabolic, nutrietal (4.65 (3.67–5.90), ENT:1.39 (1.30–1.49), circulatory: 1.84 (1.50–2.26), musculoskeletal: 1.25 (1.20–1.30) and digestive illnesses (1.09 (1.03–0.14), and injuries 1.12 (10.8–1.16). Neoplasm occurred less often: 0.70 (0.50–0.97).

Conclusion: OSA and especially OHS present significant mortality. The morbidity includes a wide range of medical disorders beside cardiovascular complications. CPAP present a complex effect on mortality with positive effect on mortality in OSA, but less effect in most diseased patients suggesting a multimodality management strategi in sleep disordered breathing patients.

P662

Survival of patients after the diagnosis of sleep-related breathing disorders

I. SARC, K. ZIHERL, M. KOSNIK, M. FLEZAR and J. GABRIJELCIC
University Clinic of Pulmonary and Allergic Diseases Golnik, Golnik, SI

Objectives: Obstructive sleep apnea (OSA) and obesity hypoventilation syndrome (OHS) constitute two major groups of sleep related breathing disorders (SRBD) with considerable SRBD-related and cardiovascular morbidity. There are scarce data available on long-term survival in these two diseases, with the few studies reporting substantial mortality in OHS patients.

Methods: Medical records of all patients who underwent diagnostic polysomnography for the first time in University Clinic Golnik between 2005 and 2010 were retrospectively reviewed in detail for clinical and laboratory data. Patients were divided in three groups: OSA and OHS patients (both groups defined according to AASM guidelines) and controls (apnea-hypopnea index – AHI < 5 and no daytime hypercapnia). Vital status was obtained from Central Population Registry.

Results: Out of 1001 patients (80% men, age 53.0 ± 11.2 years, body mass index (BMI) 33.9 ± 7.2, AHI 36.0 ± 27.3, Epworth sleepiness scale 12.6 ± 5.7), 714 (71.3%) had OSA, 116 (11.6%) had OHS and 172 (17.2%) were controls. In the mean follow-up of 3.4 ± 1.4 years 38 (3.8%) patients died. Mortality rate was 30 (4.2%) in OSA group, 5 (4.3%) in OHS group and 3 (1.7%) in controls. There was no difference in survival probability between groups (log rank $P = 0.283$). On Kaplan–Meier analysis, 1-,2-, 3-, and 5-year survival probabilities were 99.1%, 98.0%, 97.0%, and 95.4% for OSA group, 100%, 98.3%, 96.2%, and 94.7% for OHS group, and 99.4%, 98.8%, 98.8%, 97.7% for controls, respectively. Continuous or bilevel positive airway pressure (C- or BIPAP) therapy was prescribed in 543 (76.1%) of OSA and 100 (86.2%) of OHS patients. In Cox proportional hazard model adjusted for sex, age, BMI, pCO2, heart failure (HF), diabetes mellitus (DM), presence of SRBD, and prescribed C- or BIPAP therapy, age (HR 1.15, 95%CI 1.10–1.21), pCO2 (HR 2.67, 95% CI 1.58–4.53), HF (HR 3.66, 95% CI 1.59–8.39) predicted increased mortality.

Conclusions: There was no statistical difference in survival between OSA, OHS and control group. Mortality rate was mainly influenced by heart failure and higher pCO2. Mortality was lower than previously reported in treated OHS patients. Majority of patients were treated with C- or BIPAP therapy.

P663

Obesity hypoventilation syndrome: mortality and prognostic factors

K. ZIHERL, I. SARC, M. KOSNIK, M. FLEZAR and J. GABRIJELCIC
University Clinic of Pulmonary and Allergic Diseases Golnik, Golnik, SI

Objectives: The prevalence of obesity hypoventilation syndrome (OHS) is increasing. OHS is associated with considerable comorbidity, morbidity and health costs. Data on mortality in OHS patients and survival benefit of positive pressure ventilation (PAP) are lacking.

Methods: Medical records of all patients discharged with OHS from 2005 to 2010 from University Clinic Golnik were reviewed. Patients with body mass index (BMI) >30 and daytime hypercapnia in the absence of any other cause of hypoventilation, were included. Prescription of PAP, including continuous (CPAP) and bilevel (BIPAP) was recorded. Vital status was obtained from Central Population Registry.

Results: A total of 248 patients with OHS were included. Two groups were identified, 132 (53%) patients were admitted in acute exacerbation (aeOHS) and 116 (47%) under stable condition (sOHS). aeOHS patients were older (63.8 ± 12.1 versus 56.3 ± 9.7 years, $P < 0.01$), more often female (59.1% versus 33.6%, $P < 0.01$), had higher BMI (46.3 ± 9.8 versus 41.4 ± 7.7, $P < 0.01$), more often had heart failure (HF) (58.3% versus 23.3%, $P < 0.01$), arterial hypertension (92.4% versus 71.6%, $P < 0.01$), atrial fibrilation (18.9% versus 6%, $P < 0.01$), pulmonary hypertension (PH) (14.4% versus 4.3%, $P < 0.01$), diabetes mellitus (DM) (41.7% versus 23.3%, $P < 0.01$) and were less often prescribed PAP (42% versus 86%, $P < 0.01$). In a mean follow-up of 3.1 ± 1.5 years 50 (20%) patients died, 45 (34%) aeOHS and 5 (4.3%) sOHS (log rank $P < 0.01$). On Kaplan–Meier analysis, 1-,2-,3-, and 5-year survival probabilities were 88%, 78%, 70%, and 62% for aeOHS group and 100%, 98%, 96%, and 95% for sOHS group, respectively. In aeOHS group, 1-, 2-, 3-, and 5-year survival probabilities were 83%, 69%, 61%, and 50% for the group without PAP and 95%, 91%, 83%, and 83% for PAP treated group, respectively (log rank $P < 0.01$). In Cox multivariate analysis for aeOHS group adjusted for sex, age, BMI, HF, DM, PH, PAP, HF (HR 3.14, 95% CI 1.34–7.34), DM (HR 6.95, 95% CI 3.10–15.58) and PH (HR 2.58, 95% CI 1.04–6.41) were independent predictors of mortality and PAP (HR 0.39, 95% CI 0.16–0.93) was associated with improved survival. In contrast, no variable was linked to survival in sOHS group.

Conclusions: We found significant difference in mortality rates between aeOHS and sOHS group. Patients with aeOHS were older, more obese and had more comorbidities. PAP treatment independently improved survival in the aeOHS group, while heart failure, diabetes and pulmonary hypertension predicted higher mortality.

P664

Prevalence of sleepiness in professional drivers

E. DI COSCIO[1], M. MAESTRI[1], F. COSENTINO[2], N. SALVATI[3], R. BUSELLI[2], E. M. LOTTI[4], F. BARBAGLI[5], G. MICELI[5], R. ROCCHI[4], G. BATTISTA[5], M. C. SPAGGIARI[6], A. CRISTAUDO[2] and E. BONANNI[1]

[1]Neurological Clinics, Pisa, IT, [2]Department of Endocrinology and Metabolism, Orthopedics and Traumatology, Occupational Medicine, Pisa, IT, [3]Department of Statistics and Economy Applied Mathematics, Pisa, IT, [4]Department of Neurosciences, Siena, IT, [5]Department of Surgery and Bioengineering, Siena, IT, [6]Department of Neurosciences, Parma, IT

Objectives: Commercial bus drivers undergo periodical medical controls according to the Italian laws and could be screened for sleep disorders. Aim of this pilot study was to evaluate the prevalence of excessive daytime sleepiness and obstructive sleep apnea syndrome (OSAS) in a group of bus drivers.

Methods: Seven hundred and fifty-six bus drivers (727M, mean age 41 ± 8.03 years) were evaluated through screening questionnaire of the Italian Association of Sleep Medicine.

Results: According to the questionnaire, 48% presented a reduction in sleep quality and 57% a reduced duration of sleep, 28% snoring, 10% sleepiness. A percentage around 12% presented symptoms suggestive for sleep disorders and worth further investigation and referral to sleep centre.

Conclusions: The prevalence of sleep disorders seems similar to previous observation in this kind of population, although its clinical relevance should be further examined.

P665

Effects of inter-rule as opposed to inter-rate variability on the severity of the obstructive sleep apnoea syndrome

P. ANDERER[1], M. ROSS[1], A. MOREAU[1], S. THUSOO[1], R. FLIGGE[2] and G. DORFFNER[1]

[1]Philips Healthcare, Vienna, AT, [2]Philips Healthcare, Monroeville, US

Objectives: To evaluate the effects of inter-rater and inter-rule variability on the classification of the severity of the obstructive sleep apnea syndrome (OSAS) in patients with suspected OSAS based on seven manual expert scorings and Somnolyzer 24 × 7 auto scorings.

Material and Methods: Apneas and hypopneas were scored manually by 7 experts in 15 patients (8 females, 7 males, aged 28–56 years) according to the recommended AASM rule (≥ 30% drop in pressure flow signal leading to a ≥4% desaturation for hypopneas = MAN-1–MAN-7). Auto scorings were performed according to the recommended rule (=AUT_A), the alternative rule (≥50% drop leading to a ≥ 3% desaturation and/or to an arousal = AUT_B) and the 'Chicago criteria' (≥30% drop leading to a ≥ 3% desaturation and/or to an arousal and no confirmation of flow drops ≥ 50% = AUT_C).

Results: Based on a consensus scoring incorporating all 8 scorings available for the recommended rules, 4 patients were classified as normal (NO:AHI<5), 6 as mild (MI: 5 ≤ AHI>15), 2 as moderate (MO:15 ≤ AHI<30) and 3 as severe OSAS (SE:AHI ≥ 30). While AUT_A classified all patients correctly, the manual scorers misclassified between one and four patients (MAN-1: 2 MI to MO; MAN-2: 1 MI to MO, 1 MO to MI; MAN-3: 4 MI to NO; MAN-4: 2 MI to NO, 2 MI to MO; MAN-5: 1 Mo to MI; MAN-6: 2 MI to NO; MAN-7: 2 MI to NO, 1 MO to MI). Accordingly, the bias for the AHI between consensus and AUT_A scoring was lower than for consensus and any of the 7 manual scorings (AUT_A: -0.1 + -0.7; MAN-1: -3.6 + -8.2; MAN-2: 1.4 + -2.6; MAN-3: 0.5 + -2.9; MAN-4: 4.4 + -5.4; MAN-5: -0.9 + -4.1; MAN-6: -2.7 + -2.7; MAN-7: -3.1 + -3.8). Applying AUT_B changed the classification in 8 patients (4 NO to MI; 3 Mi to MO; 1 MI to SE) and AUT_C in 12 patients (2 NO to MO; 2 NO to SE; 2 MI to MO; 4 MI to SE; 2 MO to SE).

Discussion: Consensus scoring and auto scoring showed a perfect agreement for the detection of apneas and hypopneas, confirming the validity of the Somnolyzer scorings. While the inter-rater variability resulted in 1–4 classification mismatches, the inter-rule variability affected the classification results significantly. All 4 patients classified as normal according to the recommended rule showed a mildly abnormal AHI for the alternative rule and a moderately or even severely abnormal AHI for the Chicago rule. Thus, computer-assisted scoring is a valuable tool for scoring according to a defined rule and for identifying the appropriate rule for an individual patient.

All authors are Philips employees.

P666

Sleep-disordered breathing after spinal cord injury

V. RIMPILÄ[1], A. SALMINEN[1], O. KURKELA[1], E. KOSKINEN[2], T. LUOTO[2], J. ÖHMAN[2] and O. POLO[1]

[1]Unesta Research Centre, Tampere, FI, [2]Tampere University Hospital, Tampere, FI

Objectives: High spinal cord injury (SCI) affects respiratory muscles, which manifests as high incidence of sleep-disordered breathing (SDB). The purpose of this study was to investigate the prevalence of various forms of sleep disordered breathing in a clinical spinal cord injury patient cohort.

Methods: Full polygraphic sleep recording with transcutaneous carbon dioxide measurement was performed in 32 (24 men, eight women) patients with chronic spinal cord injury classified with American Spinal Injury Association (ASIA) criteria. Patients with respiratory paralysis were excluded. Sleep was staged according to conventional criteria. Apnea was scored according to AASM criteria. Sleepiness was assessed with Epworth Sleepiness Scale (ESS).

Results: Twenty-six Patients were included to the study. ASIA class (A, B, C, D) distribution was 4, 0, 4 and 18 respectively. Sleep apnea was observed in 16 patients (61.5%). The predominant apnea/hypopnea type was obstructive in 7, central in 7 and mixed in two patients. Patients with predominantly central type were all ASIA class C or D. Apnea or hypopnea occurred in two out of four patients with ASIA A level injury. In both cases the episodes were obstructive. REM-related hypoventilation, assessed as increased tcCO2 was observed in 12 patients, 7 with and 5 without concomitant sleep apnea. Three patients with apnea and 2 without had ESS more than 10.

Conclusion: Incidence of SDB was higher than would have been expected by the subjective symptoms of sleepiness. ESS above 10 did not predict SDB. SDB was obstructive in most severe injury and predominantly central in less severe cases. REM-hypoventilation occurred irrespectively of the presence or type of sleep apnea. Sleep study should be routinely performed in all patients with SCI and the clinical response of SDB to ventilatory support should be individually assessed.

P667

Gender and age differences of REM sleep-dependent obstructive sleep apnoea prevalence among Korean patients

J. S. LEE[1] and S. J. KIM[2]

[1]Pusan National University Yangsan Hospital, Yangsan, KR, [2]Seounal National University College of Medicine, Seoul, KR

Introduction: Obstructive Sleep apnea (OSA) intensity and frequency are generally severer and increased during rapid eye movement (REM) sleep due to muscle atonia and increased upper airway resistance. 'REM sleep-dependent OSA (REM-OSA)' is defined as the one in which apneas and/or hypopneas occur predominantly during REM sleep. We aimed to evaluate differences of REM-OSA prevalence according to gender and age.

Methods: We reviewed on the nocturnal polysomnographic records of 1791 consecutive OSA patients with an apnea-hypopnea index (AHI) ≥ 5/h). AHIs during total sleep time (TST), non-REM (NREM) sleep, and REM sleep (AHITST, AHINREM, AHIREM, respectively) were calculated. REM-OSA was defined as the one with AHIREM per cent AHINREM >2. Statistical comparisons were made between males and females according to the severities of OSA (mild as AHI<15, moderate as 15~30, severe as >30) and the ages (younger as age ≤ 55, older as > 55). The independent t-test and χ^2-test with linear by linear association (each with significance level of $P < 0.05$) were used for analyses.

Results: Out of 1791 OSA patients (1489 males, 302 females), total of 604 patients (429 males, 175 females) fulfilled the criteria for REM-OSA, yielding the overall prevalence of 33.7%. Females had significantly higher prevalence of REM-OSA than did males (58.3% versus 28.8%, $\chi^2 = 95.4$, $P < 0.01$). Prevalence of REM-OSA differed according to the severities of OSA. In females, prevalence of REM-OSA decreased as the severity of OSA increased (mild 74.9% versus moderate 51.5% versus severe OSA 6.1%) ($\chi^2 = 299.2$, $P < 0.01$). In males, result was the same as that of females (mild 51.7% versus moderate 31.6% versus severe OSA 4.6%) ($\chi^2 = 299.2$, $P < 0.01$). Younger females had a higher prevalence of REM-OSA than did older females (65.5% versus 51.9%, $\chi^2 = 5.7$, $P < 0.05$). But, no difference of prevalence was found between younger and older males.

Conclusion: Our results show that REM-OSA is more prevalent in females with OSA versus males with OSA and in those with mild or moderate OSA versus those with severe OSA. In females with OSA, REM-OSA seems to be more prevalent in the younger ones versus the older ones.

P668

Cardiorespiratory responses to 6-min walk test in postmenopausal obese women with obstructive sleep apnoea

V. M. M. PASSOS[1], A. M. LIMA[2], R. P. PEDROSA[3], I. M. L. BARROS[4], L. O. B. F. COSTA[5], A. C. SANTOS[6] and M. S. BRASILEIRO-SANTO[6]

[1]Federal University of Pernambuco – UFPE, Recife, BR, [2]Federal Rural University of Pernambuco – UFRPE, Recife, BR, [3]Pronto Socorro Cardiológico de Pernambuco – PROCAPE, Recife, BR, [4]Pronto Socorro Cardiológico de Pernambuco – PROCAPE, Recife, BR, [5]University of Pernambuco – UPE, Recife, BR, [6]Federal University of Paraíba – UFPB, João Pessoa, BR

Aims: To evaluate, in postmenopausal women, the effects of obesity and OSA on cardiorespiratory parameters before and after the 6-min walk test (6MWT).

Methods: Descriptive analytical, cross-sectional study. Fourty women aged 45–60 years (Age = 51.4 ± 5.2 years), sedentary and with no history of smoking for at least one year previously submitted to polysomnography were evaluated. The participants were divided into 4 groups: G1-Normal weight without OSA (BMI = 22.77 ± 1.99 kg/m^2), G2-Normal weight with OSA (BMI = 22.06 ± 2.40 kg/m^2), G3-Obese without OSA (BMI = 33.88 ± 3.09 kg/m^2) and G4-Obese with OSA (BMI = 34.01 ± 1.79 kg/m^2). All underwent clinical and anthropometric evaluation, followed by 6MWT.

Results: Apnea-hypopnea index (AHI) was different between groups, being higher in G2 (AHI = 8.94 ± 2.93 events/h) when compared to G1 (AHI = 1.78 ± 1.48 events/h) and being higher in G4 (AHI = 17.98 ± 10.73 events/h) when compared to G1 and G2 and when compared to G3 (AHI = 2.33 ± 1.74 events/h) ($P < 0.05$). In relation to respiratory parameters at rest, oxygen saturation was lower in G4 compared to G2 (SpO2 = 97.47 ± 1.46% versus 98.60 ± 0.55%, respectively), but the respiratory rate (RR) and level of perceived exertion (Borg scale) were not different between groups. Regarding to cardiovascular variables at rest, G4 had higher levels of systolic blood pressure than G1 and G2 (SBP = 136.53 ± 18.37 mmHg versus 110.20 ± 18.28 mmHg and SBP = 136.53 ± 18.37 mmHg versus 124.31 ± 9.60 mmHg, respectively, $P < 0.05$). Diastolic blood pressure in G4 was greater when compared to G1 (DBP = 89.67 ± 7.70 mmHg versus 81.31 ± 8.50 mmHg, respectively, $P < 0.05$). During recovery, heart rate was higher in G4 (HR = 77.0 ± 9.05 bpm) compared to G1 (HR = 74.33 ± 7.88 bpm) ($P < 0.05$). The other cardiorespiratory variables were not different between groups at this moment.

Conclusion: The results of this study suggest that in obese women during menopause, OSA does not cause major damage on pulmonary function and distance traveled in the 6MWT. In this population, OSA alone influenced the cardiorespiratory parameters at rest, but not in recovery from exercise, and it was demonstrated that obesity was a contributing factor to enhance the changes, especially before the submaximal test.

P669

Daytime respiratory symptoms are associated with obstructive sleep apnoea syndrome

T. M. JONASSEN, T. M. L. EAGAN and S. LEHMANN

Haukeland University Hospital, Bergen, NO

Aim: To study the relationship between day- and nighttime respiratory symptoms and obstructive sleep apnoea syndrome (OSAS) in a general Norwegian population.

Methods: An age and sex stratified random sample of all adults aged 47–48 (middle-aged) and 71–73 (elderly) living in Bergen, Norway, were invited to a cross-sectional study. Of 3506 subjects (69%) attended. Subjects were classified as having OSAS if they reported snoring, breathing cessations, and daytime sleepiness using the Karolinska Sleep Questionnaire, previously validated against polysomnography. Self-reported daytime symptoms were chronic cough, dyspnoea on climbing two flights of stairs and wheezing, and nighttime symptoms were waking with chest tightness and woken by attack of breathlessness. Three logistic regression models were fitted with OSAS as the outcome variable; one with the three daytime symptoms as main explanatory variables and two models where each of the nighttime symptoms were included separately. All models included age, sex, body mass index (BMI), waist-hip ratio and smoking.

Results: Of 10.0% of subjects with chronic cough had OSAS compared to 4.2% among those without cough ($P < 0.01$). Corre-

spondingly for the other symptoms: Dyspnoea on climbing two flights of stairs 7.7%/4.0% ($P < 0.01$); wheeze 7.7%/4.0% ($P < 0.01$); waking with chest tightness 10.3%/4.3% ($P < 0.01$); woken by attack of breathlessness 12.0%/4.3% ($P < 0.01$). Having chronic cough and dyspnoea on climbing two flights of stairs were associated with OSAS with odds ratios (OR) of 1.9 (1.2, 2.9) and 1.9 (1.3, 2.8), respectively. These relationships remained when adjusting for nighttime symptoms. Of the nighttime symptoms only woken by attack of breathlessness was associated with OSAS; OR 1.9 (1.1, 3.2).

Conclusion: OSAS should be considered in patients reporting both daytime and nighttime respiratory symptoms.

P670

Factors related job strain in patients with breathing-related sleep disorders

O. GUGLIELMI[1], B. JURADO-GAMEZ[2], F. GUDE[3] and G. BUELA-CASAL[1]

[1]Faculty of Psychology, Granada, ES, [2]Reina Sofia University Hospital, Cordoba, ES, [3]University Hospital of Santiago, Santiago, ES

Objective: The aim was to investigate the relationship between Obstructive Sleep Apnea Syndrome (OSAS) expressed by the Apnea-Hypopnea Index (AHI) and psychosocial health at work, especially work-related stress.

Method: We included 127 people who attended the Sleep Disordered Breathing Unit (mean ± SD age: 46.24 ± 8.93; sex: 64.4% male, BMI: 30.68 ± 5.23). All patients underwent an overnight polysomnography in the hospital and answered a questionnaire on general socio-demographic and health, the work stress questionnaire, Job Content Questionnaire (JCQ) and the sleep quality questionnaire Pittsburgh Sleep Quality Index (PSQI).

Results: Of the patients included in the study, 8% had an AHI <5, 22.4% had mild OSAS (AHI between 5 and 15), 12% moderate OSAS (AHI between 15 and 30) and 57.6% severe OSAS (AHI more than 30). We studied the relationship between severity of disease and work stress. Of the variables such as sex, age, level of study, job stability, presence of physical stressors at work like heat, cold, noise, chemical agents, OSAS severity and subjective sleep quality, in the logistic regression model only subjective sleep quality showed significant results associated to job strain (beta = 0.24, $P < 0.01$).

Conclusion: Obstructive Sleep Apnea Syndrome is a disorder of sleep that in addition to having serious consequences to metabolic and cerebro-vascular functioning, also affects the quality of life of the person suffering from this disorder. OSAS patients often suffer from drowsiness, fatigue, anxiety and depression and the factors responsible for these symptoms are still unclear. In the sample of patients included, work stress was associated with perceived sleep quality, whereas disease severity did not explain this aspect of the occupational health of the persons affected.

P671

Symptoms among hypertensive patients with undiagnosed obstructive sleep apnoea in primary care – a structural equation model analysis

A. BROSTRÖM[1], O. SUNNERGREN[2], P. JOHANSSON[3], E. SVENSSON[4], M. ULANDER[1], P. NILSEN[5] and E. SVANBORG[1]

[1]Department of Clinical Neurophysiology, Linköping, SE, [2]County Hospital Ryhov, Jönköping, SE, [3]Linköping University Hospital, Linköping, SE, [4]Swedish Defence Research Agency, Linköping, SE, [5]Linköping University, Linköping, SE

Objective: Obstructive sleep apnea (OSA) has been linked to hypertension in sleep clinic populations, but little is known about the symptom profile of undiagnosed OSA in hypertensive outpatients in primary care. The aim was therefore to explore characteristics associated with undiagnosed OSA in hypertensive primary care patients.

Methods: A cross-sectional design was used. A total of 411 consecutive patients (52% women), mean age 57.9 years (SD 5.9 years), with diagnosed hypertension (blood pressure > 140/90) from four primary care centres were included. All subjects underwent a full-night, home based, respiratory recording to establish presence and severity of OSA. Clinical variables (weight, height, waist circumference, blood pressure, ECG, left ventricular hypertrophy, lipid levels, renal function), medication and co-morbidities, as well as data from self-rating scales regarding symptoms/characteristics (BSAQ), insomnia (MISS), excessive daytime sleepiness (ESS), depressive symptoms (HAD) and health (SF-12) were collected during a clinical examination. Factor analyses and structural equation modelling (SEM) were used to explore the relationships between self-rated symptoms, clinical characteristics and objectively verified diagnosis of OSA.

Results: Fifty-nine per cent of the patients had an AHI >5/h indicating OSA. An exploratory factor analyses based on 19 variables yielded a six-factor model (i.e., anthropometrics, blood pressure, OSA-related symptoms, comorbidity, health complaints, and physical activity) explaining 58% of the variance. SEM analyses showed strong significant associations between anthropometrics (i.e., body mass index, neck circumference, waist circumference) (0.45), OSA-related symptoms (i.e., snoring, witnessed apneas, dry mouth) (0.47) and AHI. No direct effects of OSA on comorbidities, blood pressure, dyssomnia or self-rated health were observed.

Conclusion: OSA was highly prevalent and directly associated to anthropometrics and OSA-related symptoms (snoring, witnessed apneas and dry mouth in the morning). When meeting patients with hypertension, these characteristics could be used by general practitioners to identify patients who are in need of referral to a sleep clinic for OSA evaluation.

P672

Do cardiovascular signs and risk factors differ between hypertensive men and women with high versus low risk on the Berlin sleep apnoea questionnaire in a primary care setting?

A. BROSTRÖM[1], P. JOHANSSON[2], B. RIEGEL[3], P. NILSEN[4], B. FRIDLUND[5] and E. SVANBORG[1]

[1]Department of Clinical Neurophysiology, Linköping, SE, [2]Linköping University Hospital, Linköping, SE, [3]University of Pennsylvania School of Nursing, Philadelphia, US, [4]Linköping University, Linköping, SE, [5]Jönköping University, Jönköping, SE

Objective: To describe and compare (I) cardiovascular signs and risk factors associated with high and low risk for obstructive sleep apnea (OSA), as measured by the Berlin sleep apnea questionnaire (BSAQ), in men and women with hypertension, as well as (II) to compare traditional sleep-related symptoms between high and low-risk patients of both genders.

Methods: A cross sectional design, including 480 hypertensive primary care patients (diagnose by GP based on BP 140/90) was used. Clinical variables (weight, height, waist circumference, blood pressure, ECG, left ventricular hypertrophy, lipid levels, renal function), cardiovascular signs and risk factors (based on the

European Society of Cardiology's criteria), medication and co-morbidities, as well as data from self-rating scales regarding symptoms/characteristics (BSAQ), insomnia Minimal insomnia symptoms scale), excessive daytime sleepiness (ESS), depressive symptoms (Hospital anxiety and depression scale) and health (SF-12) were collected during a clinical examination.

Results: Seventy-one per cent of the men and 61% of the women had high BSAQ risk for OSA. The mean age of the whole population was 57.8 (±6.7) years, but age was not associated with risk for OSA. The majority (55%) of the population was female ($P < 0.05$), but male gender was more common in the group with high BSAQ risk ($P < 0.05$). No gender differences were found in either risk group regarding occurrence, loudness or frequency of snoring. Witnessed apneas, snoring disturbances and dyslipidaemia occurred more often among men with high BSAQ risk, whereas insomnia, tiredness, anxiety, increased waist circumference and family history of cardiovascular disease were more common among women. Blood pressure, left ventricular hypertrophy, arrhythmias or diabetes did not differ between the risk groups.

Conclusion: Knowledge about differences regarding gender-specific symptoms, cardiovascular signs and risk factors associated with high BSAQ risk might help healthcare personnel to identify hypertensive primary care patients in need of sleep respiratory recordings.

P673

Normal tension glaucoma assessment by retinal nerve fibre layer in patients with obstructive sleep apnoea/hypopnoea syndrome

M. AGUILAR ANDUJAR, M. D. GUERRERO SANCHEZ, B. PEREZ MORENILLA, M. RAMOS JIMENEZ and C. MENENDEZ DE LEON
Virgen Macarena Hospital, Seville, ES

Objectives: To compare parameters in relation with glaucoma: retinal nerve fiber layer (RFNL) thickness, optic nerve head (ONH) and measurements and macular thickness, in patients with obstructive Sleep Apnea/Hypopnea syndrome (OSAHS) in different intensity: mild and moderate and severe with Continuous Positive Airway Pressure (CPAP) and without it, in relation with control.

Methods: We include 26 patients who presenting snoring and daytime sleepiness. They were consecutively admitted for polysomnography exam for suspected OSAHS. All participants were subjected to complete ophthalmologic evaluation, including best-corrected visual acuity, intraocular pressure, slit lamp biomicroscopy, fundoscopy, optical coherence tomography to evaluate the RFNL, optic nerve head topography and macular thickness. This evaluation was performed again after a year of diagnosis.

Results: A total of 26 patients were recruited, including 16 patients with OSAHS and 10 controls. RNFL thickness was lower for the OSAHS patients than for the control, but not statistically significantly. Furthermore there were a relation between OSAHS intensity and reduction in RNFL thickness and between oxygen saturation reduction and RNFL thickness. When the ophthalmologic evaluation was done after one year of the diagnosis, patients with moderate/severe OSAHS with CPAP presented better maintenance in the RNFL thickness.

Conclusion: Compare with patients without OSAHS, RFNL thickness was lower in patients with OSAHS and it seems to be in relation with the OSAHS intensity. Furthermore, in patients with moderate-severe OSAHS appears to be a positive relation between CPAP use and maintenance of RFNL thickness. Data in this study are no statistically significant, so it is necessary to extend the sample size, but for the preliminary data, it appears that patients with moderate per cent severe and early use of CPAP have lower risk of developing glaucoma that patients with the same intensity of OSAHS and without CPAP.

Poster Session – Paediatrics Part I

P674

Sleep disorders in children with nervous system pathology, adenotonsillar hypertrophy and bronchial asthma

E. ABASHIDZE, L. NAMAZOVA-BARANOVA, O. KOZHEVNIKOVA and V. ALTUNIN

Scientific Centre of Child Health, Moscow, RU

Normal sleep is important for development of the physical and psychology health of the child. There are few researches on that topic. There are no data of the frequency, severity or etiology of sleep disturbances and related symptoms in this age group.

Objective: The objective of this study was to describe overnight polysomnographic sleep measures in children with diseases of nervous system, adenotonsillar hypertrophy and bronchial asthma.

Methods: Overnight sleep recordings were performed in 103 children (3–17 years old). All parents were asked to complete a sleep questionnaire about behavior of child during the sleep. Children were divided into the three groups: patients with diseases of nervous system ($n = 35$), with adenotonsillar hypertrophy ($n = 25$) and bronchial asthma ($n = 30$). The 13 healthy children completed control group.

Results: Compared to controls, children in all groups had significantly shorter duration of rapid eye movement sleep or REM sleep, smaller percentage of deep stages of non-rapid eye movement sleep or non-REM sleep and longer duration of superficial stages of nonREM sleep. It is revealed that children with sleep disturbance are more hyperactivity, irritable and tired during awake. In addition, this groups had higher scores on the insufficient sleep and sleep anxiety factors than children in the control group. The obtained data indicate decrease the quality of life in children with sleep disorders.

Conclusions: Children's sleep disorders are common and often harmful for development and well being. It is important to recognize all types of sleep problems. Persistent sleep problems in children may cause and exacerbate other somatic, cognitive and psychiatric problems. Therefore, more attention should be focused on sleep problems in children health care.

P675

Prevalence of sleep-disordered breathing symptoms and mouth-breathing among Japanese children: a community-based questionnaire study

Y. OKA[1], N. TAKAHASHI[2], F. HORIUCHI[1], Y. KAWASAKI[1], S. TANNO[1], N. TAKATA[1] and T. TANIGAWA[1]

[1]Ehime University Graduate School of Medicine, Ehime, JP, [2]Iyo Dental Association, Ehime, JP

Objectives: To describe the prevalence of sleep disordered breathing (SDB) symptoms among the community children in Japan and to elucidate its correlation with mouth breathing, that is present in SDB patients.

Methods: A questionnaire was distributed through nursery school, kindergarten, and primary school of the area and parental report of snoring, apnea, or mouth breathing were collected. Responses from 5134 community children (0–12 years of age) were included in the analysis.

Results: The prevalence of witnessed apnea (more than two days a week) was 1.0%. Habitual snoring (more than 2 days per week) was seen in 10.8% and snoring 'Always' (more than 5 days per week) was seen in 1.9% of children. Of 26.2% of children were mouth-breathers. Of the children with witnessed sleep apnea, 63.5% were mouth-breathers. Mouth breathing was significantly more prevalent (47.8%) among children with habitual snoring than in children without habitual snoring (23.6%).

Conclusion: Prevalence of apnea and snoring from our study was mostly consistent with the previous Western reports using questionnaires. As chronic snoring is considered abnormal in a pediatric population, children with signs and symptoms of SDB need to be recognized as soon as possible to receive an early treatment.

P676

Examining the relationship between sleep quality and pulmonary function in children and young adults with respiratory disorders

C. S. SENDON, J. F. CHOCANO and H. AHMAD

Eastern Virginia Medical School, Norfolk, US

Objectives: Adequate sleep is important for children; they require it for proper growth and development. Lack of sleep or interrupted sleep can have profound negative consequences on quality of life. Significant differences in sleep quality were described in adult patients with Asthma and Cystic Fibrosis (CF) but have not been evaluated in children.

Methods: This study is a single institution, prospective, observational study with 61 subjects between 10 and 25 years of age classified in two groups: Cystic fibrosis and Asthma. Thirty-one patients were studied in the Asthma group and 30 patients in the Cystic fibrosis. Patients with recent acute illness or any sleep disorders were excluded. Patients were provided an informed consent. Pulmonary function test (Spirometry) was administered. Demographic records such as age, race, height, weight, and BMI percentile were included in the database. Pittsburgh Sleep Quality Index (PSQI) questionnaire (seven components) were used for evaluate sleep quality, poor sleep quality is defined by a PSQI score >5.

Results: Mean PSQI scores were 5.51 ± 4.49 for Asthma patients, 3.36 ± 2.44 for CF patients, and 2.7 ± 1.7 for the normal control from the literature. Chi square tests showed these scores were not significantly different for Asthma and CF patients ($P = 0.270$). Significant differences between Asthma and CF patients were found for sleep disturbance ($P = 0.040$), use of sleep medication ($P = 0.011$), and sleep efficiency ($P = 0.012$). Asthma patients scored higher on the PSQI than CF patients indicating poorer sleep quality. Mean FEV1 was 86.77 ± 14.78% for Asthma patients and 79.47 ± 24.52% for CF patients. The relationship between lung function and sleep quality was not statistically significant for Asthma ($P = 0.079$) or CF patients ($P = 0.425$).

Conclusions: Asthma and CF patients in this study have worse sleep quality than the literature control patients. Asthma patients were found to have worse sleep quality than CF patients. There was no relationship between sleep quality and lung function. Clinicians taking care of patients with Asthma and Cystic Fibrosis must perform a more detailed sleep history.

P677

Influence of bronchopulmonary dysplasia and its severity on apnoea syndrome structure

N. PETROVA[1], D. IVANOV[1], Y. PETRENKO[1], O. STEPANOVA[1], N. TRESKINA[1] and I. DOBRODEEVA[2]
[1]Almazov Federal Heart, Blood and Endocrinology Centre, St. Petersburg, RU, [2]Children City Hospital 1, St. Petersburg, RU

Objective: Apnoea is a common breathing pattern in premature infants especially those with bronchopulmonary dysplasia (BPD). Our objective was to describe incidence of apnoea, including episodes of different nature, in infants with BPD at consecutive ages, and evaluate the impact of BPD severity on apnoea syndrome structure.

Methods: We performed respiratory monitoring on 25 premature infants with BPD (one case of severe, eight of moderate, and 16 of mild BPD) and 25 non-BPD preterms comparable in gestational age (26–30 weeks). Infants were examined 1–3 times at ages of <29 days, 29–50 days, more than 50 days.

Results: Similar number of infants with and without BPD had apnoea before 50 days of life. There was a tendency to decrease in apnoea incidence from first to second age interval. Ten of 20 infants with BPD examined after 50th day had apnoea, while most of non-BPD prematures where already discharged. In the first age interval less infants in whom BPD was diagnosed on the 28th day, compared to those without BPD, had central apnoea (CA) (7/13 and 22/26, respectively, $P < 0.05$), rather more demonstrated obstructive apnoea (OA) (8/13 and 10/26, respectively). At 29–50 days incidence of different types of apnoea did not vary among groups, CA prevailed. Number of BPD infants demonstrating OA dropped from 1st to 2d age interval [8/13 and 1/13, 95% confidence interval 0.23(0.06;0.40)]. After the 50th day infants with BPD demonstrated mostly CA. A whole number of 717 apnoea was revealed, 212 in BPD and 505 in non-BPD group. Infants with mild BPD had similar central apnoea (CA)/obstructive apnoea (OA)/mixed apnoea (MA) ratio in all age intervals (61%/18%21% in the first, 79%/0/21% in the second, 100%/0/0 in the third age interval) when compared to non-BPD infants (66%/18%/15%, 78%/4%/18%, 2CA/0/3MA, respectively). Infants with moderate to severe BPD tended to have more OA compared to other groups (0/1 OA/0, 50%/32%/18%, 72%/22%/6%, respectively), with statistical significance at the age of 29–50 days ($P < 0.001$ compared to mild BPD group, $P < 0.05$ – to non-BPD group). Main neurologic abnormalities frequency appeared not to differ among groups.

Conclusion: During the first month of age OA are common in infants both with and without BPD. Later, OA persist in some moderate to severe BPD infants while infants with mild illness do not differ from healthy group where abnormalities of breathing control are mostly central in origin.

P678

Impact of adenoidectomy and/or tonsillectomy on the link between cardiac vagal activity and delta sleep EEG during sleep in children suffering from sleep apnoea-hypopnoea syndrome

I. CHIMANUKA[1], J.-P. LANQUART[1], S. SCAILLET[2], J. GROSWASSER[2] and F. JURYSTA[1]
[1]Academic Erasmus Hospital, Brussels, BE, [2]Queen Fabiola Children's University Hospital, Brussels, BE

Objectives: We tested the hypothesis that adenoidectomy and/or tonsillectomy (A/T) improves the link between cardiac vagal component of heart rate variability (normalized High Frequency of HRV - HFnu-) and delta sleep that is related to deep sleep in children suffering from obstructive sleep apnea syndrome (OSAS).

Methods: Sleep ECG and EEG of 7 children aged between 13 and 35 months were recorded 5 ± 3 weeks before and 10 ± 3 weeks after A/T. Sleep parameters of the entire night as well as the cardiac vagal components of HRV (HFnu and LF/HF) and sleep parameters of the first three NREM-REM cycles were compared before and after surgery. Without 3 sleep cycles, parameters were obtained for the whole nocturnal sleep. HRV variables during REM and wake were also compared to NREM sleep. A coherence analysis was applied between HFnu and delta power. T-Test for paired samples was applied to compare variables before and after A/T. Results were expressed as mean ± standard deviation.

Results: Surgery decreased the obstructive sleep apnea index from 33.0 ± 15.1 to 2.8 ± 1.36 evts/h ($P < 0.01$). After A/T, night sleep parameters as time in bed, sleep latency, sleep period time, total sleep time, sleep efficiency as well as each sleep stage duration (stage 1–4, REM and wake) did not change in comparison to children before surgery. Across sleep stages, mean RR-interval duration, HFnu and LF/HF were similar between groups. Nevertheless, RRI decreased from NREM to REM in non-operated children ($P < 0.05$) while this difference was not found after surgery. For both groups of patients, HFnu decreased from NREM to REM ($P < 0.01$ for both groups) and wake ($P < 0.05$ and <0.01 for non-operated and operated children, respectively) and LF/HF increased from NREM to REM ($P < 0.01$ for untreated children and $P < 0.05$ for treated children). The frequency of the cross-spectrum between HFnu and delta as well as gain, phase shift or delay between occurrences of modifications in HFnu and delta signals were comparable between groups. Coherence values decreased after A/T (0.82 ± 0.18 versus 0.57 ± 0.16, $P = 0.003$ for before versus after surgery).

Conclusion: In our sample, 10 weeks after surgery, adenoidectomy and/or tonsillectomy in children suffering from moderate to severe OSAS decreased changes in RRI across sleep stages and decreased the tightness of the link between cardiac vagal influence and delta sleep despite the absence of SAHS.

P679

Relationship between snoring with sleep behavioural and movement disturbance in children

A. MOZAFARI, M. VAKIL ALIABADI and H. GHASEMI
Islamic Azad University, Tehran, IR

Background: Sleep disturbance is one of the most important subjects in pediatric medicine which its prevalence is 5% in society and have many important effects on child social function and quality of life. Sleep disturbance is seen in different kind of sign and symptom such as night terror, leg movement, walking and go to bed lately. Snoring prevalence is 12% in children that is one of the important reasons of sleep disturbance.

Methods: We have chosen 100 children with snoring as study group and 100 healthy children as control group. Their parents fill the questions about snoring and 22 item of sleep behavioural and movement disturbance (SBMD) like sleep walking, sleep talking, night terror. Pearson correlation coefficient was used to measure the strength of association between continuous variables. For analysis of qualitative parameters, we use from chi-square and if it was required, checked by fisher's exact test.

Result: The mean age of children was 6/8 years, mean height 116 cm, 41% were overweight or fatty and 52% were male. There were significant correlation among SBMD in case and control (8.54

versus 5.64 item, $P < 0.001$), snoring and adenotonsilar hypertrophy ($P < 0.001$), apnea and SBMD in case group ($P < 0.001$), but no relationship among snoring and sex ($P < 0.001$), snoring and age ($P < 0.001$) and severity of snoring with SBMD in case group.

Conclusion: This study have showed the importance of sleep medicine in children we can prevent children from many sleep disturbance with on time diagnosis of snoring. It is important that we educated sleep subject to parents for helping to achieve better sleep in children.

P680

Treatment of obstructive sleep apnoea as one of the features of the ultra-rare ROHHAD syndrome

A. GALEWICZ-ZIELINSKA and R. PODSKARBI-FAYETTE
The Children's Memorial Health Institute, Warsaw, PL

We present a case of a 9-year old boy with ROHHAD (Rapid – Onset Obesity with Hypothalamic Dysfunction, Hypoventilation and Autonomic Dysregulation Presenting in Childhood) syndrome, an ultra-rare syndrome, probably of genetic origin. Up to date only 30 cases in the world were described. Our patient is the only case of ROHHAD syndrome documented in Poland. Respiratory manifestations as well as other clinical and behavioral manifestations of the syndrome are presented and discussed. Patient underwent a thorough diagnostic process featuring polysomnographic trials backed with nasal endoscopy as well as imaging studies such as CT scans, MRIs and cephalometry. Patient's history revealed an adenoidectomy procedure at the age of six. Polysomnography results revealed a mixed-type sleep apnea with an obstructive component of 30%. Patient has been treated with a bilevel positive airway pressure mask ventilation since he was seven. Nasal endoscopy did not show any obstruction within the nose and the nasopharynx. Tonsillar hypertrophy, grade II, was diagnosed and polysomnographic results revealed an increase in overall obstruction in our patient. Tonsillectomy was performed and follow-up polysomnographic tests showed improvement in air passage. Quality of life was assessed one month after surgery showing overall improvement. Patient remains under ambulatory care of our Clinic.

P681

Nocturnal frontal lobe epilepsy is often misdiagnosed as sleep disorders in children: a case series

S. MIANO[1] and R. PERAITA-ADRADOS[2]
[1]*Sapienza University, Rome, IT,* [2]*University Hospital Gregorio Marañón, Madrid, ES*

Objectives: We present a series of children and adolescents referred with sleep disorders and/or paroxysmal events while sleeping who underwent a video-polysomnographic recording, with an extended electroencephalographic montage (Video-EEG-PSG) for suspected nocturnal seizures, sleep-disordered breathing, parasomnias, or other sleep disorders.

Methods: Patients were recruited between January and December 2010. The inclusion criterion was that the patients have their first Video-EEG-PSG recording in our laboratory. Data were retrospectely collected from the general sleep laboratory database of patients affected by sleep disorders who were diagnosed at the Sleep and Epilepsy Unit of Gregorio Marañón University Hospital in Madrid.

Results: Twenty-four out of 190 children were diagnosed with NFLE (group 1); while 166 had other sleep disorders (group 2). Among children diagnosed with NFLE, 7 were referred for sleep-disordered breathing, seven for parasomnias (five for somnambulism, one for sleep terrors, and one for sleep talking), two for insomnia, two for hypersomnia, and one for periodic limb movements, while five were referred for epilepsy. Sleep-disordered breathing was diagnosed as a comorbid condition in four children in group 1. There were no gender differences between the groups. In group 1 perinatal history was normal in most cases (21 out of 24), and a familiar history of epilepsy was found in six cases (NFLE in 2, maternal inheritance in three cases), sleep-disordered breathing or respiratory allergy in four cases, excessive daytime sleepiness and Kleine-Levin syndrome in 1, maternal depression in 1, and a mother had tics. Standard EEG was normal in most cases (21 out of 24). Interictal EEG showed epileptic discharges in 5 cases, while ictal EEG was expressed by a rhythmic activity preceded by an arousal (K complex) and/or a short background desynchronization after a K complex, superimposed movement artifacts, and autonomic changes such as tachycardia and tachypnea. All seizures were followed by stage shifts and/or a postural change and, more rarely, by short awakenings.

Conclusion: We found a high percentage of children with NFLE, often misdiagnose and associated with sleep disruption and comorbidity with other sleep disorders. We can hypothesize that epileptic seizures provoke nocturnal sleep disruption with high fragmentation, and the presence of other sleep disorders may be a trigger for nocturnal seizures.

P682

Childhood parasomnias – a developmental sleep disorder?

S. NEVSIMALOVA[1], I. PRIHODOVA[1], D. KEMLINK[1] and J. SKIBOVA[2]
[1]*Charles University, Prague, CZ,* [2]*Institute of Clinical and Experimental Medicine, Prague, CZ*

Objectives: Childhood parasomnias are believed to be a benign disorder due to immaturity of some neural circuits, synapses and receptors. The aim of our study was to find out a possible connection with further neurological developmental disorders of childhood to verify this hypothesis.

Methods: Seventy-two children (mean age 9.9 ± 5.0 years, 47 boys) were clinically examined and 88 nocturnal v-PSG and 22 v-EEG recordings were evaluated. The most frequent diagnosis were: sleepwalking in 24 children, confusional arousal in 21, sleep terror in 8, groaning and enuresis each in 7, non-specific arousal disorder in 4 patients, and REM-related parasomnia in only one child. For statistical evaluation the two-sample t-test and chi-square test were used.

Results: Perinatal risk history was found in 36% of the cohort. Developmental disorders were diagnosed in 30 children (41.5%), more frequently in combinations with: atention-hyperactivity disorder (30.5%), dyslexia and dysgraphia (13.9%), developmental dysphasia (9.7%), mild motor and/or intellectual dysfunction (6.9%). Abnormal movements in sleep, some of them also regarded as developmental, were diagnosed in 37 children (51.4%): bruxism (34.7%), periodic leg movements (25.0%), rhythmic movement disorder as well as restless legs syndrome (4.2%). Sleep-related breathing disorders were found in 29 patients (40.3%) – rhonchopathy (29.2%) and/or sleep apnea (11.1%). Association with REM parasomnias was revealed in only 8.3% patients, and with epilepsy in 4.2% cases. Only 16.8% had no comorbidity. Most of children (60%) showed 2 or 3, exceptionally up to 5 comorbidities. No statistical differences were found in evaluating their perinatal risk history or in the type of affection. Children, in whom no parasomnia was found in close relatives, had a mild but non-significant earler onset of the disease (4.4 ± 4.0 years) compared to children with a positive familial history (6.3 ± 4.3 years).

Conclusion: Parasomnias are regarded as a common and highly heritable disorder. However, our findings showed a considerable participation of perinatal risk factors and developmental disorder comorbidities that may have an etiological role to play. This can also explain why so many childhood arousal parasomnias are benign and disappear before adulthood, similarly as most of the other developmental disorders.

P683

Association of sleep patterns with emotional and behavioural adjustment in term and pre-term born children

S. LEMOLA[1], S. BRAND[2], P. HAGMANN-VON ARX[1], P. WEBER[3], E. HOLSBOER-TRACHSLER[2] and A. GROB[1]

[1]University of Basel, Basel, CH, [2]Psychiatric Clinics of University of Basel, Basel, CH, [3]University Children's Hospital, Basel, CH

The aim of the study was to assess differences in sleep patterns in term and preterm born children and their relation to cognitive and socioemotional development. We hypothesized that preterm children show lower scores in cognitive tests, have more socioemotional problems, and lower sleep efficiency than term born children. We also expected that sleep efficiency is more strongly related to socioemotional development among preterm than among term children. A sample of 50 preterm (25th–32nd gestational week) and 50 matched term born children between 6 and 10 years participated on the study. Sleep patterns were assessed by one night sleep-EEG assessment at the families' homes and parent report questionnaires. Cognitive development was assessed by subtests of the Wechsler Intelligence Scale for Children (WISC-IV), the Reynolds Intellectual Assessment Scales (RIAS), and the Intelligence and Developmental Scales (IDS). Parents reported on the children's socioemotional development by use of the Strengths and Difficulties Questionnaire (SDQ).

P684

Distribution and periodicity of leg movements during sleep in children with restless legs syndrome

W. C. M ARENDS-DERKS and A. W DE WEERD

SEIN Zwolle-Groningen, Zwolle, NL

Objectives: In patients with Restless Legs Syndrome (RLS), polysomnography (PSG) reveals excessive (periodic or at random) leg movements. In adult patients, studies have shown characteristic values in parameters of limb movements during sleep. These measures are the periodicity index (PI), the duration of the inter leg movement intervals and the time distribution over the night. The aim of the study is to describe the same parameters in children with RLS and to compare the results to those in adults.

Methods: $N = 11$ patients (Three females; median age: 8 years, range 2–16) were included if they showed leg movements with a index of at least 5/h of sleep. Leg movements were measured and assessed according to the AASM rules (2007); recording and scoring of the accompanying video PSG was done using the same rules.

Results: In contrast to the mean interval duration of 24.3 s, which we found previously in adults, no clear peak value was detected in children. The distribution of these intervals is mainly in the range of 10–20 s. During the night periodic leg movements in sleep (PLMS) have their highest prevalence in the beginning of the night with a peak in the 2 h of NREM sleep. Isolated leg movements (LMS) are more evenly spread over the whole night, with a small peak during NonREM sleep in the 7th hour of sleep. The periodicity index (PI) had a value of 0.64 in REM sleep and of 0.69 when REM and NREMsleep are taken together. The distribution over time and the PI values are approximately similar to those found in adults.

Conclusions: In a small group of patients with RLS in childhood we only partly found the characteristics in leg movements during sleep as can be seen in adult patients with RLS.

P685

Sleep, stress and psychological problems in internally displaced children

N. DARCHIA[1], N. LORTKIPANIDZE[1], M. ELIOZISHVILI[1], S. MAMUKADZE[2] and I. GVILIA[1]

[1]Ilia State University, Tbilisi, GE, [2]Tbilisi State University, Tbilisi, GE

Most evidence suggests that sleep problems in children are significant public health concern and may be linked with a variety of subsequent psycho-emotional difficulties. This work was aimed to evaluate sleep quality and associated factors in children of internally displaced (ID) families after 9 months from escaping from Shida Kartli, Georgia because of the war conflict, and to compare to the sleep of children of families from general population. We addressed the question: how much the displacement may affect sleep and psychological stability of children during their early maturation. Thirty-five children (9.5–14 years old) were studied in each group. Children completed Epworth sleepiness scale, Child Depression Inventory (CDI), Wechsler Intelligence Scale for Children-Revised (WISC-R), learning test, and were interviewed regarding the main sleep-wake characteristics. General information about children's sleep behavior, data on academic excellence and the relationship level with schoolmates was collected from parents. In addition, they were asked to fill Children's Sleep-Wake Scale (CSWS) – a 26-item measure of the following sleep quality domains: going to bed, falling asleep, maintaining sleep, reinitiating sleep, returning to wakefulness. Psychologist evaluated children's psychological status. Statistical analyses were performed using SPSS 16. Total sleep time was nearly identical in ID and non-ID children. Significant difference between sleep time on week and weekend nights was found in both groups ($P < 0.01$). Sleep onset latency was higher in ID children ($P < 0.01$). Non-ID parents reported better sleep hygiene and quality compared to the other group. Groups were statistically different on all CSWS dimensions, except returning to wakefulness. The most significant difference was found for falling asleep ($P < 0.01$). Overall sleep quality score was higher in non-ID children ($P < 0.01$). The significant difference in the signs of depression in ID and non-ID group was also revealed (9.6 versus 5.3). Intelligence scale score was small in both groups, with significant difference between groups. The learning ability of ID children was not affected by stress. Socio-economic status was significantly high in non ID families. Sleep quality was correlated with academic excellence in both group, and with depression in ID children. Findings of this study indicate that stress and displacement are risk factors for developing psychological problems and sleep disturbances in children.

Research supported by Georgian National Science Foundation Research Grant GNSF/ST07/6–237.

P686

Normative data on total sleep time perceived by adolescents

D. LÉGER[1], F. BECK[2], J. B. RICHARD[2] and E. GODEAU[3]
[1]Université Paris Descartes, Paris, FR, [2]Universite Paris Descartes/CNRS UMR 8211/Inserm U988/EHESS, Saint Denis, FR, [3]University Paul Sabatier, Toulouse, FR

There is little normative data on total sleep time (TST) available in a representative group of teen-agers.

Purpose: To explore perceived total sleep time on schooldays (TSTS) and non schooldays (TSTN) and the prevalence of insomnia among a nationally representative sample of teenagers.

Methods: Data from 9251 children aged 11–15 years-old, 50.7% of which were boys, as part of the cross-national study 2011 HBSC were analyzed. Self-completion questionnaires were administered in classrooms. An estimate of TSTS and TSTN (week-ends and vacations) was calculated based on specifically designed sleep logs. Children who reported sleeping 7 h or less per night were considered as short sleepers.

Results: TST significantly decrases between 11 yo and 15 yo, both during the schooldays (9 h 26 min versus 7 h 55 min; $P < 0.001$) and at a lesser extent during
week-ends (10 h 17 min versus 9 h 44 min; $P < 0.001$). Too short sleep was reported by 2.6% of the 11 yo versus 24.6% of the 15 yo ($P < 0.001$).

Conclusion: Despite the obvious need for sleep in adolescence, TST deeply decreases with age among children from 11 to 15 yo which may promote significant sleep debt increasing with age.

P687

Early development of sleep and circadian rhythms: child-sleep- birth cohort

O. A. SAARENPÄÄ-HEIKKILÄ[1], E. J. PAAVONEN[2], A. KYLLIÄINEN[1], P. PÖLKKI[3], T. STENBERG[4] and T. PAUNIO[5]
[1]Tampere University Hospital, Tampere, FI, [2]National Institute of Health and Welfare, Helsinki, FI, [3]University of Eastern Finland, Kuopio, FI, [4]University of Helsinki, Helsinki, FI, [5]National Institute of Health and Welfare, Tampere, FI

In early childhood, regulation of the development of sleep-wake states is under rigorous neural control, but environmental factors can affect it as documented in several cross-sectional studies. No prior studies have attempted to construct a comprehensive developmental model taking into account the genetic, biological, and environmental factors simultaneously.

Methods: The CHILD-SLEEP study recruits systematically 3000 babies during 2011–2012 from Tampere, Finland. Parental questionnaires are collected prenatally, at 3, 8 and 24 months of age, with a focus on development of sleep, emotions, and family environment. A subsample of 520 infants is randomly assigned into sleep registration groups (ACG and PSG + ACG). For the genetic analyses, blood and saliva samples are collected. A protocol for prevention and intervention of children's sleeping difficulties will be developed and implemented.

Results: The sample collection was initiated in April 2011. By March 2012, 1487 women were contacted during their visits to prenatal maternity clinics, and 1088 families had given their permission for the study. The mean age of the mothers and fathers was 30.5 years (range 17–46) and 32.4 years (range 10–57), respectively. Blood samples from 893 babies, 883 mothers and 773 fathers, and saliva samples from 48 mothers and 121 fathers were collected. PSG + ACG and ACG registrations were completed for 55 and 182 babies, 227 families participated in the preventive program for sleep disturbances, and 29 families took part in a clinical study on nightwaking. The group of snoring babies and their controls (5 per cent 6) was studied by the clinical study and PSG.

Conclusions: With systematic data collection, the project will reveal factors contributing to development of sleep and circadian rhythms, investigate trajectories of disturbed sleep, and study the long-term consequences of early sleeping difficulties. Since sleep disturbances of infants and adolescents are frequent in Finland, development and validation of a protocol for prevention of children's sleeping difficulties is likely to have a high impact on health and wellbeing of the Finnish population.

P688

Melatonin treatment in autism spectrum disorders (ASD): preliminary results

M. BOUVIER, B. CLAUSTRAT and P. FRANCO
Hospices civils de Lyon, Bron, FR

Objective: ASD patients experience more sleep disorders (SD) than the general population. Literature supports the existence of a beneficial effect of melatonin (M) treatment on SD in these patients, with few and minor side effects. However, studies with methodological limits are available.

Methods: M treatment (fast-release capsules, 2 mg) was administered for 30 days (D15–D45). Parents filled the Children's Sleep Habits Questionnaire and Insomnia Severity Index. M efficiency was evaluated by the parents with an analogical scale. Sleep was evaluated with actimetry and polysomnography (PSG) before and at the end of treatment. The 24 h M secretion was determined by measurement of 6-sulfatoxymelatonin (aMT6S) in 4 h urine samples before and after (D60) treatment. Three patients completed the protocol at time of the abstract.

Results: Patient 1 (3 years boy) went to bed and wake up earlier after treatment. Sleep efficiency was improved and sleep latency was decreased. Parents reported poor M efficiency (2/9) and side effects such as nocturnal laughs and excitation. Consequently, M dose was decreased to 0.5 mg. M secretion showed a decrease in the 20–24 h span before treatment and a major decrease in the 24–8 h span after treatment, suggesting a feed-back on the endogenous M secretion. Patient 2 (6 years boy) with Asperger syndrome presented nocturnal awakenings and upper airway resistance syndrome on PSG with normal ENT exam. Sleep efficiency was improved during treatment. Parents reported a poor M effect (3/9). M secretion profiles were normal before and during treatment. The child complained about abdominal pain. Gastro-oesoghageal reflux was evaluated and treated. Patient 3 (5 years girl) was suffering from epilepsy. M secretion showed a decrease in the 20–24 h span before treatment. Sleep efficiency was not modified by treatment. Any improvement was reported by the parents. Topiramate was related to the presence of periodic leg movements on PSG and was changed to Lamotrigine.

Conclusion: These preliminary results showed the complexity of SD in this heterogeneous syndrome. Two patients showed a decreased M secretion in the 20–24 h span, but only one had a transitory positive effect of M treatment. There were discordances between subjective and objective data, between actimetry and PSG results in particular for sleep fragmentation. All the children had a decrease of REM sleep with M. Long-term follow-up is required since M could potentially have an impact on mental health functions

P689

Analysis of EEG asymmetry before and after sleep in attention deficit hyperactivity disorder boys

M. A. GINGRAS[1], É. CHEVRIER[1], C. M. J. BRAUN[2] and R. GODBOUT[1]

[1]Hôpital Rivière-des-Prairies, Montreal, CA, [2]Université du Québec, Montreal, CA

Objectives: EEG activity before and after a night of sleep follows a normal trend of decreased power in attention deficit hyperactivity disorder (ADHD) boys (Gingras et al., ESRS 2010). ADHD adults are reported to show an atypical lateralization of Alpha and Beta wake EEG activity but this has not been evaluated in ADHD children yet. The aim of the present study was to evaluate wake EEG lateralization in ADHD boys.

Methods: Twelve boys diagnosed with ADHD but no comorbidity (age: 11.0 ± 1.2) and 15 healthy boys (age: 10.7 ± 1.6) were recorded in a sleep laboratory for two consecutive nights using a 20-electrode EEG montage. Wake EEG was recorded at 256 Hz for 5 min with eyes opened and 5 min with eyes closed, 10–15 min before lights out in the evening and after lights on in the morning. Spectral analysis of wake EEG was performed on 15 four-second artifact free epochs. Data from night 2 was submitted to Fast Fourier transform with a resolution of 0.25 Hz and cosine window smoothing. Four frequency bands were created: Delta (0.75–3.75 Hz), Theta (4.0–7.75 Hz), Alpha (8.0–12.75 Hz) and Beta (13.0–30 Hz) and Spectral data was log-transformed. A lateralization coefficient was calculated using [(Right - Left) per cent Right + Left) × 100]. EEG lateralization coefficients were compared using a 2 Groups (ADHD, Controls) × 2 Moments (evening, morning) × 4 Frequency Bands (Delta, Theta, Alpha, Beta) ANOVAs for 10 pairs of homologous electrodes, for Eyes Closed and Eyes Opened condition separately. Significant results were followed by LSD *post hoc* tests.

Results: Significant Moments × Frequency Bands interaction: Beta activity showed a right lateralization in the prefrontal area in the evening and a left lateralization in the morning (Eyes Opened condition only). Significant Groups × Frequency Bands interactions: the right lateralization of Beta activity over prefrontal, frontal and temporo-parietal areas was stronger in ADHD boys than control, in both Eyes Closed and Eyes Opened conditions. Significant Groups × Moment × Frequency Bands interactions: ADHD boys showed a stronger morning right lateralization of Alpha activity over the parietal area than controls (Eyes Opened condition only).

Conclusion: The present results support previous observations of impaired interhemispheric functional connectivity in ADHD boys. These results are also compatible with a neurodevelopmental continuity of this phenomenon from childhood to adulthood.

This research was supported by the Fonds de la recherche en santé du Québec and the Canadian Institutes for Health Research.

P690

Identifying attention-deficit hyperactivity disorder in paediatric restless legs syndrome

M. MERINO-ANDREU, O. TAPIA-CANELAS, J. LEDEZMA-SORIA and A. MARTINEZ-BERMEJO

University Hospital La Paz, Madrid, SN

Objectives: Restless Legs Syndrome (RLS) is a chronic neurological disorder characterized by an urge to move the legs, usually accompanied by uncomfortable and unpleasant leg sensations, symptoms worse in the evening or at night and they are partially relieved by movement and symptoms worse when lying or sitting. Other associated features commonly found in RLS include sleep disturbance and periodic limb movements (PLM). Paediatric RLS has a prevalence of 1.9% in school aged children and 2% in adolescents and much more frequent in children with Attention Deficit Hyperactivity Disorder (ADHD). ADHD is more likely to be diagnosed in RLS subjects and their symptoms are commonly confused. The aim of the study is to define early manifestations that can identify ADHD in RLS patients.

Methods: We have evaluated 32 subjects diagnosed of definitive RLS, divided in two groups: with or without ADHD criteria (RA+ and RA-). Various psychopathologies, severity of RLS symptoms, nocturnal polysomnography and serum ferritin levels were assessed. Diagnosis of RLS was made according to the International RLS Group rules and ADHD was identified using DSM-IV R criteria.

Results: ADHD was found in 17 (53%) subjects, with similar age distribution and male predominance in both groups. Growing pains, diurnal and nocturnal restless and RLS severity score (measured with RLS severity scale) were higher in RA+ subjects when compared with RA- subjects. In our study, polysomnographic findings were similar in both groups.

Conclusion: Our results show that, though they are commonly found as two comorbid conditions, there are clinical features that can distinguish ADHD in paediatric RLS population. We suggest that patients with RLS should be evaluated for ADHD and vice versa.

P691

Clinical characteristics and prevalence of interictal paroxysmal activity in a paediatric sleep laboratory

C. S. SENDON and J. F. CHOCANO

Children Hospital of Kings Daughters/Eastern Virginia Medical School, Norfolk, US

Objectives: Sleep and sleep breathing disorders may trigger Interictal Paroxysmal Activity (IPA) and may exacerbate preexisting seizures. We evaluated the presence of IPA in polysomnograms (PSG) performed in children suspected to have obstructive sleep apnea syndrome (OSAS). Interictal EEG abnormalities can produce transient cognitive impairment and interfere with memory consolidation.

Methods: We identified the patients with IPA through a retrospective review of PSG performed during 2006 in children <20 years of age. Spike and sharp waves were considered as representing IPA. All PSG studies included ≥8 EEG channels, including central, temporal and occipital leads. Formal electroencephalograms (EEG) performed in some of subjects were also reviewed. Height, Weight, BMI, Apnea Hypopnea Index (AHI). History of seizures, presence of neurological abnormalities and formal EEG were evaluated

Results: Two hundred twenty-four PSG were reviewed, 177 children had OSAS and 47 had a normal AHI, 22 subjects showed IPA in their PSG. Out of 22 subjects, 14 subjects (64%) had OSAS (55% was mild, 4.5% moderate and 4.5% severe), nine subjects (41%) had history of seizures, eight (36%) presented an abnormal formal EEG, and 12 subjects (55%) presented neurological abnormalities. In the group of 14 children with IPA and OSAS: seven subjects (50%) presented neurological abnormalities; five subjects (36%) presented abnormal formal EEG; five subjects (36%) had history of seizures. In the group of eight children with IPA without OSAS: five subjects (63%) presented neurological abnormalities; three subjects (38%) presented abnormal formal EEG; four subjects (50%) had history of seizures.

Conclusions: Interictal Paroxysmal Activity (IPA) was present in 10% of PSG performed in children suspected to have OSAS; IPA was present in 7.9% of children with OSAS and in 17% of children without OSAS, in the last group 7/8 (88%) had history of either seizure activity, neurological abnormalities or abnormal formal EEG, 1/8 (12%) had no history of seizure activity, neurological abnormalities or abnormal formal EEG. Neurological abnormalities, history of seizures, abnormal formal EEG and OSAS were highly associated with IPA. Appropriate EEG expertise by the sleep technologist and specialist is important to recognize and evaluate children with Interictal Paroxysmal Activity.

P692

Parasomnias in attention-deficit hyperactivity disorder

C. SORIA-BRETONES, M. GARCÍA-BELLÓN and M. A. GARCÍA-JIMÉNEZ

Hospital Virgen de la Luz, Cuenca, ES

Objectives: Our aim is to describe the prevalence of Restless Legs Syndrome (RLS) and other parasomnias in children diagnosed of Attention-Deficit Hyperactivity Disorder (ADHD) in our city, provided the high co-morbidity we find in our clinical practice.

Methods: Observational descriptive cross-sectional study in ADHD patients referred to our service for EEG since 2007 ($n = 65$).

Measures: Child's Sleep Habits Questionnaire and questionnaire based on Owen's test for RLS and Periodic Leg Movements (PLM), answered by parents by phone or live interviews.

International RLS Study Group criteria for RLS (2002) were followed.

Results: Sample age: 4–17 years old (9.9 ± 3.05).

RLS prevalence: global 18.5%; criteria of probable RLS criteria:10.8%; definitive RLS: 7.7%. Male predominance (91.7%). Compared to subjects without RLS, we find higher prevalence of bruxism (62.9%), fear of sleeping alone (62.8%) and nightmare arousals (57.1%).

Sleep disorders: 24.1% have insomnia symptoms. Some parasomnia in 20.5% of subjects, which in order of prevalence are: somniloquy, nightmares, enuresis, bruxism and sleepwalking.

Sleep habits: with increasing age, reduction of nocturnal sleep hours and increase of daytime tiredness, meaning insufficient sleep and a consequent sleep debt. 27.8% show excessive daytime sleepiness (EDS).

Conclusion: 1. RLS prevalence in ADHD turns out to be higher than expected. This is probably due to common symptoms in both disorders, which can be confused.

2. Other parasomnias and sleep disorders show similar prevalence in children with and without ADHD, in the same age range.

3. As a finding, we report progressively insufficient sleep hours in increasing ages.

This study has been possible thanks to a FISCAM grant (Foundation for Investigation of Castilla la Mancha Health System

P693

The effects of dietary sugar intake on prepubescent girls's sleep stages: a preliminary study

E. WATSON[1], S. BANKS[1], G. RIGNEY[1], M. KOHLER[1] and S. BLUNDEN[2]

[1]University of South Australia, Adelaide, AU, [2]Central Queensland University, Adelaide, AU

Objectives: This study aimed to determine whether a high sugar diet effects sleep quality and sleep architecture across the night in prepubescent girls.

Methods: Nine healthy female participants aged 10–12 years (M = 11 years 8.4 months, SD = ± 8.6 months) were recruited from four schools in Adelaide. Participants were prepubescent with a Tanner stage of one or two, with the exception of one who had a Tanner stage of four. All participants attended the sleep centre for two separate nights. On one night they consumed the standard diet (mean amount of sugar: 42.4 g ±3.18 g) and on the other night they had a sugar diet (mean amount of sugar: 74.7 g ±10.0 g); all food intake was controlled and recorded. Participants were entertained with age appropriate games and movies before going to bed at 9 pm. Sleep quality and sleep architecture was determined by polysomnography. To compare sleep architecture changes across the night, each participant's sleep was divided into three sections (first third, second third, and final third). Paired samples *t*-tests were used to examine the difference in sleep between the two diets and due to the differences in sugar consumed, a Pearson Correlation was completed between sugar and the significant findings.

Results: During the first third of the night slow wave sleep was significantly greater in the sugar diet (72% versus 51%, $t_7 = -3.53$, $P = 0.01$), with a trend towards better sleep efficiency ($t_7 = -1.8$, $P = 0.06$). During the second third of the night there was significantly less slow wave sleep (18% versus 28%, $t_7 = 2.60$, $P = 0.02$) and significantly greater REM sleep (19% versus 16%, $t_7 = -2.52$, $P = 0.02$) in the sugar diet, while in the final third, stage one and two sleep, and sleep efficiency were significantly less in the high sugar diet (3% versus 3.5%, $t_7 = 1.97$, $P = 0.05$; 43% versus 49%, $t_7 = 2.04$, $P = 0.04$; $t_7 = 1.93$, $P = 0.05$, respectively). When looking at sleep across the entire night, sleep efficiency showed no significant differences between the diets. Pearson correlations showed no significant relationships with sugar.

Conclusions: Sugar intake appears to significantly alter sleep macrostructure in prepubescent girls. Further studies are required to determine the precise relationship given the lack of an overall correlation between sleep stage changes and sugar intake in this sample.

Poster Session - Non-CPAP therapies of OSA

P694

Effects of septoplasty on sleep difficulties, nasal functions, and quality of life

G. RACIC, Z. ROJE and M. SELIMOVIC
University of Split, Split, HR

Objective: To evaluate impact of septoplasty on sleep difficulties, nasal functions and quality of life in patients with septal deviation.

Participants and methods: The study was conducted in the ENT Department, Split University Hospital, Split, Croatia from April 2007 till December 2010. It included 269 adult participants with symptomatic nasal obstruction due to septal deviation. Clinical exam (anterior and posterior rhinoscopy), Nasal Obstruction Septoplasty Effectiveness (NOSE) scale, QOL visual analog scale (VAS), and rhinomanometry before and 6 months after surgery were administered to assess the treatment outcomes. QOL was scored on 0–10 scale (0–significantly affects QOL, 10–no impact on QOL). All patients underwent septoplasty under general anesthesia.

Results: Out of 269 participants, 148 (55%) were male. According to Mann–Whitney's test there were no statistically significant differences between sexes ($P > 0.001$) in any of the examined variables (symptoms, VAS and rhinomanometry). The most commonly reported symptoms before septoplasty were difficult nasal breathing (97%), sleep difficulties (97%), and nasal stuffiness (93%). After septoplasty difficult nasal breathing was present in 120 (44%; $P < 0.001$), sleep difficulties in 152 (56%; $P < 0.001$), and nasal stuffiness in 162 (60%; $P < 0.001$) participants. The mean rhinomanometry score also showed significant improvement after septoplasty (0.31 ± 0.79 Pa versus 0.23 ± 0.75 Pa) ($P < 0.001$). NOSE score was improved from 70 (range 25–100) to 15 (range 0–65) after septoplasty ($P < 0.001$). There was a significant improvement in mean QOL VAS score from 3 (range 1–6) to 8 (range 4–10) after surgery ($P < 0.001$).

Conclusion: Septoplasty significantly decreased the reported sleep difficulties, improved reported nasal functions, as well as quality of life in the patients with nasal obstruction caused by septal deviation.

P695

Nocturnal use of the Breathe Right® advanced nasal dilator strip in patients with chronic nocturnal nasal congestion improves sleep quality and reduces daytime sleepiness (a pilot study)

J. R. WHEATLEY, S. LEE, R. PERRI, M. VERMA, W. ELIAS, C. PALME and T. C. AMIS
Ludwig Engel Centre for Respiratory Research, Westmead, AU

Introduction: Subjects with symptoms of chronic nocturnal nasal congestion (CNNC) often complain of disturbed sleep, and have a high prevalence of sleep disordered breathing (SDB). Nasal Dilator Strips (NDS) have been advocated for reducing snoring and SDB and improving sleep quality for patients with CNNC. However, objective data are lacking.

Methods: Using standard laboratory polysomnography (PSG), we studied 61 community volunteers, all reporting CNNC and disturbed sleep (43 males; age: 49.3 ± 14.8 year [mean ± SD]; BMI 28.6 ± 5.1 kg/m^2), at baseline (BL) and following 28 days of regular nocturnal use of a NDS (Breathe Right® Advanced; GSK, USA). Sleep architecture and respiratory events were quantified by PSG at BL (without NDS) and day 28 (with NDS), using current AASM rules (2007). At BL and Day 28 (with NDS), subjective sleepiness was assessed with the Epworth Sleepiness Scale (ESS), and sleep quality was assessed using a subject rated Global Assessment Scale (GAS).

Results: At day 28, sleep efficiency, total sleep time and wake after sleep onset time were unchanged from BL. Sleep onset latency (SOL) decreased from BL to day 28 (14.6 ± 19.5 mins to 9.7 ± 8.9 mins; $P < 0.05$), as did REM SOL (101.1 ± 53.5 mins to 83.4 ± 48.7 mins; $P < 0.03$). There was no change in the arousal index (AI) from BL (25.1 ± 10.9 arousals/h) to day 28 (26.0 ± 12.9 arousals/h), however, spontaneous AI decreased slightly (6.7 ± 4.4 to 5.6 ± 3.8 arousals/h; $P < 0.05$). The Respiratory Disturbance Index (20.0 ± 13.1 events/h (BL) and 22.6 ± 15.4 events/h (day 28)) and Snore Index were unchanged. The ESS decreased from 8.5 ± 4.4 at BL to 7.4 ± 4.6 at day 28 ($P < 0.04$). The GAS demonstrated improvements (all >0.5 au) at day 28 in ease of breathing, falling asleep, staying asleep, number of awakenings, falling back to sleep, sleep depth, sleep quality and feeling refreshed in the morning (all $P < 0.0001$).

Conclusions: A month's use of the Breathe Right® Advanced NDS did not reduce SDB or snoring in subjects with CNNC. However, sleep quality improved slightly both objectively (SOL, REM latency and spontaneous AI) and subjectively (GAS scores), together with a reduction in subjective daytime sleepiness (ESS). We conclude that nocturnal use of a NDS in subjects with CNNC improves sleep quality and daytime sleepiness by mechanisms other than reduction in SDB. Supported by GlaxoSmithKline.

This study was funded by GlaxoSmithKline. The study sponsor had input into the study design, data collection and analysis. However, the reported data have been analysed directly by the authors who have been responsible for writing the abstract. Any funding received for the study has been paid directly to the responsible department, and no investigators have received direct payments or consultancies in relation to this project.

P696

A multicentre evaluation of oral pressure therapy for the treatment of obstructive sleep apnoea: sleep architecture effects

I. COLRAIN[1], J. BLACK[2], R. BOGAN[3], P. BECKER[4], M. FARID-MOAYER[5], R. GOLDBERG[6], D. LANKFORD[7], L. SIEGEL[8], A. GOLDBERG[9] and A. MALHOTRA[10]
[1]SRI International, Menlo Park, US, [2]Stanford University, Stanford, US, [3]SleepMed of South Carolina, Columbia, US, [4]Sleep Medicine Associates of Texas, Dallas, US, [5]Peninsula Sleep Center, Bulingame, US, [6]Sleep HealthCenters, Phoenix, US, [7]Sleep Disorders Center of Georgia, Atlanta, US, [8]ApniCure, Redwood City, US, [9]University of California, San Francisco, US, [10]Brigham and Women's Hospital, Boston, US

Objectives: This study sought to evaluate laboratory polysomnography measures of sleep architecture and sleep stability in obstructive sleep apnoea (OSA) patients while using a new non-invasive oral pressure therapy (OPT) system (Winx(TM), ApniCure). The hypothesis was that improvements in apnoea-hypopnea index (AHI) with device use would be associated with a reduction in N1, arousal index and sleep-stage shifts, and increases in REM and N3.

Methods: Sixty-three consecutively enrolled subjects at six centres, 69.8% male, 53.6 ± 9.0 years (mean ± SD), BMI 32.3 ± 4.5 kg/m^2, with mild to severe OSA underwent laboratory polysomnography (PSG) at baseline (one night with and one without treatment in randomized order) and again following 28 nights of treatment. Total AHI and sleep architecture were assessed each night based on blind scoring by a single centralized scorer using AASM criteria. Differences between control night (Tx-) and treatment nights 1 (Tx1) and 28 (Tx28) were assessed with paired *t*-test or signed rank test. Data are presented as (median ± interquartile range).

Results: N1% was significantly reduced at Tx1 (17.8 ± 17.1, $P = 0.005$) and Tx28 (17.5 ± 14.2, $P < 0.001$) relative to Tx- (23.0 ± 21.1). REM% was significantly increased at Tx1 (18.8 ± 8.0 $P < 0.02$) and at Tx28 (18.1 ± 9.3, $P = 0.03$) relative to Tx- (16.6 ± 9.5). There were no significant changes in N3% (Tx-: 5.6 ± 12.0; Tx1: 5.7 ± 15.0; Tx28: 6.5 ± 11.8). Stage shifts to N1 sleep, overall stage shifts, total awakenings and arousals per hour (AI) were all significantly decreased at Tx1 (9.0 ± 6.0, $P = 0.002$; 26.0 ± 12.0, $P < 0.001$; 34 ± 20, $P = 0.035$; 30.6 ± 23.2, $P < 0.001$) and at Tx28 (8.0 ± 5.5, $P < 0.001$; 24.0 ± 12.5, $P < 0.001$; 29 ± 21, $P < 0.001$; 28.7 ± 20.0, $P < 0.001$) relative to Tx- (11.0 ± 8.0; 32.0 ± 16.0; 38 ± 27; 41.0 ± 23.5). The difference in AHI between Tx- and Tx1 was significantly correlated with differences in stage shifts, shifts to stage 1, AI, REM% and stage 1% (all $P < 0.01$), The same pattern of correlations was seen for differences between Tx- and Tx28 (all $P < 0.01$), with the exception of REM%.

Conclusion: Significant improvements in AHI produced by OPT were associated with anticipated changes in PSG measures, including increased sleep stability, decreased time in stage 1 sleep and increased time in REM sleep on both the first night of treatment and again after 28 days of treatment. Supported by Apnicure, Inc.

P697

A multicentre evaluation of oral pressure therapy for the treatment of obstructive sleep apnoea

I. COLRAIN[1], R. BOGAN[2], P. BECKER[3], M. FARID-MOAYER[4], R. GOLDBERG[5], D. LANKFORD[6], L. SIEGEL[7], J. BLACK[8], A. GOLDBERG[9] and A. MALHOTRA[10]

[1]SRI International, Menlo Park, US, [2]SleepMed of South Carolina, Columbia, US, [3]Sleep Medicine Associates of Texas, Dallas, US, [4]Peninsula Sleep Center, Burlingame, US, [5]Sleep HealthCenters, Phoenix, US, [6]Sleep Disorders Center of Georgia, Atlanta, US, [7]ApniCure, Redwood City, US, [8]Stanford University, Stanford, US, [9]University of California, San Francisco, US, [10]Brigham and Women's Hospital, Boston, US

Objectives: This study sought to evaluate a new non-invasive oral pressure therapy (OPT) system (Winx(TM), ApniCure) for treatment of obstructive sleep apnoea (OSA). The system is comprised of a bedside console and a soft polymer mouthpiece with tubing. The console contains a pump that creates vacuum drawing the soft palate anteriorly and stabilizing the tongue to reduce obstruction during sleep.

Methods: Sixty-three consecutively enrolled subjects at 6 centres, 69.8% male, 53.6 ± 9.0 years (mean ± SD), BMI 32.3 ± 4.5 kg/m^2, with mild to severe OSA underwent laboratory polysomnography at baseline (one night with (Tx1) and one without treatment in randomized order) and again following 28 nights of treatment (Tx28). Total apnoea-hypopnea index (AHI(/h)) and oxygen-desaturation index (>4% events) were scored blindly using AASM criteria. Epworth Sleepiness Scale (ESS) and Clinical Global Impression Severity and Change (CGI-S and CGI-C) were assessed at baseline and Tx28. OPT usage was recorded by the console.

Results: Baseline AHI (35.5 ± 24.5) was significantly reduced at Tx1 (23.1 ± 24.0) and at Tx28 (21.6 ± 21.7). Baseline ODI (29.7 ± 21.8) was significantly reduced at Tx1 (20.7 ± 22.4) and at Tx28 (19.6 ± 20.6). Clinical success defined a priori as AHI reduction ≥50% and treatment AHI ≤ 20 at Tx1 was observed in 26/63 subjects (4/15 mild, 10/18 moderate, 12/30 severe). In these 26 subjects, AHI (median (interquartile range)) was reduced from 26.2 (19.8–45.3) to 5.7 (3.6–10.0) while ODI was reduced from 19.2 (14.8–35.4) to 4.7 (2.5–9.0). For 20 subjects, Tx1 AHI was ≤ 10. Median ESS scores were unchanged in subjects who switched directly from CPAP therapy to OPT study participation and were significantly reduced from 13 (8–16) to eight (4–12) in those untreated for two or more weeks prior to OPT study participation. Average nightly usage across the take-home period was 6.0 ± 1.4 h. On CGI-C, 58% of subjects scored much improved or very much improved. There were no severe or serious device-related adverse events. Six subjects were terminated or withdrawn prior to completion of 28 nights of treatment (three for device intolerability, two for high AHI with inadequate treatment response, one for scheduling).

Conclusion: Clinically significant improvements in AHI, ODI, ESS and overall clinical status were achieved in an easily identified subgroup. Oral pressure therapy was safe and well-tolerated and nightly usage was high.

Supported by ApniCure, Inc.

P698

Evaluation of compliance with oral appliance treatment in patients with obstructive sleep apnoea syndrome

O. K. BASOGLU[1], M. S. TASBAKAN[1], C. BILGEN[1] and H. KURTULMUS[2]

[1]Ege University School of Medicine, Izmir, TR, [2]Ege University School of Dentistry, Izmir, TR

Objectives: Oral appliances (OA) are increasingly used in primary snoring and mild-to-moderate obstructive sleep apnea syndrome (OSAS). However, compliance with OA treatment is low. In this study, we aimed to assess the compliance with OA in patients with primary snoring and OSAS.

Methods: We asked questions about OA compliance by telephone visits in 116 patients (seven primary snoring, 109 OSAS) who were treated with an OA between January 2007 and September 2011.

Results: The study population consisted of 116 patients (mean age 51.5 ± 9.9 year, 77 males, BMI 29.7 ± 4.6 kg/m^2). It was observed that OA were used by 31 patients (26.7%) regularly (compliance with OA group) after a mean time of 29.9 ± 16.1 months. They used their dental device 6.3 ± 0.9 days per week and 7.0 ± 0.8 h per day. There was no difference between two groups with OA compliance and non-compliance in terms of demographic, anthropometric and polysomnographic parameters. Snoring frequency (3.9 ± 0.4 versus 1.2 ± 1.3, $P < 0.001$), snoring loudness (2.8 ± 0.9 versus 0.9 ± 1.1, $P < 0.001$), tiredness on waking (3.3 ± 1.2 versus 1.2 ± 1.2, $P < 0.001$) and Epworth sleepiness scores (9.2 ± 5.1 versus 3.2 ± 4.0, $P < 0.001$) were significantly lower after OA treatment when compared with baseline in patients with OA compliance. Excessive salivation (29.0%) and temporamandibular joint pain (22.6%) were the most commonly reported adverse events.

Conclusion: OA treatment is effective in primary snoring and OSAS patients. However, we showed that OA compliance rate was lower

than expected. Regular follow-up visits are necessary to ensure adequate treatment in these patients.

P699

Treatment success is affected by responder criteria in oral appliance therapy for obstructive sleep apnoea

T. FUKUDA[1], S. TSUIKI[1], M. KOBAYASHI[1], K. MAEDA[1], T. SASAI[1], T. KAGIMURA[2] and Y. INOUE[1]

[1]Neuropsychiatric Research Institute, Tokyo, JP, [2]Tokyo Medical University, Tokyo, JP

Objectives: Current practice parameters for oral appliance therapy for obstructive sleep apnoea suggest that oral appliances are now indicated for moderate as well as mild Obstructive Sleep Apnoea (OSA) (Kushida et al., Sleep 2006). However, this indication does not mean oral appliance is as efficacious as nasal continuous positive airway pressure (CPAP). Although some previous studies suggested excellent treatment success rates with oral appliances similarly to nasal CPAP therapy, responder criteria for oral appliance treatment differ from report to report whereas nasal CPAP usually accomplishes greater reduction in Apnoea Hypopnoea Index (AHI) to <5/h. We hypothesized that treatment success is dependent on the responder criteria in oral appliance therapy.

Methods: The study protocol was approved by the Ethics Committee of Neuropsychiatric Research Institute, Tokyo. Target subjects for analyses were patients whose baseline as well as follow-up polysomnography (PSG) was undertaken from the period between 2005 and 2011 ($N = 223$). Follow-up PSG was obtained with adjusted oral appliance in place for each subject. We defined responders as patients showing a reduction in AHI to <5/h in addition to a >50% reduction in baseline AHI (criterion 1). A different responder criterion was also defined as a >50% reduction in baseline AHI (criterion 2). Success rates were compared between the two different criteria using Chi square test. A P value of <0.05 was considered to indicate statistical significance.

Results: The baseline AHI was 21.3 ± 12.2/h (mean ± SD) in 223 patients. Only 94 patients (42%) were assumed as responders at criterion 1 while 153 patients were regarded as responders (69%) at criterion 2. There was a significant difference in the success rates between the two criteria ($\chi^2 = 44.1$, $P < 0.01$). Although all the 94 patients achieved reduction in AHI to <5/h after treatment at criterion 1, 59 out of 153 patients did not show the follow-up AHI <5/h (range 5.2–29.3) at criterion 2.

Conclusions: These findings suggest that treatment success of oral appliance therapy was easily affected by responder criteria. We conclude that both researchers and clinicians should use liberal responder criteria with caution since an application of such criteria may leave unfavourable cardiovascular outcomes even though patients were considered as ''treatment success'' by oral appliance therapy.

P700

The Snore-Breaker as a positional therapy for positional sleep apnoea

Y. L. KOORNNEEF[1], M. H. M. VLAK[2], W. F. HOFMAN[1] and H. L. HAMBURGER[2]

[1]University of Amsterdam, Amsterdam, NL, [2]Amsterdam Wake-SleepCentre, Slotervaartziekenhuis, Amsterdam, NL

Positional obstructive sleep apnea syndrome (POSAS) is defined as a 50% reduction in the apnea–hypopnea index (AHI) during non-supine sleep position compared to the AHI in supine position. About half of all patients with sleep apnea have POSAS. Little is known about the compliance and subjective improvements after treatment with positional therapy. The aim of this study is not only to assess the efficacy of positional therapy, but also the usability, compliance and subjective changes after positional therapy.

Methods: For the current study the Snore-Breaker (SB) was used for positional therapy (www.snore-breaker.nl). The SB is a device that is attached to the back of the patient with a strap and starts to vibrate when the patient lies in supine position for at least 30 s, causing the patient to turn to the side.

All patients have to fulfill the criteria for POSAS and had an AHI above five. We aim to include a total of 30 patients. Patients are randomly assigned to sleep with a normal SB (with vibration) or a placebo SB (without vibration) for 4 weeks each. Efficacy, side effects, compliance, subject satisfaction, therapy preference, Quality of Life, subjective sleep quality and subjective sleepiness are evaluated by polysomnography, questionnaires and data stored in the SB. One-way ANOVA and dependent t-tests will be used for statistical analysis.

Results: This study will be completed in July 2012. Ten patients have already been included and analysed. Preliminary analyses show a decrease in AHI and time spent in supine position with the use of the SB compared with baseline. A normal SB with vibration seems a more successful treatment compared with a placebo SB. Compliance is high, but so far no decrease in subjective sleepiness was found.

Conclusion: The SB is a simple, effective and easy to use device in POSAS. Vibration adds to the efficacy of positional training. Effects on subjective sleepiness may be small or only measurable after a longer treatment period.

P701

Role of puberty and myo-facial hypotonia in recurrence of SDB

C. GUILLEMINAULT[1], Y. S. HUANG[2], C. H. LIN[2] and P.-J. MONTEYROL[3]

[1]Stanford University, Redwood City, US, [2]Chang Gung University, Taipei, TW, [3]Bordeaux1, Bordeaux, FR

Objectives: Pubertal development may lead to recurrence of sleep disordered breathing despite previously curative surgery. We evaluated adolescents who had been previously cured of obstructive sleep apnea (OSA) following adenotonsillectomy for recurrence of sleep apnea following puberty.

Study design: Retrospective analysis of 29 adolescents (nine girls) with OSA previously treated by adenotonsillectomy: Clinical evaluation and sleep-related complaints were assessed annually from pediatric sleep questionnaire (PSQ) during sleep clinic or orthodontic follow up. Systematic cephalometric xray or 3D CT of subjects was performed by orthodontists between 12–15 years of age. Compared polysomnography at the time of OSA diagnosis, following adenotonsillectomy, and after puberty.

Results: After initial OSA diagnosis, (age 7.6 ± 1.7 years, AHI 9 ± 5, RDI 15 ± 6.4) and following adenotonsillectomy, (AHI 0.4 ± 4.4, mean RDI 0.6 ± 0.5) children were followed by orthodontist for other reasons.At pubertal evaluations (mean age of 14 years), complaints obtained from PSQ included snoring ($N = 4$), difficulty getting up in morning/going to school ($N = 12$), inattention or poor school performance within last year ($N = 13$), fatigue ($N = 10$), napping on school bus or ride home ($N = 8$), and signs of sleep phase delay ($N = 16$). Nine subjects (seven girls) were asymptom-

atic. Cephalometric comparison of subjects ($N = 20$) performed at mean age 11 years versus mean age 14 years, showed reduction of posterior airway space of 2.3 ± 0.4 mm. Polysomnography of asymptomatic subjects showed mean AHI 1.1, mean RDI 1.8, versus symptomatic subjects mean AHI 3.1, mean RDI 5.6 ± 1.2,

Conclusion: Puberty may be a risk factor for the recurrence of OSA due to enlargement and hypotonia of the tongue muscles in boys and less frequently, abnormal decent of the hyoid bone in girls.

P702

Treatment outcomes of adenotonsillectomy for children with obstructive sleep apnoea: a prospective longitudinal study

Y. S. HUANG[1], M. H. TSAI[1] and C. GUILLEMINAULT[2]

[1]Chang Gung Memorial Hospital and University, Taipei, US, [2]Stanford University Sleep Medicine Division, Stanford, US

Objectives: To evaluate the efficacy of adenotonsillectomy (T and A) in treatment of children with obstructive sleep apnea (OSA) in a 3-year prospective, longitudinal study. Analysis of the risk factors of recurrence of pediatric OSA was also performed.

Methods: Of 6 to 12 year old children with OSA documented with examination, questionnaires and polysomnography treated with T and A were followed post-operatively at post 6 months and there after for the following 3 years with similar investigation. Multivariate generalized linear modeling was used to determine contributors of suboptimal long-term post-T and A. Generalized linear models (GLM) was used to analyze the risk-factors of OSA recurrence after T and A.

Results: Eighty-eight pediatric OSA (boys = 72, 81.8%), mean age = 8.9 + 2.7 years and BMI = 19.5 + 4.6, who received T and A surgery, showed a preoperative apnea-hypopnea-index of 13.53 + 17.23 (AHI > 1100%), 6 months and then every year post-operatively the AHI was 3.47 + 8.41(AHI > 1, 40.9%), 6.29 + 10.09(AHI > 1, 35.1%), 4.8 + 8.61(AHI > 1, 31.6%) and 6.47 + 11.51(AHI > 1, 27.0%) events/h. The GLM analysis showed as significant risk-factors: higher pre-operative AHI ($P = 0.000$*), higher post operative AHI at 6, 12 and 24.months ($P = 0.000$*, 0.000*, 0.000*); higher preoperative BMI($P = 0.001$*) and increasing slope of postoperative BMI ($P = 0.000$*, 0.000*, 0.080*) for significance relationship with pediatric OSA recurrence at 3 years(AHI > 1). Preoperative age, rhinitis and enuresis also presented a trend toward recurrence of OSA 3 years post surgery.

Conclusion: The post T and A recurrent rate of pediatric OSA is about 40–30% after 3 years. The BMI, increasing slope of postoperatively BMI and the initial severity of AHI are the major risk factors of pediatric OSA recurrence.

P703

A review of the effectiveness of a clinical recommendation for weight loss in patients with obstructive sleep apnoea

F. I. CONTI-RAMSDEN, M. GLASSER, A. K. SIMONDS and M. J. MORRELL

Imperial College London, London, UK

Objectives: To investigate the effectiveness of a clinical recommendation to lose weight as an adjunct to CPAP treatment in patients with OSA, and whether any weight loss was associated with improved disease severity, sleepiness or blood pressure (BP).

Methods: A retrospective observational study of OSA patients treated with CPAP was carried out. A review of 6916 CPAP uses at the Royal Brompton Hospital, UK revealed 309 patients who had returned their CPAP machines by July 2011. Of these 309 patients 131 were excluded from the study due to CPAP intolerance ($n = 62$), switching to other treatments e.g. surgery, or ventilation ($n = 47$), transfer to another hospital or death ($n = 22$). Of the remaining 178 patients, a detailed medical record review was carried out in 89 (50%) patients, including all 35 patients where weight loss was documented in the electronic medical summary, and a random sample of 54 additional patients.

Results: The study group of 89 OSA patients was divided into a non-surgical weight loss (WL) group ($n = 42$) and a no weight loss (NWL) group ($n = 44$); three patients were excluded due to bariatric surgery weight loss. In the WL group the median (range) weight loss was 5.3 (1.3–50) kg, 5% of starting weight, over a median duration of 12 (1–138) months. Compared to the NWL group, the WL group were younger (mean ± SD WL: 54.0 ± 11.7 versus NWL: 59.7 ± 12.4 years, $P < 0.05$), and heavier (BMI, WL: 36.8 ± 6.6 versus NWL: 34.2 ± 9.8 Kg/m^2, $P < 0.05$). There was a decrease in both OSA severity and sleepiness with weight loss (oxygen desaturation index, Pre-WL: 28.7 ± 22 versus Post-WL: 11.12 ± 6.5 events/h, $P < 0.005$; sleepiness; Epworth Sleepiness Scale, Pre-WL: 10.1 ± 5.3 versus Post-WL: 6.0 ± 5.5, $P < 0.001$). There was no significant change in BP (Systolic: Pre-WL: 141.8 ± 16.5 versus Post-WL: 134.5 ± 21.1 mmHg, $P = 0.06$; Diastolic, Pre-WL: 83.5 ± 10.8 versus Post-WL: 80.8 ± 13.5 mmHg, $P = 0.75$).

Conclusion: This study supports the notion that weight loss in OSA patients using CPAP treatment reduces disease severity and symptoms of sleepiness. In addition, we found that those who were younger and heavier were more likely to achieve weight loss following clinical advice. These preliminary data may have implications for focusing weight loss resources.

Acknowledgments: This project was funded by the Imperial Undergraduate Research Opportunities Program. It was supported by the NIHR Respiratory Disease Biomedical Research Unit at the Royal Brompton and Harefield NHS Foundation Trust and Imperial College London.

P705

The use of hypnotics among patients with obstructive sleep apnoea

E. BJORNSDOTTIR[1], C. JANSON[2], E. S. ARNARDOTTIR[3], A. I. PACK[4], J. F. SIGURDSSON[3], T. GISLASON[3] and B. BENEDIKTSDOTTIR[3]

[1]University of Iceland, Reykjavik, IS, [2]University of Uppsala, Uppsala, SE, [3]University of Iceland and The National University Hospital of Iceland, Reykjavik, IS, [4]University of Pennsylvania, Philadelphia, US

Objectives: The aim of this study was to explore the prevalence of hypnotics use among patients with obstructive sleep apnea (OSA), both while untreated and two years after starting treatment with continuous positive airway pressure (CPAP). Additionally, insomnia and quality of life among patients on hypnotics was explored.

Methods: At baseline, 822 untreated OSA patients underwent a medical examination and answered questionnaires on health, quality of life by SF-12 and sleep before starting on CPAP treatment. The majority of the sample was men (81%) and the mean age was 54.9 ± 7.6 years. Altogether, 90.1% ($n = 741$) of the sample completed the 2-year follow up where baseline assessment was repeated.

Results: Altogether, 11.9% of subjects were using hypnotics on baseline compared to 14.0% at follow up. OSA patients that were using hypnotics were older, with less severe OSA, higher prevalence of restless leg syndrome (RLS) and reported lower mental and

physical quality of life. The majority (68.2%) of those who were taking hypnotics at baseline were also taking them at follow up. Subjects who were taking hypnotics were more likely to have insomnia at both baseline and follow up (baseline prevalence 84.7% versus 65.2%, $P < 0.0001$; follow up prevalence 72.8% versus 43.6%, $P < 0.0001$). There was no difference among CPAP users and non users in the prevalence and/or change in hypnotics use from baseline to follow up.

Conclusion: Untreated OSA patients who take hypnotics have less severe sleep apnea, high prevalence of insomnia and lower quality of life compared other OSA patients. The majority of those who take hypnotics at baseline continue taking the medications after starting on CPAP. Despite using hypnotics, these subjects report worse subjective sleep quality (insomnia and RLS).

Poster Session – Sleep and gender

P706

Gender differences in sleep structure produced by bright light

M. KOHSAKA[1], R. KOBAYASHI[2], N. FUKUDA[2], H. HONMA[2] and T. ISHIKANE[1]

[1]Ishikane Hospital, Sapporo, JP, [2]Hokkaido University, Sapporo, JP

Objectives: Gender difference in sleep structure has been noted in the middle aged and elderly. The purpose of this study is to investigate gender difference on sleep structure after exposure to morning bright light.

Methods: Eleven women aged 50–72 years and nine men aged 55–66 years participated in this study. All participants were in good health. Each subject signed an informed consent form prior to the study. Participants were exposed to bright light (BL: 8000 lux, 60 min) in the morning or instructed to sit in front of a lighting device without light (CL: control) for five consecutive days. This experiment was performed in a balanced crossover design. Subjects' sleep-wake patterns were recorded polygraphically for 36 consecutive hours in their homes starting from bedtime of the fourth night and ending at wake-up time of the sixth day. Sleep stages were visually scored by 20-s epoch according to the criteria of Rechtschaffen and Kales. Wilcoxon's signed rank test was used for statistical analysis between the BL and CL conditions.

Results: 1. Sleep variables in men

There were no significant differences for time in bed, sleep period time (SPT), total sleep time, sleep efficiency, number of awakenings, sleep latency, REM sleep latency and the proportion of each sleep stage to SPT between the BL and CL conditions. Neither REM density nor REM activity showed significant difference between the two conditions.

2. Sleep variables in women

Sleep latency was significantly decreased in the BL condition (16.9 ± 3.0 min) in comparison with the CL condition (27.0 ± 6.2 min). There were no significant differences for time in bed, sleep period time (SPT), total sleep time, sleep efficiency, number of awakenings, REM sleep latency and the proportion of each sleep stage to SPT between the BL and CL conditions. For the REM sleep parameter, REM activity significantly decreased in the BL condition (290.1 ± 26.3) compared to the CL condition (221.5 ± 22.6).

Conclusions: These findings indicate that effect of morning bright light on sleep was notably different according to gender. Women improved initiation of sleep after bright light exposure.

P707

Sex differences in thermal comfort preferences during bedtime

T. R. M. LEUFKENS, T. E. J. WEYSEN, E. I. S. MØST and R. J. E. M. RAYMANN

Philips Group Innovation, Eindhoven, NL

Objectives: Nowadays, it is commonplace that properties of mattresses, such as firmness and elasticity, are specifically fitted out for sexes due to differences in body weight, -size, and -shape, and associated comfort preferences. In contrast, specific thermal comfort properties in blankets and/or mattresses for males and females have received less attention. It has been shown however that overnight average body and bed temperatures in the trunk area differ significantly between men and women. The difference in bed temperature is partly caused by the isolating property of the bedding and is affecting thermal comfort. Anecdotal evidence of men feeling warm and women feeling cold in the bed may indicate that there is a need for specifically fitted thermal properties of blankets and/or mattresses for sexes. Therefore, the present study aims to investigate whether there are sex differences in thermal comfort preferences during bedtime.

Method: Thermal sleep comfort preferences were assessed by a 20 item questionnaire in a total of 85 adults (45 females and 40 males) with a mean ± SD age of 26.2 ± 6.0 years. Items consisted of a five-point Likert scale ranging from one (strongly disagree) to five (strongly agree).

Results: Female responders agreed significantly stronger than males on the statements 'I often cannot fall asleep because it is too cold', 'I think I would sleep better if I did not feel so cold', and 'When I go to bed, my feet are cold'.

In addition, females significantly more preferred wearing nightclothes, using additional blankets, and using a heating blanket prior to sleep.

Discussion: Results indicate significant sex differences in thermal comfort preferences during bedtime. Females prefer warmer bed temperatures and believe these to enhance their sleep, whereas males prefer cooler bed temperatures. In order to increase temperatures females revert to more blankets and pre-heating of the bed, suggesting that there is a need for specifically fitted thermal properties of blankets and/or mattresses for females and males.

P708

Sleep quality and quality of life in midlife women

L. LAMPIO[1], P. POLO-KANTOLA[2], O. POLO[3] and T. SAARES-RANTA[2]

[1]University of Turku, Turku, FI, [2]Turku University Hospital, Turku, FI, [3]Tampere University Hospital, Tampere, FI

Objectives: Several studies have evaluated subjective sleep quality of menopausal women with one general question and not defined the time period. This might overestimate the magnitude or frequency of sleep problems. The aim was to evaluate subjective sleep quality and its association with quality of life in premenopausal and postmenopausal women during the last three months.

Methods: A total of 158 women were recruited, of which 107 were premenopausal (44–48 years) and 51 postmenopausal (53–58 years). Menopausal status was evaluated with follicle stimulating hormone level, sleep quality with Basic Nordic Sleep Questionnaire, depressive symptoms with Beck Depression Inventory (BDI) and vasomotor symptoms with Kuppermann questionnaire.

Results: Of premenopausal women 75.7% and of postmenopausal 49.0% slept usually or always well ($P = 0.0008$). Postmenopausal women slept more restlessly ($P = 0.0008$) and had more nocturnal awakenings ($P = 0.003$). Frequency of witnessed apneas, snoring, sleep onset insomnia or use of sleeping pills was similar between the groups.

Postmenopausal women did not feel more tired than premenopausal women at daytime or in the morning. Postmenopausal women did not report more compulsory tendency to doze off at work or at leisure time (7.8% versus 3.7%, $P = 0.233$), but when not active (e.g. watching TV) they doze off more easily than premenopausal women (21.6% versus 3.7%, $P < 0.0001$). Postmenopausal women had

more depressive symptoms ($P = 0.0004$), although the average score of BDI was low in both groups. Vasomotor symptoms were more frequent in postmenopausal women ($P < 0.0001$). Fewer of postmenopausal than of premenopausal women considered their general health (58.8% versus 71.3%, $P = 0.021$) or quality of life (QOL, 72.2% versus 91.6%, $P = 0.011$) good or satisfying. The proportion of working women, shift work or work load did not differ between the groups.

Conclusions: Postmenopausal women reported worse overall sleep quality and more vasomotor symptoms as expected. Although postmenopausal women had more nocturnal awakenings, they did not report more sleep onset insomnia or non-restorative sleep compared to premenopausal women in this cohort of mostly working middle-aged women. Self-assessment of depressive symptoms, general health or global impression of QOL was impaired in postmenopausal group in comparison to premenopausal group. Our results suggest that more detailed questions of tendency to doze off result in higher rate of reported sleepiness in postmenopausal women.

P709

Relation of subjective sleep quality to polysomnography in a large representative sample of women

J. F. A. SCHWARZ[1], T. ÅKERSTEDT[1], E. LINDBERG[2], G. KECKLUND[1] and J. THEORELL-HAGLÖW[2]
[1]Stockholm University, Stockholm, SE, [2]Uppsala University, Uppsala, SE

Objectives: Polysomnography (PSG) often fails to find differences between individuals with sleep complaints and good sleepers. However, sample size and representativity may be issues involved in this lack of relation. The present study investigated the relation between subjective sleep quality and PSG in a large sample of women.

Methods: Ambulant PSG recordings were obtained on one occasion in 400 non-pregnant women (randomly selected from a representative sample, oversampling of snorers). Sleep quality was rated on a visual analogue scale the morning after the recording. Three groups with high (HSQ), intermediate (ISQ), and low sleep quality (LSQ)(cut-offs at 33 and 66 mm on the VAS) with $N = 88$, 126, and 170, respectively, were built. Three hundred eighty-four women (mean age 50 years, SD 11, Min 22, Max 73) with complete data were included.

To investigate if PSG measures (total sleep time (TST), sleep latency (SL), wake after sleep onset (WASO), number of awakenings (>60 s) (NoA), sleep efficiency,%sleep stages) differed with respect to sleep quality (categorical) and age (continuous), multiple linear regressions were applied (reference group: high sleep quality). Analyses were adjusted for AHI. An additional model including an interaction between age and sleep quality group was fitted and compared to the regression without the interaction (significance level $P < 0.05$ for all analyses).

Results: TST was significantly (sig) lower in the groups with intermediate and low sleep quality (marginal means: HSQ: 414 min; ISQ: 389 min; LSQ: 371 min) and decreased with age. SL (HSQ: 15 min; ISQ: 23 min; LSQ: 25 min), NoA (HSQ 6.7; ISQ: 7.7; LSQ: 8.2), WASO and % S1 sleep were sig. higher with low and intermediate sleep quality, and increased age. % S2 was slightly reduced only in the intermediate sleep quality group; % REM and sleep efficiency (HSQ: 89%; ISQ: 86%; LSQ: 83%) were sig. reduced in the LSQ group and with increasing age. No sig. effect of age and sleep quality was observed on%SWS. Adding an interaction between age and sleep quality groups did not improve the model fit.

Conclusions: In a large sample of women, PSG measures differed significantly in groups with different sleep quality. In particular sleep continuity, initiation and length appear to be impaired when subjective sleep quality is low. The relation of subjective sleep quality to PSG measures did not significantly change with increasing age, but age was, as expected, significantly related to differences in most PSG parameters.

The study received support from the Swedish Council for Working Life and Social Research (FAS) and the Swedih Research Council (VR).

P710

Pregnancy and sleep

C. SORIA-BRETONES, M. GARCÍA-BELLÓN, M. A. GARCÍA-JIMÉNEZ, D. ÁLVAREZ-AGUILAR, E. PÉREZ-RODRÍGUEZ, G. SÁNCHEZ-MÁRQUEZ and J. VALERO-RONCERO
Hospital Virgen de la Luz, Cuenca, ES

Objectives: Sleep disorders are often underdiagnosed during pregnancy. Our aim is to describe their prevalence, type, time of appearance and related factors.

Methods: Observational descriptive prospective study during 4 months in full term pregnant women attending Fetus Physiopathology Office ($n = 290$). Measures: self-filled questionnaires about daylife and sleep habits, sleep disorders symptoms, pregnancy features and socio-demographic data.

Clinical criteria: Diagnostic and Statistical Manual of Mental Disorders 4th edition (DSM-IV) for insomnia, Epworth scale for Excessive Daytime Sleepiness (EDS), and Walters 1995 and International Restless Legs Syndrome (RLS) Study Group 2002 for RLS.

Statistic analyisis: Descriptive measures, Pearson's chi quadrat and Fisher's exact test. Level of statistical significance: $P < 0.05$.

Results: Prevalence: 86.6% of studied women reported changes in sleep quality, quantity or habits.

Only 12% of our sample had spontaneously complained about sleep disorders without being asked. Most of them complained to midwives. The most prevalent sleep disorders are insomnia symptoms (up to 95.5%), RLS symptoms (67%), breathing disorders during sleep (snoring 50.7%, sleep apnea 5.9%), and EDS (35%). Sleep disorders are more prevalent during 3rd trimester (80.6%) followed by the 1st one (9.9%). In order of frequency, the reported related causes are polyuria, gastroesophagic reflux, muscle discomfort and fetus movements.

Sleeping habits: Increase of frequency and duration of daytime naps (78.2%), insufficient nocturnal sleep hours (48.2%), changing of usual sleep position (46.6%) and higher need of sleep-inducing techniques such as reading or watching television (37.3%).

Socio-demographic data and daily habits: negative relation between sleep disorders and regular exercise. Positive relation with workload, overweight, multiparity and age. No relation found between treatment with iron supplements and RLS symptoms.

Conclusion: 1. Sleep disorders are highly prevalent during pregnancy, due to physiological changes and other social and behavioural factors. The most prevalent is insomnia. 2. They are usually not reported by women nor Health professionals. Both must be aware about them and pay attention to their importance on quality of life and fetus' wellness. 3. Treatment with iron supplements is not effective on RLS symptoms during pregnancy; therefore they are not necessary.

P711

Sleep homeostasis in pregnant rats is characterised by higher efficiency

E. M. RUTSKOVA and M. L. PIGAREVA
Russian Academy of Sciences, Moscow, RU

Objectives: The present study aimed to investigate the effects of short term sleep deprivation (SD) on the sleep pattern in pregnant and non-pregnant rats.

Methods: Polysomnogram consisting of cortical electroencephalogram, hippocampal theta-activity and locomotor activity was recorded 24 h in 18 female Wistar rats in the ''disk-over-water'' paradigm. Animals were kept under 12/12 h light-dark schedule; 8:00 lights on. Before the experiment rats were adapted to experimental situation to be able to move across the rotating disk without falling in water. After the adaptation period polysomnogram was recorded during three consecutive days in 12 animals without disk rotation (control group 1). From the next day 6 rats underwent SD procedure with pre-set program of disk rotation from 11:00 to 14:00 during three consecutive days (experimental group 1). Another group of 6 rats were subjected to SD during 5–7th days of pregnancy (experimental group 2). Polysomnogram was also constantly recorded during three SD days. In rats forming control group 2 ($n = 6$) polysomnogram was recorded during 5–7th days of pregnancy on the immobile disk over water.

Results: Data analysis revealed that the degree of SD was the same in pregnant and non-pregnant animals. However only in pregnant rats sleep intensity increased during the first hours after SD with respect to the control values. In addition this time period was also characterized by the presence of REM sleep rebound in pregnant but not in non-pregnant rats.

Conclusion: It is concluded that homeostatic compensation of SD effects on sleep pattern works more effective in rats during the first week of pregnancy than in non-pregnant rats.

P712

Prevalence and effects of sleep disturbance in mid to late pregnancy – a pilot study

S. COCKRAM[1], F. FAIRLIE[1], P. SLADE[2] and S. BIANCHI[1]
[1]Sheffield Teaching Hospitals, Sheffield, UK, [2]University of Sheffield, Sheffield, UK

Introduction: Insufficient restorative sleep can have profound effects of biological processes including neurocognitive and emotional processing. Sleep disturbance during pregnancy is common and has been variably reported as affecting both expectant parents.

Methods: We explored the utility of a number of mechanisms of assessing sleep quality and the effects of sleep disturbance in 26 primigravid mothers and their partners at 20 weeks and 36 weeks of pregnancy. We subsequently reviewed 10 patients at 3 months postpartum to determine whether sleep disturbance or antenatal materno-fetal attachment was associated with future attachment to the newborn baby and the incidence of postnatal depression.

Results: Sleep disturbance, both subjective and objective, as assessed by actigraphy, sleep questionnaires and sleep diaries, increased in expectant mothers between the two time points. No changes in partner sleep quality or characteristics were identified. Depression scores (HADS) increased in mothers in late pregnancy ($P = 0.02$) as did materno-fetal attachment scores (MAAS questionnaire). No correlations were identified between quality, quantity or deterioration of sleep and depression or attachment quality scores. Ten patients utilised a commercially available neuro-cognitive battery (CogState). No change in detection, identification or recall was noted between the two time points. Ten patients completed a postnatal attachment questionnaire. High levels of attachment were noted. Strong correlations were identified between 'time spent in attachment mode' at 20 weeks and quality of attachment at 3 months post-delivery ($R^2 = 0.46$). This effect weakened at 36 weeks ($R^2 = 0.17$). Surprisingly strong associations were noted between the global attachment score at 20 weeks and the degree of postnatal hostility toward the child at 3 months ($R^2 = 0.58$). This association weakened at 36 weeks of pregnancy ($R^2 = 0.13$). Only 1/10 patients attained a clinical diagnosis of postnatal depression (PND). Prenatal questionnaire scores were unable to predict the development of PND.

Conclusions: Sleep quality deteriorates in expectant mothers as pregnancy progresses but not in partners. Maternofetal attachment increases throughout pregnancy as do depression scores. Neurocognitive function is preserved. Antenatal attachment questionnaires do not predict postnatal depression symptoms but did predict postnatal attachment.

P713

Pre-eclampsia and pregnancy-induced hypertension among women later diagnosed with obstructive sleep apnoea

B. BENEDIKTSDOTTIR[1], E. S. ARNARDOTTIR[1], E. BJÖRNSDÓTTIR[1], A. PACK[2] and T. GISLASON[1]
[1]Landspitali University Hospital, Reykjavík, IS, [2]University of Pennsylvania School of Medicine, Philadelphia, US

Introduction: It is estimated that 10% of pregnancies are affected by hypertension worldwide and one-half of all are due to preeclampsia. An association between obstructive sleep apnea syndrome (OSA) and the development of preeclampsia or gestational hypertension has been observed, but large studies are lacking in this field. The aim of this study is to estimate the prevalence of reported preeclampsia among women when they later were diagnosed with OSA.

Material and methods: The OSA women ($n = 156$) were a part of the Icelandic Sleep Apnea Cohort. They were newly diagnosed with moderate or severe OSA, mean AHI 42.6(±20.0), mean ODI 32.0 (±20.0). They all answered a questionnaire including questions about health, sleep, symptoms of OSA and preeclampsia. Those who answered that they had been diagnosed with preeclampsia (PE) or pregnancy induced hypertension (HT) were defined as having had PE and HT.

Results: Among the 156 OSA women 146 reported having been pregnant. Among them 31% reported that they had during pregnancy been diagnosed with preeclampsia and 37% that they had pregnancy induced hypertension. This is much higher when compared to reports about same disorders from women in the general population. When the OSA women reporting preeclampsia were compared to OSA women not reporting PE, they were more likely to be more obese (BMI 35.6 m^2, (±6.3) versus 32.5 m^2, (±5.3), $P = 0.002$), be younger (mean age 56.1 versus 59.6 years, $P = 0$, 01), be current smokers (29% versus 13%). In a multivariate logistic regression, they are also more likely to report nocturnal sweating and morning headaches after adjusting for significant demographic factors. No significant differences were found in OSA severity, insomnia, cardiovascular diseases, diabetes, obstructive lung diseases, restless legs syndrome between OSA women reporting PE and those who did not.

Conclusion: In a prospective cohort of female patients with obstructive sleep apnea one third of them reported having had preeclampsia or hypertension during pregnancy which is three times more often than reported in the general population. These women

were compared to other OSA women more obese, younger, more often smokers and reporteted night time sweatening and headache upon wakening more often. These findings show an association between OSA among women and preeclampsia/pregnancy induced hypertension and raise the question how these conditions are related to each other.

P714

Erection – desaturation – apnoeas. A story of nose?

D. CUGY

Unité Hypnologie and Chronobiologie Clinique, Bordeaux, FR

Initial observation: Video Polysomnography recording in a 59 years old man shows a characteristical sequence beginning with an erection followed by saturation falling (which evolves from 97% to 93%) and then appearance of obstructive respiratory events. This sequence is preceded by a REM sleep period interrupted by an awakening followed by a supine position change. Saturometry signal analysis does not allow to made relationship between desaturation episode arising with respiratory sleep events nor with position change.

We attempted to estimate reproducibility of this observation on polysomnography coupled with erectometry realized within pelvis surgical assessments.

Material and methods: Eight patients benefited from a coupling recording polysomnography (MICROMED) and erectometry (RIGI-SCAN).

Results: Seven patients on eight presented episodes of night-erection. Sixteen episodes of erection were observed. Elevan episodes of erection associated to desaturations were found at five patient's. Both patients who did not present these phenomena were carrier of an important SAOS (IAH of 35/hour for one of the patients and 70 /h for the second). Ten sequences associating erection-desaturation-apneas were identified on 16 observed erections (62%)

Discussion: Nasal congestion was reported for Sidenafil (1) as side effect for phosphodiesterase inhibitors. Cornets nasal tissue answers in a similar way that corpora cavernosa and can participate in nasal obstruction during erection episodes usually observed in paradoxal sleep. Global mechanism of observed events requires a detailed research

Bibliographie: (1) Trimarchi & al Nasal congestion after visual sexual stimulation with and without sildenaWl (Viagra®): a randomized placebo-controlled study, Eur Arch Otorhinolaryngol (2008) 265:303–306 DOI 10.1007/s00405-007-0452-4.

Poster Session – Learning and memory

P715

Sleep and real-life gross-motor learning

K. HOEDLMOSER, J. BIRKLBAUER, P. EIBENBERGER, E. MUELLER and M. SCHABUS
University of Salzburg, Salzburg, AT

In the last decades, growing evidence has supported the hypothesis that sleep plays a functional role in the consolidation of memory, including procedural memories and motor learning in particular. Regarding the latter domain, available data suggest that sleep promotes the offline processing of fine-motor skills (e.g., finger tapping). However, corresponding data on gross-motor skills involving whole body movements remain extremely scarce, despite their utmost importance in our everyday life.

We tested 12 healthy male subjects (M = 25.75 years, SD = 4.17) using a between-subjects design. Each subject either participated in one of the following conditions: (i) 'SLEEP' – 8 h sleep during the night after learning in the evening, or (ii) 'WAKE' – 8 h wakefulness during the day after learning in the morning. In both conditions participants had to learn a real-life task: riding an inverse steering bicycle (cf. http://www.sleepscience.at/en/research) and were tested after training (TEST 1) as well as post-8 h-sleep or 8 h-wakefulness (TEST 2). Gross-motor performance was assessed during riding the inverse steering bicycle 5×30 m in a straight-line by the two variables 'time taken [s]' and 'standard deviation (SD) of steering angle [°]'. Sleep in comparison to wakefulness appears to support gross-motor performance concerning speed: condition 'SLEEP': TEST 1: 16.21 s (SD = 3.90), TEST 2: 17.03 s (SD = 5.24); condition 'WAKE': TEST 1: 15.79 s (SD = 3.01), TEST 2: 20.36 s (SD = 7.05). Furthermore, subjects participating in the 'SLEEP' condition showed almost no overnight decrease in gross-motor performance accuracy, indicated by an average SD of steering angle of 11.34°(SD = 4.97) during TEST 1 and 11.97°(SD = 4.11) during TEST 2, whereas subjects participating in the 'WAKE' condition reduced their performance from 10.26° (SD = 2.73) to 12.29° (SD = 4.32). Concerning our hypothesis regarding sleep spindles and its impact on gross-motor performance we found a robust effect for the relationship between fast (13–15 Hz) sleep spindle number and gross-motor performance increase over night ($r^6 = -0.869$; $P = 0.025$): subjects showing more fast sleep spindles during the night following inverse steering bicycle training were those being able to enhance gross-motor performance overnight.

These findings provide evidence that a retention interval containing sleep obviously helps to maintain learning of a real-life gross-motor task, whereas a period of wakefulness even leads to a performance decrease.

P716

The effects of sleep and time on semantic memory stabilisation and integration

A. REID and G. GASKELL
University of York, York, UK

Objectives: Two experiments explored the role of time/sleep on consolidation and stabilisation of new information that varied in its consistency with existing semantic memory. In a modified retroactive interference paradigm, A–B and A–C pairs contained novel (N) 'A' words (e.g. stunch) paired with real 'B' and 'C' words (e.g. horse, cat). Each pair was used in a size judgement task, with feedback on the correct response. Size relations across each triplet were semantically either congruent (e.g. 'horse > stunch > cat') or incongruent (e.g. 'cat > stunch > horse'). Participants were tested 20 min or 24 h later. We predicted that time/sleep and congruency would influence memory for A-B pairs in the 24 h condition. Furthermore, for this condition we predicted better integration of congruent information with existing knowledge.

Methods: In Experiment 1 participants learned the size relationship between 20 A–B pairs as described above. After a 15-min break 20 A–C pairs were learned. Half the A–B–C triplets formed a congruent size relationship while half did not. Lists were trained to 80% criterion. At test participants completed size judgements on the trained pairs and compared novel items with untrained words (generalisation). Coarse sleep stage data were collected in the 24 hr group using single channel Electroencephalography (EEG). Experiment 2 was identical except the training criterion was 95%.

Results: Analyses showed that A–C accuracy exceeded that of A–B items for the 20 min, but not 24 h, group. Furthermore, new information that was the least compatible with existing knowledge, the incongruent A–C list, resulted in the most errors after 24 h. In generalisation, a large negative correlation between B–C size difference and accuracy emerged at a delay, such that smaller (informative) differences facilitated performance. Lastly, stage 2 sleep was correlated with list performance and generalisation measures.

Conclusions: The reduction of retroactive interference in the 24 h group supports previous research indicating that sleep facilitates the restoration of weak memories (Drosopoulos et al. 2007). Further, congruency with existing knowledge also influenced performance, with incongruent relationships leading to poorer memory. Lastly, generalisation after a delay capitalised on the informational value of the learned relationships. These findings fit with systems-level consolidation in which new semantic memories become integrated with existing knowledge over time.

P717

Compensatory parietal activation during an episodic memory task following one night of total sleep deprivation

C. HARAND, F. BERTRAN, F. MÉZENGE, M. GAUBERT, J. GONNEAUD, R. LA JOIE, N. MOREL, B. DESGRANGES, F. EUSTACHE and G. RAUCHS
INSERM Research Unit U1077, Caen, FR

Objectives: Sleep deprivation after learning does not necessarily result in overt changes in behaviour, but rather in a covert reorganization of brain activity subserving performance. Using functional Magnetic Resonance Imaging (fMRI), we investigated the neural bases of episodic memory retrieval in subjects allowed to sleep or totally sleep-deprived during the first post-learning night.

Methods: On day 1, 35 young healthy participants (mean ± SD: 22.2 ± 2 years) learned a series of pictures. Immediately after learning, half of them were allowed to sleep at home ($n = 18$, Sleep group) while the others were totally sleep-deprived during the first post-learning night ($n = 17$, TSD group). On day 4, after two recovery nights, fMRI data were acquired during a recognition task and analyzed using SPM5. The contrast of interest 'Hits – correct rejection' in the TSD group was masked by the same contrast in

Sleep subjects (exclusive mask, $P < 0.05$) to reveal brain areas specifically activated in TSD participants but not in Sleep ones.

Results: Recognition performance did not differ between groups (mean ± SD: Sleep group: 84.2 ± 10.1; TSD group: 84.7 ± 8.7; $P > 0.87$). The analysis of fMRI data revealed a partially overlapping hippocampo-cortical neural network subserving memory retrieval in each group (pcorr < 0.05). However, higher responses were found in TSD participants, but not in Sleep ones (exclusive mask at $P < 0.05$) in the inferior parietal lobule bilaterally (IPL, $P < 0.001$). A whole brain regression analysis revealed that activity in the right IPL was positively correlated with recognition accuracy ($P < 0.001$). Then, we performed psychophysiological interactions (PPI) to determine whether the functional connectivity between various brain areas was influenced by the sleep status during the post-learning night. We showed that the left and right hippocampi were functionally connected with the left IPL in TSD participants, but not in Sleep ones ($P < 0.001$).

Conclusion: Group comparisons, regression and PPI analyses highlight the involvement of the IPL in episodic memory following sleep deprivation. Activity in this area may be interpreted as a compensatory mechanism to maintain performance at the same level than in Sleep participants.

P718

Sleep-dependent consolidation of schema-conformant and non-conformant items

S. J. DURRANT[1], N. HENNIES[2], S. A. CAIRNEY[2] and P. A. LEWIS[2]
[1]University of Lincoln, Lincoln, UK, [2]University of Manchester, Manchester, UK

Objective: Sleep plays an important role in neural reorganisation which underpins memory consolidation. The gradual replacement of hippocampal binding of new memories with intracortical connections helps to link new memories to existing knowledge. This process appears to be faster for memories which fit more easily into existing schemas. Here we seek to investigate whether this more rapid consolidation of schema-conformant information is facilitated by sleep, and the neural basis of this process.

Methods: Participants learned a set of 32 (consolidated) melodies in the first encoding session, and a further (unconsolidated) 32 melodies in a second encoding session 24 h later. Each session contained three blocks, and within a block every melody was played three times in succession with a different timbre each time, and participants were asked to identify which timbre was playing. Half of the learned melodies conformed to a tonal schema possessed by all enculturated Western listeners, and half of the melodies violated this schema.

The second session was immediately followed by a recognition test for all 64 learned melodies, plus 32 novel lures. Participants indicated whether or not they had heard a melody before, and also how confident they were about their answer on a scale of 1 to 3. During the recognition test, participants' brain activity was monitored with fMRI.

Results: Behaviour was analysed with a 2 × 2 ANOVA with factors Schema (conformant, non-conformant) and Consolidation (consolidated, unconsolidated). This revealed a main effect of Schema ($F_{1,17} = 4.446$, $P = 0.050$), a main effect of Consolidation ($F_{,17} = 16.071$, $P = 0.001$) and a significant Schema x Consolidation interaction ($F_{1,17} = 11.468$, $P = 0.004$), with recognition of schema-conformant items better if consolidated. The amount of REM sleep obtained predicted the greater recognition after consolidation ($r = 0.511$, $P = 0.015$).

The imaging data revealed greater activation for the unconsolidated melodies in the right hippocampus, while greater activation for the consolidated melodies appeared bilaterally in the putamen. Activation in the left putamen was predicted by the amount of REM sleep obtained ($r = 0.750$, $P = 0.0003$).

Conclusion: These data show that rapid consolidation of schema-conformant items may depend on REM sleep. At a neural level, the consolidation is represented by decreased involvement of the hippocampus and increased involvement of the striatum, also related to the amount of REM sleep obtained.

P719

Sleep facilitates acquisition of implicit phonotactic constraints in speech production

G. GASKELL[1], J. A. WARKER[2], R. FROST[1], J. GUEST[1], R. SNOWDON[1] and A. STACKHOUSE[1]
[1]University of York, York, UK, [2]University of Scranton, Scranton, PA

Objectives: Much of language learning involves the acquisition and modification of statistical relationships between linguistic elements. Previous research has shown that the phonemic composition of speech errors is malleable such that artificial constraints on the combinations of phonemes that co-occur can be learned in the lab [1]. However, second-order constraints, which involve particular combinations of phonemes in specific syllable positions, tend to be found only after the first day of testing. Here we addressed whether sleep affects the acquisition of these implicit constraints using a nap paradigm.

Methods: Participants ($N = 38$) were required to produce syllables in time with a metronome at a fast rate designed to elicit speech errors. The target syllable sequences contained two phonemes (/f/ and /s/) that were restricted to either onset or coda position depending on the nature of the vowel. After 48 training sequences, half the participants had a 90-min nap and the other half were asked to watch a film for a similar duration. All participants were then given a further session of 96 repetition sequences to examine whether implicit phonotactic constraints had been learned. Finally, participants were tested on their ability to generalise this knowledge more explicitly when asked to pick the sequence that matched their training constraints from two visually presented novel alternatives.

Results: For the nap ($P < 0.001$) but not the wake group ($P = 0.198$), speech errors at test adhered to the constraints provided by the training materials. Furthermore, the sleep group showed an ability to generalise this knowledge to new materials, whereas the wake group were at chance in this task. Analysis of polysomnography data suggested that generalisation ability was correlated with spindle activity on central electrodes.

Conclusion: These results suggest that sleep facilitates the abstraction and generalisation of speech knowledge from a limited input dataset. The speech error elicitation paradigm demonstrates that this process operates on implicit knowledge, but at the same time is able to facilitate explicit judgements of form. We interpret the data in the context of systems consolidation models of sleep.

1. Warker, J. A., Dell, G. S., Whalen, C. A., & Gereg, S. (2008). Limits on learning phonotactic constraints from recent production experience. Journal of Experimental Psychology-Learning Memory and Cognition, 34, 1289–1295.

P720

State-dependent consolidation of cross-modal integration

N. HENNIES[1], M. LAMBON RALPH[1], T. HAYES[1], P. HUGH[1], S. J. DURRANT[2] and P. A. LEWIS[1]

[1]University of Manchester, Manchester, UK, [2]University of Lincoln, Lincoln, UK

Objective: Sleep facilitates processes that contribute to semanticisation, such as statistical learning or the unitisation of information. Cross-modal integration represents another crucial element of semantic memory formation. Here, we seek to investigate the effects of sleep and time dependent consolidation on the integration of cross-modal information using a novel category learning paradigm.

Methods: Participants performed a multimodal category learning task (MCL), in which stimuli were categorised into two classes as quickly as possible. Each stimulus was characterised by an image (Asian character), a location, and a pitch. Category assignment was predefined based on obvious image characteristics. Integrated information about location and pitch was also sufficient for correct categorisation, but participants were not aware of this hidden structure. Participants categorised 48 stimuli repeatedly over five blocks. Because location and pitch information preceded the image for every stimulus, abstraction of the hidden structure was associated with speeded reaction time. Categorisation of the same images without location or pitch information served as a control task. The MCL and the control task were repeated with a novel set of stimuli after a consolidation interval, which differed across four groups (20 min, 24 h, 12 h-day, or 12 h-overnight (including sleep)). There were 13 participants in each group.

Results: Before the consolidation interval, there was no between-group difference in performance and no difference in performance within groups between the MCL and the control task. After the consolidation interval, however, both the 24 h and the 12 h-day group, performed significantly faster in the last block of the MCL compared to the control task (One-sample *t*-test, 24 h: $P = 0.015$, 12 h-day: $P = 0.002$). This effect was not observed in either the 20 min group ($P = 0.226$) or 12 h-overnight group ($P = 0.390$).

Conclusion: These data show that participants can integrate cross-modal information in the context of a category learning task, and suggest that this skill develops in a time-dependent manner. Interestingly, this effect was observed after consolidation across wake but not sleep, suggesting that cross-modal integration may rely upon a different form of state dependent consolidation than other semanticisation processes.

P721

Does sleep help in extracting semantic knowledge from episodic experience?

M. SCHÖNAUER, E. BAYKARA, A.-K. LORENZ, J. MÜLLER, F. PARGENT and S. GAIS

LMU Munich, Munich, DE

Objectives: One recent theory regarding the effect of sleep on declarative memory is that sleep allows hippocampal episodic memory to become integrated into semantic neocortical networks, a process called semanticization. In a series of experiments, we investigated the behavioural aspects of this hypothesis.

Methods: In Study 1, subjects were presented with 80 images of birds and invented bird family names. During later recall, they had to recognize individual images and classify old and new images into families. In Study 2, subjects learned 40 series of holiday pictures. Each series showed the one person on holiday. Later, they were shown photos of the same persons in a different context and asked to remember the name of the person and the topic of the holiday (e.g. 'Egypt', 'Camping', 'Beach'). In addition, 80 previously shown images were presented with some detail masked out. Here, subjects had to recall what was shown under the mask. In Study 3, subjects saw abstract objects differing in colour, pattern and shape. For pairs of items, they had to judge, which item ranked higher. To do this task, they had to remember the individual items and extract a general underlying rule. Knowledge of the rule and memory for individual items was tested later. Finally, Study 4 tested whether subjects who had learned lists of words were quicker to find visually (thrust - truths) or semantically (thrust - shove) similar words later. All fours studies compared conditions where subjects slept between initial learning and recall with conditions where subjects stayed awake.

Results: In none of the four studies we could find any significant difference between sleep and wake conditions. Subjects were able to recognize visual items, categorize new images, extract general information from series of presentations, and remember visual detail with similar performance after sleep and wakefulness. Single or repeated presentation of items was of no importance either. Semantic or visual aspects of words were equally quickly accessed, as was item and rule information.

Conclusion: Together, these studies suggest that the abstraction of rules underlying previously learned material does not seem to be a primary function of sleep. Although these studies have negative results, we believe that they do not represent experimental failures to find an effect (Type II Error). Instead, we believe that they provide an important clue on how sleep does and does not affect memory consolidation.

P722

The effects of nap duration on the consolidation of declarative and procedural memories

K. TAO and M. HAYASHI

Hiroshima University, Higashihiroshima, JP

Objectives: A number of studies have demonstrated that declarative and procedural memories improve across nocturnal sleep. The relationship between memory consolidation and sleep stages has been under discussion. Nocturnal sleep contains all of the sleep stages so that it is difficult to eliminate the influences of each sleep stage. Then we focused on a daytime nap to examine the influence of sleep stage 2 and slow wave sleep (SWS) for memory consolidation.

Methods: Forty participants trained paired association and finger tapping sequence tasks at noon and were tested at 5 pm. At 2 pm., 29 participants (18–24 year) took a nap including sleep stage 2 ($n = 13$) or SWS ($n = 16$), while the others remained awake ($n = 11$).

Results: The mean total sleep time was 17.4 (2.7) min in sleep stage 2 group and 52.9 (5.4) min in SWS group. Performance of paired association tended to improve for those who took a nap containing SWS compared to those who stayed awake, and positively correlated with EEG delta band power (r72, $P < 0.05$). Although performance of finger tapping sequence did not differ among the groups, it positively correlated with EEG sigma band power which reflects fast spindle activity (r76, $P < 0.05$).

Conclusion: These results suggest that SWS is necessary to consolidate the memory trace of declarative memory, and that fast spindle concerns procedural memory.

P723

Revisiting Scrima's hypothesis of REM and NREM sleep contributions in memory consolidation and resistance to retroactive interference for verbal material

G. DELIENS, R. LEPROULT, D. NEU and P. PEIGNEUX
Université libre, Brussels, BE

Objectives: Scrima (1982) hypothesized that Rapid Eye Movements sleep (REM) contributes consolidating recently acquired memories, whereas non-REM (NREM) sleep contributes preventing retroactive interference on the newly acquired material. We tested this hypothesis in a controlled morning nap paradigm aimed at producing predominant post-training REM or NREM sleep episodes. Indeed, REM can be observed in short naps under appropriate homeostatic and circadian conditions, by depriving the end of the night of sleep (richer in REM sleep) then allowing a nap in the morning when REM circadian propensity is high (see Tinguely et al., BMC Neurosci 2006: 7: 2).

Methods: Twenty-five volunteers (mean age 26.2 ± 4.7 years) slept in the laboratory under polysomnographic (PSG) control for 6 h after sleep onset (±midnight). At 9:00 in the morning, they learned a list of 28 unrelated word pairs (A), then at 10:00 were allowed to sleep again or kept awake, under EEG control. They were then awakened after 45 min. At 12:00, a novel list of word pairs (B) was learned just before delayed recall of list A. List B was composed of 50% word pairs in which the first word of the pair was presented in list A, hence creating interference. The same procedure was repeated one month later in the other condition (morning sleep versus wake).

Results: Average sleep duration during nap was 32.5 ± 9.6 min. Ten subjects exhibited REM sleep (mean REM duration 5.7 ± 4 min, NREM S2 16.4 ± 10.9 min) whereas 13 exhibited deep NREM stage 3 (S3) sleep (mean S3 5.4 ± 1.7 min, S2 24.4 ± 7.6 min). Recall of word pairs not subjected to interference (NIP) was similar in nap and wake conditions ($P > 0.3$), also in nap conditions with versus without (a) REM ($P > 0.3$) or (b) NREM S3 sleep ($P > 0.17$). Interference effects (correct recall of NIP minus word pairs with interference [IP]) were found in nap ($P < 0.001$) but not in wake ($P > 0.09$) condition (interaction effect $P < 0.04$). In naps however, interference effects weakened after sleep with versus without NREM stage 3 ($P < 0.05$), whereas no difference was found between naps with versus without REM sleep ($P > 0.3$).

Conclusion: Our results partially support Scrima's hypothesis that NREM, or at least slow wave sleep (NREM S3) protects novel memories against interference. Indeed, interference effects were decreased after naps containing slow wave sleep. At variance, we failed to evidence REM sleep-related consolidation effects. Hence, future studies should further confront and investigate these issues.

This study was supported by a FNRS (Fonds National Belge de la Recherche Scientifique) grant CC 1.5.184.10F. GD is supported by FNRS. A Brains Back to Brussels 2010 post-doctoral grant supports RL.

P724

Does sleep favours generalisation of visual-texture discrimination skills?

G. DELIENS, Y. SCHROEDER, G. TINGUELY and P. PEIGNEUX
Université Libre, Brussels, BE

Objectives: It is known that post-training sleep improves performance in a retinotopic manner in the visual texture discrimination (VTD) task (e.g. Karni et al. 1994). Here we tested the hypothesis of a sleep-dependent generalization of visual discrimination abilities.

Methods: In the Wake group, subjects ($n = 16$, mean age 25.1 ± 2.2 years) practiced VTD at 9:00 (learning) and 19:00 (testing) after an active wakefulness period. In the Sleep group, subjects ($n = 16$, mean age 23.9 ± 1.6 years) learned at 20:00 and were retested at 8:00 after a night of sleep. In each condition, participants received monocular training on the left or right eye ($n = 8$/subgroup). An eyepatch occluded vision with the untrained eye. In the VTD task, subjects had at each trial to report 2 targets presented simultaneously: the identity of the centrally displayed (foveal vision) rotated letter (T or L), and the vertical/horizontal orientation of 3 aligned diagonal bars, located laterally at 2.29–3.43° of visual angle (peripheral vision) in a 19 × 19 horizontal bars background. At learning, 10 blocks (51 trials/block) were administered. Stimulus onset asynchrony (SOA) decreased between blocks (360, 260, then 220 to 60 msec by 20 msec-steps). The shortest SOA allowing 80% correct responses both for letter and orientation was computed. At testing, blocks were administered likewise, with the first SOA set at the best SOA at learning + 40 msec, under 4 conditions in a fixed order: same visual quadrant (SVQ) at trained (TE) then untrained (UE) eye, other visual quadrant (OVQ) at TE then UE. Performance was computed as the SOA difference between learning and each test condition (i.e. SOA difference = 0 means no improvement)

Results: SOA was similar between trained eyes ($P > 0.3$) and groups ($P > 0.7$) at learning. At delayed testing, t-tests against the null value hypothesis disclosed significant SOA improvement in the Sleep group for TE and UE on SVQ (ps < 0.001), and a nearly significant improvement for UE-OVQ ($P < 0.06$) but not TE-OVQ ($P < 0.12$). In the Wake group, effects were non-significant in all conditions (P range >0.3 < 0.8).

Conclusion: Our results confirm prior findings that visual perceptual skills benefit from sleep both for trained and untrained eyes in the same visual quadrant. Additionally, our results suggest that sleep may also favours generalization of visual discrimination abilities to untrained visual quadrants, besides retinotopic specificity in V1. GD is supported by FNRS (Fonds National Belge de la Recherche Scientifique, Belgium)

P725

The role of stage 2 in the consolidation of an engaging motor learning task across multiple post-learning nights of sleep

C. D. HIGGINSON, K. R. PETERS and C.T. SMITH
Trent University, Peterborough, CA

Objectives: The purpose of the present study was to examine how sleep architecture is affected by the acquisition of a complex motor learning task over three post-learning recording nights.

Methods: Participants included 24 university students (Mage = 21.00, SD = 2.83) randomly divided into a learning group ($n = 12$) and a control group ($n = 12$). The complex motor learning task was Rock Band Beatles. Participant's sleep was recorded polysomnographically over 5 consecutive nights. The second recording night was used as the baseline measure. On the evening of the third recording night, those in the learning group underwent a 1-h learning session in the video game Rock Band Beatles using both the guitar and drum instruments. Control participants viewed a concert DVD during this time. Sleep was recorded for three nights following acquisition of the task, with a retest 1-week post-learning. A series of 2(group) × 4(night) mixed design ANOVAs were performed on the percent of stage 2 sleep, slow wave sleep (SWS) and rapid-eye movement (REM) sleep. Additionally, a series of correlation coeffi-

cients were calculated between these sleep parameters during each post-learning night and the percent improvement on the task at retest.

Results: Preliminary results (10 participants included; 4 controls) of the ANOVAs revealed a main effect of group for the percent of stage 2 sleep [$F_{1,8} = 4.60$, $P = 0.06$]. The learning group had significantly more stage 2 (M = 49.13, SD=3.86) than the control group (M = 43.79, SD = 3.86). No other significant differences were found for the percent of SWS or REM sleep between the groups. The correlation analyses revealed significant, positive relationships between the percent of stage 2 sleep during the first post-learning night and the percent improvement at retest on song 1 guitar (r = 0.87, $P = 0.02$), song 2 guitar (r = 0.80, $P = 0.06$) and song 1 drums (r = 0.84, $P = 0.04$).

Conclusion: These preliminary results suggest that stage 2 sleep may be involved with consolidation of a complex motor task.

P726

Nap-related consolidation in learning the grammar and vocabulary of a novel language

J. MIRKOVIC and G. GASKELL
University of York, York, UK

Objectives: Various aspects of language learning are influenced by memory consolidation (e.g. Dumay & Gaskell, 2007; Tamminen et al. 2010). In infants, sleep-related consolidation aids abstraction: short post-learning naps have been beneficial in abstracting underlying grammars in artificial language paradigms (e.g. Hupbach et al. 2009). Here, we investigated the influence of a 90-min nap in adults learning both the vocabulary and grammar of an artificial language.

Methods: We used a word-picture matching task to simulate grammar and vocabulary learning. Half the novel words had a specific determiner/suffix combination (e.g. determiner: tib, suffix: -esh) and were paired with pictures of typically female occupations (e.g. tib scoiffesh - ballerina). The other half had a different determiner/suffix combination and were paired with pictures of male occupations (e.g. ked, -ool in ked jorool; sailor). After training, participants took a 90-min break filled with either a nap with polysomnography or awake control. All were then assessed for grammatical and vocabulary knowledge. In the first grammatical test, participants saw the novel word and its matching picture (e.g. scoiffesh – ballerina) and selected the appropriate determiner. In a second task, participants saw a new set of words and pictures, half consistent with the grammar of the training set, and half inconsistent. The vocabulary measures were explicit recall, where participants viewed the pictures from the training set and had to name them in the novel language, and auditory translation recognition, where participants indicated whether a novel word matched its English translation.

Results: The groups showed equivalent performance in training ($P = 0.314$). At test, there was a dissociation between the influence of intervening sleep on grammar and vocabulary performance. For grammar, there were no significant differences between groups in either test, with both groups showing good grammatical knowledge. In contrast, participants who napped after learning performed better on vocabulary tests (e.g., nap: 94% of the novel words correctly matched to their English translation equivalents, versus wake: 85%, $P = 0.024$).

Conclusions: The findings show that, in adults, naps may not aid the process of grammar abstraction in a novel language, but vocabulary learning clearly benefits from sleep. These results suggest that the arbitrariness of the mapping may determine the involvement of sleep in learning and consolidation.

P727

Effects of sleep on knowledge integration and automaticity of processing: word learning and numerical cognition

E. THAM and G. GASKELL
University of York, York, UK

Objectives: Two experiments investigated whether sleep benefits memory for new numerals and words by examining automaticity in the activation of meanings, using Size Congruity Effects (SCEs) and Semantic Distance Effects (SDEs) in a second-language learning paradigm. SCEs occur when comparing semantic/font size of item-pairs: responses are faster when both dimensions are congruent. SDEs involve swifter semantic size judgements for distant compared with closer items. We predicted participants who slept before testing would show stronger SCEs and SDEs for the new items than participants remaining awake. Based on existing literature, we also hypothesized that differences in automaticity would be related to components of sleep, namely slow-wave sleep (SWS) and sleep spindle activity.

Methods: In Experiment 1, participants learned 9 Malay words in the evening/morning, and were tested after an equivalent period of sleep or wakefulness. During testing, participants compared congruent and incongruent item-pairs differing in relative physical-font and semantic size. Participants had to select the semantically larger item ignoring font size, first using English/existing (baseline) stimuli and then Malay words. In Experiment 2, participants learned 9 novel numerals instead of words. The training and testing procedure was similar to that of the first experiment. Sleep polysomnography data was collected in both experiments.

Results: Mixed ANOVAs revealed that for word stimuli (Experiment 1), participants who slept compared to remaining awake, exhibited stronger SCEs and SDEs for Malay comparisons. The above results were not confounded by circadian factors as there were no equivalent differences for English stimuli. Furthermore, the strength of SCE and SDE effects for Malay comparisons was correlated with participants' sleep spindle activity and SWS respectively. In contrast, there was no significant difference in performance between the wake and sleep groups when comparing both novel and existing numerals (Experiment 2); and no significant relationship between the strength of SCE/SDE and unique sleep components.

Conclusion: Findings suggest that although offline wakeful consolidation is sufficient for numerical learning, sleep is crucial in enhancing automaticity of processing meanings in new word learning. Moreover, SWS and sleep spindles are both associated with memory consolidation, helping to strengthen new word memories and integrate them with existing knowledge.

P728

Characteristics of theta waves during wakefulness – a marker of synaptic strength?

S. FATTINGER[1], S. KURTH[2], M. RINGLI[3], O. JENNI[3] and R. HUBER[3]
[1]ETH Zurich, Zurich, CH, [2]University of Colorado Boulder, Boulder, CO, [3]University Children's Hospital Zurich, Zurich, CH

Objectives: With increasing duration of wakefulness, sleep pressure and the synchronisation of neuronal activity increases, which might be due to an increase in the strength of cortico-cortical connectivity (Vyazovskiy et al., 2009). This increase in synchrony is followed by a gradual net decrease during subsequent sleep indicating an overall reduction of synaptic strength. In the spontaneous electroencephalogram (EEG) these changes in synaptic strength

are best reflected in the slope of slow waves (SW, 1–4.5 Hz) during non-rapid-eye-movement (NREM) sleep: the steeper the slope the higher synaptic strength. Pre-pubertal children show increased markers of synaptic strength compared to adults. A recent study in rats reported evidence for a close relationship between the electrophysiological origin of sleep SW and theta activity during wakefulness. Our aim was to investigate whether in children theta waves, and in particular their slopes, might be used as markers of changes in synaptic strength during the day.

Methods: We recorded 4 min of spontaneous waking high density (hd) EEG (128 channels) in the evening and morning, right before and after sleep in 11 healthy children (8.7–12.6 years). ICA was performed to remove heart rate, muscle or eye movements artefacts (26.4 ± 7.2 (mean ± SD) components were rejected). After band pass filtering (Chebyshev Type II, 2.5 to 15 Hz), theta waves (TW, 6.25–8 Hz) were detected as negative signal deflection between two consecutive positive peaks.

Results: We found increased theta activity by ~68.6% (±23.7%, $P < 0.001$) and increased amplitudes of detected TW in the evening compared to the morning ($P < 0.001$). The slopes of TW still exhibited a significant increase from morning to evening when controlling for the amplitude increase (slope of TW at an amplitude of 10 μV, morning: 300.5 ± 5.0 μV/s (mean ± SD), evening: 305.8 ± 6.6 μV/s, $P < 0.05$; slope of TW at an amplitude of 4 μV, morning: 128.9 ± 3.3 μV/s, evening: 134.5 ± 4.5 μV/s, $P < 0.01$).

Conclusion: In our children theta activity increased from morning to evening. Under baseline condition no such increase was reported for adults. This age difference may be due to a faster build-up of sleep pressure during the day in children compared to adults. Such an increase in sleep pressure during the day might reflect an increase of synaptic strength. The slope increase of TW from morning to evening might represent a marker of this increased synaptic strength.

P729

EEG sigma and slow wave activity during NREM sleep correlate with overnight declarative and procedural memory consolidation

C. NISSEN, J. HOLZ, H. PIOSCZYK, B. FEIGE, K. SPIEGELHALDER, C. BAGLIONI and D. RIEMANN

University Medical Center Freiburg, Freiburg, DE

Objectives: Previous studies suggest that sleep-specific brain activity patterns such as sleep spindles and EEG slow wave activity (SWA) contribute to the consolidation of novel memories. The generation of both sleep spindles and SWA relies on synchronized oscillations in a thalamo-cortical network that might be implicated in synaptic strengthening (spindles) and downscaling (SWA) during sleep.

Methods: This study further examined the association between EEG power during NREM sleep in the spindle (sigma, 12–16 Hz) and slow wave frequency range (0.1–3.5 Hz) and overnight memory consolidation in 20 healthy subjects (10 men, 27.1 ± 4.6 year).

Results: We found that both EEG sigma power and SWA were positively correlated with the pre-post sleep consolidation of declarative (word list) and procedural (mirror tracing) memories.

Conclusions: These results, although only correlative in nature, are consistent with the view that processes of synaptic strengthening (sleep spindles) and synaptic downscaling (SWA) might act in concert to promote synaptic plasticity and the consolidation of both declarative and procedural memories during sleep.

P730

The relationship between sleep spindles and memory consolidation is dependent on slow wave sleep activity

R. COX, W. F. HOFMAN and L. M. TALAMINI

University of Amsterdam, Amsterdam, NL

Objectives: Sleep spindles have been implicated in episodic memory consolidation. Indeed, various spindle measures increase after learning, and/or correlate with memory retention over sleep. As the benefits of sleep for declarative memory performance are specifically related to SWS, spindles during SWS might be particularly relevant. However, previous studies on spindles and memory did not distinguish between sleep stages with and without slow waves. We, therefore, investigated the relation between memory retention and sleep spindles in stage 2 sleep without slow oscillations and in SWS involving both spindles and slow oscillation. In addition, sleep architectural and power measures for different frequency bands were correlated with memory retention.

Methods: Subjects ($N = 19$) were exposed to a film fragment (9.30 am). Memory for film content was assessed both immediately and following an 11-h retention interval, containing a 2-h nap under polysomnographic registration. For stage 2 sleep and SWS separately, spindles were detected (algorithm similar to Ferrarelli's) and power was determined in various frequency bands. Sleep spindle density (spindles count/min), as well as the power parameters and relative occurrence of sleep stages, were correlated with retention.

Results: We found a 60% higher spindle density during deep sleep than during light sleep ($t = -5.1$; $P < 0.001$). Average spindle amplitudes and durations, however, did not differ from light to deep sleep. With regard to spindle density and memory retention, we found a strong and highly significant positive correlation during SWS ($r = 0.75$, $P = 0.001$), but none whatsoever during stage 2. These results remained similar after controlling for pre-sleep memory performance and are thus not secondary to influences of encoding success on subsequent spindle density. None of the sleep architectural or power measures correlated robustly with memory retention.

Conclusions: Contrary to expectations, we found higher spindle density during deep than during light sleep. Elementary spindle physiology seemed to be unaffected by sleep depth. We showed that, during SWS, spindle density is related to memory retention. These findings suggest a central role of SWS-related spindles in the neural mechanisms underlying declarative memory consolidation. This is in line with studies suggesting that spindles are more effective at potentiating cortical networks when in the presence of an attendant slow oscillation.

P731

Reactivating newly learnt words during slow wave sleep triggers REM-mediated integration of new memories and existing knowledge

J. TAMMINEN[1], M. LAMBON RALPH[2] and P. LEWIS[2]

[1]University of London, Egham, UK, [2]University of Manchester, Manchester, UK

Objectives: Previous research has shown that nocturnal sleep facilitates the integration of newly learnt words into existing stores of lexical knowledge. Here, we seek to establish if this lexical integration is also seen after a 90-min daytime nap, and whether auditory replay of the new words during slow wave sleep (SWS) enhances lexical integration and subsequent recall of these new words.

Methods: Forty subjects learnt 34 novel fictitious words (e.g. dolpheg) which overlapped phonologically with existing words (e.g.

dolphin) at 11 am. At 1 pm, after an immediate test of recall of the words, word meanings, and lexical integration, half of the subjects slept for 90 min (nap group), and half remained awake watching a DVD (wake group). A retest took place after this consolidation opportunity. Critically, half of the novel words were replayed to the nap group over loudspeakers during SWS.

Results: Lexical integration was measured by comparing recognition times (RT) to existing words for which a new overlapping word had been learnt (e.g. dolphin) with RTs to control words for which no new overlapping word had been learnt (e.g. cathedral). As in earlier work involving nocturnal sleep, lexical integration (revealed by an inhibitory RT effect on existing words with a novel word neighbour) was observed only after a nap ($P = 0.05$, all ps>0.05 in wake group). Free recall of novel words declined in the wake group ($P < 0.05$) but remained unchanged in the nap group. Reactivation did not impact significantly upon any of the memory tests. Interestingly however, the emergence of the lexical integration effect in the nap group was predicted by time spent in rapid eye movement (REM) sleep ($r = 0.47$, $P = 0.04$), and this effect was carried only by the reactivated words ($r = 0.54$, $P = 0.01$, non-reactivated: $r = 0.02$, $P = 0.94$).

Conclusion: REM sleep has been implicated as a brain state which facilitates activation of wide semantic networks of information. This is supported by our finding that REM sleep is involved in integrating new words with existing lexical knowledge. However, we observed this only in novel words that were reactivated during SWS. Our finding fits well with the suggestion that spontaneous reactivation of new memories during SWS tags these memories for subsequent strengthening during REM. We propose that auditory replay of a subset of novel words during SWS may have lead to more prominent tagging of these words, followed by increased reliance on REM-dependent consolidation.

P732

Slow oscillation amplitudes and up-state lengths relate to memory improvement

D. P. J. HEIB[1], K. HOEDLMOSER[1], H. GRIESSENBERGER[1], J. ZEITLHOFER[2], G. GRUBER[2], P. ANDERER[2] and M. SCHABUS[1]
[1]University of Salzburg, Salzburg, AT, [2]Medical University of Vienna, Vienna, AT

Objectives: There is growing evidence for an active involvement of sleep on memory consolidation. Besides hippocampal sharp wave-ripple complexes and sleep spindles, slow oscillations (SO) appear to play a key role in the process of sleep-associated memory consolidation. Indeed, the induction of slow oscillations during sleep (Marshall, Helgadottir, Molle, & Born, 2006) provided first evidence for a causal role of slow oscillations in declarative memory consolidation. Furthermore, there is evidence that the amplitude of slow oscillations increase during a night after learning a declarative memory task in comparison to a control night (Mölle, Eschenko, Gais, Sara, & Born, 2009). In motor learning such increases were even linked to overnight memory performance changes (Huber, Ghilardi, Massimini, & Tononi, 2004). However, it is unresolved whether learning-induced changes alter the slow oscillation amplitude and effect overnight memory gains in performance.

Methods: Twenty-four subjects (12 men) aged between 20 and 30 years participated in a randomized, within-subject, multicenter study. Subjects slept three times for a whole night in the sleep laboratory with complete polysomnography. Whereas the first night only served for adaptation purposes, the two remaining nights were preceded by an explicit word-pair task (learning night) or by a non-learning control task. Slow oscillations were detected in non-rapid eye movement sleep over electrode Fz according to standard criteria (Massimini, Huber, Ferrarelli, Hill, & Tononi, 2004). The Peak-to-peak amplitude and length of slow oscillations were analyzed. For analysis we focused on subjects showing overnight memory enhancement (I+) versus no enhancement (I-).

Results: The peak-to-peak amplitude change from the control night to the learning night differed tendentiously between I+ and I- ($F_{1,20} = 4.85$, $P = 0.05$). Whereas I+ exhibited an amplitude increase I- showed a decrease. Across groups data reveals that overnight memory change correlates with higher SO peak-to-peak amplitude changes ($r20 = 0.41$, $P < 0.05$). Furthermore, the positive – but not the negative – SO phase length was significantly correlated with overnight memory gains ($r20 = 0.388$, $P < 0.05$).

Conclusion: Overnight (declarative) memory improvement is associated with subtle changes in slow oscillation amplitude as well as the positive SO phase duration.

P733

EEG theta synchronisation during retrieval indicates overnight memory consolidation

D. P. J. HEIB[1], K. HOEDLMOSER[1], W. KLIMESCH[1], H. GRIESSENBERGER[1], J. ZEITLHOFER[2], G. GRUBER[2], P. ANDERER[2] and M. SCHABUS[1]
[1]University of Salzburg, Salzburg, AT, [2]Medical University of Vienna, Vienna, AT

Objectives: Research on the beneficial effect of sleep for memory is anything but new. It is supposed that newly acquired memory traces become stable during sleep by integrating them into neocortical networks. During wakefulness, successful memory retrieval is related to the extent of EEG theta synchronization: remembered in comparison to non-remembered items show a stronger theta synchronization. Thus, consolidating effects of sleep are expected to be reflected by changes in theta synchronization from retrieval before to retrieval after a night of sleep.

Methods: A total of 24 subjects (12 males, mean age = 24.95 year) participated in the present study. In the evening each participant learned 160 word pair associates. After a short break, a first cued recall session (R1) was conducted. Now, only the first word of each pair was presented (cue) and subjects were instructed to report the respective corresponding word (target). Recall performance was tested again on the subsequent morning after 8 h of sleep (R2).

EEG was recorded during recall as well as during sleep. Preliminary analysis focused on the percent change in theta power from pre to post appearance of all cue words over electrode Cz. Theta changes were compared between correct remembered target words (HITS) and non- remembered items (MISSES) as well as between evening R1 and morning R2 recall.

Results: In R1, theta synchronization was stronger for HITS than MISSES ($P = 0.003$). However, this difference was no longer existent after a night of sleep during morning R2 recall as theta power increased for MISSES. By contrast, theta power for HITS did not differ between R1 and R2. Interestingly, the amount of theta power increase from R1 to R2 for MISSES was positively correlated with the spectral power in the low spindle range (11–13 Hz) during the first hour of sleep ($P = 0.003$).

Conclusion: It is concluded that the inability to recall an associated target word in the evening (R1) might lead to a (further) encoding of the respective cue word. Thus, for MISSES, only the cue words might

benefit from the nightly consolidation process. It is speculated that the increase in theta power for MISSES from R1 to R2 is reflecting exactly that overnight strengthening of the cue words. This assumption is supported by the fact that overnight theta change is correlated with the spectral power during sleep in a frequency range (11–13 Hz) previously related to sleep associated consolidation processes.

P734

The associations between sleep spindle activity, general cognitive ability and declarative learning

A. MARIC[1], C. LUSTENBERGER[2], R. DÜRR[3], P. ACHERMANN[3] and R. HUBER[2]

[1]University Hospital Zurich, Zurich, CH, [2]University Children's Hospital Zurich, Zurich, CH, [3]University of Zurich, Zurich, CH

Objectives: Studies report sleep dependent performance improvement in declarative memory tasks which, at times, is correlated to sleep spindle activity (SpA). SpA also reflects intellectual abilities. The thalamoreticular nucleus and the thalamocortical system are the generators of sleep spindles and enable efficient encoding and processing during wakefulness. We examined if the relationship between SpA, intelligence measures and declarative learning reflect the efficiency of the thalamocortical system.

Methods: Fifteen subjects performed an unrelated word-pair task in the evening and in the morning. Overnight performance improvement and initial acquisition rate, a measure of learning efficiency, were recorded for both recalls. All-night SpA (EEG power between 12–15 Hz during Non-REM sleep) was calculated for the C4-A1 derivation. General cognitive ability was assessed by information processing speed (ZVT). Another six subjects were trained on the same word pair task, with 5 min wakefulness between two recalls. Their performance improvement was compared to the overnight performance improvement after 2 h of sleep.

Results: Information processing speed (1.6 ± 0.3 1/s, mean ± SD) and SpA (8.3 ± 3.9 μV2) were positively correlated ($r = 0.55$, $P < 0.05$). In addition, SpA correlated negatively with the overnight performance improvement (+4.6 ± 1.9 correct answers; $r = -0.77$, $P < 0.005$) and positively with the initial acquisition rate (75.5 ± 9.3%; $r = 0.78$, $P < 0.005$). Performance improvement after 5 min wakefulness (+5.2 ± 4.2 correct answers) was similar to the one observed after one night of sleep ($P = 0.43$).

Conclusion: SpA is associated with general cognitive ability and learning efficiency but not with overnight performance improvement. SpA might therefore reflect the efficiency of the thalamocortical network. Furthermore, the performance improvement in the present experiment is not sleep dependent. Thus, sleep spindles are rather a marker for learning during encoding in wakefulness, i.e. learning efficiency, than contributing to learning itself. In summary, a more efficient thalamocortical system is thought to process information more efficiently, which is probably an important aspect of intellectual ability.

This work was supported by the Swiss National Science Foundation and the Swiss Research Foundation on Mobile Communication.

Poster Session – Cognition and disease

P735

Relationship between sleep and effectiveness of rehabilitation in hemiplegia patients after stroke

K. HAYASHIDA[1], S. HIGUCHI[2], J. KAJIWARA[1], K. KAI[1], K. ZAITSU[2], K. SETSU[1] and F. HATTORI[1]
[1]Nagao Hospital, Fukuoka, JP, [2]Kyushu University, Fukuoka, JP

Recent studies have demonstrated that sleep enhances procedural memory and motor learning. Although the effect of sleep on motor learning is reduced by aging, it is suggested that motor learning was accelerated by sleep in old patients with stroke. However, the effects of quantity and quality of sleep on motor learning in stroke patient remain unclear. In this study, relationships between sleep variables and effectiveness of rehabilitation in hemiplegia patients after stroke were examined.

Fifteen consecutive stroke patients (mean age: 60.3 ± 11.7 years) admitted to a convalescent rehabilitation ward volunteered to participate in this study. Patients with severe dementia or higher brain dysfunction were excluded. Subjects gave written informed consent for participation in the study, which was approved by the research ethics committee of Nagao hospital. An actigraph (Actiwatch-L) was placed on the unaffected wrist for one week to estimate an actual sleep time, wake after sleep onset (WASO) and sleep efficiency. The Functional Independence Measure (FIM) scale was used to accesses the effectiveness of rehabilitation. The FIM assesses the degree of assistance required by the patient in order to perform motor and cognitive tasks of everyday life. The FIM gain is the difference between the total FIM on admission and the total FIM on discharge. The FIM efficiency (FIM gain divided by the length of stay) is used for an index to evaluate the rate of functional improvement.

Significant positive correlations were found between the actual sleep time and the discharge motor FIM score (r = 0.659), between the actual sleep time and the FIM efficiency (r = 0.703), between WASO and length of stay(r = 0.785), and between the sleep efficiency and the discharge motor FIM (r = 0.723). From stepwise multiple regression analysis, only the actual sleep time was significant for the mean FIM efficiency (R^2 = 0.49, P = 0.003). This study is first to demonstrate the relationship between sleep and effect of rehabilitation in hemiplegia patients after stroke in actual clinical situation. The results suggest that motor learning by sleep relates to the improvement of effectiveness of rehabilitation.

P736

Specific memory effects of continuous positive airway pressure in patients with obstructive sleep apnoea

S. HATIF, F. MARCHAND and P. FOSSATI
Service de Psychiatrie, Paris, FR

The objectives of the study was to better understand the effects of continuous positive airway pressure (CPAP) treatment on memory in patients with obstructive sleep apnea (OSA).

Methods: Thirteen patients with OSA were administered neuropsychological tests of short-term and working memory as well as long term verbal and visuo-spatial memory prior to CPAP treatment, and at 6-month follow-up treatment. Adherence to CPAP treatment was measured for each participant. Statistical analyses were conducted to examine the difference of memory performance on memory tests before and after CPAP treatment.

Results: Performance on verbal digit span and performance on non verbal episodic memory were statistically different after CPAP treatment (t = -3.8, P < 0.05 and t = -4.2, P < 0.05 for immediate recall and t = -4, P < 0.05 for delayed recall). Performance on working memory and performance on verbal episodic memory were not different prior and after CPAP treatment (t = -0.7, P > 0.05, t = -1.3, P > 0.05, t = -0.80, P > 0.05).

Conclusions: These preliminary findings indicate that CPAP treatment effects are memory specific, depending on the processing and the cerebral areas implicated. Digit verbal span and non verbal episodic memory seems to share passive storage processing (phonological loop) related to parietal and occipital areas. On the other hand, working memory and verbal episodic memory rather depend on encoding and retrieval processing related to fronto-temporal areas.

P737

Sleep-disordered breathing and cognitive impairment among patients with heart failure

C. HJELM[1], A. STRÖMBERG[1], K. ÅRESTEDT[2], A. BROSTRÖM[3]
[1]University Hospital Linköping, Linköping, SE, [2]University of Kalmar, Linköping, SE, [3]Linköping University, Linköping, SE

Background: Heart failure (HF) and sleep disordered breathing (SDB) are two often coexisting problems among elderly. Severe left ventricular dysfunction, systolic hypotension, apnoeic events and cerebral hypoperfusion can be potential causes for cognitive impairment. Few studies have, however, investigated the effects of SDB on cognitive function in patients with HF. The aim of the present study was to (I) describe cognitive function in community dwelling HF patients with and without SDB and (II) to investigate predictors for cognitive dysfunction.

Methods: A descriptive cross-sectional design was used and 137 consecutive community dwelling HF patients (68% male), mean age 71 year (SD 10), 58% in NYHA class II were included. Clinical examinations (weight, height, blood pressure, medication and co-morbidities), respiratory recordings (Apnea Link), actigraphy (SenseWear) and self-rating scales regarding insomnia (Minimal Insomnia Symptom Scale), daytime sleepiness (Epworth Sleepiness Scale) and depression (Patient Health Questionnaire) were used. Cognitive function was measured with Mini-Mental State Examination (MMSE), Trail making A and B, Rey Ostereich Complex Figure, Word knowledge, Memory of a story and Block Design.

Results: Fourty-four percent of the total group had SDB (AHI > 15) and 22% impaired cognitive function. The mean score for MMSE was significantly lower for those with SDB compared to those without SDB (28.0 + 1.6 versus 28.5 + 1.7, P < 0.05). The occurrence of mild cognitive dysfunction and cognitive dysfunction on the MMSE did not differ between the groups. Measures of psychomotor speed and executive functions did not differ, neither did semantic- and episodic memory or spatial abilities. Linear regression revealed that BMI was associated to psychomotor speed (P < 0.05), and age to executive functions, visual-spatial perception and construct memory (P < 0.05). Higher education was associated to performance in semantic memory and smoking to episodic memory (P < 0.05). Insomnia was associated with global cognition and psychomotor speed (P < 0.05), and saturations time<90% with spatial performance (P < 0.05). No associations were found for AHI, nadir saturation,

daytime sleepiness, NYHA class, systolic blood pressure, diabetes or depression.

Conclusion: Cognitive dysfunction was quite uncommon in this HF population. The predominance of mild HF and the relatively low proportion of patients with SDB might explain the lack of associations to cognitive function.

P738

Visual-spatial attention in OSA is slow to be captured, slow to be released

D. N. EDER, O. RAGNARSSON, M. KARIMI, L. GROTE and J. HEDNER

University of Gothenburg, Gothenburg, SE

Objectives: To characterize pre-conscious attention in obstructive sleep apnea (OSA). The capture of attention begins with the selection of potentially relevant information from continuous sensory inflow and the launching of processes which facilitate higher level processing: Phasic arousal (Alerting) sharpens sensory intake and evaluation and Orienting entails the disengagement and shift of attention from one focus to another. These processes have not previously been characterized in OSA.

Methods: We used a visual covert orienting paradigm (based on the Attention Network Test) to study the functional structure of visual attention processes over time in 47 normals (25% [Median] 75% age 44[59]65 year) and 26 sleep clinic patients (age 44[57]66 years) diagnosed with OSA (RDI 27[39]56) and EDS (ESS 6[11]18). Subjective fatigue was markedly higher in OSA (Fatigue Impact Scale: control 5[20]40, OSA 12[43]77). Spatial Orienting is elicited by presenting a cue signaling the location of an upcoming target. Alerting is elicited by a cue which signals the temporal onset of the target. Alerting is defined as the difference in response times (RT) between temporal- and un-cued trials and Orienting as the difference between temporal- and spatial-cued trials. Snapshots of these attention functions at different stages of processing are obtained by presenting targets at 1 of 5 intervals (200, 400, 600, 800, or 1000 ms) following the onset of the cue. Orienting and Alerting effects were estimated using linear mixed effects models and are presented as estimates of contrasts (differences) between groups flanked by 95% confidence limits (cl Delta cl). All reported effects are statistically significant ($P < 0.003$)

Results: Orienting in OSA was inhibited at 200 ms (Delta-110 -54 2 ms), not engaged until 400 ms and failed to disengage over subsequent intervals (maximum 600 ms: Delta 43 120 197 ms.) Alerting was similar between groups at all target intervals except at 1000 ms, where OSA patients were markedly inhibited (Delta-179 -94 -8 ms).

Conclusion: Spatial attention in OSA was abnormal: Slow to re-orient from its previous focus and once captured, very slow to disengage. Alerting in OSA displays a exaggerated inhibition which necessarily limits rapid re-activation. These patterns are sharply atypical and suggest a functional deficit in visual-spatial attention processing which could be particularly limiting in dynamic sensory environments such as driving.

P739

Cortisol and sleep architecture: an associative role in cognitive functioning in Addison's disease patients

M. HENRY, K. G. F. THOMAS and I. ROSS

University of Cape Town, Cape Town, ZA

Objectives: While it is well established that high cortisol levels may impair cognitive functioning (memory), there is no convincing evidence to explain the mechanisms by which cortisol deficiencies affect cognition. Since cortisol plays a key role in the initiation and maintenance of different sleep stages, it has an important influence on the process of memory consolidation that takes place during sleep. This study aimed to investigate the impact of alterations in cortisol levels on sleep architecture and subsequently on memory, using Addison's disease (AD) patients to investigate the effects of low cortisol levels. Only subjective measures will be presented here, and an objective sleep study will be conducted later to investigate the effects of cortisol levels on sleep architecture and cognitive functioning. We aimed to characterise sleep and memory complaints of AD patients, hypothesising that on subjective measures, AD patients would report significantly poorer sleep quality and more memory complaints compared with healthy controls.

Methods: Twenty AD patients and twenty healthy controls were recruited to complete the Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), and the Cognitive Failures Questionnaire (CFQ).

Results: Analysis of total PSQI score revealed a statistically significant between-group difference ($P < 0.001$), with Addison's patients experiencing worse sleep quality. On analysis of the seven individual components of the PSQI, Addison's patients' scored significantly worse on five components. No significant differences were found on the sleep disturbances or daytime dysfunction components, or on the ESS score. Analysis of the CFQ scores revealed a statistically significant between-group difference on Retrieval ($P = 0.021$), with Addison's patients reporting poorer memory retrieval. No significant differences were found on Clumsiness (motor awkwardness) or Intention (prospective memory). Data from a further 55 participants in each group will be collected and analysed later in the year.

Conclusion: Patients with AD appear to report poorer sleep quality and memory functioning but not more daytime dysfunction compared with healthy controls. Should a relationship between sleep architecture and cognition be established in the objective sleep study, results could indicate that altered sleep architecture might serve as one underlying mechanism for the memory deficits frequently reported by AD patients.

P740

The effect of sleep on procedural memory consolidation in adults with attention deficit hyperactivity disorder

C. SAUTER, J. PAUL, M. COLLA, A. PETER, C. GARBAZZA, C. DUJARDIN, J. KOLLEK, M.-L. HANSEN and H. DANKER-HOPFE

Charité University Hospitals, Berlin, DE

Objectives: Adults with attention deficit hyperactivity disorder (ADHD) very often report impaired sleep quality, which may result in exacerbation of symptoms and decrements in performance during the day. Since sleep is essential for memory consolidation, impaired sleep may lead to deterioration in memory performance. To date studies on memory consolidation during sleep in ADHD adults are lacking. In the present study effects of sleep on memory consolidation in adults with ADHD as compared to age and sex-matched controls were analysed.

Methods: In total, twenty adults with the diagnosis of ADHD and 20 age and sex matched controls will be enrolled in the study. Participants spend two nights at the sleep laboratory for adaptation purposes and for diagnosis of sleep disorders. The second night

serves as a baseline night. At an interval of 1 week subjects undergo two experimental nights, which are separated by one week. In the experimental nights subjects are trained either on a procedural (mirror tracing) or on a declarative memory task (word pair association) prior to a full-night polysomnography (PSG) in a randomised balanced cross-over design. In addition in each experimental night a control task, which corresponds to the learning task of the other experimental night, is applied. Objective and subjective sleep quality are analysed. Sleep is evaluated according to the AASM criteria. Performance in the learning and control tasks is compared within and between study groups.

Results: Preliminary results from 15 adults with ADHD (10 female, five males; age: 35 ± 8 years) and 15 age and sex-matched controls (age: 36 ± 8 years) showed no differences in sleep macrostructure between the baseline and the experimental nights and between groups. Both groups showed an improvement in accuracy of the procedural memory task in the morning. ADHD patients furthermore showed an improvement in the speed component of the procedural task. Performance gain in the procedural memory task was not related to sleep macrostructure.

Conclusion: Sleep quality did not differ between ADHD patients and age and sex-matched controls in any of the baseline and experimental nights. ADHD patients seem to benefit more from sleep in terms of procedural memory consolidation than the control group. However, the improvement in performance was not related to sleep macrostructure.

Poster Session - Neurophysiology: neurotransmitters

P741

The influence of sodium oxybate and sleep on reward processing: an fMRI study

J. HOFMEISTER, V. STERPENICH, K. IGLOI, M. DESSEILLES, M. GSCHWIND and S. SCHWARTZ
University of Geneva, Geneva, CH

Objective: Sodium oxybate (SO; Xyrem®) has been approved in most countries for treatment of narcolepsy with cataplexy. It acts as a GABA(B) receptor agonist, improving disrupted sleep, decreasing sleep onset latency, and increasing slow waves activity (SWA) in narcoleptic patients as well as in healthy subjects. Here, we tested (1) whether SO influences brain network related to reward processing and (2) whether changes in sleep induced by SO affect reward processing in healthy subjects on the next day.

Method: Nineteen subjects were given SO or placebo (PL) over two distinct fMRI sessions. Each subject performed a game-like task after SO/PL administration in an evening session (1). PSG was recorded in the following night. On the next day, a second session of game-like task was performed during the afternoon (2). During the game-like task, subject could win or lose points by rapidly detecting a target. We compared brain activity during winning or losing points after SO or PL, during the evening session and after the sleep.

Results: At behavioural level, subjects detected the target more rapidly after negative cues (potential losses) immediately after SO, suggesting increased risk aversiveness in these subjects. Subjects also often pressed too early under SO for positive cues (potential gains), suggesting an increased impulsivity for obtaining rewards. After one night of sleep under SO (versus PL), we observed no other modification in reaction times.

At the fMRI level, during the evening session, subjects under direct influence of SO (as compared to PL) showed significant activation in an error monitoring network (including the anterior cingulate) when they are losing for cues signaling large potential gains, and activated significantly more a network related to reward processing (including the ventral putamen) when they are actually winning for these same cues, suggesting that SO enhances reward sensivity.

After a night of sleep modified by SO (versus PL), we found a significant activation of the bilateral amygdala and right insula when subjects lost large amounts of points, suggesting that changes in sleep after SO administration may have an effect on error processing and emotional reactivity on the next day. The analysis of sleep data will be also presented.

Conclusion: SO (as compared to PL) influences reward functions at both the behavioral and brain level.

This work is supported by UCB

P742

Sleep and motor function after GHB and baclofen administration in healthy rats and rats with focal cerebral ischaemia

A. HODOR, S. PALCHYKOVA, B. GAO and C. BASSETTI
University Hospital of Berne, Berne, CH

Objectives: There is still no effective treatment available for stroke patients. Promotion of neuroplasticity during recovery may represent an alternative therapeutic strategy. Sleep has been implicated in facilitation of neuroplasticity. Sleep promoting drugs, gamma-hydroxybutyrate (GHB) and baclofen (Bac), administered during the acute phase after ischemia showed neuroprotection. We investigated (1) changes in sleep induced by GHB and Bac in healthy rats, (2) stroke outcome following Bac administration beyond the acute phase in a rat model of focal cerebral ischemia.

Methods: (1) Adult male rats ($n = 26$) were implanted with EEG/EMG electrodes. GHB (150 or 300 mg/kg), Bac (10 or 20 mg/kg) or saline were administered 1 h after light onset and offset. (2) Rats subjected to middle cerebral artery occlusion (MCAo) were treated with Bac (10 mg/kg) or saline. First injection, done 24 h after MCAo, was followed by two daily injections during 10 consecutive days. Animals were assigned to the ischemia/Bac, sham/Bac or ischemia/saline group ($n = 8$ per group). Functional recovery was evaluated by single pellet reaching test (SPR).

Results: (1) GHB and Bac caused abnormal behavior (immobile flat body posture, limbs stretched sideways, eyes opened) and physiology (hypersynchronous slow waves in EEG) lasting up to 413 min. Amount of vigilance states was evaluated after the end of the abnormal state. Bac increased NREM sleep in the light and dark phase (16 and 91 min, respectively; $P < 0.05$, paired *t*-test). REM sleep was enhanced by 12 min in the dark ($P < 0.05$). Time of Bac administration affected NREM sleep episode duration and frequency. Thus, during the light phase Bac increased the duration of NREM sleep episodes ($P < 0.01$), but reduced their frequency ($P < 0.05$), while during the dark phase only episode frequency was increased ($P < 0.0001$). GHB had no effect on vigilance states. EEG spectral analysis is in progress. (2) SPR performance dropped to 0 immediately after MCAo in both ischemic groups and recovered slowly in the course of 1.5 month. Bac-treated ischemic rats showed slightly better performance than saline-treated rats, but the group difference did not reach statistical significance. The data collection is ongoing.

Conclusion: Our results indicate that GHB and Bac induced subanesthetic state distinct from physiological sleep, confirming previously published mouse data. Bac treatment increased the amount of sleep after the end of drug-induced state.

This study was supported by UCB Pharma S.A. Belgium, Allée de la Recherche, 60, B - 1070 Brussels

P743

Metabolic effects of sodium oxybate

G. LUCA and M. TAFTI
University of Lausanne, Lausanne, CH

Gammahydroxybutyrate (GHB) (sodium oxybate, Xyrem®), is used in sleep medicine for the treatment of narcolepsy with cataplexy. One of the side effects observed in treated patients is weight loss.

Aim: To investigate metabolic changes after acute, short-term and chronic administration of GHB in different mouse strains.

Methods: In four different experiments we have evaluated both the acute and chronic metabolic changes induced by the drug. For acute metabolic changes blood was assessed at 1 h after the drug administration. In a second step, mice were studied in the calorimetric chambers for 8 days: 4 baseline days and 4 days under drug administration, in randomized order. Food and water intake, respiratory ratio (RER), oxygen consumption and CO2 production, locomotor activity and weight were measured. For chronic metabolic changes mice were studied 4 weeks under placebo or 300 mg GHB/kg/day. Lean mass, fat mass, and water content were assessed by

EchoMRI. Weight was monitored weekly. This experiment was carried out on two mouse strains: C57BL6 and Ob/Ob mice.

Results: No differences were found between treated and control mice regarding cholesterol, triglyceride, glucose, and free fatty acids measured in serum after acute administration of GHB. Calorimetric results suggest that after 4 days of treatment there is a decrease in RER, independent of food intake, which may point to a shift in the substrate used for energy production from carbohydrates to lipids. After chronic treatment there were no significant differences between treated and control C57BL6 mice for fat mass, lean mass, or water content, but treated mice showed a more balanced distribution of fat mass and lean mass. GHB treated mice gained less weight than matched controls. In Ob/Ob mice there were no differences between treated and control groups regarding fat mass, lean mass or water content and the decrease in weight observed in treated mice was not significantly different from the control mice.

Conclusions: Weight loss as response to GHB treatment in humans is also observed in C57BL6 mice, but the significant change in weight gain found in C57BL6J mice was not observed in Ob/Ob mice. This finding suggests that changes in weight (both in wild-type mice and humans) under GHB treatment are independent of the leptin regulation.

Supported by FP7-People, Marie Curie Actions, NINA Project 238665 and UCB Pharma

P744

Effects on sleep of the induction of a torpor-like state in the rat

M. MASTROTTO[1], F. DEL VECCHIO[1], A. AL-JAHMANY[1], R. AMICI[1], M. CERRI[1], D. MARTELLI[2], E. PEREZ[1], D. TUPONE[3] and G. ZAMBONI[1]

[1]University of Bologna, Bologna, IT, [2]Florey Neuroscience Institutes, Melbourne, AU, [3]Oregon Health and Science University, Portland, OR

Introduction: The periods of torpor are typically followed by the occurrence of high-Delta power NREM sleep (NREMS) (1). In the present study, this phenomenon was investigated in rats through the induction of a torpor like state by the pharmacological inhibition of the Rostral Ventromedial Medulla (RVMM), a key area in the central nervous control of metabolism, promoting thermogenesis (2).

Methods: Eighteen male Sprague-Dawley rats (300–350 g) were surgically implanted, under general anaesthesia (Diazepam, 5 mg/kg, i.m., ketamine, 100 mg/kg, i.p.), with electrodes for chronic EEG recording, a thermistor for the detection of the hypothalamic temperature (Thy), a catheter for arterial blood presssure recording, and a microcannula for drug delivery within the RVMM. Before the experiment, animals were exposed for three days to ambient conditions that are known to favor the occurrence of a natural torpor bout: ambient temperature (Ta) 15°C, constant darkness and a high-fat diet. Three groups of animals were microinjected within the RVMM (1 injection/h, for 6 h) with the GABAA agonist muscimol (1 mM, 100 nl; Group 1 ($n = 6$) and Group 2 ($n = 6$)) or with saline (0.9%, 100 nl, group 3 ($n = 6$)). One hour after the last injections, Ta was raised to 28°C for groups 1 and 3, and to 37°C for Group 2 to favour the return to normothermia.

Results: In both Group 1 and 2, a deep hypothermia was observed during the 6-h microinjection period (Thy fell to 22.80 ± 0.8°C) which was accompanied by a decrease of EEG activity and a progressive shift of the EEG spectral power towards the low-frequency region. After the injection period, EEG activity showed a progressive increase and the EEG spectral power shifted to the high frequency region. In particular, after the recovery of normothermia, a powerful intensification of Delta power in NREMS was observed, which lasted about 6 h. The peak in Delta power was significantly higher in Group 1 than in Group 2 ($P < 0.01$). No significant effects were observed in Group 3.

Conclusion: The dynamics of EEG changes during and after the torpor-like state induction were similar to those described in natural torpor. The increase in Delta power in NREMS was attenuated under environmental conditions promoting the restoration of normothermia, suggesting a role for the degree of sympathetic activation during restoration in its determination.

1. Deboer T, Tobler I. Sleep. 2003; 26: 567–72.
2. Morrison S, Nakamura K. Front Biosci., 2011; 16: 74–104.

P745

Brainstem auditory-evoked potentials during human sleep and sleep-like chloral hydrate effect

E. MEDINA-FERRET[1], M. PEDEMONTE[2] and R. A. VELLUTI[1]

[1]Hospital de Clinicas, Montevideo, UY, [2]Facultad de Medicina CLAEH, Punta del Este, UY

Objectives: Brainstem auditory evoked potentials (BAEP) shifts during sleep are still under discussion. Authors have reported latency shifts related to body temperature thus excluding sleep effects. Our previous results in animal models (Velluti 2008) (1) – recording the auditory nerve potential as well as the unitary activity at the cochlear nucleus, lateral superior olive and inferior colliculus- have revealed shifts in firing patterns when animals asleep, being our hypothesis that at least subtle changes must occur in the human sleep.

Methods: In this pilot study, results are shown during natural sleep and a sleep-like state produced by Cloral Hydrate (CH). Volunteers without any pathology were stimulated with alternating clicks (80 dB SPL, 10 /s) and BAEP were recorded together with on-line sleep polysomnographic control, during natural sleep and under CH hypnotic dose. The experimental design was to record during the afternoon nap (“siesta” from 1:00 to 4:00 pm) with monitored skin temperature and responses studied also in the frequency domain (new technical approach).

Results: 1. Analyzing waves VI and VII during natural sleep stage 2, a significant decrease in wave VII amplitude was observed. Moreover, the FFT study, in the frequency domain exhibited significant differences between wakefulness and sleep stage 2 power spectra in 200 Hz band. **2.** Effects of CH sleep-like stage 2. During afternoon naps, significant wave V latency increase was depicted in comparison with wakefulness, without skin temperature shifts. Studying the BAEP (I, V) in the frequency domain significant decrease in the power spectra were obtained during sleep-like stage 2 in comparison with a waking epoch.

Discussion and conclusion: Changes observed comparing physiological sleep and CH sleep-like are different, pointing that mechanisms underlying pharmacological induced sleep are not the same than those involved in physiological sleep.

1. Velluti R. A. The suditory system in sleep (2008) Elsevier-Academic Press

P746

Alpha2/ alpha3 gamma-aminobutyric acidA receptor subtype selective positive allosteric modulator TPA023 effects on sleep/wake and electroencephalogram spectrum in the rat

L. E. APPEL, E. A. SHANKS, W. F. SEIDEL, D. M. EDGAR, K. A. WAFFORD

Eli Lilly, Windlesham, UK

7-(1,1-Dimethylethyl)-6-(2-ethyl-2H-1,2,4-triazol-3-ylmethoxy)-3-(2-flurophenyl)-1,2,4-triazolo[4,3-b]pyridazine (TPA023) and diazepam are positive allosteric modulators (PAMs) at gamma-aminobutyric acidA (GABAA) receptors. Although both drugs are anxiolytic and anticonvulsant, diazapem is sedative but TPA023 is not. TPA023 is a triazolopyridazine which is structurally different from conventional benzodiazepines that bind at this site on the receptor. Unlike nonselective benzodiazepines (BZD), TPA023 lacks efficacy at alpha1 and alpha5-subunit containing GABAA receptors, exerting its effects through alpha2 and alpha3-subunit containing receptor subtypes (1). The lack of modulation on alpha 1-containing receptors is proposed to underlie the absence of sedation observed with TPA023.

Benzodiazepine receptor ligands (diazepam) including alpha-1 subunit preferring compounds (zolpidem) decrease sleep latency and increase sleep time in animals and humans and include concomittant changes in the electroencephalogram (EEG). This study compares the alpha2/3 selective PAM TPA023 with the non-selective hypnotic diazepam using EEG analysis.

Experiments were performed in accordance with the Animal (Scientific Procedures) Act 1986. Adult male Wistar rats were surgically implanted to measure EEG and Electromyogram (EMG) together with locomotor activity, body temperature, feeding and drinking. Acute oral administration of TPA023 3–10 mg/kg and diazepam 10–60 mg/kg delivered at CT-18 were evaluated using SCORE2000TM. Diazepam decreased sleep onset latency and increased NREM sleep at all doses, while TPA023 produced no effect on these variables. Both drugs decreased REM sleep, locomotor activity, and EEG delta-power in NREM sleep, together with increases in beta-power; the latter suggests that the EEG changes in spectral power are not mediated by alpha1-containing receptors, as well as being independent to the changes in sleep/wake vigilance. These results are consistent with studies in BZD-insensitive mutant mice where diazepam-induced changes to the EEG spectrum are mediated via its activity at the alpha2-containing subtype (2).

1. Atack J.R et al. (2006) JPET 316:410–422.
2. Kopp, C et al. (2004) PNAS 101:3674–3679.

P747

Metabotropic glutamate receptor subtype 5 availability and sleep deprivation: a positron emission tomography study in healthy humans

S. C. HOLST[1], K. HEFTI[1], J. SOVAGO[2], A. BUCK[3], S. AMETAMEY[4], M. SCHEIDEGGER[1], R. DÜRR[1], A. BAUMER[1], B. GOMEZ-MANCILLA[2], E. SEIFRITZ[5] and H.-P. LANDOLT[1]

[1]University of Zurich, Zurich, CH, [2]Novartis Institutes for Biomedical Research, Basel, CH, [3]University Hospital Zürich, Zurich, CH, [4]ETH, PSI and USZ, Zurich, CH, [5]Psychiatric University Hospital, Zurich, CH

Preclinical evidence suggests that metabotropic glutamate receptors of subtype 5 (mGluR5) modulate glutamatergic neurotransmission and play important roles in brain oscillatory activity and neuronal plasticity. Activation of mGluR5 stimulates the synthesis of Fragile X mental retardation protein. Fragile X syndrome, a common form of inherited mental retardation and autism, is caused by a (CGG)*n* repeat polymorphism in the Fragile X mental retardation 1 gene (FMR1). We recently observed in healthy adults that mGluR5 availability in the brain is significantly increased after sleep deprivation. Here we investigated whether these changes are related to sleep deprivation-induced changes in subjective and objective measures of sleepiness and genetic variation in FMR1.

Methods: Twenty-three healthy men completed two experimental blocks separated by one week. The blocks included two positron emission tomography scans with the highly selective radioligand, 11C-ABP688, conducted after nine (control condition) and 33 h (sleep deprivation condition) of wakefulness in randomized, cross-over fashion. Binding of 11C-ABP688 in each scan was normalized to cerebellum, a brain region with unaltered mGluR5 availability after prolonged wakefulness. The EEG was recorded simultaneously during the roughly 1-h PET scans and subjects were alerted via the intercom in case of sleep. Statistical tests included Spearman or Pearson correlation analyses.

Results: The number of CGG repeats in FMR1 varied between 17 and 44 among all subjects. The repeat numbers correlated with waking EEG alpha/beta activity (11–30 Hz) in the control condition, and with theta, alpha and low beta activity (6.5–19.5 Hz) after sleep deprivation (P_all <0.05). In the control condition, theta power (7–8.5 Hz) also correlated with global mGluR5 availability (P_all <0.05). Sleep deprivation increased stage 1 (3.6 versus 2.1 min), stage 2 (8.8 versus 2.9 min) and slow wave sleep (1.1 versus 0.0 min) when compared to sleep control (P_all <0.07). The sleep deprivation-induced increase in global mGluR5 availability correlated with the increases in subjective sleepiness, as well as in intermittent stage 1 sleep (P_all <0.05) during scanning.

Conclusion: Our data indicate that the sleep deprivation-induced increase in cerebral mGluR5 density is associated with subjective and objective measures of elevated sleepiness. Furthermore, our data suggest that FMR1 genotype and mGluR5 availability affect EEG activity in healthy adult men.

P748

Pro-cognitive potential of metabotropic receptors (Glur5) blockade: evidence from sleep behaviour and cortical network oscillations in rodents

A. AHNAOU[1], X. LANGLOIS[1], T. STECKLER[1], H. HUYSMANS[1], P. TE RIELE[1], L. RAEYMAKERS[1], J. BARTOLOME[2] and W. DRINKENBURG[1]

[1]Janssen Pharmaceutical Companies of Johnson and Johnson, Beerse, BE, [2]Janssen Pharmaceutical Companies of Johnson and Johnson, Toledo, ES

Objectives: Pharmacological manipulation of the metabotropic glutamate (mGlu5) receptors may be critical for the treatment of many neurological and psychiatric disorders. MGlu5 receptor blockade limits neuronal damage induced by a hyperactivity of N-methyl-d-aspartate (NMDA) receptors, therefore linked to process of neurodegeneration/neuroprotection. Whereas, positive modulation of mGlu5 receptors may alleviate the profound glutamatergic hypo-function observed in schizophrenia. Sleep has a primary role in the regulation of brain plasticity and cognition, hence cognitive impairment associated with sleep disturbances is a core feature of patients with Alzheimer and schizophrenia diseases. The mGlu5-NMDA receptors

signaling is fundamentally involved in cognitive functions; therefore the present studies used mGlu5 receptor antagonists (MTEP and MPEP) and positive allosteric modulators (ADX and AZ) to clarify whether blockade or allosteric activation of mGlu5 receptor signaling would have beneficial effects on sleep and facilitates oscillatory indexes of cortical networks communication in rats.

Methods: Effects of systemic MPEP and MTEP (1, 3 and 10 mg/kg) and oral ADX and AZ (10, 30 and 100 mg/kg) were characterized on sleep-wake architecture, electroencephalogram variables and cortical network oscillations in rats.

Results: MGlu5 receptor blockade consistently consolidated deep sleep and enhanced sleep efficiency, whereas allosteric activation increased waking and decreased deep sleep. Cortical oscillations in the theta (4.5–6 Hz) and gamma (30–50 Hz) frequency ranges were prominent in field potentials following blockade of the mGlu5 receptor, whereas only theta oscillations were promoted after allosteric activation. Future studies will address the circadian profile of vigilance states in mutant mice deficient in mGlu5 receptor as well as changes of the receptors density in the rat brain using [3H]MPEP autoradiography in order to examine the functional interaction between receptor activity and biological effects.

Conclusion: Our pharmacological evidence highlights the ability to differentiate the pharmacology of mGlu5 blockade from that of allosteric activation, and furthermore suggest that sleep and cortical network oscillations may provide a valuable animal-clinical interface for studying mGlu5 receptor signaling. The beneficial effect on sleep and the dynamic changes in cortical oscillations might underpin cognitive potential of mGlu5 receptor blockade.

P749

Insomnia in the mouse after in utero exposure to antidepressant treatment

E. LACOMBE[1], C. PRENAT[1], V. FABRE[1], G. VODJDANI[2] and J. ADRIEN[1]

[1]Inserm, Paris, FR, [2]CNRS, Paris, FR

Serotonin selective re-uptake inhibitors (SSRI) are of increasing use in pregnant women, but their long-term effects on the child are largely unknown. Such putative effects on sleep regulation were examined in the adult progeny of mice treated with SSRI during gestation.

Methods: C57/BL/6 gestating females were treated from the first until the last day of gestation with fluoxetine (18 mg/kg/day in drinking water). Control animals drank plain water. Polygraphic sleep recordings were made at 8–16 weeks of age in the progeny exposed to prenatal fluoxetine treatment (FLX) or water (Control). Vigilance states (wakefulness, slow wave sleep and REM sleep) were analyzed in basal conditions, and after a restraint stress challenge of 90 min duration.

Results: In basal conditions, both male and female FLX mice exhibited an increase in the duration of wakefulness (+16% and +10% of that in the control groups, respectively), and a concomitant decrease in slow wave sleep (-16.8% and -11%) associated with enhanced beta/delta ratio in the EEG spectral power. REM sleep (REMS) duration was not modified.

After 90 min of restraint stress, control mice displayed an increase of REMS amounts appearing 2 h after the end of the stress period and lasting for 6 h (+54% and +135% of no stress conditions for males and females, respectively). In the FLX groups, females exhibited the same sleep modifications as controls. FLX male mice presented a smaller and non significant increase of REMS amounts (+22%), but this increase was delayed so as to begin 4 h after the end of stress period and to last for about 8 h thereafter.

In conclusion, in utero exposure to fluoxetine in mice promotes persistent disturbances in sleep organization and EEG activity that evoke those of chronic insomnia and seem to be gender-dependent, since only the male progeny is strongly affected. These modifications are associated with a delayed response of sleep to stress.

P750

Effects of corticotropin releasing factor on sleep homeostatic response and Fos expression in the preoptic hypothalamus

I GVILIA[1], R. SZYMUSIAK[2] and D. MCGINTY[2]

[1]Ilia State University, Tbilisi, GE, [2]UCLA, Los Angeles, CA

Objectives: Corticotropin releasing factor (CRF) has a sleep-suppressing effect. We evaluated the hypothesis that suppression of sleep by CRF is mediated through interactions with preoptic sleep-active neurons.

Methods: Rats were subjected to 2 h sleep deprivation (SD) followed by either intracerebroventricular (icv) administration of CRF (0.5 μg/3 μl, $n = 6$) or saline ($n = 6$). All rats were then allowed 90 min undisturbed sleep, followed by euthanasia and cardiac perfusion. Brain sections cut through the median preoptic nucleus (MnPN) and ventrolateral preoptic area (VLPO) were processed for immunostaining for c-Fos protein and glutamic acid decarboxylase (GAD).

Results: CRF-treated rats spent significantly less time in both nonREM sleep (28.8 ± 5.5% versus 54.7 ± 7.9%) and REM sleep (3.7 ± 1.2% versus 11.1 ± 2.0%) during post-SD recovery, compared to control rats. Also, CRF-treated versus control rats exhibited significantly lower numbers of MnPN Fos+/GAD+ cells (in rostral MnPN: 26.8 ± 3.6 versus 41.3 ± 4.8; in caudal MnPN: 11.3 ± 1.5 versus 26 ± 3.7) in the condition of post-SD recovery sleep, whereas Fos+/GAD+ cell counts for VLPO sites did not change significantly, compared to vehicle. Single Fos+ cell counts in both the MnPN and VLPO were significantly increased in CRF-treated versus control rats (in rostral MnPN: 125.2 ± 15.3 versus 47.3 ± 2.1; in caudal MnPN: 82.2 ± 7.8 versus 32.5 ± 3.8; in VLPO cluster: 19.2 ± 0.6 versus 14.2 ± 1.1; in extended VLPO: 45.5 ± 5.6 versus 23.7 ± 4.3).

Conclusion: Our findings suggest that icv CRF injection (1) suppresses Fos expression in MnPN GABAergic neurons and (2) activates MnPN and VLPO nonGABAergic neurons. The changes in preoptic neuronal activity may contribute to CRF-induced suppression of post-SD recovery sleep.

P751

Excitation by glucose of sleep-promoting neurons in the ventrolateral preoptic nucleus: a new link between sleep and metabolism

C. G. VARIN[1], A. RANCILLAC[2], H. GEOFFROY[2], P. FORT[1], T. VITALIS[2] and T. GALLOPIN[2]

[1]University C Bernard Lyon1, Lyon, FR, [2]CNRS UMR 7637, ESPCI ParisTech, Paris, FR

Objectives: One of the main functions of sleep is likely to replenish brain energy stores depleted during wakefulness enlightening the close relationship between metabolism and the control of vigilance states. However, the direct influence of metabolic signals on the activity of neurons responsible for the induction and the maintenance of sleep remains to be established. To address this crucial point, we attempted here to determine whether and how the sleep-promoting

neurons previously characterized ex vivo within the ventrolateral preoptic area (VLPO) are responsive to variations of extracellular glucose concentration.

Methods: Brain coronal slices containing the VLPO were obtained from 14 to 18 days old mice. Patch-clamp recordings were performed on VLPO neurons and responses were monitored following changes in extracellular glucose. Then, pharmacological experiments coupled with single-cell RT-PCR were designed to elucidate the pathway responsible for these effects.

Results: As previously reported in rats, sleep-promoting neurons in mice VLPO are also endowed with a potent calcium low threshold spike (LTS). Further, these LTS neurons were dose-dependently excited by glucose within physiological range (EC50 = 4.06 mM). This excitatory effect was specific to LTS neurons since co-distributed non-LTS neurons within the VLPO did not depicted any response to changes in extracellular glucose concentration. Furthermore, our results suggest that this glucose-dependant excitation is mediated by the catabolism of glucose leading to an increase in intracellular ATP production and eventually to a closure of ATP-sensitive potassium channels (KATP). Indeed our pharmacological investigation revealed that LTS neurons exhibited functional KATP channels. Using perforated-patch recordings, we further found that decreasing glucose concentration induced an outward current reversing near the expected K+ equilibrium potential. Finally, this glucose-induced potassium current was reversed by tolbutamide, a KATP channel blocker.

Conclusion: These results demonstrated for the first time a direct and specific action of glucose on the activation of neurons responsible for sleep onset and sleep maintenance. Such mechanism could take part in the metabolic control of sleep.

P752

Neurovascular coupling mediated by sleep-promoting neurons within the ventrolateral preoptic nucleus

A. RANCILLAC[1], C. G. VARIN[1], H. GEOFFROY[1], M. GUILLE COLLIGNON[2], F. LEMAÎTRE[2], C. AMATORE[2], T. VITALIS[1] and T. GALLOPIN[1]

[1]CNRS UMR 7637, Paris, FR, [2]CNRS UMR 8640, Paris, FR

Objectives: The hypothalamic ventrolateral preoptic nucleus (VLPO) contains neurons responsible for triggering and maintenance of slow wave sleep. Recently, our team discovered ex vivo that VLPO sleep-promoting neurons are sensitive to glucose, the brain's main metabolic fuel. Indeed, their firing rate increases with glucose concentration (see abstract of Varin et al., ESRS 2012). To sustain neuronal function, the brain developed ''neurovascular coupling'' mechanisms to increase blood flow in activated regions. Here we investigated whether VLPO sleep-promoting neurons could act as metabolic regulators by controlling the local blood vessel tone.

Methods: The VLPO is punctuated by radial arterioles, among which a large arteriole was systematically identified, running down the center of the VLPO. Using infrared videomicroscopy in mouse brain slices preparations, we monitored blood vessels diameter changes according to specific experimental paradigms.

Results: We showed that a rise in extracellular glucose concentration induced dose-dependent vasodilation with an EC50 of 3.8 mM. As we found that VLPO sleep-promoting neurons express the neuronal isoform of the Nitric Oxide (NO) synthase, we tested whether vasodilatations induced by glucose could be due to NO released by VLPO sleep-promoting neurons. Indeed, in the presence of a NO scavenger the amplitude of vasodilatations induced by glucose was significantly reduced. Through amperometric detection of NO with a platinized carbon ultramicroelectrode, we quantified in situ NO flux following an increase in glucose concentration. Finally, evoked firing of single VLPO neuron in whole-cell configuration confirmed their ability to transduce neuronal signals into vascular responses.

Conclusion: This study demonstrates that glucose-induced activation of VLPO sleep-promoting neurons lead to local vasodilation in the VLPO via NO release that in turn increases local glucose supply. This mechanism could constitute an auto-excitatory loop within the VLPO to maintain and consolidate the neuronal activity thereby helping to maintain slow-wave sleep.

P753

Cholinergic basal forebrain neurons mediate histamine-induced cortical activation

J. C. ZANT, S. ROZOV, H.-K. WIGREN, P. PANULA and T. PORKKA-HEISKANEN

University of Helsinki, Helsinki, FI

The basal forebrain (BF) is a key structure in regulating both cortical activity and sleep homeostasis. It receives input from all ascending arousal systems, and is particularly highly innervated by histaminergic neurons. Previous studies clearly pointed to a role for histamine as wake-promoting substance.

We used *in vivo* microdialysis and pharmacological treatments in rats to study which EEG spectral properties are associated with histamine-induced wakefulness and whether this wakefulness is followed by increased sleep and increased EEG delta power during sleep. We also investigated by which BF neurons the histamine-induced cortical activation is mediated.

Histamine levels increased immediately and remained constant throughout a 6 h sleep deprivation, returning to baseline levels directly afterwards. During the spontaneous sleep-wake cycle a strong correlation between wakefulness and extracellular histamine concentrations was observed, which was not affected by the time of day. Perfusion of histamine into the BF increased wakefulness and cortical activity, without inducing recovery sleep. Perfusion of a histamine receptor 1 antagonist decreased both wakefulness and cortical activity. Lesioning the BF cholinergic neurons abolished these effects.

Taken together, these results show that BF cholinergic activation by histamine is important in sustaining a high level of cortical activation, and that a lack of BF cholinergic activation by histamine may be important in the initiation and maintenance of NREM sleep. The level of histamine release is tightly connected to behavioral state, but does not convey information about sleep propensity.

P754

Pharmacogenetic activation of preoptic area GABAergic neurons increase NREM sleep

Y. SAITO[1], N. TSUJINO[1], M. MIEDA[1], K. SAKIMURA[2] and T. SAKURAI[1]

[1]Kanazawa University, Kanazawa, JP, [2]Niigata University, Niigata, JP

Objectives: Neurons in the preoptic area (POA), especially the ventral lateral preoptic area and the median preoptic nucleus, fire rapidly during sleep and cease firing during wakefulness. These neurons carry GABA, and thought to play an important role in initiation and maintenance of sleep by sending inhibitory projections

to the arousal systems that reside in the brain stem. Recently, several evidence have suggested that orexinergic neurons in the hypothalamus, which play a critical role in maintaining arousal, are also influenced by these neurons. To elucidate the roles of these neurons in regulation of orexin neurons, we pharmacogenetically stimulate these sleep-active neurons.

Methods: We used Gad1-Cre knock-in mice, in which Cre recombinase is exclusively expressed in GABAergic neurons. We used an adeno-associated viral vector to deliver hM3Dq or hM4Di to Cre-expressing GABAergic neurons in the POA.

Results: Pharmacogenetically stimulation of POA GABAergic neurons resulted in increase of NREM sleep accompanied by inhibition of activity of orexin neurons.

Conclusion: These observations suggest that the POA GABAergic neurons are important in inhibition of arousal regions including hypothalamic orexin neurons.

P755

Orexin changes in experimentally immunised rats by TRIB2

T. KODAMA, S. TANAKA, Y. HONDA, K. HONDA, M. HONDA
Tokyo Metropolitan Institute of Medical Science, Tokyo, JP

Narcolepsy, a typical hypersomnia, shows daytime sleepiness and cataplexy as primary symptoms. The allele of the HLA (DQB1*0602) and T-cell receptor alpha are strongly associated with the morbidity. It is also reported that cataplexy is improved by the intravenous administration of IgG. These evidences indicate the contribution of autoimmune mechanism, however, the details remain unknown. Recently, Cvetkovic-Lopes et al. reported about 30% narcolepsy patients have antibodies to Tribbles homolog 2(TRIB2) protein in the serum, which is highly expressed in orexin neurons. We also have confirmed the presence of antibodies to TRIB2 in Japanese narcolepsy patients.

Objectives: We investigated the changes in orexin of the rat brain experimentally immunized by TRIB2 for clarifying whether (1) orexin neurons are degenerated by the attack of TRIB2 antibody or (2) TRIB2 antibody increases in the serum due to the loss orexin neurons.

Methods: Twenty-five 6 week-old female SD rats were housed in the sound attenuated light controlled cages and were given every other week the subcutaneous injection of keyhole limpet hemocyanin (KLH), 30 microgram TRIB2 conjugated to KLH (TRIB2), or saline(control). The IgG titers were also checked every other week. After the IgG titer rise, orexin concentration in CSF was measured using Elisa kit. The rat brains are stained immunohistochemically to investigate the change of orexin neurons.

Results: The percent ratio to the average CSF orexin level of age matched control group was calculated. Orexin in both KLH and TRIB2 group decreased significantly compared to the initial value. Orexin levels of 16 week, 18 week and 20 week-old rats in KLH group are 114.16% + 14.05, 61.96% + 4.90, and 81.18% + 10.67(mean + SEM), respectively. Similarly, these in TRIB2 group of 16 week, 18 week and 20 week are 97.75% + 8.38, 77.56% + 8.12, and 73.84% + 8.65, respectively. There was no significant difference between KLH and TRIB2 group. Contrary to expectation, there was no change in orexin neurons of either group in histological study. Prepro-Orexin mRNA level did not show any significant difference between two groups.

Conclusion: This result may suggest that the general activation in immune system has the effect on the regulation of orexin synthesis.

P756

The contribution of baroreflex and central autonomic commands to cardiac control during the wake-sleep cycle is modulated by ambient temperature but does not depend on hypocretin neurons activity

V. LO MARTIRE, S. BASTIANINI, C. BERTEOTTI, A. SILVANI and G. ZOCCOLI
University of Bologna, Bologna, IT

Objectives: Hypothalamic neurons releasing hypocretin (HCRT) control wake-sleep behaviour, cardiovascular system and body temperature, and their loss entails narcolepsy. Cardiac autonomic control is exerted by two major nervous mechanisms: baroreflex and central autonomic commands (CAC). The related contributions of baroreflex and CAC to cardiac autonomic control can be assessed by the cross-correlation function (CCF) between spontaneous fluctuations of heart period (HP) and those of systolic blood pressure (SBP) (Silvani et al., Sleep, 33:355–361, 2010). CCF yields the linear correlation coefficient between HP and BP as a function of the time-shift between these variables. We investigated whether the loss of HCRT neurons may cause alterations in the sleep-dependent cardiac autonomic control at different ambient temperature (Ta).

Methods: Narcoleptic mice with genetic ablation of HCRT neurons ($n = 11$) and wild-type controls ($n = 12$) were implanted with a telemetric BP transducer and electrodes for discrimination of wake-sleep states. After two weeks of recovery, signals were continuously recorded and the CCF between HP and BP was computed in each mouse during the different wake-sleep states (wakefulness, non-rapid-eye-movement sleep and rapid-eye-movement sleep) at each Ta of exposure (30°C, 20°C) in random order. Data were analyzed by 3-way ANOVA with mouse strain, wake-sleep state and Ta as factors. In case of significant interaction effects, the simple effect of the mouse strain was tested using *t*-tests with $P < 0.05$ considered to be statistically significant.

Results: Ta showed an important effect on the CCF profiles in each behavioral state. This was particularly evident during rapid-eye-movement sleep when cardiac rhythm was mainly modulated by baroreflex control at 20°C, whereas central autonomic commands prevailed at 30°C. In spite of these behavioral-dependent changes in cardiac control produced by the exposition to different Ta, the modulating effect of Ta on CCF was the same in both mouse strains: no significant differences in CCF profiles were found between narcoleptic and control mice.

Conclusion: These results demonstrate that cardiac autonomic modulation by baroreflex and CAC is influenced by ambient temperature and wake–sleep cycle but does not depend on the integrity of HCRT signaling.

P757

Effects of ambient temperature on blood pressure during sleep in narcoleptic mice with genetic ablation of hypocretin/orexin neurons

C. BERTEOTTI, S. BASTIANINI, V. LO MARTIRE, A. SILVANI and G. ZOCCOLI
University of Bologna, Bologna, IT

Objectives: Hypothalamic hypocretin/orexin (HCRT) neurons are involved in various physiological processes including wake-sleep behaviour, cardiovascular system, metabolic rate and body temperature. These physiological processes are strongly interrelated and the hypothalamus plays a critical role in their control. HCRT neurons

are lost in narcolepsy, a rare debilitating neurological disorder, characterized by excessive daytime sleepiness, cataplexy, sleep fragmentation and occurrence of sleep-onset rapid-eye movement episodes. We investigated whether the HCRT neurons mediate the effects of sleep and ambient temperature (Ta) on blood pressure (BP).

Methods: Narcoleptic mice with genetic ablation of HCRT neurons ($n = 11$) and wild-type controls ($n = 12$), both with mixed genetic background (75% C57Bl/6J-25% DBA/2J) were kept on a 12-h light-dark cycle, and free access to food and water. Animals were implanted with a telemetry BP transducer (TA11PA-C10, DSI) in the abdominal aorta and electrodes for discriminating wake-sleep states. After two weeks of recovery, simultaneous sleep and BP recordings were performed on mice undisturbed and freely moving in their own cages at 20°C and 30°C for 48 h at each Ta. Data were analyzed by 3-way analysis of variance and *t*-tests (significance at $P < 0.05$).

Results: The main effects of wake-sleep state and Ta, their interaction effect, and the wake-sleep state x mouse strain interaction effect on BP were statistically significant. BP changed with ambient temperature, increasing with decreasing Ta. The effect of Ta on BP was significantly lower in rapid-eye-movement sleep (REMS) than either in non-rapid-eye-movement sleep (NREMS) or wakefulness, in both mice strains. BP was higher in wakefulness than either in NREMS or REMS. Sleep-related decrease in BP was significantly reduced in narcoleptic mice at each Ta, both in the dark and light periods, and particularly during REMS.

Conclusion: These data indicate that HCRT neurons play a critical role in mediating the effects of sleep but not those of ambient temperature on blood pressure in mice. HCRT neurons may thus be part of the central neural pathways that mediate the phenomenon of blood pressure dipping on passing from wakefulness to sleep. This concept may have clinical implications in patients with narcolepsy with cataplexy, who lack HCRT neurons.

P758

Functional alterations of locus ceruleus noradrenergic neurons in orexin neuron-ablated mice

N. TSUJINO[1], T. TSUNAMATSU[2], A. YAMANAKA[3], M. WATANABE[4], Y. KOYAMA[5] and T. SAKURAI[1]

[1]Kanazawa University, Kanazawa, JP, [2]National Institute for Physiological Science, Kanazawa, JP, [3]National Institute for Physiological Science, Okazaki, JP, [4]Hokkaido University, Sapporo, JP, [5]Fukushima University, Fukushima, JP

Objectives: Narcoleptic patients and animals show behavioral instability not only in wakefulness state but also in non-rapid eye movement sleep. Instability in wakefulness states has been thought to be due to deficiency of orexins, neuropeptides produced in the lateral hypothalamic neurons. However, the neuronal mechanism that explains sleep-instability in this disorder has remained totally unknown, because firing of orexin neurons ceases during sleep in healthy animals. We hypothesized that chronic compensatory changes occured in wake-promoting neurons in narcolepsy. To evaluate this, we examined firing pattern of serotonergic neurons and noradrenergic neurons in the brain stem, two important neuronal populations for the regulation of sleep/wakefulness states.

Methods: We recorded single-unit activity of serotonergic neurons and noradrenergic neurons in the DR and LC of wild-type and narcoleptic mice *in vivo* along with simultaneous recordings of EEG/EMG to monitor sleep stages. Activities of noradrenergic neuron in LC were recorded by slice patch clamp. Excitatory and inhibitory inputs to NA neuron were analyzed by immunohistochemistry.

Results: Serotonergic neurons showed normal firing pattern during all sleep/wakefulness stage in narcoleptic mice. On the other hand, firing frequency of noradrenergic neurons in the LC was higher in narcoleptic mice during wakefulness and NREM sleep. Using slice patch clamp recording, sIPSC and mIPSC of noradrenergic neuron in narcoleptic mice were significantly reduced as compared with wild-type. There is no obvious change in apparent density of excitatory and inhibitory terminals in LC by immunohistochemistry.

Conclusion: These results suggested that the change in firing frequency of noradrenergic neuron in narcoleptic mice might be due to functional change of GABAergic inputs. These alterations might play roles in sleep abnormality in narcolepsy.

P759

Genetic dissection of orexin signalling in neuronal networks involved in wakefulness regulation and cataplexy

A. VASSALLI[1], S. LI[1], J. M. DELLEPIANE[1], Y. EMMENEGGER[1], C. SCHRICK[1], G. PLAZZI[2], P. FRANKEN[1] and M. TAFTI[1]

[1]University of Lausanne, Lausanne, CH, [2]University of Bologna, Bologna, IT

It is now recognized that the neurotransmitters orexins (OXs; hypocretins) elicit appropriate levels of arousal to engage in exploratory and goal-directed behaviors depending on physiological needs. OX neuron cell bodies are exclusively located in the lateral hypothalamus and directly innervate and excite a multitude of brain targets, including wake-promoting monoamine groups, such as noradrenergic (NA), dopaminergic (DA), histaminergic, serotonergic neurons, as well as cholinergic neurons. Furthermore, OX neurons receive a large variety of afferents. The anatomical and functional complexity of the OX system is thus considerable. A challenge is to unravel the relative functional contributions of these pathways in distinct OX functions.

To attain a comprehensive understanding of the function of the OX circuit, we have re-assessed the OX null (OX KO) mutant mouse and developed new behavioral criteria of cataplexy identification. This led us to a number of findings shedding new light on the process of cataplexy, both at the behavioral and polysomnographic levels. Unlike the current static view of cataplexy as a PS-like dissociated state, we provide a dynamic picture of cataplexy as a reproducible sequence of distinct phases characterized by distinct EEG signatures. We have in particular identified bursts of high-power theta activity confined to the frontal cortex and correlated to cataplexy onsets. The neural substrates underlying these previously unrecognized frontal signals are being characterized.

To unravel the underlying neural pathways of cataplexy and other aspects of orexin-mediated wakefulness regulation, we have created conditional knockout (CKO) alleles of each OX receptor gene and generated mice in which selective OX target neuron populations are depleted of either one or both OXRs, using Cre/loxP techniques. Because OX neurons massively innervate the NA and DA systems intimately involved with narcolepsy symptoms, we are first analyzing behavioral state regulation in NA and DA neuron-specific OX1R and OX2R deficient mouse models, generated by crossing our mice to Dopamine-beta-hydroxylase-driving Cre and Dopamine transporter-driving Cre mice, respectively. The differential set of EEG characteristics that we have found to define the progression of a cataplexy attack in OX null mice, and their behavioral correlates, can now be interrogated with a finer resolution into the neuronal network.

P760

Search for neurons mediating functions of orexin as a wakefulness-stabiliser

E. HASEGAWA[1], M. YANAGISAWA[2], T. SAKURAI[1] and M. MIEDA[1]
[1]Kanazawa University, Kanazawa, JP, [2]University of Texas Southwestern Medical Center, Dallas, TX

Objectives: Loss of orexin neurons is associated with narcolepsy in the human, highlighting a critical role of orexin neuropeptides in the maintenance of wakefulness. Orexin-/- mice, as well as mice lacking both of two orexin receptors (Ox1R-/-;Ox2R-/- mice), display a phenotype strikingly similar to narcolepsy: abrupt behavioral arrests with muscle atonia (cataplexy), sleep-onset REM sleep (SOREM) and fragmented sleep/ wakefulness states. They are clear that application of exogenous orexins excites many types of neurons in slice preparation, including those of TMN, DR, LC, and LDT/PPT, and application of orexin directly into the LC, TMN, and LDT promotes wakefulness and suppresses NREM and REM sleep *in vivo*. However, neurons directly downstream to orexin neurons in physiological conditions, i.e., neurons activated by endogenous orexins and mediate their wake-promoting and REM-suppressing effects, have remained uncertain.

Methods: To identify such neurons, we searched for monoaminergic and cholinergic nuclei in which local rescue of Ox1R or Ox2R expression in Ox1R-/-;Ox2R-/- mice ameliorates their narcoleptic phenotype. To rescue of Ox1R or Ox2R expression, Ox1R-/-;Ox2R-/- mice were injected with recombinant AAV vectors.

Results: Cell-nonspecific rescue of Ox2R in the dorsal and median raphe by AAV vectors prevented SOREM sleep, while rescue of Ox1R in the locus coeruleus (LC) increased duration of wakefulness to values close to those of wildtype mice. We further examined serotonergic and noradrenergic neuron-specific rescues of orexin receptor in the raphe and LC, respectively, and reproduced the results of cell-nonspecific rescue experiments, at least partially. Furthermore, it was clear that dorsal raphe serotonerigic neurons and LC noradrenergic neurons project to several nuclei implicated in sleep/wake regulation.

Conclusion: These results suggest that dorsal raphe serotonerigic neurons and LC noradrenergic neurons function as neurons directly downstream to orexin neurons to prevent SOREM and to stabilize wakefulness, respectively.

P761

Wake-promoting effects of ONO-4127, a prostaglandin DP1 receptor antagonist, in hypocretin deficient narcoleptic mice

Y. SAGAWA, N. SAKAI, S. CHIKAHISA, M. SATO, S. CHIBA and S. NISHINO
Stanford University, Palo Alto, CA

Objective: Over 90% of narcoleptic patients receive pharmacological treatments; amphetamines and modafinil are the two major classes of compounds used for the treatment of excessive daytime sleepiness (EDS) associated with narcolepsy. These treatments are not always satisfactory due to their incomplete management and unpleasant side effects. PGD2 or DP1 receptor agonists promote sleep, while a PGD2 synthase inhibitor promotes wakefulness in animals. It was recently reported that ICV perfusion of ONO4127, a selective DP1antagonist, enhance wakefulness in rats. In the current study, we evaluated the wake-promoting effects of ONO-4127 in orexin/ataxin-3 transgenic (Tg) narcoleptic and wild type (WT) mice and compared the efficacy with that of modafinil.

Methods: Mice ($n = 6$–8 for each genotype) were surgically attached to the headstage for EEG and EMG monitoring. Two drug doses (6.0×10–5 M, 2.9×10–4 M) or vehicle were administered at 1 μl/min with a microdialysis probe aimed at the basal forebrain (BF; the horizontal limb of the diagonal band) in each mouse in light (ZT2 to ZT8) and dark (ZT 14 to ZT 20) periods. Modafinil (30 m and 100 mg/kg, p.o. at ZT 2 and ZT14) was administered in these mice for the comparison.

Results: The infusion of ONO-4127 to the BF markedly increased wake and reduced NREM and REM sleep in both WT and Tg mice. ONO-4127 at 6.0×10–5 M and 2.9×10–4 M, increased 6 h cumulative wake amount by 45.8%, 62.4%, and reduced NREM by 30.2%, 41.4% and REM sleep by 32.5%, 42.7% (compared to the vehicle sessions) in WT mice in the light period, and increased wake by 37.6%, 51.9%, reduced NREM by 32.0%, 47.8% and REM sleep by 63.8%, 71.4% in Tg mice. In the dark period, ONO-4127 increased wake by 20.6%, 31.8%, reduced NREM by 36.9%, 56.4% and REM sleep by 14.5%, 30.6% in WT mice, and increased wake by 24.5%, 38.7%, reduced NREM by 38.3%, 59.5%, and reduced REM sleep by 31.6%, 59.9% in Tg mice. The wake promoting potency of ONO-4127 (2.9×10–4 M) is roughly comparable to that of modafinil (100 mg/kg p.o). ONO-4127 reduced the direct transition from wake to REM sleep (DREM) in Tg mice (by 67.6%, 100%), while modafinil did not reduce DREM. The effects of ONO-4127 was site specific, and perfusion of ONO-4127 to the thalamus did not increase wake.

Conclusion: Possible use of prostaglandin DP1 antagonists for the treatment of EDS associated with narcolepsy is suggested. DP1 antagonists may also reduce cataplexy, as ONO-4127 reduced DREM in Tg mice.

Research supported by a contract with Ono Pharmaceutical Co. Ltd.

P762

The 'love-hormone' and sleep: correlates of intra-nasal oxytocine administration

D. NEU[1], V. NAGANT[1], P. VERBANCK[1] and M. MIKOLAJCZAK[2]
[1]Université Libre, Brussels, BE, [2]Université Catholique de Louvain, Louvain-La-Neuve, BE

Introduction: There is accumulating evidence that in humans, sex hormones as oxytocin (OXT) have psychological effects beyond their basic and physically direct reproductive actions. Important anxiolytic effects are also observed with increased levels of OXT. The neural substrate for anxiolytic effects of OXT has been suspected in limbic areas, in particular in the amygdala. Anxiolysis, a state of calm, and 'being relaxed' are generally related to and linked with lowered vigilance or even sleepability. Induced lowered vigilance can in terms be related to somnolence (3). Whether OXT can rise or influence sleepability and how these effects of OXT can be related to vigilance in healthy subjects, remains unknown. The objective of the present study is to observe objective influence of OXT on monitored vigilance states within a controlled trial.

Methods: Within a randomized placebo-controlled double blind cross-over trial, twelve healthy young men were recruited. Each subject was randomly assigned to intra-nasal placebo or OXT after 2 weeks of stable sleep-wake schedules (T1). Within the cross-over design, each subject underwent 2 weeks later the same test battery under the same conditions (T2). Multiple Sleep Latencies (MSLT) and psychomotor vigilance test (PVT) trials and visual analog scales for fatigue and sleepiness (VAS-F, VAS-S) have been carried out at several fixed time points under both conditions with the exactly same procedure and monitoring for stable sleep-wake schedules during the

4 weeks of study protocol by means of ambulatory wrist actigraphy, before and between both testing conditions.

Results: MSLT recordings showed more total duration of sleep states and appearances of daytime REM-sleep without any prior deprivation under the OXT condition. However, VAS-F, VAS-S and PVT did not show significant differences in mean reaction times between both conditions (placebo or OXT).

Conclusion: The relationships between sexual function related hormones and electrophysiological brain activity remain certainly underexplored. We think that standardized measures of EEG monitored vigilance states combined to behavioral assessments can increase our insight regarding these issues. Adjunctive measures of vigilance and stress related hormones should probably be investigated in parallel within future endeavors in this field.

P763

Drug effects on wake versus sleep auditory thresholds

M.H. BONNET[1] and D.L. ARAND[2]

[1]Wright State University, Springboro, OR, [2]Kettering Medical Center, Kettering, OH

Previous work has shown that a number of medications produce significant changes in auditory thresholds in both awake and sleeping subjects. The current study sought to compare changes in auditory thresholds during sleep and wake to determine the extent to which changes are state specific.

Six normal males slept in the sleep laboratory for nine non-consecutive nights. Ss were awakened 5–8 times per night from stage 2 sleep with a screening audiometer through an earphone insert. Ss also had waking auditory threshold measurements made prior to lights out and following each of the awakenings from sleep. On the first four nights after adaptation, Ss received either placebo, caffeine 400 mg, flurazepam 30 mg, or pentobarbital 100 mg in a random order 15 min prior to lights out.

Each night was divided into five time periods and multiple observations within a time period were averaged. Overall significant medication effects on wake and sleep arousal threshold have been previously reported. For the current analyses, the data were plotted and the area under the curve for each quarter of the night for each drug and placebo was calculated. For the values obtained from sleep arousal threshold, the wake area value was subtracted so that wake effects and independent sleep effects could both be evaluated and compared. Then each medication area value was divided by the corresponding placebo area value to provide comparable unitless data. All of the derived data were entered into a single ANOVA with repeated measures effects for quarter of the night (3 df), medication condition (2 df), and sleep versus wake observation (1 df).

The ANOVA showed a significant main effect for medication ($F = 18.2$, $P < 0.001$; overall ratio means were 0.82, 1.36, and 1.20 respectively for the caffeine, flurazepam and pentobarbital conditions with caffeine different from both sedatives). However, there were no other statistically significant ANOVA findings for other main effects or any interaction (all $P > 0.25$) including all effects for sleep versus waking.

The current data extend previous findings by showing that medication-induced increases and decreases in auditory threshold occur independently in waking threshold and in arousal threshold when asleep even when controlled for changes in waking threshold. Of more interest, changes in auditory threshold corrected as a proportion of placebo threshold values were of similar magnitude when subjects were awake as they were when subjects were asleep.

P764

Caffeine delays markers of maturation in juvenile rats

N. OLINI, S. KURTH and R. HUBER

University Children's Hospital Zurich, Zurich, CH

Objectives: Caffeine is a widely consumed stimulant. A lot is known about its metabolism and its molecular and cellular action in the central nervous (CNS) system. A major effect of caffeine on the CNS is the inhibition of the adenosine receptors which leads to alterations in sleep wake regulation.

Adolescence is a critical period for brain development during which a massive reorganization of cortical connectivity takes place. These connectivity changes are reflected in prominent changes in the sleep EEG slow wave activity (SWA). Even though there is increasing consumption of caffeinated beverages by adolescents, little is known about effects of caffeine on adolescent neurobehavioral development. Therefore, we examined the effects of caffeine application during this critical period on behaviour, anatomical structure and the sleep EEG in juvenile rats.

Methods: Twenty-nine Sprague Dawley rats were individually housed and maintained on a 12 h/12 h light-dark cycle. Food and water was given *ad libitum*. Electrocorticogram (ECoG) and electromyogram (EMG) were continuously recorded for 3 weeks starting from postnatal day 25 (P25). A subgroup of animals ($n = 13$) received caffeinated drinking water between P30 and P35 (0.15 g/l). ECoG signals were filtered and subjected to a Fast Fourier Transform for 4-s epochs. Vigilance states were visually scored. For behavioural analyses, videos were recorded twice during free exploration on P28 and P42. Histological analyses were conducted at similar ages (P30, P42, $n = 6$).

Results: Juvenile rats show an inverted *U*-shaped time course of sleep SWA as found in humans. Peak SWA is reached at around P30. In our rats the critical period of cortical maturation is reflected in a strong decrease of SWA (P30 versus P38, $P < 0.05$), an increase in exploratory behaviour (P28 versus P42, $P < 0.01$) and a reduction of cell density (P30 versus P42, $P < 0.05$). The application of caffeine during this critical period diminished the reduction of SWA (sham versus caffeine, $P < 0.05$) and tended to show a lower increase of exploratory behaviour (sham versus caffeine, $P = 0.06$). Moreover, the cell density at older age was significantly higher after caffeine treatment (sham versus caffeine, $P < 0.05$).

Conclusion: Our results show behavioural, structural and electrophysiological changes after a caffeine treatment in the rat and suggest that caffeine delays maturation during a critical period.

Poster Session - Shift work

P765

The length of time that shift-working nurses have for themselves on days off is associated with recovery from work

T. KUBO[1], M. TAKAHASHI[1], M. SALLINEN[2], Y. KUBO[3] and H. SUZUMURA[4]

[1]National Institute of Occupational Safety and Health, Kawasaki, JP, [2]Finish Institute of Occupational Health, Helsinki, FI, [3]Jikei University School of Medicine, Tokyo, JP, [4]Aichi Medical University, Aichi, JP

Objectives: Shift-working nurses often have occasional days off due to their shift schedules. This situation may affect their possibilities to recover sufficiently before the next shift cycle begins. This study examined whether the length of leisure time that shift-working nurses have for themselves on days off is associated with their recovery from fatigue, sleep and how satisfied they are with their days off.

Methods: Thirty shift-working nurses from a university hospital participated in the study. They were instructed to record their leisure activities (work-related, domestic work, shopping, watching TV, and sports) for 16 days at awakening and bedtime using a self-reported log (divided into 30-min sections). Shopping, watching TV, and sports were categorized as ''leisure time for myself.'' Subjective fatigue (1 = very low to 10 = very high) and satisfaction with days off (visual analogue scale) were retrospectively rated at bedtime. Throughout the study, sleep was measured with an actigraph (AW64 [Mini Mitter Co.]). Later, days off were divided into the longest and shortest days (''long'' day, 11.4 ± 0.7 h., ''short'' day, 1.8 ± 0.3 hrs.), based on the length of ''leisure time for myself.'' Satisfaction with days off was compared between the two days using paired *t*-tests. The fatigue and sleep data were analyzed using two-way mixed repeated analysis of covariance (condition [''long'' day, ''short'' day], day [dayshift before day off, day off]). Covariates included age, partner (yes/no), children (yes/no), and shift schedule (two-shift system, three-shift system).

Results: The level of satisfaction with days off was significantly higher in the category of ''long'' days compared to the category of ''short'' days. The same relationship held for sleep efficiency, but sleep duration did not show such a pattern. Subjective fatigue significantly decreased from a day shift to the subsequent day off. A marginal significant interaction was observed for subjective fatigue ($P = 0.097$). A post-hoc test showed that fatigue levels during days off were significantly lower in the category of ''long'' days compared to the category of ''short'' days.

Conclusion: Our findings show that the length of leisure time that shift-working nurses have for themselves on days off is associated with their satisfaction with these days, recovery from fatigue, and sleep quality.

Acknowledgment: This study was supported by a Grant-in-Aid for Young Scientists (start-up).

P766

Sleep restriction at sea affects solo sailors' reaction times

R. HURDIEL and D. THEUNYNCK

Université du Littoral Côte d'Opale, Dunkerque, FR

Objective: The aim of the study was to record sleep durations during short offshore solo sailing races and to compare reaction times pre-race versus post-race.

Materials and Methods: Nineteen sailors took part in three different single-handed races of 24 h, 36 h and 50 h duration; 12 completed the study with full compliance. The sleep/wake schedule for each sailor was recorded with actigraphs and an electronic sleep diary from the day before the start until the end of the race. Reaction times (RTs) were measured on board with a 5 min simple reaction time (SRT) test. Pre-race RTs were recorded in the mid-day before the race and post-race RTs immediately after the race.

Results: Sailors slept 8 h 32 min ±39 min the last night before the race. Mean sleep duration recorded during the 24 h race was 22 ± 30 min (2 ± 1 naps; 2 sailors did not sleep at all); during the 36 h race it was 92 ± 34 min (6 ± 3 naps); and during the 50 h race it was 172 ± 122 min (8 ± 2 naps). Number of lapses (RTs > 500 ms) on the SRT was significantly greater after the race compared to before ($t = -3.47$; $P = 0.005$). The reciprocal transform (mean 1/RT*1000) was also significantly different ($t = 4.67$; $P = 0.001$), as were the slowest 10% of RTs ($t = -5.04$; $P < 0.001$) and the fastest 10% of RTs ($t = -4.65$; $P = 0.001$). No difference was found for false starts ($t = -1.68$; $P = 0.12$).

Discussion: These results show that sleep restriction affects SRT test outcomes in solo sailors (as they do in the general population), suggesting elevated performance and safety risks while at sea. Our results also indicate that a 5 min SRT test is sufficiently sensitive to reveal that solo sailors suffer from performance impairment due to sleep restriction. Work is in progress to provide innovative solutions to managing sleep, fatigue, and competitiveness during offshore solo sailing races.

P767

The effects of a 6 h on/6 h off maritime watch system on sleep

P. DONOFRIO[1], A. DAHLGREN[2], M. BARNETT[3], M. LÜTZHÖFT[4], A. KIRCHER[4], M. GILLBERG[5], G. KECKLUND[1] and T. ÅKERSTEDT[1]

[1]Stockholm University, Stockholm, SE, [2]KTH Royal Institute of Technology, Stockholm, SE, [3]Warsash Maritime Academy, Warsash, UK, [4]Chalmers University of Technology, Gothenburg, SE, [5]Karolinska Institutet, Stockholm, SE

Objective: Fatigue at sea is involved in a number of maritime accidents and the work schedule (watch system) seems to be an important factor since it involves two periods of work and two periods of sleep per day. One important factor may be the amount and quality of sleep obtained in watch systems that displace sleep to the day and evening. The present study aimed to investigate polysomnographical sleep on a schedule with 6 h off and 6 h on during a one-week maritime bridge simulator study of sleep and fatigue.

Methods: Two teams of nine officers participated working a 6/6 watch schedule during a week ''at sea''. Team one worked 00–06 and 12–18, and participants were allowed to sleep between 06 and 12 (morning sleep) and 18–24 (evening sleep), team two worked 06–12 and 18–24, and participants were allowed to sleep between 12–18 (afternoon sleep) and 00–06 (night sleep). All subjects were submitted to a 24 h polysomnography (EEG, EOG and EMG) on the second and third day.

Results: Team one slept significantly less during morning sleep (179 ± 9 min) than during evening sleep (211 ± 10 min) and team two slept more during night sleep (230 ± 9 min) than during afternoon sleep (127 ± 10) ($P < 0.01$ for both). Team one had a significantly lower sleep efficiency during morning sleep (80.7 ± 3%)

than during evening sleep (87.2 ± 3). Team two had a higher efficiency during night sleep (86.7 ± 3) than during afternoon sleep (73.9 ± 3) (both $P < 0.05$). REM sleep in team one increased dramatically from 14.5 ± 3% during morning sleep to 26.6 ± 4% during evening sleep ($P < 0.01$). Team two had around 15% of REM sleep for both night and afternoon sleep. Stage1 min showed a strong effect of watch in both groups. Team one increased from 15.8 ± 3 min during morning sleep to 40.0 ± 3 during evening sleep ($P < 0.001$). The second team increased from 29 ± 3 min during night sleep to 40.6 ± 3 during afternoon sleep. SWS% did not show any differences between watches. The total amount of sleep was 390 and 357 min ($P < 0.10$) for the two teams for a 24 h period, with no differences between the teams for the other variables.

Conclusions: The 6 h on/6 h off system resulted in a clear split sleep pattern, which may lead to higher sleepiness, with afternoon sleep being most negatively affected, presumably for both circadian and homeostatic reasons (prior amount of sleep), and with consequences for the total amount of sleep per 24 h day that is lower than what may be necessary for optimal alertness.

P768

Do long-haul truck drivers show individual differences in response to night shifts?

M. PYLKKÖNEN, A. HENELIUS, H. K. HYVÄRINEN, S. JAGADEESAN, K. PETTERSSON and M. SALLINEN

Finnish Institute of Occupational Health, Helsinki, FI

Objectives: The prevalence of sleepiness amongst shift workers is highest during night shifts. We examined whether some professional drivers are more often sleepy than others during these shifts. In addition, we studied factors associated with this possible individual difference.

Methods: Forty-nine long-haul truck drivers (mean age 37.6 year) volunteered. Data was collected during a 2-week period with a minimum of two night shifts. The data consisted of a total of 214 night shifts.

The outcomes included sleep–wake rhythm measured by a diary and an actigraph, sleepiness measured hourly during shifts by the Karolinska Sleepiness Scale (KSS), and use of sleepiness countermeasures measured by a diary. Individual factors were measured by a questionnaire. A shift was defined as ''sleepy shift'' if at least one of the KSS ratings was ≥6.

Results: Eleven drivers had all, 26 drivers some, and 12 drivers none of their night shifts defined as ''sleepy shifts''. The proportion of the first night shifts was higher for the drivers with ''sleepy shifts'' only (44%) than for those with some (36%) or no (33%) ''sleepy shifts''. The night shifts of the drivers without ''sleepy shifts'' were, on average, 1.5 h earlier than those of the other drivers ($P < 0.05$). Shift duration (mean 11 h) did not differ between the groups.

The drivers with ''sleepy shifts'' only slept less than the drivers without ''sleepy shifts'' prior to the first night shift (mean 7.1 versus 8.6 h; $P < 0.05$) and between successive shifts (mean 5.5 versus 6.2 h; $P < 0.05$). The proportion of the first night shifts preceded by a nap was higher for the drivers with ''sleepy shifts'' only (44%) than for the other drivers (15%, 24%).

The proportion of night shifts during which the drivers used sleepiness countermeasures was higher for drivers with ''sleepy shifts'' only (88%) than for those with some (68%) or no (28%) ''sleepy shifts''. The most used countermeasures amongst the sleepiest drivers were caffeine (47% of the cases), talking with other people (37%), and increasing the volume of radio (21%). Of the individual factors, daily sleep need was higher for the drivers with ''sleepy shifts'' only (mean 8.3 h) than for those with some (7.7 h) or no (7.3 h) ''sleepy shifts''.

Conclusions: Our results suggest that some professional drivers are repeatedly sleepier than others during night shifts. These differences seem to be associated with multiple factors related to sleep, shift and individual characteristics, and with the use of sleepiness countermeasures.

P769

Effects of prophylactic nap on junior doctors' cognitive performances in an emergency department

D. ZIDOUR[1], M. CHENNAOUI[2], F. SAUVET[2], P. VANBEERS[2] and E. SAGUI[1]

[1]HIA LAVERAN, Marseille, FR, [2]IRBA, Bretigny, FR

Objectives: Emergency room medical interns experience sleep-deprivation induced attentional and memory impairments, which may reduce quality of care. The purpose of this study was to determine if short prophylactic naps before shifts improve cognitive performance during and after shifts.

Methods: Each subject had to perform between two and six shifts with or without a nap beforehand. Attentional and cognitive performance were determined by measuring reaction times to the ''simple'' and ''inverted'' subtests of the Standardized Tests for Research with Environmental Stressors (STRES) battery. Memory performance was assessed using the number of errors in the grammar subtest of the STRES battery. Three measurements were obtained: before (T0), at 2 am (T1) and after the shift (T2). Periods of wakefulness and sleep were recorded by actimetry. Twenty-three subjects performed 87 shifts: naps were taken before 26 shifts and naps were not taken before 61 shifts.

Results: After adjusting for coffee or stimulant consumption, attention at T1 was better in subjects who had taken a nap beforehand (nap group) as compared with subjects who did not take a nap (no nap group). After the shift at T2, the benefits of the nap had disappeared, but greater attention was associated with variables describing quality of sleep throughout the shift. No variable was associated with improved memory performance during (T1) or after (T2) the shift.

Conclusions: This study found that a short prophylactic nap benefitted attentional but not memory performance in emergency room interns. This result is in agreement with what has been described in truck drivers. The benefit of this type of nap for attentional performance appears to be effective for at least 11 h post-nap.

P770

Influence of sleep deprivation on the health of medical staff working in night shift

S. BAJRAKTAROV[1], N. MANUSEVA[2], G. NOVOTNI[3], S. ARSOVA[1], K. RICHTER[4] and A. NOVOTNI[1]

[1]Faculty of Medicine, Skopje, MK, [2]University Psychiatry Clinic, Skopje, MK, [3]University Neurology Clinic, Skopje, MK, [4]Schlafflabor, Klinikum Nurnberg, Nurnberg, DE

Introduction: Working in night shifts and high stress on the working place are important characteristics of jobs in the health sector mainly because of the possible negative effects on the health and the safety of the medical stuff. Shift work with night shifts in health workers is connected with increased number of sleep disorders, more mental health problems, dissatisfaction with the job, decreased work activity

and increase of cardiovascular /digestive diseases and absence from work. The influence of the night shifts is mainly because of the affection of natural circadian rhythm of the person resulting in increased risks over theirs bio-psycho-social integrity.

Aim: To measure the influence of quality of sleep over somatic and psychic health of the health workers working in night shifts according to the SF-36 Health Survey questionnaire.

Method: The study was cross sectional, administered in two psychiatric services in Skopje, Macedonia, on representative stratified sample of 60 health workers working in night shifts and 60 health workers working only in one dayshift. The groups were age matched and were grouped according to their specialty.

Results: According to the results of the SF-36 Health Survey questionnaire the group with the night shift has increased depression, disordered sleep and fatigue. These are the reasons for leaving the night service.

Conclusion: Decreased quality of sleep is correlated with negative implications on the social functioning and quality of life of the night shift workers.

P771

Sleep and fatigue associated with levels of worktime control and worktime variability: a cross-sectional investigation

M. TAKAHASHI[1], T. KUBO[1], X. LIU[1], F. TOGO[2], A. SHIMAZU[3], K. TANAKA[4] and T. UCHIYAMA[5]

[1]National Institute of Occupational Safety and Health, Kawasaki, JP, [2]The University of Tokyo Graduate School of Education, Tokyo, JP, [3]The University of Tokyo Graduate School of Medicine, Tokyo, JP, [4]Graduate School of Medical Science Kitasato University, Sagamihara, JP, [5]Kakogawa Works, Kobe Steel, Kakogawa, JP

Objectives: Perceived ability to control over working times, worktime control (WTC), is generally advantageous to health and well-being at work. It is unclear if more variable working times when coupled to greater WTC may lead to unfavourable consequences. The present study aimed at evaluating how both WTC and worktime variability (WTV) were associated with sleep and fatigue in day-working individuals.

Methods: A total of 2206 employees in a manufacturing worksite responded to a questionnaire (response rate = 83%, 2147 men, 59 women, mean age 42 ± 14 year). This study selected 1085 daytime workers (747 fixed, 333 flextime, five others). We measured WTC, WTV, sleep (Pittsburgh Sleep Quality Index, PSQI), fatigue, fatigue recovery after a night's sleep, weekly work hours, psychosocial work characteristics, and sociodemographic variables. WTC was assessed as the extent of influencing five aspects of working times (1 = very little to 5 = very much): (i) length of a workday, (ii) starting and finishing times of a workday, (iii) taking of breaks during the workday, (iv) scheduling of vacations and paid days off, and (v) taking of unpaid leave. The total score was computed and divided into three categories (low, moderate, high) by tertile. WTV was assessed by the alternative questions (1 = yes, 2 = no) about having or not having to work (i) the same number of hours every day, (ii) the same number of days every week, and (iii) with fixed starting and finishing times. The total score was calculated and divided into two categories (less versus more variable) by a cut-off of three. Analysis of variance was conducted with the factors of WTC and WTV, adjusted for age, work schedule (fixed versus non-fixed), occupation, weekly work hours, psychosocial work characteristics (quantitative job overload, job control, social support at work).

Results: More variable group showed significantly poor sleep than less variable group for total sleep time and PSQI global and component (sleep duration, daytime dysfunction) scores. As supported by a significant interaction between WTC and WTV, high WTC and more WTV was found to be significantly greater fatigue than high WTC but less WTV. The similar but non-significant results were obtained for recovery from fatigue.

Conclusion: These data indicate poor conditions of sleep associated with more variable working times, and also raise concerns for increased fatigue under more variable working times despite high worktime control.

P772

Selection into shift and night work

J. AXELSSON[1], G. KECKLUND[2], P. GUSTAVSSON[1] and A. RUDMAN[1]

[1]Karolinska Institute, Stockholm, SE, [2]Stockholm University, Stockholm, SE

Objectives: Selection factors may be an important mediator of the relationship between shift and night work and impaired health. The aim was to investigate if factors already during higher education (e.g. demographical and health behavioral factors) are more prevalent amongst individuals working shift-work or permanent night work one year after graduation.

Methods: Three national cohorts of nursing students (n = 1155, 1702, and 1459) filled out a questionnaire before graduating and after one year in work life. The sampling frame constituted the total population of last semester nursing students from all 26 universities in Sweden (in the autumns of 2002, 2004 and 2006, respectively). At baseline, the response rate varied between 68 and 73%, and 92%, 92%, and 78% for the respective cohorts one year post graduation. Data from the baseline questionnaires was used to predict future work schedules of 3-shift (including night, 26%), and permanent night (5%). Other work schedules were: day shift (Mon-Fri, 8%), 2-shift (morning/evening, 54%), other schedules (6%). Reported effects have a P-level of <0.05.

Results: The typical 3-shift worker was a single healthy male nurse. More specifically, socio-demographic predictors for working 3-shift one year post graduation were being male, living alone, having no children, regular alcohol consumption, being a non-smoker, having ideal BMI, and high self-rated health. With respect to choosing permanent night work one year post graduation, the characteristic nurse had more often children, smoked, had high BMI and lower self-rated health as measured at the time of graduation.

Conclusions: We found that selection into shift- and night work was mainly related to demographical variables and to some degree to life-style and health factors. While selection into 3-shift work was related to a wide range of 'positive' health factors, the opposite was true for those starting to work permanent night work, largely supporting and extending on recent work (1). Thus, selection into three shift-work seem to largely relate to factors that also promote health while the opposite seem true for selection into permanent night work.

References

1. Nabe-Nielsen et al., Cardiovascular risk factors and primary selection into shift work Scand J Work Environ Health 2008;34(3):206–212

P773

Sleep diaries for shift workers

M. LAMY, E. BASTILLE-DENIS and A. VALLIÈRES
Université Laval, Québec, CA

Introduction: Sleep diaries have long been the preferred method for collecting data on self-reported sleep over time in insomnia research. Only a few studies were dedicated to daily self-reports of sleep difficulties associated with shift work. The aim of this study is to qualitatively document the use of sleep diaries in the context of shift work and to present a diary template that reflects the reality of shift work

Method: The sample included 46 shift workers (86.9% women; mean age = 35.4 years old) taking part in a study on bio-psychosocial factors involved in the evolution of shift work sleep disorder. Among them the first 10 were given a sleep diary used in previous insomnia studies. This sleep diary consisted of 7-day report presented on a single page with a column for each day of the week. This format is similar to the one proposed recently as a consensus sleep diary by a committee of experts. The other 36 participants received a diary with a 24-h scale on each page. Both sleep diaries included six questions on sleep and wake time, and a question on medication, alcohol and caffeine use. Both formats used a sleepiness rating scale (Likert scale from ''1'' to ''7) to be completed after each sleeping period.

Results: 55.5% of the total sample (26 out of 46 participants) reported at least 3 sleep periods per day when working at night, 41.3% reported two sleep periods per day and only 1 participant reported 1 sleep period per day. The first 10 participants were unable to comply with the 7 columns for each day of the week diary. All of them reported that this version did not reflect the reality of their sleep schedules. A few added an extra column in order to report transitions before and after night shift. Most of them did not report napping periods as they consider that they had more than one sleep period per day rather than a nap. Most of them wanted to comment on their sleep difficulties occurring at different time point. The 36 participants using the second sleep diary format did not report any of these difficulties.

Conclusion: Qualitative reports suggest that within the context of shift work, sleep diaries need to be adjusted in order to capture the sleep patterns over 24 h. Moreover, this tool will help clinicians to better investigate difficulties with sleep in the shift work population and to develop a treatment plan that better suits the reality of shift work sleep disorder.

Support: Supported by the Canadian Institutes of Health Research (#197171).

P774

Influence of night shift work on the nurses psycho-social functioning

S. BAJRAKTAROV[1], N. MANUSEVA[2], D. DIMOVSKI[2], E. MICEVA-VELICKOSKA[2], V. CHALOVSKA-SAMARDJISKA[2], V. VUJOVIC[1] and A. NOVOTNI[1]
[1]Faculty of Medicine, Skopje, MK, [2]University Psychiatry Clinic, Skopje, MK

Introduction: Nurses working in night shifts are suffering from sleep disorders which are affecting their functionality and quality of life. The influence of the night shift is based on the disturbed circadian rhythm of the person resulting in increased risks on the bio-psycho-social integrity of the person.

Aim: To measure the influence of the quality of sleep and disturbed sleep on the daily functioning of the nurses working in night shift through parameters of the Epworth Sleepiness Scale.

Method: The study included 30 nurses working in night shift and control group of 15 nurses with day shift only. We used Epworth Sleepiness Scale.

Results: There were significant differences in the total score between the groups. Only on the question for the sleepiness during sitting and talking to someone there was no significant difference.

Conclusion: The decreased quality of sleep has negative influence on the activity of the medical nurses working in night shifts in their working place and also in their social functioning and quality of life. Accumulated deficits in sleep in the investigated group could lead to more severe problems in their everyday functioning such as excessive sleepiness during the day, substandard sleep and fatigue. Decreased quality of sleep is connected with negative implications in relation to social functioning and quality of life.

P775

Association of shift work sleep disorder with increased leukocyte count

P. VANTTOLA[1], S. PUTTONEN[1], K. VIITASALO[2] and M. HÄRMÄ[1]
[1]Finnish Institute of Occupational Health, Helsinki, FI, [2]Finnair Health Services, Vantaa, FI

Objectives: Shift work has many undesirable health outcomes such as metabolic and cardiovascular disease. We have earlier reported an association of shift work and systemic inflammation. Now we tested the hypothesis that specific sleep disturbance related to shift work may predispose to increased inflammation indicated as elevated leukocyte levels.

Methods: The study involved 687 full time shift workers of a Finnish airline company (386 men). Shift work sleep disorder (SWSD) was defined by six items assessing symptoms of sleep difficulties and tiredness in relation to work shifts and days off. Participants (N = 198) who reported always or often having at least one work shift related difficulty and did not report having any difficulty more than seldom on holidays were classified into the SWSD group. All the other participants were classified into the non-SWSD group (N = 489). Blood samples were drawn after a 12 h fasting.

Results: Multinomial logistic regression analyses adjusted for age, sex and recent infectious diseases indicated that monocyte count was higher in the SWSD group than in the non-SWSD group (mean ± SD 6.3 ± 1.7% and 6.0 ± 1.6% respectively, B = 0.2, $P < 0.01$). In separate analyses for men and women, the association was significant only in men (mean ± SD 7.1 ± 1.6% and 6.3 ± 1.6% respectively, B = 0.3, $P < 0.001$). No significant effects were found in lymphocyte, granulocyte or overall leukocyte counts.

Conclusion: SWSD appears related to increased monocyte count among male shift workers but not among female shift workers. The results imply that individuals suffering from work shift related difficulty in sleep or tiredness may be more vulnerable to inflammation. Whether the increase in monocyte level is a chronical state remains to be solved by future longitudinal follow-up studies.

P776

The importance of circadian flexibility and shift system characteristics in evaluating the tolerance to shift work

N. MARCOEN, D. PIETERS, M. VANDEKERCKHOVE, O. MAIRESSE, J. WUYTS and E. DE VALCK
Vrije Universiteit Brussel, Brussels, BE

Objectives: Both the inter - individual variability in the human circadian rhythm and the characteristics of the shift system itself are important in evaluating the effects of shift work. The first aim of this

study was to determine the flexibility of the internal circadian system in a group of employees working in 8 h rotating shifts, as well as to relate this level of flexibility to the tolerance to shift work. The second aim was to compare the effects of working in an 8 h versus 12 h shift system.

Methods: Male shift workers (mean age 39 year, SD = 9, $n = 27$) working at a petrochemical plant completed the Dutch version of the Standard Shift Work Index. They also kept a sleep diary and wore a wrist actigraph during three consecutive night shifts. These measurements were completed in an 8 h shift system and were repeated at least 4 months after the implementation of a 12 h system. Circadian flexibility, operationalized as the total shift in internal circadian phase from night 1–3, was determined by 2 h measurements of saliva melatonin level across each night shift. Regarding the outcome measures, we focused on the mean total sleep time (TST) for the three consecutive night shifts and on subjective estimation of sleep disturbance, general wellbeing, social disruption and job satisfaction.

Results: The observed association between circadian flexibility (mean phase shift 110 min, SD = 126) and mean TST was moderate (sleep diary: r = 0.43, $P < 0.05$, $n = 17$) to large (actigraphy: r = 0.52, $P < 0.05$, $n = 14$). More flexible subjects also reported a higher job satisfaction, r = 0.45, $P < 0.05$, $n = 14$. The results regarding the comparison between shift systems indicated that subjects objectively gained more sleep in the 8 h system in comparison with the 12 h system, z = -2.38, $P < 0.05$, $n = 8$. However the change to a 12 h system seemed not to cause any subjective disturbance regarding sleep, social life and job satisfaction and even produced a lower disturbance in general wellbeing of the subjects, z = -2.48, $P < 0.05$, $n = 27$.

Conclusion: The inter- individual flexibility of the circadian rhythm appeared to be a pivotal factor in evaluating the effects of shift work. Regarding shift system characteristics, the change from the 8 h to 12 h system seemed beneficial to the general wellbeing of the employees, despite a somewhat shorter sleep duration in the latter.

P777

Job strain, sleep and napping in shift-working nurses

M. HÄRMÄ, M. SALLINEN, C. HUBLIN, M. KIVIMÄKI, J. VAHTERA and S. PUTTONEN

Finnish Institution of Occupational Health, Helsinki, FI

Objectives: Exposure to high job strain and shift work challenge employees sleep. On-duty napping is an effective countermeasure to fatigue. However, there is little research on spontaneous napping and 24-h sleep amount in shift workers. This study explores the effects of long-term job strain on napping and total sleep length among shift working nurses.

Methods: The subjects were 95 shift-working female health care professionals (average age 47.3 years, range 31–60) from the Finnish Public Sector Study. Based on the 2008 survey results, hospital wards with either high or low average level of job strain were identified. Nurses who had evaluated their own job strain high in high-strain wards (HJS; $n = 42$) or low in low-strain wards (LJS; $n = 53$) were recruited. Main sleep periods and naps were measured across a 3 week period using actigraphy and sleep diary. Naps were recorded with 15 min accuracy.

Results: The mean daily sleep length across measurement period was 6:49 h and did not differ between HJS group (6:46 h) and LJS group (6:51 h). Sleep was shortest after night shifts (4:25 h) and the longest after days off (7:21 h). Taking naps was associated with perceived sleeping difficulties. Only two participants (8%) with sleep disturbances often or frequently took naps ≥2 times a week whereas 19 individuals (28%) among those with sleep disturbances seldom or never took naps ≥2 a week. Nurses in the LJS group took more often naps before a night shift than nurses in the HJS group (79% versus 52%, $P < 0.01$). Ninety-three per cent of subjects had ≥1 nap during the measurement period and 22% napped ≥2 a week in both job strain groups. Approximately two thirds of the participants had a nap/sleep before at least one night shift, after at least one morning shift or during at least one day off during the 3 week period. Even then, over half (54%, $n = 51$) experienced often severe sleepiness during night shift.

Conclusion: Our results suggest that job strain plays only a small role in the amount and rhythm of sleep among shift working nurses. High job strain is associated with lower frequency of napping before night shifts. Shift working nurses nap frequently, but they would need to sleep more to ensure alertness at work and recovery from work.

P778

Changes in positive and negative affect across two weeks of simulated night shift

M. JACKSON[1], D. GRANT[2], G. BELENKY[2] and H.P.A. VAN DONGEN[2]

[1]Victoria University, Melbourne, AU, [2]Washington State University, Spokane, WA

Objectives: Self-reported mood has been shown to fluctuate across the day, exhibiting a circadian rhythm. However, in several laboratory studies with continuous wakefulness, positive affect (PA) and negative affect (NA) appeared to be differentially influenced, where PA showed a circadian rhythm, whereas NA did not. Whether the temporal profiles of PA and NA are also dissociated in a simulated night work schedule with daytime sleep has not been studied. This study examined whether there are differential temporal profiles of PA and NA during simulated night shift work, as compared to simulated day shift work.

Methods: $N = 42$ healthy subjects (ages 27.5 ± 5.6 year; 13f) participated in an in-laboratory experiment under controlled conditions. A total of 29 subjects were assigned to a simulated night shift condition; the remaining 13 were assigned to a simulated day shift condition. Both conditions involved 2 weeks of shift work with a break of up to 58 h halfway through. Time in bed was 10 h per day in both conditions; in the night shift condition (time in bed: 10:00–20:00 h), sleep was placed 12 h out of phase relative to the day shift condition (time in bed: 22:00–08:00 h). On shift work days, the Positive Affect Negative Affect Schedule (PANAS) was administered 4 times per day (22:00, 01:00, 04:00, 07:00 for night shift, 10:00, 13:00, 16:00, 19:00 for day shift). Mixed-effects ANOVAs were performed to examine the effects of condition and time of day on PA and NA.

Results: PA tended to be higher in the day shift condition compared to the night shift condition ($F_{1,1637} = 3.57$, $P = 0.059$), whereas there was no significant difference between conditions for NA ($F_{1,1637} = 0.01$, $P = 0.93$). There was a significant condition by time of day interaction for PA ($F_{3,1631} = 15.71$, $P < 0.001$), with PA decreasing more across the night shifts than the day shifts. There was no significant interaction for NA ($F_{3,1631} = 1.87$, $P = 0.13$).

Conclusion: This study supports and extends previous findings of PA and NA exhibiting different patterns across the day, with PA displaying circadian variation under controlled laboratory circumstances, but not NA. PA was degraded during periods of circadian misalignment. These findings may have implications for understand-

ing the higher prevalence of mood disturbance in shift work populations.

P779

Sleep quality as a mediator in the relationship between doctors' worktime control and patient safety

P. TUCKER, E. BEJEROT and T. ÅKERSTEDT
Stockholm University, Stockholm, SE

Objective: Poorer worktime control is associated with greater sleep disturbances. The fatigue that results from poor quality sleep may pose a threat job performance. Thus the current study seeks to determine whether the relationship between doctors' worktime control and their perceptions of the risk of medical error is mediated by sleep quality.

Method: A representative sample of doctors in Sweden (N = 1534) completed a questionnaire about working conditions, wellbeing and patient safety (response rate 53.1%). Worktime control was measured by two items which asked respondents: (1) whether they could influence their work hours; and (2) whether they had access to flexitime (response options ''yes'', ''yes, to some extent'' and ''no''). Concerns about patient safety were measured by two items which asked respondents: (1) how much they worried about the risk of making mistakes (five response options from ''no, never'' to ''yes, constantly''); and (2) how often they felt that their workload increased the risk of malpractice (four response options from ''daily'' to ''less than once a month''). Sleep quality was measured by the Karolinska Sleep Quality Index (KSQI), calculated as the mean score of responses to four items which asked participants how often they had experienced each of the following sleep symptoms in the last three months: difficulty falling asleep, repeated awakenings with difficulty falling back to sleep, too early (final) awakening and interrupted / restless sleep (range of possible scores: 1 – Never; 5 – Always/5 times or more per week).

Results: There were significant associations between both worktime control measures, both patient safety measures and scores on the KSQI. Mediation analyses (Sobel test for mediation) indicated that the associations between each worktime control measure and each patient safety measure were mediated by sleep quality ($P < 0.0001$ in each case).

Conclusion: Worktime control allows doctors to optimise the fit between the demands of their work schedule, and their own personal needs and circumstances. In doing so, it facilitates sleep and recovery between duty periods, thereby enhancing job performance and promoting patient safety.

P780

The relationship between chronotype and sleep in shift workers with and without shift work sleep disorder

T. SIMON, E. BASTILLE-DENIS and A. VALLIÈRES
Laval University, Québec, CA

Objectives: Research about the influence of chronotype on sleep in shift work populations has shown inconsistent results. Some studies indicate that evening types show better adaptation to shift work and have more efficient diurnal sleep than morning types, while other studies have failed to replicate these findings. Moreover, no study to date has examined the influence of shift work sleep disorder (SWSD) in the relationship between chronotype and sleep. The present study aimed to investigate the association between chronotype and the duration of the diurnal sleep periods in shift workers with or without SWSD.

Methods: The sample included 34 workers (85% women; mean age = 36 years old). Eighty-eight per cent of which worked on night shifts and 12% of which worked on rotating shifts. SWSD was assessed using a semi-structured interview. Participants completed a chronotype questionnaire then wore an actigraph during two weeks. For each work night, total sleep time (TST) was calculated from the actigraph's report for the 24 h period (24 h-P), for the main diurnal sleep period (MDS-P) and for the naps. The score on the chronotype questionnaire was used as a continuous variable (lower scores = greater eveningness, higher scores = greater morningness).

Results: Correlation analyses showed no association between chronotype and TST for the 24 h-P. Results remained the same when taking diagnosis into account. However, there was a significant negative association between TST during the MDS-P and the chronotype ($r = -0.46$, $P < 0.05$). When participants were split according to diagnosis, this association was only found in those with SWSD ($r = -0.68$, $P < 0.01$). There was also a significant positive association between chronotype and TST during naps ($r = 0.42$, $P < 0.01$). Again, this association was only present among those with SWSD ($r = 0.65$, $P < 0.01$).

Conclusion: Sleep during the 24 h period does not vary according to chronotype or diagnosis of SWSD. However, sleep during main diurnal sleep period, which occurs immediately after shift work, is significantly shorter among workers with SWSD who show a greater morningness tendency. These same workers take significantly longer naps than other shift workers. Thus, future studies should consider the SWSD diagnosis when examining the relationship between chronotype and sleep.

Supported by the Canadian Institutes of Health Research (#197171). Scholarship from the Institut de recherche Robert-Sauvé en santé et en sécurité du travail (IRSST)

P781

Shift work and characterisation of sleep quality in Brazilian nurses

M. DE MARTINO for the ''grupo de estudo''

Objective: To characterize the quality of sleep in nurses working in shifts and at night.

Method: For the sleep quality was applied Pittsburgh Sleep Quality Index (PSQI),in a total of 239 nurses, the research was type eexploratory and descriptive. Approved by the Ethics Committee of the University of Taubaté, São Paulo, Brazil, No 441/06.

Results: The females were predominant (90.79%), the average age old was between 20 and 29 (42.68%). With regard to working hour, 67.36% work during the day. As the sleep quality, 83.26% have bad quality. In relation to sleep latency scores were: 28.45% with zero score, 37.66% between 1 and 2, 24.27% between 3:04 and, between 9.62% 5 and 6. The duration of sleep 60.70% sleep 7 h or more, 26.36% sleep between 6 and 7 h, 7.11% sleep between 5 and 6 h, and 5.86% sleep <5 h. As regards the sleep efficiency, 9.62% efficiency have 85% or greater; 4.60%, between 75% and 84%, 4.60%, between 65% and 74%, and 81.17% ≤ 60%. Sleep disorders are presented in 92.47% of nurses. Regarding the use of sleep medication, 89.54% reported no use. Dysfunction present during the day, 80.75%. The subjective sleep quality was: 16.32%, very good, 59.41% good, 21.34%; bad, and 2.93.

Conclusion: We evaluated the conditions of work and identified the problems in the hospital and shifts in sleep quality. It is suggested to invest in health promotion programs to improve the quality of work life.

P782

Work-related sleep problems vary according to work schedule

E. FLO[1], S. PALLESEN[2], N. MAGERØY[3], B. MOEN[2] and B. BJORVATN[1]

[1]Norwegian Competence Center for Sleep Disorders, Bergen, NO, [2]University of Bergen, Bergen, NO, [3]Haukeland University Hospital, Bergen, NO

Objectives: Shift work related sleep/sleepiness problems may be due to both aspects of the shifts (i.e. morning, evening and night shifts) and the work schedules (i.e., permanent versus rotational schedules). We used the Bergen Shift Work Sleep Questionnaire (BSWSQ) to evaluate shift work related insomnia (i.e., pervasive sleep and sleepiness problems for each day shifts, evening shifts and night shifts) in different schedules. We investigated morning shift insomnia (i.e., differences between workers on permanent morning, two-shift rotations of morning/evening, and three-shift rotations of morning/evening/nights workers), evening shift insomnia (i.e., differences between workers on two- and three-shift rotations workers), night shift insomnia (i.e., differences between permanent night and three shift rotation workers) and rest-day insomnia (i.e., differences between all mentioned schedules).

Methods: One thousand and five hundred eighty-six nurses (response rate 80.9%, 91.2% females) completed the BSWSQ, measuring insomnia symptoms the last 3 months, separately for each shift, and rest-days. We report the prevalence of participants who ''often'' or ''always'' experience both a sleep problem (problems with sleep onset or sleep maintenance) and a sleepiness/tiredness problem in relation to a shift, defined as shift related insomnia (separate scores for morning-, evening- and night shifts and rest-days). Chi- square analyses were conducted for each morning-, evening- night- and rest-day insomnia and workers on the permanent and rotational schedules.

Results: Differences between work schedules regarding shift related insomnia were found. Morning shift insomnia showed no difference between the permanent morning schedules, two- and three-shift rotation schedules. The two-shift rotation schedule showed higher evening shift insomnia frequencies than three-shift rotation schedule (29.8% and 19.8% respectively). Night shift insomnia was more frequent among three-shift rotation workers compared to the permanent night schedule (67.7% and 41.7% respectively). The rest-day insomnia was more prevalent among permanent night workers compared to two- and three-shift rotations (11.4% compared to 4.2% and 3.6%, respectively).

Conclusion: The Insomnia prevalence differed between the work schedules and shifts; with generally higher frequencies for three-shift rotations and night shifts. However, insomnia was present in all shifts and schedules, highlighting the need for a multifaceted outlook on sleep and shift work.

P783

Atherosclerotic risk factors and social jetlag in rotating shift-workers

T. KANTERMANN[1], F. DUBOUTAY[2], D. HAUBRUGE[3], D. FOY[4], S. HAMPTON[4], M. KERKHOFS[5], A. SCHMIDT-TRUCKSÄSS[6] and D.J. SKENE[4]

[1]Charité University Hospitals, Berlin, DE, [2]CBMT, Charleroi, BE, [3]ArcelorMittal Industeel Belgium, Charleroi, BE, [4]University of Surrey, Guildford, UK, [5]Free University of Brussels, Charleroi, BE, [6]University of Basel, Basel, CH

Objective: Pulse wave velocity (PWV; a marker for atherosclerotic risk), glucose, insulin and social jetlag (difference between mid-sleep time on workdays and days off used as a marker of circadian disruption) were measured in rotating shift-workers (fast clockwise (CW), slow counterclockwise (CC)), and day workers (DW), to test for differential effects in different shift rotations.

Methods: Seventy-seven male steel workers (42 ± 7.6 years, mean ± SD) completed questionnaires on demographics, health, stimulants, sleep, social and work life, social jetlag and chronotype (mid-sleep time on free days corrected for sleep deficit on workdays). We measured PWV, blood pressure (BP) and heart rate (HR) between 08:00 and 12:30 h in controlled posture conditions (no caffeine/smoking/exercise) in 63 workers, of which 37 provided fasting blood samples (06:00–08:00 h) for assessment of plasma glucose and insulin.

Results: Age, body mass index (BMI), waist-hip-ratio (WHR), BP, HR, smoking, coffee consumption and chronotype did not differ between shift-workers and day workers. Shift-workers (CW, CC) reported significantly more stomach upsets (+44.8%, $P = 0.021$), digestion problems (+42.3%, $P = 0.017$), weight fluctuations (+38%, $P = 0.008$) and social jetlag ($P = 0.001$). The CW and CC workers did not differ in ratings of how shift-work affected sleep, social and work life. There was no significant difference in PWV (covariates: age, BP) between the three groups. In all workers combined, HR and social jetlag were significantly positively correlated ($r = 0.309$, $P = 0.021$, adjusted for age). Glucose was significantly higher in DW (6.1 ± 0.4 mM, mean ± SEM) compared to CW (4.7 ± 0.3 mM) ($P = 0.022$, covariates: age, BMI, WHR). There was no difference in insulin levels between the three groups.

Conclusions: Although PWV was not different between the two shift-rotations this pilot study shows first evidence of HR being associated with social jetlag. The observed differences between different shift rotations and day workers warrant further studies of this type.

Supported by the DFG (German Research Foundation) and the 6th Framework Project EUCLOCK (018471).

Poster Session - Quality of sleep

P784

Quality of sleep, sleepiness and family functioning in adolescents

S. H. PUCCI and M. G. PEREIRA
University of Minho, Braga, PT

Objectives: (1) To analyze the relationship among sleepiness, family functioning, quality of sleep and sleep habits; (2) To find the best predictors of quality of sleep; (3) To find best predictors of family functioning.

Methods: A sample of 202 adolescents from both genders, ages between 15 and 18 participated in the study. The instruments used were: Epworth-Billings Sleepiness Scale modified (EBSS), Howard Family Sleep Questionnaire (HFSQ), Pittsburgh Sleep Quality Index (PSQI) and a Socio-Demographic Questionnaire that addressed alcohol, tobacco and caffeine consumption and parent's knowledge about drugs.

Results: Results showed a positive relationship between family functioning and quality of sleep, sleepiness and family functioning and between quality of sleep and sleepiness. The predictors of family functioning were: lower level of parents' knowledge of drugs, mother's smoking, number of soda drinks with caffeine drank by the adolescent per day, sleepiness and quality of sleep. The model explained 28% of variance. The predictors of quality of sleep were: having a person in the family with sleep problems, number of energy drinks consumed per week, more sleepiness and worse family functioning and the model explained 26% of variance.

Conclusion: Results showed a need for intervention regarding health promotion in adolescents, concerning a healthy diet and prevention of substance use. These interventions should include parents since there seems to be a relationship between adolescents' life style and family functioning including parent's life style.

P785

Sleep quality – objective and subjective data analysis

M. ZAKEVICIUS[1], V. LIESIENE[2], R. GRIKSIENE[1], R. MASAITIENE[3] and O. RUKSENAS[1]
[1]Vilnius University, Vilnius, LT, [2]Institute of Neuromedicine, Kaunas, LT, [3]Vilnius Sapiegos Hospital, Vilnius, LT

Objectives: Researchers are still debating on what determines rest sense after the sleep. A lot of attention today is paid for sleep fragmentation and its impact on sleep's restorative functions. The purpose of our study was to analyse a sleep fragmentation by scoring various arousals (microarousals (MA), vegetative (VA) and behavioural (BA) arousals) and to evaluate their relation with subjective sense of rest after the sleep without paying attention to the type of insomnia.

Methods: The whole night polysomnograms of 60 subjects (30 men, 30 women), who were patients of sleep disorders laboratory, were analyzed according to their stage composition and arousals. Arousal indices (AI) were calculated for all three types of arousals. The sleep quality was evaluated using the Pittsburgh sleep quality index (PSQI).

Results: MAI value in total sleep time (TST) – 5.8 ± SD 4.1 – was highest among all three arousal types. BAI in TST was 4.8 ± SD 2.7 and VAI in TST was 3.0 ± SD 2.4 Average PSQI value in subjects was 13.0 ± SD 4.4. The strongest and significant correlation was between PSQI and MAI ($r = 0.42$; $P < 0.001$). There was no significant correlation between PSQI and other two types of AI. The only significant correlation from all sleep stages was between the duration of NREM stage 4 and PSQI ($r = -0.3$; $P < 0.05$).

Conclusion: Microarousal density is important for the subjective sense of rest after the sleep. Correlations between PSQI and AI show that for subjective rest sense MA are more important than other arousal types. That could suggest that cortical arousals are more important – make more damage to the sleep's restorative functions – than the ones that involve other systems (vegetative or behavioural).

P786

Effect of pulsed GSM 900 MHz exposure on polysomnography-based sleep quality: an intra- and inter-individual perspective

H. DANKER-HOPFE[1], P. ANDERER[2], H. DORN[1], T. BOLZ[3] and C. SAUTER[1]
[1]Charité University Hospitals, Berlin, DE, [2]Medical University of Vienna, Vienna, AT, [3]IMST GmbH, Kamp-Lintfort, DE

Objective: To look at possible RF-EMF effects on physiological parameters like sleep quality at an individual level, data collected in a study supported by the Federal Agency for Radiation Protection, Germany (Danker-Hopfe et al. 2010) were reanalysed.

Methods: In a double-blind, randomized, sham-controlled cross-over study possible effects of a pulsed GSM 900 MHz electromagnetic field on sleep was analysed in 30 healthy young men (mean age ± SD: 25.3 ± 2.6 years). An adaptation night was followed by nine study nights in the laboratory, in which subjects were exposed to three exposure conditions (Sham, GSM 900 and WCDMA/UMTS) in an individually randomized order. All nights were scored according to the AASM standard and all three nights/condition and subject were used individually in the analysis increasing the sample size from 30 to 270, or nine individual GSM/Sham comparisons per subject, respectively. The number of sleep parameters analysed in the present paper was restricted to those 13 variables which are recommended by the AASM standard (Iber et al. 2007) for clinical reports.

Results: Overall nine out of the 13 sleep variables did not show an overall statistical significant difference between SHAM and GSM exposure. Time (min and% of TST) spent in stage N1 was significantly shorter (3.8 min, 4.2% of TST) under GSM exposure as compared to Sham. Furthermore time spent in rapid eye movement sleep was significantly higher (5.6 min, 4.5% of TST) under GSM exposure as compared to Sham. Overall none of the sleep variables which are in a first line indicative of a disturbed sleep, like sleep onset latency, wake after sleep onset and/or the sleep efficiency index, was affected by GSM exposure. At the individual level, significant effects were seen for all variables ranging from five subjects (stage N3) to 13 subjects (stage N1). However, except for the REM sleep parameters, significant differences in both directions (higher and lower values under GSM exposure) are observed at the individual level. In all individuals who showed significant differences in stage R sleep the amount of REM sleep (min and% TST) was higher in the GSM exposure condition.

Discussion: The data underline that at the individual level there are differences in sleep parameters, however these differences are not consistent and at the group level are not apparent. For stage N1 the observed differences are indicative of a better sleep under exposure.

P787

Research of new food materials for improvement of sleep quality

I. KAMADA[1], K. SUZUKI[1], H. KAMBAYASHI[1], T. GOKITA[1], H. IWASAKI[1], M. KOIDE[1], M. MURAKOSHI[2], K. SUGIYAMA[3], H. NISHINO[4], M. YOSHIDA[5] and Y. URADE[6]

[1]Lion Corporation, Odawara, Kanagawa, JP, [2]Lion Corporation and Kyoto Pref. University Med., Odawara, Kanagawa, JP, [3]Lion Corporation and Ritumeikan University, Odawara, Kanagawa, JP, [4]Kyoto Pref. University Med. and Ritumeikan University, Kyoto, JP, [5]SleepWell Corporation, Osaka, JP, [6]Osaka Bioscience Institute, Osaka, JP

Objectives: In recent years, the average amount of sleep-time in Japan has been decreasing. However we can't spend enough time sleeping because of busy schedules. Under this circumstance, we tried to search for new food materials for improving the quality of sleep. In this study, we examined the sleep-promoting activity of selected materials by recording and analyzing electroencephalogram (EEG) after administration of each material to mice, and then we evaluated the effects of the sleeping condition of humans using a portable EEG during sleep.

Methods: Animal study; We implanted EEG-EMG electrodes to C57BL/6N mice and tested the sleep-promotion effects of the materials. Test samples including a vehicle control were administrated by p.o. 10 min before the dark period, and then the data was recorded for 24 h, from the onset of the dark period to the end of the light period.

Clinical study: The participants were selected by the Pittsburgh Sleep Quality Index score, which is equal to or higher than 5.5 points. They took a material about an hour before sleep and an EEG during sleep were both recorded. Furthermore, a subjective evaluation using the MA version of the OSA sleep questionnaire was surveyed, and a growth hormone was also measured by using a morning urine sample.

Results: Animal study; In 50 candidates, we found that seven materials, such as a kind of sake yeast and European ash tree extract, have the possibility for increasing the number of stage transitions from wakefulness to non-REM sleep. There was no significant difference between each material and the vehicle control, indicating that the seven materials do not affect EEG power density of non-REM sleep. It was suggested that the seven materials have the possibility to induce natural sleep.

Clinical study: The results of the EEG analysis showed that the initial stage of sleep deepened. In addition, subjective evaluation showed remarkable results of sleepiness regarding awakening, sleep maintenance, dreaming and the fatigue of awakening. Furthermore, it was observed that the quantity of the growth hormone in morning urine tends to increase by the intake of each material.

Conclusion: In human studies, we confirmed that seven food materials deepened the initial stage of sleep. The OSA sleep questionnaire survey also showed that seven materials have improved subjective sleep. In conclusion, it was indicated that seven materials have the possibility to improve both subjective and objective sleep quality.

P788

Effects of a new bed on sleep structure in healthy subjects

A. DUBOIS[1], F. DUFOREZ[1], M. ELBAZ[2], G. DELAUTRE[3] and D. LÉGER[2]

[1]European Sleep Center, Paris, FR, [2]Hôtel-Dieu, Paris, FR, [3]APL, Paris, FR

Objectives: This research aimed to demonstrate the effect of a new bed on sleep, based on the hypothesis that new beds can improve sleep quality in subjects having difficulty sleeping.

Method: In order to demonstrate the effect of a new bed on the sleep of healthy subjects, we studied polysomnographic sleep recordings of 14 volunteers (seven young adults and seven older adults). All participants were recorded twice at the Centre du Sommeil et de la Vigilance at the Hôtel-Dieu hospital in Paris, once sleeping on a bed at least ten years old, and once on a new bed, in random order. Both beds were of the same size and type. In addition to the objective data analysed, subjective data were collected via Vis Morgen and Spiegel questionnaires.

Results: On a subjective level, the results did not reveal any significant difference between nights spent on an old bed and nights spent on a new bed, for either age group. On an objective level, in terms of the sleep macrostructure, there was no significant difference between subjects sleeping on an old bed and subjects sleeping on a new bed. Total sleep time and the proportions of SWS and REM remained constant in both situations, for both young and old subjects. The microstructure of the subjects' sleep, however, did reveal significant differences. The Periodic Limb Movement (PLM) index was significantly higher on old beds than on new beds ($P < 0.04$). Subjects, mostly in the older group, moved more on old beds, without this affecting the macrostructure of their sleep. Similarly, the number of micro-awakenings per hour is higher among subjects sleeping on old beds than for the same subjects sleeping on new beds ($P < 0.05$).

Conclusion: A new bed can offer an objective improvement in the quality of sleep microstructure, especially among older people.

Poster Session - Cardiovascular and metabolic consequences of SDB

P789

Incidence of sleep apnoea in ischaemic heart disease

A. MOZAFARI and S. FARZAM
Islamic Azad University, Tehran, IR

Background: Obstructive sleep apnea (OSA), a common form of SDB, is highly prevalent in adults with approximately 20% adults having at least mild OSA. One of the most associated consequences is cardiovascular sequel. Incidence of sleep apnea in IHD is about 50%, but mostly remains undiagnosed. This study aimed to assess the incidence of sleep apnea in IHD patients whether pulse oximetry can predict apnea in this group of patients.

Materials and methods: A randomized sample of 60 adult patients referred to Post CCU was selected. Patients with respiratory and CNS problem and using of sedative drugs were excluded. All participants including post AMI, CHF and acute coronary syndrome underwent the portable device and pulse oximetry. The portable monitoring device included a small recording unit to monitor the change in nasal pressure with respiration using a nasal cannula. Apneas, Hypopneas, Desaturation, Epworth Sleepiness Score were and Anthropometric parameters evaluated and recorded for participants. Data were analyzed and compared using SPSS version 15 software.

Results: From April through September 2011, we randomly performed 60 tests with nasal cannula and pulse oximetry. Of these, mean age was 61 ± 11, 61.7% were female, neck circumference 39.3 ± 3.3 and BMI 28.9 ± 6.4 kg/m^2. Patients with Epworth Sleepiness Scale > 10 were in 45%, snoring in 73% and finally mean Apean-Hypopnea Index (AHI) was 21.9 ± 17, AHI over than 15 in 61.7% and AHI > 30 in 18.3%.

There were no relationship between AHI > 15 and ESS > 10 (*P* value 0.471), AHI > 15 and ESS > 16 (*P* value 0.106), AHI > 15 and BMI (*P* value 0.602) and AHI and sex (*P* value o.725). There were significant correlation between AHI more than 15 and (ODI) > 10(*P* value 0.0001, OR: 9.180, CI 2.67–31.50) and AHI > 30 and ODI>10 (*P* value 0.042, OR: 4.89 CI 0.95–25).

Conclusion: In according to this data, incidence of AHI > 15 were 61.7% in IHD patients. There were no significant correlations among AHI > 15 and sex, BMI and ESS in IHD patients, but significant relationship between AHI > 15 and ODI > 10. Sensitivity and Specificity of ODI>10 for detection of AHI > 15 were respectively.

P790

Sleep-disordered breathing and its association with metabolic syndrome

J. CARRILLO[1], C. VARGAS[2], M. ARGANDOÑA[3], I. BASTIAS[1] and C. BETANCUR[4]
[1]Felix Bulnes Clinical Hospital, Santiago, CL, [2]University of Santiago, Santiago, CL, [3]Public Assistance Emergency Hospital, Santiago, CL, [4]San Sebastian University, Concepción, CL

Introduction: The metabolic syndrome (MetS) is a clinically effective way of detecting individuals with a higher risk of cardiovascular diseases and/or type 2 diabetes, and it has a strong association with the obstructive sleep apnea syndrome (OSAS). On the other hand, it has found an association between habitual snoring (S) with blood hypertension and obesity, but not with MetS as such. The aim of this work is to study the association between sleep disordered breathing with MetS, through S, as a symptom marker, and suspicion of OSAS, as more severe clinical form.

Methodology: We conducted a cross-sectional study with data from the National Health Survey 2009–2010, implemented by the Epidemiology Department of Ministry of Health in Chile. The study subjects were administered a sleep questionnaire, underwent anthropometric measurements, blood pressure measurements and biological samples for the detection of MetS, according to consensus criteria of the IDF-ATP. We compared the prevalence of MetS between the S (snore all or most days) and non-snorers (nS), and between the group with suspected obstructive sleep apnea syndrome (S-OSAS+) (habitual snoring, nocturnal breathing pauses and excessive daytime sleepiness) and those who did not meet the criteria of suspicion (S-OSAS-). Using a logistic regression model adjusted for age, sex, BMI, socioeconomic status and smoking, we examined the association of S and S-OSAS+ with MetS.

Results: The population sample was of 5412 subjects with a mean age of 46.6 ± 18.8 years (IQ = 32–61), of which 2198 (40.6%) were men. Of the total sample, 2963 (54.7%) subjects were S, and 2141 (39.6%) were nS. On the other hand, 213 (3.9%) subjects had S-OSAS+, and 4686 (86.6%) were S-OSA-. Of the total, 3348 (61.9%) completed all the necessary parameters, and of these, 1129 (33.7%) subjects met the diagnostic criteria for MetS. The S group had significantly more MetS than nS group (42.6% versus 22%, $P < 0.001$), with an OR = 1.24 (95% CI, 1.01–1.52). The S-OSAS+ group also had significantly more MetS than the S-OSAS- group (60% versus 32%, $P < 0.001$), with an OR = 1.89 (95% CI, 1.16–3.07).

Conclusions: In the population sample studied, the S group has greater risk of MetS than nS group. This risk is even greater in those with S-OSAS+. These results suggest that sleep disordered breathing are an independent risk factor for metabolic syndrome in the adult population in Chile.

P791

Sleep apnoea in patients after acute myocardial infarction

O. LUDKA[1], L. GALKOVA[1], M. MIKOLASKOVA[1], Z. MIHALOVA[1], J. HLASENSKY[1], A. DROZDOVA[1], L. GACIK[1], T. KARA[2] and J. SPINAR[1]
[1]University Hospital Brno, Brno, CZ, [2]ICRC Brno, Brno, CZ

Introduction: Sleep represents a state of physiological rest for the cardiovascular system which can be in a great deal disrupted by sleep-disordered breathing (SDB). The most common type of SDB is the obstructive sleep apnea occurring in 9% of middle-aged females and 24% of middle-aged males. The pilot project data indicate a possible close pathophysiological correlation between myocardial infarction and sleep apnea (SA). SA has also been connected by some small studies to a higher morbidity and mortality rate in subjects with a cardiovascluar disease. Early diagnosis and treatment disposes therefore of an ability to greatly improve the life quality and furthermore to decrease morbidity and mortality rate of the latter patients.

Aim: To determine the prevalence of SA in patients who have suffered an acute myocardial infarction (AMI).

Methods: Consecutive patients admitted to our department in 2010 with the diagnosis of AMI were enrolled. All of them underwent complete clinical, biochemical examination and ECG examination at the time of admission. Minimally after 48 h after the admission and condition stabilisation every patient was examined with the mobile device ApneaLink - a non-invasive examination analyzing air flow in the airways and monitoring the oxygen blood saturation during the night. Sleep apnea or hypopnea occurrence were classified according to standard criteria of the American Academy of Sleep Medicíne (AASM).
Results: Two hundred five patients (74% men), age 65 years, BMI 29 kg/m^2, ST elevation AMI 63%, localization of AMI - anterior wall 37%, inferior wall 37%, lateral wall 7%, other 19%, left ventricle ejection fraction 49%. Apnea-hypopnea index (AHI) <5 23%, AHI ≥5 and <15 35%, AHI ≥15 and <30 22%, AHI ≥30 20%.
Conclusion: According to the AASM criteria 77% of post AMI patients had SA. It is much more than in common population.
Discussion: The presented project showed high prevalence of SA in patients who have suffered an AMI. If the worse prognosis hypothesis in SA patients are to be confirmed, there is a high benefit in examining all the patiens post AMI, on the potential simultaneous SA occurrence. This way can evaluate a rising opportunity to identify a new risk factor and to eliminate it via a corresponding therapy.

P792

Instantaneous increase in arterial blood pressure related to sleep-disordered breathing

H. HEIN, M. BOSSE and H. NÄGELE
St. Adolf-Stift, Reinbek, DE

Purpose: Sleep disordered breathing is known to increase arterial blood pressure and sympathetic activity. It is an accepted cause of arterial hypertension. We examined instantaneous changes in blood pressure related to single events of sleep disordered breathing like obstructive, mixed and central apneas and hypopnoeas, dependent of sleep stage, desaturations and arousals.
Setting: Sleep laboratory in a teaching hospital
Methods: We analyzed polysomnographic records of 41 patients, 15 women/26 men, age 57 ± 10 years, body-mass-index 30.6 ± 4.8 kg/m^2, apnea-hypopnea-index 32.6 ± 19.2/h. Data were manually scored according to AASM-criteria. Only parts of the records without any artifacts over 3 min were used for the further evaluation. Arterial blood pressure was calculated beat to beat via a validated pulse transit time method. We obtained data of 6946 respiratoy events: 1195 obstructive/293 mixed/233 central apneas and 5225 hypopneas.
Results: Following a respiratory event systolic blood pressure increased by 17 ± 9.4 mmHg, diastolic blood pressure ascended by 6.8 ± 3.3 mmHg, with little difference for the type of the event and little difference for the sleep stages, except a lower increase in stage N3. The amplitude of the desaturation exhibited a low correlation with arterial pressure changes: 0.23 for the systolic and 0.08 for the diastolic pressure. Arterial blood pressure increased significantly more after respiratory events followed by an EEG-arousal (systolic/diastolic 17.8 ± 9.3/7 ± 4 mmHg) than after events without an EEG-arousal (systolic/diastolic 16.6 ± 9/6.7 ± 3.8 mmHg).
Conclusions: Arterial blood pressure changes induced by sleep disordered breathing are more pronounced if the events were followed by an arousal. The extent of desaturations has little influence. Blood pressure increase was lower in stage N3 compared to REM, N1 and N2. Financial disclosure: no sponsoring

P793

Sleep apnoea syndrome is associated with prolongation of QRS duration only in women

F. ROCHE, V. PICHOT, S. CELLE, A. DACOSTA, C. ROMEYER BOUCHARD, E. ACHOUR, E. SFORZA and J.-C. BARTHÉLÉMY
University Hospital, Saint-Etienne, FR

Increased QRS duration is associated epidemiologically with enhanced risk of serious cardiac ventricular arrhythmias even in the absence of authentic bundle branch block. Many cardiovascular diseases including hypertension, left ventricular hypertrophy, heart failure can cause such an intraventricular conduction disorder. Sleep apnea syndrome (SAS) may also directly or indirectly represent another risk factor of increased QRS duration. However, only a cohort study of unselected subjects regarding sleep disorders symptoms evaluating all traditional risk factors could provide an answer to this medical question.
Methods: Four hundred eighty women and 323 men, all volunteers aged 68 years at inclusion in the study (PROOF SYNAPSE cohort) were able to benefit from a computerized ECG analysis (GE Marquette Software) to calculate HR, PR interval, mean 12-leads QRS complexes duration, QT and corrected QT duration. All subjects included had never presented any cardiovascular or heart rhythm also received an ambulatory polygraphic recording. We looked for statistical relationships involving the existence of an incidental sleep disorder (apnea plus hypopnea index "AHI" >15 /h) and ECG abnormalities by stratifying the analysis by gender. All subjects with right or bundle branch block were excluded from the analysis.
Results: In the subgroup of women only, the average duration of QRS was found longer (83 ± 9 ms versus 80 ± 9 ms, $P < 0.03$) in volunteers who had an AHI > 15 (176 of the 480 women). No other ECG parameter is found altered in the group of women suffering from sleep apnea. We find a significant linear correlation in women between QRS duration and expressed as logAHI ($R = 0.15$, $P < 0.002$). In multiple regression, the QRS duration is correlated independently with the same variable (logAHI) after adjustment for systolic and diastolic blood pressure (clinical and ambulatory), taking antihypertensive medication, for the presence of type 2 diabetes and for BMI. No significant relationship was not found in men between QRS duration and other parameters of the resting ECG and the presence or severity of SAS.
Conclusion: Presence of undiagnosed sleep apnea is associated with a modest but significant prolongation of QRS duration in women only. However, the lengthening of the QRS complexes is very modest and the overall male and female SAS subjects remains in the values used as normal. The consequences of such minor myocardial conduction defect remains to be defined.

P794

The role of sleep-related breathing disorders in systemic inflammation

N. TROESTER[1], M. PALFNER[1], A. AVIAN[2], M. DOMINCO[1], G. KOVACS[1] and H. OLSCHEWSKI[1]
[1]Division of Pulmonology, Graz, AT, [2]Department for Informatics and Statistics, Graz, AT

Objective: Sleep related breathing disorders (SRBD) are associated with both obesity and inflammation. While the causal relation between obesity and SRBD is established, the causality between inflammation and SRBD remains unclear. This study aimed to investigate these relationships using SRBD treatment as intervention.

Methods: Retrospective study of 783 patients referred to a pulmonary sleep laboratory for polysomnography. In 383 patients diagnosed with SRBD a second polysomnography was performed after final titration with positive airway pressure therapy. Apart from polysomnographic data like apnoea-hypopnoea-index (AHI), longest duration of respiratory event and minimal O2 saturation during sleep, at both time points weight, height, body mass index (BMI), HDL cholesterol, LDL cholesterol, total cholesterol, C-reactive protein (CRP), triglyceride, fasting glucose, and HbA1c were measured. SRBD therapy was regarded as successful if AHI dropped below 15/h and as therapy failure at AHI > 15 /h.

Results: SRBD therapy results were good (AHI < 5/h) in 72.6%, acceptable (AHI 5–15 /h) in 21.4% and regarded as failure (AHI >15 / h) in 6%. In the groups with successful therapy, CRP levels decreased significantly (-25% and -1.4%; $P < 0.001$, respectively) while body weight and BMI increased significantly (+0.74% and +1.5%, $P < 0.001$) as well as triglycerides (+7.7%, $P < 0.001$).

In the group with initially pathological CRP (>5 mg/l), changes in CRP were even more pronounced: CRP decreased significantly in the success as well as the acceptable treatment group ($P < 0.0001$; $P = 0.007$, respectively) and decreased also in the failure group, but not significantly ($P = 0.573$).

Conclusion: SRBD but not obesity causes an inflammatory response that is responsive to SRBD therapy.

P795

Localized microstructural cerebral lesions in central sleep apnea could be modified by therapeutic intervention

T. DUNING, A. HEIDBREDER, M. DEPPE and P. YOUNG
University Hospital of Muenster, Muenster, DE

Objectives: The exact underlying pathomechanism of central sleep apnea (CSR) is still unclear. A dysfunction of respiratory control centers in the brainstem was suggested by some authors. However, conventional MRI fails to identify primary or secondary structural changes of the brainstem in most cases.

Innovative and improved MRI techniques, such as Diffusion Tensor Imaging (DTI), now allow far more subtle assessment of microstructural degenerative cerebral changes. The aim of this study was to investigate, (1) if patients with CSR show a specific pattern of degenerative cerebral changes, and (2) whether these microstructural changes could be modified by therapeutic intervention.

Methods: Eleven patients from our sleep laboratory underwent a cardiorespiratory polysomnography and a detailed clinical examination. After diagnosed with CSR, CPAP therapy was initiated in all patients. Cerebral MRI scans were obtained before introducing CPAP therapy and after 3 month of using CPAP. We applied different MR-imaging techniques, ranging from semiquantitative measurement of white matter hyperintensities (WMH) and automated calculation of brain parenchyma volumes up to DTI to detect even subtle neural changes.

Voxel-wise differences in white and gray matter values between CSR patients and 44 healthy controls were statistically evaluated by analysis of covariance. Furthermore, a longitudinal analysis was used to detect microstructural changes in white or gray matter after 3 month of CPAP therapy.

Results: Only DTI analysis showed differences between patients and healthy controls. Voxel-based DTI-analysis revealed a widespread decline in CSR patients when compared to the healthy controls, significantly exceeding the WMH on conventional MRI. The microstructural damage was mainly focussed on the brainstem and frontal cerebral regions. The longitudinal analysis of DTI data revealed voxel clusters of decreased as well as increased fiber integrity, indicating neuronal plasticity. Interestingly, the microstructural changes were also restricted to the brainstem and frontal cerebral regions.

Conclusion: Microstructural damage in the brainstem and in connecting frontal white matter tracts might trigger sleep-disordered breathing with CSR. These localized structural changes could be modified by therapeutic intervention (CPAP). DTI seemed to be more sensitive and specific than conventional structural MRI and also other advanced MR analyses tools in detecting these subtle structural changes.

P796

Comorbidities and intake of cardiovascular medications are the best predictors of mortality in patients with obesity-associated hypoventilation treated with long-term noninvasive ventilation

J. C. BOREL[1], B. BUREL[2], R. TAMISIER[2], S. DIAS-DOMINGOS[2], P. LEVY[2] and J.-L. PÉPIN[2]
[1]AGIR à dom, Meylan, FR, [2]Hospital A. Michallon, Grenoble, FR

Background: The higher mortality rate in patients with obesity-associated hypoventilation is a strong rationale for long term noninvasive ventilation (NIV). The impacts of comorbidities, medication and NIV compliance on survival of these patients remain largely unexplored.

Methods: Observational cohort of hypercapnic obese patients initiated on NIV between March 2003 and July 2008. Anthropometric measurements, pulmonary function, blood gases, nocturnal SpO2 indices, comorbidities, medication, conditions of NIV initiation and NIV compliance were used as covariates. Survival curves were estimated by the Kaplan–Meier method. Univariate and multivariate Cox models were used to assess predictive factors of mortality.

Results: One hundred and seven patients (56% women), in whom NIV was initiated in acute conditions (36%), were followed during 43 ± 14 months. The 1, 2, 3 years survival rates were 99%, 94%, and 89%, respectively. In univariate analysis, death was associated with older age (>61 years), low FEV1 (<66% predicted value), male gender, BMI×Time, concomitant COPD, initiation of NIV in acute condition, use of inhaled corticosteroids, ß-blockers, nonthiazide diuretics, angiotensin-converting enzyme inhibitors and combination of cardiovascular drugs (one diuretic and at least one other cardiovascular agent). In multivariate analysis, combination of cardiovascular agents was the only factor independently associated with higher risk of death (HR = 5.3; 95% CI: 1.18; 23.9). Female gender was associated with lower risk of death.

Conclusion: Cardiovascular comorbidities represent the main factor predicting mortality in patient with obesity-associated hypoventilation treated by NIV. In this population, NIV should be associated with a combination of treatment modalities to reduce cardiovascular risk

P797

Correlation between obesity and sleep apnoea syndrome

C. L. ARDELEAN, D. R. DIMITRIU, S. M. FRENT, V. TUDORACHE, D. F. LIGHEZAN and S. MIHAICUTA
Victor Babes Hospital, Timisoara, RO

Body: Introduction Obesity is a common comorbidity in patients with sleep apnea syndrome (SAS)

Aims and objectives: Analysis of obesity in patients with sleep apnea syndrome

Methods: Between June 2005 and June 2009 we evaluated 968 consecutive patients with suspected OSAS, using the Epworth sleepiness questionnaire, anthropometric data for body mass index and AC, somnography or polysomnography (AHI assessment). We use univariate statistical analysis of data related to BMI in four layers to assess the relative risk (RR) of developing SAS

Results: Seven hundred twenty-seven male (75.1%), 241 female (24%), age 52 ± 11.89 years (6–84), AHI 34.10 /h ± 27.41, AC 120.06 cm ±15.10 (88–157), mean BMI 33.06 ± 6.32 kg/m^2 (17–56). BMI > 25 kg/m^2 (84%). Obesity grade1 (35%), grade2 (22%), grade3 (14%).

In univariate statistical analysis, obesity RR = 2.57, $P = 0.004$ (moderate predictor); Overweight RR = 2.33, $P = 0.095$(moderate predictor). Obesity grade 1 RR = 2.67, $P = 0.043$(moderate predictor), obesity grade 2 RR = 3.97, $P = 0.012$(strong predictor), obesity grade 3 RR = 3.78, $P = 0.027$(strong predictor).

Mean BMI, RR = 2.37, $P = 0.040$.

Conclusions: Correlation between obesity and sleep apnea syndrome is strong.Mean BMI is a moderate predictor for SAS ($P = 0.040$). Obesity grade 2 and 3 are strong predictors for SAS ($P = 0.012$ and $P = 0.027$).

P798

Obesity at patient with sleep apnoea syndrome and comorbidities

C. L. ARDELEAN[1], D. R. DIMITRIU[1], S. M. FRENT[2], V. TUDORACHE[2], D. F. LIGHEZAN[2] and S. MIHAICUTA[2]

[1]Victor Babes Hospital, Timisoara, RO, [2]Victor Babes University of Medicine and Pharmacy, Timisoara, RO

Body:

Introduction: Patients with sleep apnea syndrome and comorbidities have a high degree of obesity.

Aims and objectives: Analysis of body mass index (BMI) in patients with sleep apnea syndrome (SAS)and comorbidities.

Methods: Between June 2005 and June 2009 we evaluated 968 consecutive patients with suspected OSAS, using the Epworth sleepiness questionnaire, anthropometric data for body mass index and AC, somnography or polysomnography (AHI assessment). We evaluate the correlation between IAH and BMI in multiple linear regression and mean values were compared at patients with SAS and comorbidity by Student's t test in patients with equal variances and Welch correction in patients with unequal variances.

Results: Seven hundred twenty-sevne male (75.1%), 241 female (24%), age 52 ± 11.89 years (6–84), AHI 34.10 /h ± 27.41, AC 120.06 cm ±15.10 (88–157), mean BMI 33.06 ± 6.32 kg/m^2 (17–56). BMI>25 kg/m^2 (84%). Obesity grade 1 (35%), grade 2 (22%), grade3 (14%).

BMI in patients with hypertension (31.43 versus 34.21 kg/m^2 kg/m^2, $P < 0.001$) and COPD (32.56 versus 34.42 kg/m^2, $P < 0.001$. Multiple linear regression, correlation AHI and BMI is directly proportional, r = 0.2839, $P < 0.001$(highly statistically significant)

Differences between groups with AHI ≥ 10 and 0–9 AHI regarding BMI were not statistically significant, $P = 0.069$. This contradictory result may be explained by high prevalence obesity in entire group (84%) and the importance of local distribution of fat, predominantly in the upper regions of the body.

Conclusions: Patients with hypertension and overlap syndrome have a high degree of obesity. In multiple linear regression, correlation AHI and BMI is directly proportional, r = 0.2839, $P < 0.001$(highly statistically significant.

P799

Increased carbonic anhydrase activity is associated with nocturnal hypoxia in patients with obstructive sleep apnoea

T. WANG, D. ESKANDARI, M. KARIMI, D. ZOU, L. GROTE and J. HEDNER

University of Gothenburg, Gothenburg, SE

Objectives: Obstructive Sleep Apnea (OSA) is characterized by intermittent hypoxia and most likely derangement of CO2 metabolism in local tissue. The enzyme carbonic anhydrase (CA) plays a fundamental role in CO2 metabolism in various tissue compartments. CA activity in patients with OSA has not been studied. We hypothesized that CA activity in blood is altered by sleep disordered breathing and that kinetics of this system may influence expression of disease and its complications.

Methods: Fourty patients (31 males, mean age 53 year, mean BMI 31 kg/m^2), referred to the sleep clinic with suspected OSA were randomly selected. Overnight polygraphy recording and morning venous blood sampling was performed. Arterial blood gases were obtained in 21 additional patients with various degree of hypoventilation. Patients returning to the clinic after initiation of CPAP treatment were resampled for venous blood when possible. CA activity was assessed by pH change over time reflecting conversion of CO2 to HCO3- and H+ over 120 s in an in-vitro assay. The Area Under the Curve (AUC) was used to quantify CA activity in venous blood.

Results: Mean Apnea Hypopnea Index (AHI) was 32.5 [1–98], oxygen desaturation index (ODI4%) 33.7 [0.3–109] and mean nocturnal oxygen saturation (SaO2) 93% [86–97%] ($n = 40$). A decreased nocturnal mean SaO2 was associated with an increase in CA conversion speed (Spearman's P, rs=0.4, $P = 0.01$) while there was only a trend for ODI ($P = 0.09$). A linear up-regulation of CA activity occurred in relation to decreasing PaO2 (rs = 0.68 $P = 0.001$) but not PaCO2 ($P = 0.65$) in patients with various degrees of hypoventilation. Interestingly, an above mean CA activity was associated with higher risk of diagnosed hypertension and high office systolic pressure >140 (Fisher's exact test $P = 0.03$) and diastolic pressure > 90 ($P = 0.02$). There is a tendency towards decreased CA activity after CPAP treatment, although more data is required to make further analysis.

Conclusion: Periodic nocturnal hypoxemia in OSA and established hypoxia in hypoventilation are both associated with up-regulation of CA activity. Altered CA activity may act to sustain periodic breathing and could possibly be associated with modified hemodynamic control in various states associated with hypoventilation.

P800

Particularities of the association of resistant hypertension in patients with sleep apnea syndrome

S. M. FRENT, E. ENGELHARDT, V. TUDORACHE,
C. L. ARDELEAN, D. R. DIMITRIU and S. MIHAICUTA

University of Medicine and Pharmacy Victor Babes, Timisoara, RO

Aim: Identify the significant characteristics in patients who associate sleep apnea and resistant hypertension.

Methods: We included in the study 145 patients with resistant hypertension (RHT) out of 1194 consecutive patients suspected of SAS, evaluated in our lab over a period of 8 years (2001–2009) by sleep questionnaires, anthropometric measurements, polisomnography for apnea-hypopnea index (AHI) (values: normal 0–4, mild 5–14, moderate 15–29, severe over 30) and history of ST. We used descriptive analysis of data, analysis of distribution of variables and statistical correlations tests.

Results: In the study group 75 were males (52%) and 69 females (47%), age 56.778 ± 9.00 years (range 31–84), BMI 36.231 ± 6.85 (range 20–61) and the mean AHI 46.312 ± 24.9. Nine (6.2%) of the patients with RHT had AHI<10, while the other 136 (93.8%) had an AHI>10. Seventy three of patients with RHT (50.34%) were smokers. The most frequent comorbidities in patients with RHT were: coronary artery disease (15.17%), heart failure (5.51%) and diabetes (1.37%), while 46.2% of these patients associated multiple comorbidities.

Conclusion: Resistant hypertension is associated with more elderly subjects, with higher BMI and smokers. Severe OSA is an important risk factor for RHT. A large number of RHT patients present with multiple comorbidities.

P801

Sleep apnoea syndrome in acute stroke: a one-year prospective study. First results

J. SLONKOVA, M. SEDLAKOVA, Z. SOLDANOVA, M. KOLIBACOVA, M. STORKANOVA and P. NILIUS
University hospital Ostrava, Ostrava, CZ

Objectives: Sleep apnoea (SA) is a risk factor for stroke, it can appear after stroke or it could be worsened by this event.We plan enroll 100 patients and follow them for one year to discover abnormality in breathing in acute phase with monitoring the dynamics of clinical status in sleep apnoea events and its influence in clinical outcome.We excluded patient with no deficit in admission and patient in coma on artificial ventilation.

Methods: Prospective analysis of 53 patients from planned 100 in the first acute phase of stroke enrolled from January 2011 till September 2011.We collected demographic data,we performed two polysomnografic studies(PSG) within one week after stroke,we plan repeat PSG study in month 3 and 12 after stroke.We collect demographic data, Barthel index,Rankin,NIHSS,QOLIE-31,Pitsburgh questionnaire,we perform neuropsychological examination with aim of discover cognitive decline.Our hypothesis whish is to be proved that high degree of SA causes worse results in examinated parametres.We use statistical metric methods(%, average,standard deviation, 5% level of significance, 95% confidence interval,tests: Pearson,Chi2,Fischer, data from Excel Microsoft are transfered into IBM SPSS version 18.Control group –patient with apnoea/hypopnoea index (AHI) <5.

Results: We enrolled 42 men (79.2%), 11 women (20.8%).Average age 63.6 ± 11.8 years,SA in 69.8%, no ventilation abnormality in 30.2%. 28.3% AHI 5–15, 22.6% AHI 16–30, 24.5% AHI more than 30.Correlation between SA and stroke: $P = 0.021$.Mean age of men 62.5 ± 12.7, mean age in women 66.6 ± 7.2.SA was found in 60% men and 81% women.Higher prevalence of carotic stroke in group of patients with SA and in control group.Atherosclerotic etiology.More often day strokes.Hypertension in both groups, diabetes mellitus is not mostly present.Overweight is statistically significant $P = 0.005$ in SA patients. Pulse variation mostly in men $P = 000.5$.There was only one patient with central typ of SA. We plan to enroll 100 patients and follow them for one year each.

Conclusions: Stroke and SA is mostly present in elderly obese patients,more in men, heartbeat instability mostly in men.SA mostly diagnosed in patients with history of SA,but not examined or treated.Regular prevention examinations should be performed,obesity avoidance is deeply recommended,questionnaires about snoring, sleep ventilation abnormalities should be regularly included into screening examination,especially in higher risk group of the patients.

P802

Increased overnight blood pressure in pregnancy is associated with snoring but not with apnoea/hypopnoea index (AHI) or oxygen desaturation

P. L. JOHNSON[1], A. J. ROBERTSON[2], G. LEE[3], S. MIDDLETON[1], A. MAKRIS[3], A. HENNESSY[2] and C.E. SULLIVAN[1]
[1]University of Sydney, Sydney, AU, [2]Campbelltown Hospital, Sydney, AU, [3]Liverpool Hospital, Sydney, AU

Introduction: Sleep disordered breathing (SDB) is increased in women with gestational hypertension (GH). SDB severity is measured by the apnea/hypopnea index (AHI) and oxyhaemoglobin desaturation. Previous findings from research into GH and SDB have found that, although subtle changes in the inspiratory flow profile i.e. flow limitation, were present in polysomnography, the AHI was low and oxygen desaturation minor. We therefore measured overnight blood pressure, snoring and polysomnography in pregnant women to ascertain the relationships between various components of SDB and blood pressure during sleep.

Methods: Thirty pregnant women (12 with GH) were studied in their own homes. Polysomnography (EEG, EOG, EMG, airflow using nasal cannula, respiratory movement using inductive plethysmography and oxyhaemoglobin saturation) was performed using the Embletta™ device. Snoring was recorded using a SonoMat™, a thin mattress in which sensors measure and record sound and movement. Overnight blood pressure was recorded using SpaceLabs™, which uses an arm cuff that inflates every 20–30 min.

Results: There were no relationships between AHI or mean and minimum SaO2 and blood pressure ($r^2 < 0.15$ in all measurements). However, snoring was associated with an increased overnight blood pressure. Higher percentages of snoring were associated with higher average and maximum sleeping blood pressure. Women who snored for >30% of the night had significantly higher overnight BP than women who snored for <20% of the night. These findings were true for women with and without gestational hypertension.

Conclusion: Overnight snoring, but not AHI or oxygen desaturation, is associated with increased overnight blood pressure in pregnant women.

P803

Characteristics of apnoea-related desaturation and cardiac function in obstructive sleep apnoea syndrome

B. FALUDI, A. TRUNK and I. HERNÁDI
University of Pécs, Pécs, HU

Obstructive sleep apnea syndrome (OSAS) is characterized by repetitive pharyngeal wall obstruction, snoring, and oxygen desaturations with the well known consequences on the sleep architecture and daytime functions. It is also known, that the major outcome of the disease covers the wide spectrum of the cardiovascular and cerebrovascular diseases, and cognitive dysfunction. All of these are consequence of accumulation of the effect of single apneas during long period (years). Less is known about the consequence of the single apnea events.

The effect of single apneas on blood pressure, repetitive sympathetic activation, intrathoracal pressure and cardiac arrhythmias are well documented, but little is known about the characteristic of apnea related desaturations and cardiac changes.

In order to elucidate, we used the polygraphic recordings of OSAS patients. Using the time difference between the onset of apnea and onset of desaturations (delta(A–D)), duration of apnea, oxygen desaturations level and the apnoe related heart rate changes, by the

aid of MATLAB based program we calculated trend curve of delta (A–D) and apnoe duration, distribution of the O2 desaturations, delta (A–D) and apnoe induced heart rate changed, and cluster analysis of apnea duration and heart rate change and cluster analysis of oxygen desaturation and heart rate changes. Different parts of the recordings were compared by the same methods.

Our results shows that the time difference between the onset of apnea and desaturation is not a random delay, characteristic trends can be found. Our preliminary results show three different subtypes: short delay, long delay and gradual increasement in delay between the onset of the apnoe and desaturation. It may depends on the cardiovascural background (athero- and arteriosclesois, cardiac failure, etc.) of the patient.

Comparison of different part of the sleep period (selected on the base of the trend curves of the apnea length and delta (A–D)related events) may provide better insight into the regulation and reaction to the apneas of the organism.

P804

Breathing pattern changing during stroke

Z. SZAKACS and K. POZSEGOVITS
Military Hospital, Budapest, HU

Objectives: We investigate the prevalence and behavior of sleep-related breathing disorders (SRBDs) associated with a first-ever stroke.

Methods: We prospectively studied 51 consecutive patients admitted to our stroke unit. Complete neurological assessment was performed to determine parenchymatous and vascular localization of the neurological lesion. A portable respiratory recording study was performed within 24 h after admission (acute phase), and subsequently after 7 day (subacute phase), and 90 day (stable phase). Various types of sleep respiratory disturbances (SRD), obstructive apneas [OA], hypapneas [HYP], central apneas [CA], and Cheyne-Stokes breathing [CSB] pattern have been described.To show the time course of SRBD after the neurological disease has stabilized. The following discussion tries to establish to what extent SRBD is a consequence of acute phase or whether it remains when neurological impairment is stable or fully recovered.

Results: Functional abilities were assessed by the NIH Stroke Scale (NIHSS). There were not correlation between neurological dysfunctionality and the presence type of SRBD in the acute phase. There was not correlation between neurological topography and the presence or type of SRBD in the acute phase. The BMI did not change significantly between the studies. We did not found significant (t test for paired data) reductions in the CA, OA, HYP until three month. There was a strong trend toward a reduction in CSB was observed. in the subacute and stabil phase. We found a strong tendency, but not significant (*t* test for paired data) reductions in the SUM and CSB, but the other pathological events were not significantly different across both studies. When considering obstructive and central apneas plus hypopneas, no significant change was observed from baseline. Therefore differences in SUM were probably due mainly to a reduction in the CSB.

Conclusion: In conclusion, SRBD are frequent in patients with stroke, with the prevalence of SRBD two to three times higher than expected from the available epidemiological data in Hungary. Although the relationship between both conditions remains intriguing, overall current data suggest that obstructive apnea could act as a risk factor, whereas CSB could be the consequence of stroke. On the evidence of the results should suggest using autoservo BPAP during acut phase in stroke.

P805

The effect of hypoxia and desaturation on the level of C reactive protein levels in patients with obstrutcive sleep apnoea syndrome

I. BERNATH and Z. SZAKACS
Military Hospital, Budapest, HU

Objectives: The question of C reactive protein (CRP) levels being elevated in patients with OSAS is controversial, particularly because of the confounding impact of obesity and other cardiovascular diseases and medication on CRP levels. There are many published reports on this topic, some demonstrating independent relationships between CRP and OSAS, whereas others do not show significant relationships after adjustment for relevant confounding variables. The aim of this study was to evaluate the possible impact of different desaturation profiles in othervies severe OSAS cases ont he CRP levels, thus giving a clue for better understanding of prior inconsistencies.

Methods: The study population comprised four subgroup of patients.Group 1. Severe OSAS N: 238 (AHI more than 30 /h) with intermittent hypoxia and reoxigenation -oxigen level lower than 90% during apnea but higher than 90% during interpnea-.Group 2. Severe OSAS N:184 (AHI more than 30 /h) without hypoxia - oxigen level higher than 90% during apnea and interpnea-, but desaturation exceeding 4%.Group 3. Sever OSAS N:113 (AHI: more than 30/h) without hypoxia and desaturation not exceeding 4%.Group 4. Control patients N: 80 without OSAS, hypoxia or sleep fragmentation (AHI and arousal index <5 /h).Men/age 30–50 years; BMI 26–30 kg/m^2/ with positive history of treated hypertension were recruited following diagnostic polysomnography. Patients with therapy resistent hypertension, or with other vascular or metabolic comorbidities were excluded. Baseline blood samples were obtained while the patient was fasting, in the early morning. Serum levels of CRP were measured in the detection range 0.01 to 40 mg/l; normal range: 0–5 mg/l.

Results: Int he four groups CRP levels were the follows: Group 1.: 7.2 ± 1.2 mg/l, group 2.: 2.8 ± 0.3 mg/l, Group 3.: 1.8 ± 0.4 mg/l, Group 4.: 2.4 ± 0.6 mg/l.

Conclusion: Sleep-disoredered breathing cases characterised by intermittent hypoxia/reoxigenation were potent risk factor for elevated CRP levels, while cases with normoxemia along with or without desaturation did not represent elevated risk for increased CRP levels.This finding should be considered when recruiting OSAS patients for future studies investigating the relation between OSAS and inflammation mediated vascular diseases.

P806

Increased expression of adipose tissue hypoxia inducible factor- 3 in obese patients with obstructive sleep apnoea

D. ESKANDARI[1], D. ZOU[1], M. JERNÅS[2], B. OLSSON[1], P. ANDERSSON[2], L. GROTE[2] and J. HEDNER[2]
[1]University of Gothenburg, Gothenburg, SE, [2]Sahlgrenska Academy, Gothenburg, SE

Introduction: The adipose tissue is a major secretory organ that may maintain low grade inflammation in obesity. The effect of intermittent hypoxia on adipose tissue hypoxic gene expression has not been extensively studied. We addressed expression of hypoxia

inducible factor (HIF)-1 and HIF-3 in adipose tissue of obese patients with obstructive sleep apnea (OSA).

Methods: Ten morbidly obese OSA patients (seven female, age 53 ± 11 year and BMI 41 ± 2 kg/m^2) underwent ambulatory polygraphy recording and subcutaneous fat biopsies were obtained before and after initiation of continuous positive airway pressure (CPAP) treatment. DNA microarray was used to analyze the expression of HIF subtypes 1alpha and 3alpha (splices 1–7) in adipose tissue.

Results: The apnea hypopnea index (AHI), oxygen desaturation index (ODI) and ESS were 42[6–86] *n*/h, 42[9–79] *n*/h and 9[0–16]. HIF-3alpha1 expression at baseline was linearly correlated with AHI and ODI (r = 0.794, 0.842, $P = 0.006$, 0.002, respectively). HIF-1alpha and HIF-3alpha (splices 2–7) were not related with the degree of hypoxia. CPAP treatment significantly reduced AHI, ODI, ESS and diastolic blood pressure. There was no change in HIF-1alpha and HIF-3alpha (splices 2–7) expression after CPAP while HIF-3alpha (splice 1) decreased from 233 ± 37 to 187 ± 64 ($P < 0.05$).

Conclusion: Adipose tissue HIF-3 alpha expression is increased in relation to severity of nocturnal intermittent hypoxemia in obese OSA patients and CPAP treatment could reduce the expression. Our findings suggest there is a regulatory interplay between different subtypes of HIF in fat tissue. Increased HIF-3 alpha expression may play a modulatory role in the association between hypoxia, fat tissue and low grade inflammation.

P807

Multiparametric evaluation of vascular function in lean, normotensive patients with obstructive sleep apnoea

R. M. BRUNO, L. ROSSI, M. FABBRINI, E. DURANTI, E. DI COSCIO, M. MAESTRI, P. GUIDI, G. FRENZILLI, A. SALVETTI, S. TADDEI, L. GHIADONI and E. BONANNI

University of Pisa, Pisa, IT

Objectives: Patients with obstructive sleep apnea, a condition highly comorbid with hypertension and obesity, exhibit accelerated vascular aging and renal damage. The aim of the study was to perform a comprehensive evaluation of vascular function in patients with obstructive sleep apnea and no cardiovascular risk factors.

Methods: Forty patients with moderate-severe obstructive sleep apnea (20 with, 20 without cardiovascular risk factors) and 20 matched healthy controls were enrolled in the study. Renal vasodilating capacity (nitrate-induced change in resistive index), endothelium-dependent vasodilation in the brachial artery, carotid-femoral pulse wave velocity and carotid stiffness were measured. Oxidative stress parameters, serum E-selectin, endothelial nitric oxide synthase (eNOS) and leukocyte adhesion molecules RNA expression, and endothelial progenitor cell markers were also evaluated.

Results: Obstructive sleep apnea patients without cardiovascular risk factors presented reduced endothelium-dependent dilation (3.7 ± 2.1 versus 6.1 ± 3.0%, $P < 0.05$), increased serum E-selectin (49.8 ± 11.5 versus 38.9 ± 17.9 ng/ml, $P < 0.05$), and impaired renal vasodilating capacity (6.0 ± 4.3 versus 10.4 ± 6.1%, $P < 0.05$), as compared to controls. Furthermore, eNOS expression was reduced, while oxidative stress parameters and leukocyte adhesion molecule were similar to controls. Patients with obstructive sleep apnea and cardiovascular risk factors exhibit also increased aortic and carotid stiffness, increased renal resistive index and intima-media thickness, and reduced expression endothelial progenitor cell markers.

Conclusions: Obstructive sleep apnea is characterized by endothelial dysfunction and activation and impaired renal vasodilating capacity even in the absence of cardiovascular risk factors; reduced eNOS expression, but not oxidative stress, might be responsible for this early alteration.

P808

Predictors for systemic arterial hypertension at patients with obstructive sleep apnoea - hypopnoea syndrome

S. D. MIHAICUTA[1], C. L. ARDELEAN[1], D. COSMA[1], O. C. DELEANU[2] and S. M. FRENT[1]

[1]University of Medicine and Pharmacy, Timisoara, RO, [2]University of Medicine and Pharmacy, Bucharest, RO

Obstructive sleep apnea (OSA) is an important risk factor for systemic arterial hypertension (SH).

Aim: Identify the best predictors for SH in patients with obstructive sleep apnea – hypopnea syndrome.

Material and results: We included prospectively 489 consecutive patients (pts) with clinically suspected OSA. The pts were included and followed-up for a mean period of 7 years by sleep questionnaires, anthropometric measurements, polisomnography for apnea-hypopnea index (AHI) (values: normal 0–4, mild 5–14, moderate 15–29, severe over 30) and history of ST. We evaluated the Odds Ratio (OR) together with 95% confidence interval (CI) in a univariate analysis and the independent variables in order to identify the most important predictors for ST. In the study population 346 males (71%) 143 females (29%), age 50 ± 12 years (range 18–84 years) were included. The Body Mass Index (BMI) was 34 ± 6 kg/m^2 (range17–56 kg/m^2) and the mean AHI 36/h ± 28. Systemic hypertension was found in 59% patients. The mean time from the diagnostic of SH was 7 ± 5 years. The structure of the population regarding SH was classified following the European Society of Hypertension 2007 Guidelines as follows: from the 59% of pts with SH 11% with high normal values, 15% stage I hypertension, 29% stage II hypertension, 8% stage III hypertension. AHI in all 3 levels (mild, moderate and severe), with reference normal, is extremely significant ($P < 0.001$) in hypertensive patients. Still, only severe OSA is the strongest predictor for hypertension, OR 3.2 ($P < 0.001$, CI 1, 67–5, 59). Mild and moderate OSA did not significantly influence the appearance of systemic hypertension ($P < 0.14$, OR 0.58, CI 0.29–1.20, $P < 0.24$, OR 1.52, CI 0.76–2.86). SH is a weak predictor for OSA in univariate analysis, $P = 0.045$, OR 1.76, CI 1.01–3.08.

Conclusion: Patients with OSA are exposed to a higher risk of developing SH. A strong predictor for SH is only severe OSA.

P809

The impact of sleep apnoea on regional cerebral blood flow

Y. SVIRYAEV[1], N. ZVARTAU[1], L.S. KOROSTOVTSEVA[1], A. A. STANZHEVSKII[2], A. O. KONRADI[1], N. A. KOSTENIKOV[2] and A. L. KALINKIN[3]

[1]Almazov Federal Heart, Blood and Endocrinology Centre, St Petersburg, RU, [2]Russian Research Institution of Radiology and Surgery Technology, St Petersburg, RU, [3]Federal Research Clinical Centre of Speciaized Medical Care and High Technology, Moscow, RU

Objectives: Sleep apnea is known to be associated with the higher risk of stroke (Valham F. et al., 2008), and regional cerebral blood flow pathological changes could mediate this association. The objective of our study was to evaluate the impact of sleep apnea episodes on the 18-fluorine deoxyglucose (18 FDG) brain distribution at positron emission tomography.

Design and methods: 18 FDG brain distribution was examined [Ecat Exact 47, Ecat Exact HR+, Germany, tissue metabolic activity was assessed by «Standard Uptake Value (SUV)»] in 10 hypertensive

subjects (eight males) during wakefulness and drug-induced (diazepam 10 mg) sleep. Sleep-breathing disorders were defined by screening device (ApneaLink, ResMed, Australia). We found 12 areas of reduced 18-FDG accumulation in OSAS subjects: left and right frontal lobes (one subjects in each case); left and right parietal lobes (one subject in each case); anterior part of left cingulate gyrus ($n = 1$); left and right subconvex area ($n = 3$ and $n = 1$); mediobasal areas of right temporal lobe ($n = 4$); left and right caudate nucleus ($n = 5$ and $n = 7$); left and right thalamus ($n = 5$ and $n = 6$). Comparative analysis included only 6 loci; it did not show any difference of SUV, however, the 18 FDG brain distribution tended to decrease in the area of both caudate nuclei: in the left one 7.5 ± 0.7 versus 6.7 ± 0.7 ($P = 0.08$), and in the right one – 7.7 ± 0.4 versus 7.0 ± 0.7 ($P = 0.07$) during wakefulness and drug-induced sleep, respectively. According to the sleep study mean apnea-hypopnea index during examination was 35.4 episodes per hour of sleep.

Conclusions: Hypertensive patients with OSAS seem to have a decreased glucose metabolism during sleep compared to the awake state.

P810

Rhythms of EEG and blood pressure changes during episodes of obstructive sleep apnoea

M. SIEMINSKI[1] and M. PARTINEN[2]

[1]Medical University of Gdansk, Gdansk, PL, [2]Vitalmed Research Centre, Helsinki, FI

Objectives: The aim of our study was to analyze the rhythms of EEG power changes during the episodes of obstructive sleep apnea (OSA) and their relation to changes of blood pressure (BP).

Methods: Polysomnographic studies of five patients (five men, mean age 63, 6 years) diagnosed with OSA syndrome were analyzed. From each patient 10 episodes of OSA, lasting at least 30 s were selected for analysis. Each episode was divided into 5-s epochs, including 15 s before and after the episode. Those 15-s periods were not overlapping with another episodes of OSA. For each epoch mean alfa+beta and delta EEG waves power was calculated with fast Fourier transformation (A + B FFT and D FFT). Mean values of systolic and diastolic BP for each epoch were also calculated. Then the calculated values were compared for the following epochs: 15–10 s before the episode, first and third epoch of apnea, 15–10 s before the end of episode, 5 s before the end of episode and 10–15 s after the end of episode.

Results: For A + B FFT we have observed no changes before the episode, then significant decrease during the episode with significant increase after the episode. For D FFT there were no changes before the episode, a significant increase during the episode and significant decrease after the episode. Systolic and diastolic BP was significantly increasing before the episode, then significantly decreasing during the episode and again significantly increasing after the episode.

Conclusion: We have observed a regular and repetitive pattern of changes in EEG waves power and BP values during episodes of apnea, with A + B FFT changes following the changes of BP and D+FFT behaving oppositely to A + B FFT.

P811

Altered immune status in patients with arterial hypertension and severe obstructive sleep apnoea

E. ELFIMOVA, A. AKSENOVA, P. GALITSIN, A. RVACHEVA, K. ZYKOV, A. LITVIN and I. CHAZOVA

Russian Cardiology Research and Production Complex, Moscow, RU

Preliminary data of the study investigating peculiarities of inflammatory response and endothelial function in patients with arterial hypertension and obstructive sleep apnea syndrome.

Objective: It is known that obesity, chronic sleep deprivation, daytime sleepiness, impairment of growth hormone secretion affects immunity. OSAS is a disease associated with most of this conditions.

The aim: To evaluate the lymphocyte subset analyses in patients with arterial hypertension (AH) and obstructive sleep apnea syndrome (OSAS).

Design and methods: Eight male patients with AH (office BP 150 ± 5.6/91.3 ± 7.8 mmHg) and severe OSAS (AHI 66 ± 15), otherwise healthy, aged 39.5 ± 10 years lymphocytes phenotyping was performed by flow cytometry (Cytomics FC500; Beckman Coulter, USA).

Results: Pts with AH and severe OSAS were examined for levels of CD3+,CD3+/CD4+, CD3+CD8+, CD3-CD(16 + 56), CD3+CD(16 + 56), CD19+, CD3+CD25+, CD4+CD25+, CD50+, CD3+CD50+, CD3-HLA-DR+, CD3+HLA-DR+, CD3+CD95+.

The levels of CD3-HLA-DR+ (14.0 ± 7.97 versus 8.5 ± 3.3) and CD3 + CD (16 + 56) (7.85 ± 5.22 versus 5.0 ± 2.3) and CD 50+ (97.8 ± 2.34 versus 90.0 ± 10.0) were statistically higher in comparison with normal values, whilst CD3+HLA-DR+ (2.51 ± 1.64 versus 6.0 ± 3.1), CD3 + CD95 + (32.32 ± 10.7 versus 42.0 ± 9.0) were significantly lower.

Conclusion: Patients with AH and OSAS have altered immune status: increase of the percentage of CD3-/HLA-DR+ and CD3+CD (16 + 56) peripheral lymphocytes and decrease of CD3+/HLA-DR+ lymphocytes together with decrease of CD3+ CD95+. These data suggest, that both CD4+ and CD8+ T-cell compartments, as well as the regulation of CD95+ expression on T-cells, should be targeted for further study. Knowing of the underlying inflammatory mechanism could lead to understanding of disease progression and development of cardiovascular complications.

P812

Circulating endothelial progenitor cells in patients with arterial hypertension, obesity and severe obstructive sleep apnoea syndrome

E. ELFIMOVA, A. AKSENOVA, P. GALITSIN, A. RVACHEVA, K. ZYKOV, A. LITVIN and I. CHAZOVA

Russian Cardiology Research and Production Complex, Moscow, RU

Background: Arterial hypertension (AH), obesity and obstructive sleep apnea syndrome (OSAS) – are those co-morbidities frequently associated. OSAS is known to have an additional impact on endothelial dysfunction. Circulating endothelial progenitor cells (EPCs) are known for their potential in the process of cardiovascular damage and repair. It is shown it some studies that patients with OSAS have increased levels of circulating endothelial cells and endothelial microparticles while reduced amount of circulating endothelial progenitor cells.

The aim: To evaluate the number of circulating endothelial progenitor cells (EPCs) in patients with Arterial Hypertension (AH), obesity

and severe Obstructive Sleep Apnea Syndrome in comparison with control group.

Materials and methods: there were included 8 male patients with AH 148.8 ± 5.74/ 91.8 ± 6.79 mmHg, severe OSAS (AHI 65.8 ± 24.7) and obesity (BMI 37.2 ± 5.1) and 6 male patients with AH 149.8 ± 9.30/94.6 ± 11.6 mmHg, obesity (BMI 36.5 ± 5.9), but without OSAS (AHI 4.2 ± 1.4). Both groups were matched by age, cardiovascular risk factors and were otherwise healthy. EPCs – CD34 + CD133 + CD309(VEGF-2/KDR+) were isolated and quantified from peripheral blood samples, obtained in the fasting condition, following sleep studies - by flow cytometry (Cytomics FC500, Beckman Coulter, USA).

Results: Patients with AH and OSAS had higher percentage of CD34+ cells (1.025 [0.61–1.955] versus 0.6 [0.4–0.82], $P = 0.043$) and absolute count of EPC/10 ml (296 [221.5–843.0] versus 108 [27.3–280.2], $P = 0.043$).

Conclusions: In the preliminary data of the study investigating peculiarities of inflammatory response and endothelial function in patients with arterial hypertension and obstructive sleep apnea syndrome - patients with OSAS and AH, otherwise healthy showed increased number of circulating EPC in comparison to the matched group of obese AH patients without OSAS. It is planned to continue recruitment of the patients for further evaluation of obtained data.

P813

Relationship between sleep apnoea syndrome, plasma gamma-glutamyl-transferase levels and cardiovascular risk

L. PUIU[1], A. DIDILESCU[2], A. PETROVAN[3], F. GLIGA[4], E. TABACU[5], M. MAN[6], M. MARC[7] and F. MIHALTAN[8]

[1]Pneumophthisiology Hospital, Baia-Mare, RO, [2]Carol Davila, University of Medicine and Pharmacy, Bucharest, RO, [3]University Hospital for Infectious Diseases, Cluj-Napoca, RO, [4]Pneumology Hospital, Targu-Mures, RO, [5]Marius Nasta'' Pneumology Institute, Bucharest, RO, [6]Clinical Pneumology Hospital, Leon Daliello, Cluj-Napoca, RO, [7]Pneumology Hospital, Timisoara, RO, [8]Marius Nasta'' Pneumology Institute, Baia-Mare, RO

In Sleep Apnea Syndrome (SAS) the episodes of hypoxia/reoxygenation and the prooxidant activity of gamma-Glutamyl-Transferase (gamma-GGT) results in the generation of reactive oxygen species that promote oxidative stress, the earliest stage in pathogenesis of atherosclerosis lesions.

Objectives: The aims of our study were to assess the relationship between obstructive sleep apnea and plasma gamma-GGT levels and to test the hypothesis that this relationship is strengthened by oxidative stress, in SAS patients, comparing to a control group.

Methods: Two Romanian groups, consisting of 40 patients diagnosed with SAS and 26 healthy controls, were recruited. All subjects underwent cardiorespiratory poligraphy. Plasma levels of gamma-GGT, total cholesterol (TC), triglycerides, low density lipoprotein cholesterol (LDL-c), high density lipoprotein cholesterol (HDL-c), glycemie, C-Reactive Protein (CRP), thrombocytes, uric acid and albumin were assessed. Statistical analysis was performed using Pearson correlations tests, two tailed *t*-test and one-way ANOVA test.

Results: In the SAS group, correlations were found as follows: gamma-GGT and triglycerides (r = -0.30; $P = 0.05$); gamma-GGT and uric acid (r = 0.52; $P = 0.003$); gamma-GGT and glycemie (r = 0.40; $P = 0.02$); apnea/hypopnea index (AHI) and gamma-GGT (r = 0.37; $P = 0.04$); thrombocytes and CRP (r = 0.48; $P = 0.001$), while in the control group between oxygen desaturation index (ODI) and TC (r = 0.59; $P = 0.001$); ODI and LDL-c (r = 0.58; $P = 0.001$); AHI and triglycerides (r = 0.47; $P = 0.01$); CRP and HDL-c (r = -0.64; $P = 0.0004$). With regard to the smoking status, hypopneas number and the TC/HDL-c ratio were statistically significant higher in smokers than in nonsmokers ($P = 0.01$; respectively, $P = 0.02$).

Conclusions: In SAS patients, plasma gamma-GGT level predicts outcomes by adding to information provided by traditional risk factors for cardiovascular disease. Thus, gamma-GGT could be considered an early biomarker for oxidative stress and, possibly an independent risk marker for metabolic syndrom and the development of subclinical atherosclerosis.

P814

Analysis of anthropometric data at patient with sleep apnoea syndrome and co-morbidity

C. L. ARDELEAN[1], D. R. DIMITRIU[1], M. PETRUI[1], S. M. FRENT[2], V. TUDORACHE[2], D. F. LIGHEZAN[2] and S. MIHAICUTA[2]

[1]Victor Babes Hospital, Timisoara, RO, [2]Victor Babes University of Medicine and Pharmacy, Timisoara, RO

Introduction: Patients with sleep apnea syndrome and comorbidities have a high degree of obesity.

Objective: Analysis of abdominal circumferences (AC) in patients with sleep apnea syndrome (SAS) and comorbidity

Material and methods: Between June 2005 and June 2009 we evaluated 968 consecutive patients with suspected OSAS, using the Epworth sleepiness questionnaire, anthropometric data for body mass index and AC, somnography or polysomnography (AHI assessment). We evaluate the correlation between IAH and AC in multiple linear regression and mean values were compared at patients with SAS and comorbidity by Student's t test in patients with equal variances and Welch correction in patients with unequal variances.

Results: Seven tweny-seven male (75.1%), 241 female (24%), age 52 ± 11.89 years (6–84), AHI 34.10 /h ± 27.41, AC 120.06 cm ±15.10 (8–157), mean BMI 33.06 ± 6.32 kg/m^2 (17–56). BMI > 25 kg/m^2 (84%). Obesity grade1 (35%), obesity grade2 (22%), obesity grade3 (14%). AC in patients with AHI ≥10 (120.6 cm versus 118.33 cm, $P = 0.042$), in patients with hypertension (120.06 cm versus 117.77 cm, $P = 0.008$) and in patients with COPD (127.78 cm versus 118.59, ($P < 0.001$). Multiple linear regression, correlation AHI and AC is nonlinear, r = 0.228, weak correlation, $P < 0.001$.

Conclusions: Patients with hypertension and overlap syndrome have a high degree of obesity. SAS is an important step that links obesity and hypertension in some individuals.

P815

Co-morbidities at patients with sleep apnoea syndrome

C. L. ARDELEAN[1], D. R. DIMITRIU[1], S. M. FRENT[2], M. PETRIU[1], V. TUDORACHE[2], D. F. LIGHEZAN[2] and S. MIHAICUTA[2]

[1]Victor Babes Hospital, Timisoara, RO, [2]Victor Babes University of Medicine and Pharmacy, Timisoara, RO

Introduction: Hypertension and other comorbidities are important diseases that accompany sleep apnea syndrome (SAS) or may be caused by SAS.

Aim: Complete evaluation of patients with suspected SAS by international protocols.

Methods: One thousand two hundred ten patients with suspected SAS were divided according to blood pressure in three lots: LotA-Nonhypertension, LotB-hypertension, LotC-resistant hypertension. We collected general data, medical history, sleep questionnaires,

anthropometric measurements (neck circumference NC, abdominal circumference AC), somnography for apnea-hypopnea index (AHI), oxygen desaturation index (DI), comorbidities and measured mean values, standard deviation, 95% confidence interval (CI).

Results: Lotul A: 40% (481), age = 47.38 ± 13.3, BMI = 31.31 ± 6.2, NC=42.82 ± 4.77, CA = 113.17 ± 16.1, AHI = 32.25 ± 26.9, Epworth = 8.87 ± 4.83, DI = 20.76 ± 26.2.

Diabetes mellitus(DM) 2.48%, coronary disease(CD) 4.55%, heart failure(HF) 1%, arrhythmia 10%, ≥2 associated comorbidities 5.5%. Lotul B: 48% (584), age = 54.25 ± 10.3, BMI = 34.48 ± 6.66, NC = 44.15 ± 4.67, CA = 119.68 ± 15.2, AHI = 42.79 ± 27.6, Epworth = 10.39 ± 4.98, DI = 30.24 ± 27.9. DM 2%, CD 17%, HF 6.5%, arrhythmia 25%, ≥2 associated comorbidities 17.5%. Lotul C: 12% (146), age = 56.77 ± 9.0, BMI = 36.23 ± 6.85, NC = 44.76 ± 4.96, CA = 122.25 ± 15.2, AHI = 46.31 ± 24.9, Epworth Scale = 11.52 ± 4.9, DI = 31.29 ± 28.7. DM 1.3%, CD 15.2%, HF 5.51%, arrhythmia 40%, ≥2 associated comorbidities 46.2%. SAS was present in 75% normotensive patients, 88% hypertensive patients and 94% patients with resistant hypertension.

Conclusion: SAS and comorbidities are more common in patients with hypertension and resistant hypertension. Most of these patients are obese, with increased abdominal circumference, increased daytime sleepiness, low oxygen saturation.

P816

Respiration sinus arrhythmia during sleep

W. JERNAJCZYK[1], I. MUSINSKA[1], L. WOLKOW[1], T. JAKUBCZYK[1], B. WEST[2] and M. LATKA[3]

[1]Institute od Psychiatry and Neurology, Warsaw, PL, [2]Mathematics and Information Science Directorate, Army Research Office, Durham, NC, [3]University of Technology, Wroclaw, PL

Objectives: Respiration sinus arrhythmia (RSA) is a well known mechanism that affects heart rate variability of awake subjects. On an electrocardiogram this phenomenon is manifested as subtle changes in the R-R interval which are synchronized with respiration. The R-R interval is shortened during inspiration and prolonged during expiration. We have recently found that in awake subjects the coupling between respiratory and cardiovascular systems may occasionally become deranged. The shortening of R-R interval may take place not only during inspiration but may continue during the most part of expiration. The end of expiration triggers the dramatic rebound of the R-R interval length. In this way, the length of adjacent R-R intervals may increase by as much as 50%. The goal of this study is to verify whether this effect may be observed during sleep.

Methods: The polysomnography was performed for six healthy subjects during two consecutive nights. The polysomnograms were visually scored. The computer generated R-R time series were visually verified to eliminate motion artifacts. The polysomnograms were analyzed in the neighborhood of points where the length of the consecutive R-R intervals increased by more than 35%.

Results: Respiration sinus arrhythmia during sleep in most cases leads to gentle modulation of heart rate. However, occasionally the shortening of R-R interval during inspiration continues until it is reset during the following inspiration. This resetting leads to conspicuous jumps of R-R intervals as in the case of awake subjects. Surprisingly, in many cases the jumps of the R-R interval is preceded by K-complex localized between two adjacent inspirations.

Conclusion: The presence of K-complexes in the close neighborhood of sudden changes of heart rate seems to provide an independent confirmation of their sleep protection function.

P817

Analysis of whole blood clot microstructure confirms a hypercoagulable state in obstructive sleep apnoea syndrome

M. M. WILCZYNSKA[1], K. LEWIS[1], S. STANFORD[2], M. J. LAWRENCE[2], L. NICOLLE[1] and P. A. EVANS[2]

[1]Prince Philip Hospital, Llanelli, UK, [2]NISCHR Haemostasis Biomedical Research Unit, Swansea, UK

Objectives: Obstructive sleep apnoea syndrome (OSAS) is the co-existence of daytime sleepiness and repetitive episodes of the passive upper airway collapse during sleep. It is an independent risk factor for cardiovascular disease including hypertension, arrhythmias, heart failure, stroke and cardiovascular death. Although precise mechanisms remain unclear a pro-thrombotic state is partly implicated.

Fibrin clot structure corresponds closely with the pro-thrombotic state. Its quantitative analysis can provide information regarding hypercoagulable state. We have developed a new biomarker to measure clot quality in whole blood by fractal analysis. Gel point (GP) describes functional change from viscoelastic fluid into viscoelastic solid. At the GP, the fractal number (Df) describes the microstructure of the incipient clot and studies on 120 volunteers suggests a normal Df of 1.74 + 0.07 in a healthy state. We wanted to see if Df is altered in OSAS and if it is affected by Continuous Positive Airways Pressure (CPAP) treatment.

Methods: Eighteen patients with OSAS (16 males, mean body mass index (BMI) = 37.3 kg/m^2, mean age 60 years, mean 4% Dip-rate (DR) = 41.8 events/h (on Visilab limited channel sleep study). Nine controls with similar symptoms but negative sleep studies (seven males, mean BMI = 34.7 kg/m^2, mean age 48.8 years, mean 4% DR = 5.8 events/h. Whole blood was collected at 4 pm and after sleep the following morning. Samples were tested for routine clotting profiles, thromboelastography and the novel biomarkers: GP, Df. Those with OSAS had morning blood tests after their first night of auto-titrating CPAP (average 7 h).

Results: Mean Df for OSA at 4 pm = 1.706. Mean Df for controls at 4 pm = 1.741 (P = 0.02). Mean Df for OSA at 7.30 am = 1.734. Mean Df for controls at 7.30 am = 1.748(P = 0.35). Within OSA there was an increase in Df after sleep (P = 0.026) but it was reversed after one night of CPAP Df = 1.695 (P = 0.02). There were no statistically significant differences at any time point for routine coagulation and platelet function tests.

Conclusion: Those with OSAS have a normal prothrombotic state in the afternoon but significantly higher prothrombotic state in the morning, possibly secondary to the hypoxia-reoxygenation events and catecholamine surges. Morning pro-thrombotic state improves after a single night of CPAP use. Df appears a new and sensitive marker that could highlight patients at vascular risk and be used to monitor response to CPAP therapy.

P818

Resistin as a marker of impaired glucose tolerance in OSA patients

R. CHERNEVA, O. GEORGIEV, D. PETROVA, A. CAKOVA and V. MITEV

University Hospital, Sofia, BG

Background: The role of different clinical parameters regarding inflammation and oxidative stress has largely been debated in the etiology of impaired glucose tolerance in OSA patients.

Aim: To determine the plasma levels of resistin in patients with OSA and impaired glucose tolerance and compare them to those with normal blood glucose. To determine the effect of BiPAP on resistin levels.
Materials: Thirty patients with newly diagnosed OSA have participated in the study. OSA was defined using a full polysomnography study. The glucose metabolism was investigated applying an oral glucose tolerant test. Both blood glucose and IRI were determined on the 0, 60th, 120th, 180th minute. Eighteen patients were with newly diagnosed impaired glucose tolerance (IGT). Twelve patients had normal blood glucose (NBG). Plasma levels of resistin (RayBio # ELH –resistin - 001) were determined in both groups.Eighteen patients received BiPAP.Eleven remained without treatment.
Results: The immuno-reactive insulin (IRI) was 25.29 mU/l in IGT patients. In patients with NBG, IRI was 21.3 mU/l. Body mass index (BMI) did not differ significantly between patients with IGT and NBG. BMI was 40, 42 in patients with IGT and 41.7 in those with NBG. Apnea-hypopnea index (AHI – 60.8) was higher in patients with NBG compared to those with IGT (AHI – 50.6).Resistin was higher – 4.46 ng/ml in IGT patients compared to NBG – 3.98 ng/ml. IRI in IGT patients was 25.29 mU/l and correlated best to the plasma levels of resistin ($P < 0.05$). In the treated patients resistin decreased – 5.9 /4.5 ng/ml. In those without treatment resistin changed from 4.3/3.4 ng/ml.
Conclusion: The commonly used clinical parameters – BMI, AHI were higher in patients with OSA and normal blood glucose. They are not reliable clinical markers for the early detection of impaired blood glucose metabolism in OSA patients. Only resistin correlated to the levels of immmuno-reactive insulin. It could be applied as an early detection marker and therapeutic target of impaired blood glucose metabolism in OSA patients.

P819

Role for human epithelial cells in intermittent hypoxia-induced airway inflammation

C. PHILIPPE[1], E. ESCUDIER[2], D. ISABEY[3] and M.-P. DORTHO[4]
[1]AP-HP Hopital Tenon and INSERM, Paris, FR, [2]AP-HP Hopital Trousseau and INSERM, Paris, FR, [3]INSERM U955, Créteil, FR, [4]AP-HP Hopital Bichat and INSERM, Paris, FR

Background: Obstructive sleep apnea is associated with systemic inflammation related to intermittent hypoxia. Whether the increased neutrophil and IL-8 levels in induced sputum reflect systemic inflammation or airway inflammation is unknown.
Objective: To assess the potential role for airway epithelial cells in airway inflammation induced by intermittent hypoxia.
Methods: Human nasal epithelial cells were cultured at an air-liquid interface allowing differentiation to airway epithelial cells. After intermittent hypoxia, epithelial cell-conditioned media were assessed for matrix metalloproteinase expression, growth factors, and cytokines. Chemotactic effects of conditioned media on human neutrophils were evaluated. Direct effects of intermittent hypoxia on migration of neutrophils from healthy volunteers and obstructive-sleep-apnea patients were compared.
Results: Intermittent hypoxia for 24 h significantly increased MMP-9 and MMP-2 expression and pro-MMP-9 activation ($P < 0.05$), IL-8 (5112 ± 3923 versus 2455 ± 2738 pg/ml, $P < 0.05$), PDGF AA (396 ± 225 versus 189 ± 73 pg/ml, $P < 0.05$), and VEGF (1250 ± 993 versus 220 ± 229 pg/ml, $P < 0.05$) compared to normoxia. TGF alpha, TGF beta, IL-1, and IL-6 were unchanged. Neutrophil chemotaxis was dramatically enhanced by conditioned media (112.00 ± 4.80% versus 0.69 ± 0.43%, P = 0.0053). Intermittent hypoxia increased spontaneous and IL-8-induced neutrophil migration. Migration was greater with neutrophils from patients than from controls.
Conclusion: These data suggest a specific inflammatory response of human nasal epithelial cells to intermittent hypoxia, independently from systemic events. In patients with obstructive sleep hypoxia, the systemic response to intermittent hypoxia may amplify the local inflammatory response. Between 2009 and 2012, MPO has been memeber od scientific committee, principal investigator or co-investigator of researchs funded by ResMed, Philips et Bioprojet; has been invited speaker in symposia oragnized by Vitalaire, Philips, IPSEN had received travel grants from Orkyn' et UCB.

P820

Genetic determinants of cardiovascular disease in women with obstructive sleep apnoea

P. BIELICKI[1], M. BARNAS[1], J. LUIZA[2], K. BRZOSKA[3], R. PLYWACZEWSKI[2], M. MUMOR[1], T. STEPKOWSKI[3], R. CHAZAN[1], M. KRUSZEWSKI[3] and P. SLIWINSKI[2]
[1]Warsaw Medical University, Warsaw, PL, [2]Institute for Tuberculosis and Lung Diseases, Warsaw, PL, [3]Institute of Nuclear Chemistry and Technology, Warsaw, PL

Obstructive sleep apnea is the most common cause of respiratory disorders during sleep. This disease affects mostly middle-aged men, but it is also seen in women.
It is well known that breathing problems during sleep increase the risk of cardiovascular complications such as arterial hypertension, coronary heart disease and stroke. Attempts were made to identify subjects with OSAS who are particularly susceptible to serious cardiovascular complications. One of the directions for this research is the assessment gene polymorphism of the genes potentially associated with an increased risk of cardiovascular diseases.
Aim of the study: Evaluation of some genetic polymorphisms that may affect the incidence of cardiovascular disease in women with obstructive sleep apnea.
Material and methods: The study included randomly selected 151 women, with OSAS (defined as daytime sleepiness and AHI > 5 /h), aged 60.5 ± 9.0 years. They all filled a questionnaire concerning the prevalence of cardiovascular diseases. Gene polymorphism for: SREBF1, HIF1A, FTO and ALOX5AP genes was assessed.
Results: Arterial hypertension was diagnosed in 107 (70.9%), coronary heart disease in 24 (15.9%), myocardial infarction in five (3.3%), and stroke in six (4.0%) women. Correlation analysis of selected gene polymorphisms with the diagnosis of these diseases showed a statistically significant correlation between the SREBF1 CNS homozygous AA gene and stroke (in 4 out of 6 women were homozygous AA, $P < 0.001$) and a higher incidence of coronary heart disease (33% versus 15.9%, $P < 0.05$) and myocardial infarction (25% versus 3.3%, $P < 0.0001$) in FTO heterozygous AG women compared with the control group.
Conclusions: Determination of polymorphism of certain genes may be useful in assessing the risk of cardiovascular complications in women with OSAS

P821

Genetic determinants of diabetes mellitus type 2 in patients with obstructive sleep apnoea

M. BARNAS[1], P. BIELICKI[1], L. JONCZAK[2], K. BRZOSKA[3], R. PLYWACZEWSKI[2], M. KUMOR[1], T. STEPKOWSKI[3], R. CHAZAN[1], M. KRUSZEWSKI[3] and P. SLIWINSKI[2]

[1]Warsaw Medical University, Warsaw, PL, [2]Institute for Tuberculosis and Lung Diseases, Warsaw, PL, [3]Institute of Nuclear Chemistry and Technology, Warsaw, PL

Obstructive sleep apnea is the most common cause of respiratory disorders during the sleep. It is well known that breathing problems during sleep increase the risk of cardiovascular diseases, including diabetes. We tried to identify patients with OSAS who are particularly at risk of these complications. One of the directions for this research is the assessment gene polymorphism of the genes potentially associated with the above mentioned complications.

Aim of the study: To assess the polymorphism of selected genes potentially associated with the incidence of type 2 diabetes in patients with obstructive sleep apnea.

Materials and methods: The study included 600 randomly selected OSAS patients (OSAS was defined as daytime sleepiness and AHI> 5/h) aged 57.4 ± 10.3 years (25.2% women). They all filled a questionnaire concerning the prevalence of cardiovascular diseases. Gene polymorphism for: TCF7L2, SREBF1, SREBF2, OSBPL10, HIF1A, FTO, APOA5 i ALOX5AP was determined.

Results: Type 2 diabetes was diagnosed in 121 (20.2%) subjects. Correlation analysis of selected gene polymorphisms with type 2 diabetes in the whole group showed a significant relationship only for the APOA5 heterozygous CG gene. Of the 60 heterozygous CG APOA5 gene subjects, diabetes was diagnosed in 20 (33.3%); as mentioned above patients with diabetes accounted for 20.2% in the entire group ($P < 0.05$). An additional analysis for different subgroups showed a significantly higher incidence of type 2 diabetes in women with heterozygous CG ALOX5AP gene (33.7% versus 21.6% in males, $P < 0.05$) and in individuals over 40 years of age with heterozygous CT OSBPL gene (20.9% versus 14.8% of the population below the age of 40 year, $P < 0.05$).

Conclusions: Determination of polymorphism of certain genes may be useful in assessing the risk of type 2 diabetes in selected groups of patients with OSAS.

P822

Circulating microRNA 92a in patients with acute ST-segment elevation myocardial infarction with obstructive sleep Apnoea Syndrome

H. WANG and Y.Z. LIN

Guangxi People's Hospital, Nanning, CN

Objective: To investigate the relationship between circulating micr-oRNA 92a(miR-92a) and patients with ST-segment elevation myo-cardial infarction (STEMI) compliance with obstructive sleepapneasyndrome(OSAS), influence of percutaneous coronary intervention (PCI) and continuous positive airway pressure (CPAP) on miR-92a as well.

Methods: We studied 37 males using polysomnography: 20 sub-jects with OSAS and a 17-subject control group. An OSAS-validated sleep questionnaire covering the most important cardiovascular risk factors was applied to all subjects. Furthermore, patients received a complete general physical examination and biochemistry test with lipid profile. To determine the regulation of miR-92a, we detected it in peripheral blood mononuclear cells (PBMCs) of 24 patients with STEMI with OSAS (group STEMI and OSAS), 58 patients with STEMI without OSAS (group STEMI without OSAS), 50 healthy volunteers as group control. All patients accepted emergency PCI therapy.20 of 24 patients with STEMI and OSAS accepted CPAP therapy. Blood was taken before, 24 h after PCI therapy and one week after admission in patients with STEMI.

Results: Circulating level of miR-92 was higher in patients with STEMI before PCI therapy than group control (11.54 ± 9.34 versus 4.42 ± 3.12, $F = 8.09$, $P = 0.006$), and miR-92a would be down-regulated after emergency PCI therapy(6.33 ± 5.13 verssus 11.54 ± 9.34, $F = 2.26$, $P = 0.13$). In admission, The level of miR-92a was higher in patients with STEMI and OSAS than those without OSAS (13.83 ± 7.32 versus 10.03 ± 8.26, $F = 13.234$, $P = 0.001$). Expression of miR-92a decreased after CPAP therapy in patients with STEMI and OSAS after PCI (5.06 ± 3.77 versus 7.62 ± 4.91, $F = 5.977$, $P = 0.018$).

Conclusions: In STEMI patients, the expression of circulating miR-92a is up-regulated. PCI therapy may suppress such up-regulation. Circulating miR-92a is also up-regulated in patients with OSAS, and it can be down-regulated by CPAP therapy. Our data suggest that miR-92a might have potential for diagnosis and therapeutic application in the prevention and treatment of STEMI and OSAS.

Poster Session - SDB: epidemiology and diagnosis Part II

P823

Cortisol and psychological and physical health in males with obstructive sleep apnoea

S. CENTOFANTI[1], R. BYRNE[2], P. CATCHESIDE[3], N. ANTIC[3], D. MCEVOY[3], A. CLOW[4] and S. BANKS[1]
[1]University of South Australia, Adelaide, AU, [2]Flinders University, Adelaide, AU, [3]Adelaide Institute for Sleep Health and Flinders University, Adelaide, AU, [4]University of Westminster, London, UK

Objectives: Obstructive Sleep Apnoea (OSA) is known to deleteriously impact physical and psychological health. Cortisol, a hormone characterised by a marked circadian rhythm and stress responsiveness, is also thought to be affected in OSA. However it is unknown if diurnal patterns of cortisol secretion are connected with physical or psychological health outcomes in OSA. The purpose of this pilot study was to assess the relationship between cortisol and psychological and physical health in OSA patients.

Methods: Twenty-nine adult males diagnosed with OSA (AHI 42.9 ± 16.1; Age 53.4 ± 8.7) undertook the 2-day in-home study. Participants completed the Depression-Anxiety-Stress Scale (DASS-21) and the Short Form 36 Health Survey (SF-36) to measure psychological and physical health respectively. Salivary cortisol samples were collected immediately upon awakening, every 15 min thereafter until 45 min and 12 h post-awakening to measure the diurnal pattern of cortisol secretion, with diurnal decline calculated as peak minus the 12 h cortisol level.

Results: Data were analysed using Pearson correlations. While not statistically significant a trend for a negative association between cortisol diurnal decline and stress (r = -0.30, $P = 0.059$) and anxiety (r = -0.30, $P = 0.059$) was observed. Depression (r = -0.04, $P = 0.420$) and physical health were not associated with cortisol (r = 0.16, $P = 0.204$).

Conclusions: Trends in the current data suggest there may be links between stress, anxiety and the diurnal pattern of cortisol secretion in individuals with OSA. Further investigation is needed to examine if there are causal relationships between these factors.

P824

Association of sleep-disordered breathing symptoms and maternal hyperglycaemia

B. IZCI BALSERAK
The University of Pennsylvania, Philadelphia, PA

Sleep disturbances and changes in pregnancy may impair glucose mechanism. This study aimed to examine associations of sleep-disordered breathing, sleep and nap duration with 1-h glucose challenge test levels in pregnant women after controlling for known risk factors for gestational diabetes. Pregnant women ($n = 104$) who underwent full polysomnography and a glucose challenge test (GCT), and completed the Multivariable Apnoea Prediction and Pittsburgh Sleep Quality Indexes were studied. Bivariate and multivariable logistic regression analyses were performed.

Over 13% participants reported habitual snoring in the first-trimester. Only 9.3% women with normoglycaemia (GCT < 135) were habitual snorers, whereas 45.5% women with hyperglycaemia-(GCT ≥ 135) had habitual snoring ($P < 0.001$). Sleep-disordered breathing symptoms (loud snoring, snorting/gasping and apnoeas), (odds ratio (OR) 2.85; 95% confidence interval (CI) 1.50–5.41; $P = 0.001$) and total nap duration (OR 1.48; 95%CI 0.96–2.28; $P = 0.08$) were associated with hyperglycaemia. After adjusting for confounders, sleep-disordered breathing symptoms (OR, 3.37; 95%CI, 1.44–8.32; $P = 0.005$) and nap duration (OR, 1.64; 95%CI, 1.00–2.681.02; $P = 0.05$) continued to be associated with hyperglycaemia. However, the primary outcome measure, the apnea/hypopnea index in the first-trimester was not significantly associated with hyperglycaemia (OR 1.03; 95%CI 0.83–1.28; $P = 0.77$).

Sleep-disordered breathing symptoms and nap duration are associated with hyperglycaemia. We found no association between sleep duration and hyperglycaemia. Research is needed to determine whether women with sleep-disordered breathing and/or daytime-napping are at risk for gestational diabetes.

P825

Towards a diagnostic method for obstructive sleep apnoea and upper airway resistance syndromes based on features extracted from the envelope of the breathing signal

E. A. VIVALDI, A. BASSI, J. DIAZ and J. ARANCIBIA
Universidad de Chile, Santiago de Chile, CL

Objectives: The development of a new tool for the diagnosis of sleep breathing disorders that, unlike the apnoea/hypopnea index (AHI), evaluates breathing by assessing continuous feature variables instead of counting events, and can detect both obstructive sleep apnoea (OSA) and upper airway resistance syndrome (UARS).

Methods: The signal analyzed is the pressure transducer airflow (PTAF) of standard polysomnography. The envelope curve of the signal is obtained using the Hilbert transform. For every 30-s epoch of recording, the envelope's coefficient of variation (ECV) is calculated, i.e., the ratio between the standard deviation and the average of the envelope curve through the epoch. ECV is a continuous, scale-invariant index. In addition, a smoothed version of the envelope is generated to filter out irregularities within the time span of a single breathing cycle. The coefficient of variation of the smoothed envelope (SECV) is then calculated.

Results: Normal breathing is characterized by a steady envelope curve; it hence presents a low ECV. In disrupted breathing, a fluctuation of the envelope curve is observed. The fluctuation becomes more prominent as the disturbance is more severe, and increasingly higher ECVs are obtained. OSA patterns present fluctuations that span through several breathing cycles, while UARS patterns present fluctuations within a breathing cycle due to the flattening of the PTAF signal contour caused by airflow limitation. Thus, ECV discriminates both OSA and UARS from normal breathing, while SECV is specifically sensitive to OSA. When the sequence of ECV and SECV values for each epoch are displayed as two all-night curves, a comprehensive view of the breathing pattern evolution is obtained. These curves can be presented in the same time axis along with the hypnogram, body position or other relevant variables, so that synchronous variations are evidenced. Additionally, a histogram of the distribution of ECVs and SECVs can summarize the respiration quality throughout the study.

Conclusion: This new, easy to calculate, informative diagnostic tool offers a continuous intensive index that can characterize and individualize the overall dynamics of sleep breathing. Being process-oriented, it diverges from the AHI event-oriented approach. It overcomes well known AHI's shortcomings inherent to event thresh-

old definition that can be critical in subtler alterations of respiratory signals as in mild to moderate OSA and UARS.
Grant Fonis SA10I20034

P826

Clinical characteristics of obesity hypoventilation syndrome patients: comparison with obese obstructive sleep apnoea syndrome patients

O. K. BASOGLU and M. S. TASBAKAN
Ege University School of Medicine, Izmir, TR

Objectives: Obesity hypoventilation syndrome (OHS) is characterized by obesity, daytime hypercapnia, and sleep-disordered breathing in the absence of lung or respiratory muscle disease. The aim of this study was to compare characteristics of OHS and obstructive sleep apnea syndrome (OSAS) patients and to identify clinical predictors that should prompt clinicians to measure arterial blood gases.

Methods: Out of 1495 OSAS patients, 823 (55.1%) were diagnosed as obese OSAS and 52 (3.5%) were OHS. Demographic and anthropometric features, lung function tests, blood gas analysis, polysomnographic findings of OHS patients were compared to obese OSAS patients.

Results: The rate of females (50% versus 32.7%, $P = 0.015$) and body mass index (40.8 versus 35.8 kg/m^2, $P = 0.003$) were higher in OHS when compared to obese OSAS patients. Waist ($P < 0.0001$) and hip ($P = 0.003$) circumferences were wider, lung volumes and PaO2 were lower ($P < 0.0001$), whereas PaCO2 and HCO3 were increased ($P < 0.0001$) in patients with OHS. Epworth sleepiness scores of OHS patients were higher (13.9 versus 11.3, $P = 0.004$) but AHI was similar in two groups (52.9 versus 46.2, $P > 0.05$). Lowest and mean SpO2 and also sleep time with SpO2 < 90% were decreased in OHS ($P < 0.0001$). Multivariate analysis showed that hypercapnia was significantly associated with body mass index ($P = 0.003$), PaO2 ($P = 0.001$) and HCO3 ($P < 0.0001$).

Conclusion: It was shown that OHS patients have increased body mass index, daytime sleepiness, PaCO2 and HCO3, and decreased lung functions and PaO2 levels than obese OSAS patients. Hypoxemia and increased bicarbonate levels in obese OSAS patients should prompt clinicians to exclude OHS.

P827

The influence of obstructive sleep apnoea on thyroid hormone

M. L. ANDERSEN, C. GUINDALINI, L. BITTENCOURT and S. TUFIK
Universidade Dederal De Sao Paulo, Sao Paulo, BR

Objectives: Studies have demonstrated an association between the obstructive sleep apnea syndrome (OSAS) and hormone levels alterations. The aim of this study was to examine the influence of OSAS on the hormonal profile of men from a population-based sample in Sao Paulo, Brazil.

Main outcome measures: OSAS was estimated according to clinical symptons and full-night polysomnography.

Methods: The Epidemiologic Sleep Study (EPISONO) was a population-based study of sleep and associated risk factors in Brazil's largest city, Sao Paulo. This study adopted a probabilistic three-stage cluster sampling approach. Polysomnographies and fasting blood samples were collected for all subjects. OSAS diagnosis was defined according ICSD 2. A total of 466 men aged 20–80 years at the time of their enrollment in EPISONO were assessed. The percentage of men who participated in EPISONO, but refused to participate in our study was 2.3%.

Results: The prevalence of OSAS complaints in the study cohort was 41.2% overall. OSAS was significantly associated with higher levels of TSH compared to healthy subjects, even after correction for age and body mass index (Odds ratio: 1.10; 95%CI: 1.01–1.20; $P = 0.03$). Cortisol, testosterone (free and total), progesterone, FSH, LH, prolactin, and estradiol levels did not differ between OSAS and healthy groups, after the adjustment for potential confounders.

Conclusion: OSAS is a relatively common sleep disorder phenomena, especially among men. Since TSH is relevant to the integrity of the hormonal system, the marked increase in TSH levels found in OSAS men could have negative impact in several functions. These findings can provide additional provides progress towards the understanding of the influence of this sleep breathing disorder on thyroid function, and encourage clinicians to evaluate thyroid function in patients with OSAS.

P828

Small vessel disease in patients with obstructive sleep apnoea

J. PRETNAR-OBLAK, A. COPI, M. PRAZNIK, M. ZALETEL, B. ŽVAN, A. KOREN, A. RESMAN-GASPERSIC and L. DOLENC-GROŠELJ
Ljubljana Medical Center, Ljubljana, SI

Objectives: Obstructive sleep apnea (OSA) is a common sleep disorder associated with increased body mass index, metabolic syndrome, hypertension etc. Complications, such as stroke and cognitive impairment are common. Several studies have shown that patients with OSA have small vessel disease. However, they were never compared to controls with similar risk factors without OSA. The aim of this study was to show that OSA is an independent risk factor for small vessel disease. We tested the hypothesis that small vessel disease was more common in patients with OSA compared to controls with similar cerebrovascular risk factors.

Methods: Magnetic resonance imaging of the head was performed in patients with OSA (17 patients, 15 male and two female, aged 51.5 ± 9.8 years) and 16 age- and gender-matched asymptomatic controls with similar cardiovascular risk factors. FLAIR sequences were used to analyse images and Fazekas scale was used for evaluating the severity of small vessel disease. In addition, a partial Fazekas scale was used to evaluate each brain lobe separately.

Results: Significantly less OSA patients had a normal MRI exam - Fazekas 0 (OSA: 29.4% versus controls 53.3%). OSA patients had a higher Fazekas score compared to controls; Fazekas 1 (OSA: 41.2% versus controls 26.7%), Fazekas 2 (OSA: 29.4% versus controls 20.0%). There was a significant difference in the partial Fazekas score in all the lobes, however the biggest difference among the two groups was in the temporal lobe.

Conclusions: Patients with OSA have more small vessel disease lesions with a possible predilection for temporal lobes compared to controls with similar risk factors. OSA is probably an independent risk factor for small vessel disease.

P829

Use of the pictorial Epworth Sleepiness Scale in adults with Down's syndrome

E. A. HILL[1], D. FAIRLEY[1], S. VAN PUTTEN[2], S. COOPER[3], J. F. FORBES[1], L. WILLIAMS[1] and R. L. RIHA[4]
[1]University of Edinburgh, Edinburgh, UK, [2]Down's Syndrome Scotland, Edinburgh, UK, [3]University of Glasgow, Glasgow, UK, [4]NHS Lothian and University of Edinburgh, Edinburgh, UK

Objectives: Adults with Down's syndrome (DS) are predisposed to sleep apnoea (SA), which can manifest as excessive daytime sleepiness (EDS) and behavioural and emotional disturbances. The Epworth Sleepiness Scale (ESS) is a widely-used tool for measuring subjective EDS. The pictorial version of the ESS (pESS) was developed to improve ease of use of the ESS by people with diminished literacy, and so may be suited to persons with intellectual disabilities such as Down's Syndrome (DS). The objective of this study was to assess the usefulness of the pESS in a population of adults with DS.

Methods: A sleep questionnaire, including the pESS, was sent to 650 adults (age ≥ 16 year) with DS and their families/carers living in Scotland. Standard statistical analysis was undertaken using SPSS 17 (Chicago, IL).

Results: Of 288 responses (44%), 257 were valid for analysis (144 males, 111 females, two unspecified). Mean age was 31 ± 11 years (no significant gender difference). BMI was 29.8 ± 7.3 kg/m^2, with females significantly heavier (P = 0.002).

The PESS was fully completed by 222 responders, partially completed by 30 and not completed by five. The mean total score on fully completed pESS was 7 ± 5 out of a possible 24, with males significantly sleepier (P = 0.007). EDS (PESS > 10) was evident in 20% of responders. Seven per cent had a total score of 0. Of the partially completed questionnaires, the most commonly omitted items were: item 1 – ''Sitting and reading'' (77%); item 5 – ''Lying down to rest in the afternoon when circumstances permit'' (27%); and item 3 – ''Sitting inactive in a public place e.g. theatre or a meeting'' (23%). Additional information had been written on 23% of the partially completed pESS questionnaires. Five people noted ''N/A'' or ''don't know'' in response to item 1, one of whom was blind. ''N/A'' or ''don't know'' was noted by four responders with reference to item five, with two reporting that they did not lie down to rest in the daytime. Three responders reported other additional support needs (blindness; cerebral palsy) or generally limited understanding.

Conclusion: This is the first study examining the use of the pESS in an adult DS population. The questionnaire was generally well-accepted, although further investigation of the specific types of error and difficulties encountered during completion is required. Modification of the questions used in the ESS and pESS to improve validity in this specific patient group may be appropriate. The study is ongoing.

P830

The diagnostical importance of polysomnography in children with obstructive sleep apnoea syndrome

I. BURDULADZE[1], A. CHIKADZE[2], L. KHUCHUA[2], M. JIBLADZE[2] and R. SHAKARISHVILI[2]
[1]Research Institute of Clinical Medicine, Tbilisi, GE, [2]P.Sarajishvili Institute of Neurology, Tbilisi, GE

Objectives: The syndrome of obstructive sleep apnea (OSA) is a frequent, albeit under-diagnosed condition in children, which may lead to substantial morbidity if left untreated. At the same time, the role of the overnight sleep study for the diagnosis of OSA is clear. The purpose of the present study was to investigate the night sleep structure in children with OSA using polysomnography (PSG) method.

Methods: Five male children (mean age 8.0 years) with clinical manifestation of OSA (history of loud snoring during three or more nights per week, breathing difficulties during sleep, unusual sleeping positions, morning headaches, daytime fatigue, irritability and behavioral problems) were investigated. All children appeared to have tonsillar hypertrophy found by laryngological examination. All of them underwent a PSG. Sleep questionnaire were completed (with parents' comments) and the main sleep parameters (sleep latency period, sleep efficiency, sleep stages, rapid eye movement (REM), apnea/hypopnea index, awakenings, respiratory arousal index, periodic leg movements, etc.) were calculated in all cases.

Results: There was not found any paroxysmal, pathological activity during day routine EEG and sleep, neither locally nor diffusely in the children. However, the significant changes were revealed in the structural organization of sleep. We found the night sleep organization with normal saturation and low desaturation indexes. According to the PSG report, the main criteria of the sleep study were the following: sleep latency-10 min, REM-22%, II stage-42%, III stage-11%, respiratory arousal-11%, saturation-96%, desaturation index-1, snoring index-38, apnea index-1–2. In particular, the episodes of central Central Apnea (CA) and obstructive apnea (OA) were observed with low indexes (CA Index 1.5–2.5; OA Index 0.2-0.6) in all cases, mainly plagued with EEG-Arousals, snore-arousals and LM-arousals.

Conclusions: 1. Investigation of night sleep by using PSG can help researchers to reveal variability of sleep architecture during the different clinical presentation of OSA in children.

2. PSG study in those children did not establish a clear relationship between tonsillar hypertrophy and frequency of apnea episodes.

3. PSG can help sleep specialists in distinguishing OSA from benign snoring.

4. An overnight PSG including multiple channels aiming to monitor sleep state, as well as EEG, respiratory and cardiac parameters is the only specific diagnostic study of OSA.

P831

Polysomnographic variables in OSAS patients with excessive daytime sleepiness

B. GULBAY, T. ACICAN, F. CIFTCI, M. ERDEMIR ISIK and Z. ONEN
Ankara University School of Medicine, Ankara, TR

Objective: To compare polysomnographic and demographic characteristics of obstructive sleep apnea (OSA) patients with or without excessive sleepiness assessed by Epworth sleepiness scale (ESS).

Method: Eighty-two adult patients (28 F, 54 M) with a diagnosis of OSAS by polysomnography (AHI > 15 /h) were retrospectively assessed in two groups in respect of presence (ESS > 10) or absence (ESS < 10) of excessive daytime sleepiness (EDS) according to ESS score.

Results: Forty-six patients had an ESS score >10. OSAS patients with daytime sleepiness were younger (P = 0.01) and their arousal index and apnea hypopnea index (AHI) were higher (P = 0.017 and 0.042, respectively). Although statistically non-significant, OSAS patients with EDS were more obese and their sleep latency and sleep efficiency in polysomnography were lower. In addition, in OSAS patients with EDS the superficial sleep phase (NREM 1–2) was more whereas deep slow sleep (NREM 3), REM sleep, and average oxygen saturation at sleep were lower (P > 0.05). Thirty of

patients with EDS (65.1%) had nocturnal oxygen desaturation while the same value in the group without EDS was 58.3%. In multiple regression analysis the arousal index, total AHI, and age were all effective in determination of ESS score ($P = 0.002$). As a result, OSAS patients with EDS have a more severe disease, with a worse sleep-associated respiratory pattern and more fragmented sleep compared to OSAS patients without EDS. Rather than a single factor, factors such as severity of OSAS, arousal index, and age are determinants of ESS score that demonstrates the presence of EDS.

P832

Weak associations between insomnia, daytime sleepiness and measures of obstructive sleep apnoea severity were strengthened after adjustment for age, gender and depression in a Norwegian, community-based sample

H. HRUBOS-STRØM[1], I.H. NORDHUS[2], G. EINVIK[1], T. DAMMEN[3] and H. HRUBOS-STRØM[1]

[1]Akershus University Hospital, Lørenskog, NO, [2]University of Bergen, Bergen, NO, [3]University of Oslo, Oslo, NO

Objectives: There is an ongoing debate regarding the association between subjective sleep complaints and measures of objective sleep in obstructive sleep apnea (OSA). The aims of the present study were to assess symptoms of insomnia and daytime sleepiness among participants of the Akershus Sleep Apnea Project (ASAP) and to study associations between these complaints and measures of OSA severity adjusted for age, gender and symptoms of depression.

Methods: A questionnaire was mailed to 30 000 age- and gender stratified Norwegians aged between 30–65 years. The response-rate was 55.72%. A clinical sample of 535 responders (54.58% male, mean age 48.51 years, standard deviation (SD) 11.26) was included in the ASAP. In this study, 17 persons with sleep time <240 min or no REM sleep registered were excluded leaving a study sample of 518. Subjective sleep complaints were evaluated by the Bergen Insomnia Scale (BIS, range 0–42) and the Epworth Sleepiness Scale (ESS, range 0–24). Objective sleep was assessed by in-hospital polysomnography. Depression was assessed by the Beck Depression Inventory (BDI). Associations were evaluated by correlation and multiple linear regression. Age, gender and BDI sum score were all entered in the models.

Results: Mean BIS score was 14.46 (SD 9.55). Mean ESS score was 8.70 (SD 4.23). Both mean scores were approximately 0.50 SDs above Norwegian general population norms. Median Apnea Hypopnea Index (AHI) was 6.35 (Interquartile range 16.63) and mean average oxygen saturation was 94.44 (SD 1.79). Mean BDI score was 7.39 (SD 6.54). In univariate analyses, the BIS score was correlated with average oxygen saturation (Pearsons r = -0.15, $P < 0.005$). The ESS score was not significantly associated with any sleep variable in univariate analyses. In multivariate analyses, BIS score was independently associated with average oxygen saturation, beta (b) = -0.74, (-1.18 to -0.29, $P < 0.01$, adjusted $R^2 = 0.32$). In multivariate analyses ESS score was independently associated with logarithmically transformed AHI, b = 0.67 (0.34–1.00, $P < 0.01$, adjusted $R^2 = 0.13$).

Conclusion: Symptoms of insomnia and daytime sleepiness were independently associated with average oxygen saturation and AHI respectively. Weak univariate associations were strengthened in multivariate analyses. Thus, adjustment for age, gender and depression should be considered when associations between subjective sleep complaints and measures of objective sleep in OSA are assessed.

P833

The co-occurrence of interictal discharges and nocturnal seizures in children with sleep-disordered breathing

S. MIANO, A. TABARRINI, O. VITELLI, A. R. MAZZOTTA, R. CASTALDO, F. BIAGIARELLI and M. P. VILLA

Sapienza University, Rome, IT

Objectives: Sleep breathing disorders (SDB) may trigger paroxysmal events during sleep such as interictal discharges (ID) and pre-existing seizures. We previously found a high percentage of ID and nocturnal seizures in children with sleep apnea syndrome (OSAS). In this study we aimed to confirm and evaluate the natural history of these association.

Methods: Video-polysomnographic studies were performed in a population of children recruited consecutively for suspected OSAS, from April 2009 to March 2010, with no previous history of epileptic seizures. All sleep studies included ≥8 electroencephalographic (EEG) channels. We collected data at the first evaluation and at the follow-up.

Results: We found 61 children who met the criteria for primary snoring, nine of them showed ID, while 122 children met the criteria for OSAS and 19 of them showed ID. In total, 28 out of 183 children with SDB showed ID (15.3%). We did not find differences in sleep respiratory parameters, age and sex, between children with and without ID. Moreover, we found sharp waves over centro-temporal regions in 14 children (group A), dysrhytmic theta activity and spikes and poly-spikes over frontal region in six children, associated with suspected ictal arousals (group B), and slow waves and/or dysrhytmic theta activity with superimposed sharp waves in 8 children (group C). Group C was younger than group A and B (mean age of 4.0 ± 1.2, versus 6.1 ± 0.3, versus 9.6 ± 4.9 years, $P < 0.05$), and had a higher apnea-hypopnea index compared to group A (7.5 ± 4.3, versus 1.8 ± 2.4 events/hour of sleep). The apnea hypopnea index of group B was 20.8 ± 31 events/hour of sleep.

Moreover 37 subjects out of all sample underwent polysomnographic recordings at 6 months or 1 year after treatment, and we found that three out of five children with ID at baseline did not showed ID at follow-up, while five children out of 32 without ID at baseline, showed residual OSAS and ID, with nocturnal seizures in three of them.

Conclusions: We confirm that children with SDB had a higher percentage of ID and nocturnal seizures. Some of them showed ID associated with primary snoring, while others showed ID and/or nocturnal seizures associated with OSAS or with residual sleep disease after treatment. We suppose that the former group may express a simple comorbid between interictal discharges and snoring, while the latter may be a subgroup of children who develop ID and/or nocturnal seizures in relation to sleep respiratory events.

P834

Professional and frequent driving habits in the European Sleep Apnea Database

M. KARIMI, J. HEDNER and L. GROTE for the ESADA

Objectives: Obstructive sleep apnea (OSA) is associated with an increased risk for motor vehicle accidents (MVA's). Current legislation in many European countries list untreated OSA as a condition associated with impaired capability to drive. Treatment of OSA leads to a reduced risk for MVA's. Sleep clinics spend a substantial part of their resources to optimize OSA treatment in drivers. The current study captured license status and driving distance reported by OSA

patients included in the multinational European Sleep Apnea Database (ESADA) cohort.

Method: The ESADA database includes consecutive patients with suspected OSA referred to 23 sleep centers in 16 European countries. Reported parameters were obtained by regular visits at the sleep center in association with an overnight study for OSA diagnosis in 8078 patients. Driving license (DL) status was defined according to current EU driver license classifications (A to E) and mean yearly driving distance was recorded.

Results: Four thousand six hundred seventy-six individuals (males 59% and females 55%) reported exclusively AB license status and 923 (males 15% and females 2%) reported additional CDE status. Males reported a higher yearly driving distance (21.847 ± 478 km versus 10.681 ± 347 km, $P < 0.001$). No DL was reported by 2488 patients (31%). Approximately 63% of patients with severe OSA (AHI ≥30 /h) have a DL. Patients with CDE license tended to be younger, less morbid and used less medication. Measures of central obesity (waist and neck) were slightly elevated in CDE drivers whereas OSA severity and subjective daytime sleepiness were similar in AB and CDE drivers (AHI 24.5 /h and 25 /h, ESS = 10 in both groups, *n*.s). Interestingly, 43% of all patients with a DL were frequent drivers (driven distance >15.000 km/year) and 35% (15%) of all male (female) frequent drivers suffered from severe OSA (AHI ≥ 30 /h).

Conclusion: Information from this large multicentre database suggests that professional as well as frequent drivers with significant sleep apnea are highly prevalent among patients investigated for OSA. Specific considerations in terms of diagnostics as well as treatment initiation and follow-up may be considered among professional or frequent drivers. Classification of driving habits should be included into the clinical routines at sleep centers and prospective outcome studies are warranted.

Support: The ESADA study is supported by enabling grants from RESMED and PHILIPS RESPIRONICS. The ESADA network has been supported by the EU COST Action B 26.

P835

Elevated pancreatic polypeptide and leptin levels in obstructive sleep apnoea: sex differences

F. DELEBECQUE, L. MORSELLI, R. LEPROULT, K. TEMPLE, H. WHITMORE, J. SYKES, D. A. EHRMANN and E. VAN CAUTER
University of Chicago, Chicago, IL

Pancreatic Polypeptide (PP) and leptin are two hormones that play a role in appetite regulation. PP secretion is stimulated by food intake and proportional to caloric content, and is thus involved in the short-term regulation of appetite regulation. In contrast, leptin does not increase significantly after a meal and contributes to the long-term regulation of energy balance. Leptin levels are elevated in obesity, considered as a state of leptin resistance. PP levels are reduced with obesity. PP is also thought to be an indicator of pancreatic vagal tone in the basal state. There is evidence that cardiac sympatho-vagal balance is altered in Obstructive Sleep Apnea (OSA), with a decrease in daytime para-sympathetic activity. We therefore hypothesized that OSA may be associated with alterations of the levels of PP and leptin in obese men and women, which may have an adverse impact on appetite regulation.

Following a night of polysomnography and a 2-h oral glucose tolerance test (OGTT) with sampling at 30-min intervals, obese men ($n = 52$, BMI: 36 ± 7 kg/m^2) and women ($n = 57$, BMI: 39 ± 9 kg/m^2) were divided into those with OSA (men $n = 38$, women $n = 25$) and those without OSA (men $n = 14$, women $n = 32$). Plasma PP and leptin levels were measured by radioimmunoassay (ALPCO, Salem, NH and Millipore, Billerica, MA respectively).

All statistical analyses were controlled for sex, age, race risk, BMI and AHI. Variables were log transformed when appropriate. In women, the presence of OSA was associated with higher circulating PP levels ($P < 0.0001$), and PP levels increased with the severity of OSA (as assessed by the AHI). These findings may reflect increased resistance to PP and its appetite-suppressive effects. In contrast, in men, PP levels were not elevated by the presence of OSA, but instead decreased with the severity of OSA. Sex differences were also observed for the impact of OSA on leptin levels. In men, we detected no significant impact of the presence of OSA. In contrast, in women, increased severity of OSA was associated with higher leptin levels. ($P < 0.03$ for sexxlogAHI interaction).

These findings demonstrate for the first time that the impact of OSA on hormones regulating appetite is greater in women than in men, suggesting a greater risk of weight gain in women.

This work was supported by the NHLBI grant, R01HL75025, by the NIDDK grant P60DK-020595, by the NIA grant PO1-AG11412 and by the NIH grants MO1-RR-00055 and P50 HD057796.

P836

Use of a questionnaire to screen obstructive sleep apnoea in patients evaluated with home sleep studies

R. DUARTE and F. MAGALHÃES DA SILVEIRA
Sleep – Laboratório de Estudo dos Distúrbios do Sono, Rio De Janeiro, BR

Objectives: Full polysomnography (PSG) remains the gold standard to diagnose obstructive sleep apnoea (OSA). However, it is labor intensive and expensive to perform. The aim of this study was to evaluate a screening questionnaire in the diagnosis of OSA obtained by portable monitor (PM).

Methods: Prospective study of adult patients referred to a Brazilian sleep center from January 2008 to February 2012. All patients were studied with PM (ApneaLink Plus – ResMed) and completed a questionnaire named ACHaR. This model has 4 dichotomized variables: snoring, hypertension, neck circumference, and reports of nocturnal gasping/chocking; total score of 0–4 points. A score of two or more points was taken to indicate high risk for OSA. For the diagnosis of OSA and moderate/severe OSA was used a cutoff of apnoea/hypopnoea index (AHI) = 5 and 15 events/h, respectively. Our questionnaire was compared to AHI by receiver operator characteristic curves and area under the curve (AUC). All reported *P* values were two-tailed.

Results: Of 228 screened patients with ACHaR, 91.2% were classified as having high risk and 8.8% were classified as having low risk of OSA. Both prevalence of OSA and prevalence of moderate to severe OSA were different between the two groups (high and low risks): 89.9% versus 50.0% with $P < 0.001$ and 63.0% versus 10.0% with $P < 0.001$, respectively. For OSA diagnosis, ACHaR questionnaire had sensitivity = 94.9%, specificity = 32.2%, positive predictive value (PPV) = 89.9%, negative predictive value (NPV) = 50.0%, accuracy = 86.4%, and AUC = 0.741 (95% CI = 0.640–0.841). For moderate/severe OSA diagnosis, ACHaR questionnaire had sensitivity = 97.7%, specificity = 18.9%, PPV = 62.9%, NPV = 90.0%, accuracy = 65.3%, and AUC = 0.710 (95% CI = 0.641–0.779).

Conclusion: Our questionnaire had good accuracy for OSA diagnosis by PM, showing to be a useful tool in outpatients with suspected OSA.

P837

Proportion of patients with Obstructive Sleep Apnoea among snorers in Bulgaria– a Varna obstructive sleep apnoea survey

M. MILKOV[1] and F. KIROV[2]
[1]*Medical University of Varna, Varna, BG,* [2]*University Hospital, Sveta Marina, Varna, BG*

Obstructive Sleep Apnea (OSA) is a well recognized risk factor for cardiovascular disease and stroke. Bulgaria is leading the list of mortality from stroke in EU. So far there are no published studies on the impact of OSA on stroke incidence in Bulgaria. The aim of this study is to assess the effect of OSA on stroke incidence by setting up a registry of patients with OSA in the rural and urban area of Varna. A database system was created including all out patient referrals with snoring problems and MEZAM or polysomnography performed. From 148 snoring cases (age from 19 to 74), 82% had mild to severe OSA. None of these patients were under specific treatment. Two third (67%) had elevated blood pressure and/or hypercholesterolemia. Only 12% of diagnosed OSA patients accepted CPAP treatment. The preliminary results from the registry suggest a significant importance on OSA on stroke incidence in Bulgarian male population. Follow-up studies are required in order to quantitatively assess the impact of OSA.

P838

Screening for sleep apnoea syndrome and hypersomnolence in Social Security health examination centres by targeting a high-risk population

G. DELORD[1], M. ELBAZ[2], H. GAMBLE[1], D. LÉGER[2], B. VARSAT[1] and O. VERON[2]
[1]*Caisse Primaire d'Assurance Maladie de PARIS, Paris, FR,*
[2]*Université Paris Descartes, Paris, FR*

Objectives: To investigate the feasability of screening for sleep apnea syndrome (SAS) and hypersomnolence (HS) in Health Examination Centres by targeting a population at increased risk (diabetics, hypertensives, and obese subjects). To recommend the subjects identified as being at increased risk to consult a Sleep Centre for further investigation.

Methods: During a routine Social Security health examination, subjects aged 40 years and over completed the Berlin and Epworth questionnaires. Additional questions on medical history, sleep duration and medication were added. Subjects known to have SAS or HS were excluded from the analysis.

All consenting subjects and their General Practitioner (GP) were informed of the results by post. Those identified as being at high risk for SAS with the Berlin questionnaire and/or having an Epworth score >15/24 were encouraged to contact a Sleep Centre for further investigation. After three months, those identified at high risk were asked to complete a short questionnaire on their follow-up investigations.

Results: Five hundred twenty-nine questionnaires were returned, of which 11 were excluded due to known sleep disorders or recent sleep studies. The average age was 53.6 years (SD = 8.4, range = 40–73) and 51.5% were male. The exposed group was defined as subjects with hypertension, diabetes, obesity, or a combination of these conditions (n = 120) and the non-exposed group was defined as subjects with none of the three conditions (n = 398).

73 (14.1%) subjects were identified as being at "high risk" of SAS by the Berlin questionnaire. Among the exposed group, 57/120 (47.5%) were classified as high risk, whereas in the non-exposed group, 16/398 (4.0%) were "high risk"; Odds ratio = 21.39 (95% CI: 11.72 to 40.59). Eighteen subjects (3.5%) subjects had an Epworth score >15/24: 4/120 (3.33%) among the exposed and 14/398 (3.52%) among the non-exposed; Odds ratio = 0.95 (95% CI: 0.31–2.93).

To date, 24 of the 85 high risk subjects have replied to the folow-up questionnaire (response rate = 28%). Seventeen have already consulted their GP, of whom 11 have had sleep studies (seven confirmed SAS: four mild, two moderate and one severe) and three are awaiting further investigation.

Conclusion:

The preliminary results of this study suggest:

1. That screening for SAS and HS is feasible in Health Examination Centres,
2. That sleep explorations are more efficient among a targeting a population at increased risk of SAS.

P839

The trend of familial Aggregation in snoring

J. LIU
Guangxi Sleep Respiratory Disease Centre, Nanning, CN

Objective: To investigate the correlation between snoring in parents and children and to understand the genetic predisposition to snoring.

Methods: A sampling survey of 11 163 residents over the age of 14 from 2862 households was conducted in Guangxi, China, between January 2003 and March 2005. The Odds ratio (OR) of snoring and the epidemiology of obstructive sleep apnoea/hypopnoea syndrome (OSAHS) were evaluated. The survey data were collected by using physical examinations and household questionnaire surveys. Each questionnaire surveyed both respondents and their cohabitants. The first person to complete the epidemiological survey was used as the index to establish the standard family for this study. There were two forms for the standard family: the index person together with his or her siblings (at least two over the age of 14 years) and parents and the index person together with his or her spouse and their children (at least two over the age of 14 years). The extent of snoring was defined according to the evaluation criteria used in china and abroad. Based on the pattern of snoring in the parents, the surveyed families were divided into four groups: group A, no snoring in parents; group B, snoring in fathers; group C, snoring in mothers; and group D, snoring in both parents.

Results: A total of 329 standard families were surveyed. The data showed that there were 168 (51.06%), 118 (35.87%), 18 (5.47%) and 25 (7.60%) standard families in groups A, B, C and D, respectively. The analysis showed that the or of snoring in children gradually increased from 4.3% in group A, to 12.8% in group B, 17.3% in group C and 25.4% in group D. These differences were significant. Further investigation showed that the or of snoring in sons gradually increased from 6.2% in group A to 17.6%, 22.9% and 37.5%, in groups B, C and D, and that this difference was also significant. Meanwhile, the OR of snoring in daughters did not increase significantly. The analysis of the ORs for the standard families showed that when group a was used as a control, the OR of snoring in children in groups B, C and D was 3.25 (95% CI: 1.81–5.84), 4.64 (95% CI: 1.96–10.96) and 7.55 (95% CI: 3.61–15.79), the OR of snoring in children in group D was affected the most,there was no significant difference between groups B and C.

Conclusions: There are trend of familial aggregation in snoring, the sons appear to have higher risk to snoring in families erther snoring in father or mother.

P840

Prevalence of obstructive sleep Apnoea symptoms and risk factors in Armenia

M. PETROSYAN

St. Nerses the Great Medical Center, Yerevan, AM

Objectives: Obstructive sleep apnea (OSA) is a common medical condition with significant adverse consequences. OSA awareness among population and physicians in Armenia is quite low. This study is aimed to estimate the prevalence of OSA symptoms and risk factors in Armenian population, which has not been investigated so far.

Methods: This is a population based cross-sectional study of 1500 randomly selected adults from the capital city and regions of the country. The risk of OSA was assessed by the Berlin questionnaire (BQ). The responders were also asked about the availability of daytime sleepiness, insomnia, chronic medical condition, chronic drug use, nasal congestion, smoking habits and snoring awareness as a sign of serious disease.

Results: Overall 1500 people were interviewed, 818 men (54.5%) and 682 women (45.5%) with mean age of 48.3 ± 15.4 and mean BMI of 28.6 ± 6.4. Based on the BQ criteria 44% of responders were identified as being at high risk of OSA. This risk was significantly higher in men compared to women (49% versus 37% $P < 0.001$). Male gender increased the odds to be at high risk of OSA by 1.6-fold (OR 1.6, 95% CI 1.3–2.0, $P < 0.001$). In both genders OSA risk significantly increased with age, achieving the maximum level of 60% at the age of 50–69 and declining to 45% after the age of 70. Men under 50 were at higher risk of OSA than women (42% versus 19%, $P < 0.001$). After 50 the risk to have OSA was almost the same in men and women (57% versus 56%). Obesity, chronic disease, chronic drug use, nasal congestion and smoking were associated with high risk of OSA. Despite the high prevalence of snoring and OSA symptoms, OSA awareness among responders was extremely low.

Conclusion: The study revealed a high level of OSA symptoms and risk factors among Armenian population. Almost every second male and every third female could benefit from evaluation for OSA. This study may enhance the OSA diagnostics and treatment in Armenia.

P841

Sleep-disordered breathing and its association with depressive syndrome

C. BETANCUR[1], J. CARRILLO[2] and C. VARGAS[3]

[1]San Sebastian University, Concepción, CL, [2]Felix Bulnes Clinical Hospital, Santiago, CL, [3]University of Santiago, Santiago, CL

Introduction: Depression is a highly prevalent disease and is often associated with sleep disorders. On the other hand, there is evidence that the obstructive sleep apnea syndrome (OSAS) is a risk factor for depression. However, there is little evidence on the relationship of sleep-disordered breathing (SDB) in general, with depression. The aim of this study is to examine the association between SDB with the depressive syndrome, through habitual snoring (S) as a symptom marker, and suspicion of OSAS, such as more severe clinical form.

Methodology: We conducted a cross-sectional study with data from the National Health Survey 2009–2010, implemented by the Epidemiology Department of Ministry of Health in Chile. The subjects studied were recorded socio-demographic and anthropometric, and were applied a sleep questionnaire, and the latest version corrected and adapted from the CIDI-SF. We compared the prevalence of depressive syndrome (DS) in the last year between the S (snore all or most days) and non-snorers (nS), and between subjects with suspected OSAS (S-OSAS+) (habitual snoring, nocturnal breathing pauses and excessive daytime sleepiness) and those without suspected OSAS (S-OSAS-), through a chi-square test. Using a logistic regression model adjusted for sex, age, BMI, educational level, smoking and alcohol consumption we examined the association of S and S-OSAS+ with DS.

Results: The population sample was of 5412 subjects with a mean age of 46.6 ± 18.8 years (IQ = 32–61), of which 2198 (40.6%) were men. Of the total sample, 2963 (54.7%) subjects were S, and 2141 (39.6%) were nS, and 213 (3.9%) subjects had S-OSAS+, and 4686 (86.6%) were S-OSAS-. On the other hand, 718 (15.4%) achieved DS score. The subjects S showed higher prevalence of DS than nS (17.2% versus 13.5%, $P < 0.001$) and OR = 1.35 (95% CI, 1.11–1.65). In turn, S-OSAS+ subjects also presented a higher prevalence of DS than S-OSAS- (39.5% versus 14.6%, $P < 0.001$) and OR = 4.14 (95% CI, 2.87–5.96).

Conclusions: Our results show that there is an association between SDB and DS. From a population sample, the S group has a higher risk of DS than nS, and this risk is considerably higher for subjects in group S-OSAS+. This suggests that SDB are an independent risk factor for DS in the adult population in Chile.

A Study Based on National Health Survey 2009–2010, Ministry of Health, Chile.

P842

Behavioural hyperventilation as a cause of central sleep apnoea: a report of three cases

D. PEVERNAGIE[1], A. MARIMAN[2], N. VANDENBUSSCHE[1], E. TOBBACK[2], S. OVEREEM[1], L. DELESIE[2], H. JANSSEN[1] and D. VOGELAERS[2]

[1]Sleep Medicine Centre Kempenhaeghe, Heeze, NL, [2]University Hospital Ghent, Ghent, BE

Central sleep apnea (CSA) is a disorder characterized by repetitive episodes of decreased ventilation due to complete or partial reduction in central neural outflow to the respiratory muscles. Hyperventilation plays a prime role in the pathogenesis of CSA. Chronic heart failure and dwelling at high altitude are classical conditions in which CSA is induced by hyperventilation.

Hyperventilation syndrome (HVS) is a prevalent behavioural condition in which minute ventilation exceeds metabolic demands, resulting in hemodynamic and chemical changes that produce characteristic dysphoric symptoms. HVS is frequently due to anxiety disorder and panic attacks.

Until present, medical literature has focused primarily on daytime symptoms of behavioural hyperventilation. It is currently unknown how HVS may affect sleep. We report on three cases in which behavioural hyperventilation was associated with occurrence of significant CSA, as confirmed by polysomnography (PSG). Case 1 is a 9-year-old girl who suffered from severe insomnia with difficulties initiating sleep. This was consistent with a panic reaction that was conditioned by a previous psychological trauma and that was elicited by fear for going to bed. Hyperventilation started during an initial phase of wakefulness and continued through the subsequent transitions to stage 1 and 2 non-rapid eye movement (NREM) sleep, causing sequences of protracted CSA and severe oxygen desaturation. Case 2 is a 32-year-old man who suffered from nocturnal migraine attacks. An attack triggered a prolonged awakening during which he started to hyperventilate. Respiratory rate increased significantly and repetitive CSA events were observed in subsequent episodes where NREM 1 sleep was re-initiated. Case 3 is a 43-year-old woman who suffered from HVS in the context of generalised anxiety disorder, caused by several stressful life events. PSG demonstrated increase in respiratory amplitude and

baseline oxygen saturation associated with clusters of CSA, throughout the entire sleep period. In all three cases, CSA was not present during normal tidal breathing in steady sleep.

These cases illustrate that behavioural hyperventilation may compromise sleep quality by inducing CSA. Therefore, behavioural hyperventilation should be added to the list of known causes of CSA.

P843

Clinical utility of nocturnal oximetry as a first-line investigation for obstructive sleep apnoea

R. SANEFUJI[1], Z. TIPPU[2], H. LYONS[1] and C. KOSKY[1]

[1]Guys and St Thomas' Hospital, London, UK, [2]Guys, King's and St Thomas' Medical School, London, UK

Objectives: Nocturnal polysomnography (NPSG) is the accepted gold standard investigation for the diagnosis of obstructive sleep apnoea (OSA), but its availability and cost are limiting factors for its use as a first line investigation. Nocturnal oximetry is a validated alternative which is more readily available.

We present our experience of using nocturnal oximetry as a first line investigation in the diagnosis of OSA in a national tertiary referral centre for sleep disorders. This is available to patients in our unit within approximately 14 days as opposed to a 6 week delay in arranging a NPSG.

Methods: One hundred sixty consecutive patients referred with possible OSA underwent nocturnal oximetry at our unit and were followed prospectively. The >4% oxygen desaturation index (ODI) of >10 /h and typical desaturation trace on oximetry were used for diagnosis of OSA.

Results: Average age of 160 recruits was 47.3 years (range 20–81 years) and 49 (30.6%) were female. Body Mass Index (BMI) was known in 109 patients and average BMI was 33.6 kg/m^2 (21.7–63.2 kg/m^2). Average >4% ODI was 19.6 /h (SD 23.5).

87 (54.4%) patients had oximetry results compatible with OSA. Fourty nine (30.6%) had normal oximetry and OSA was excluded. Oximetry was non-diagnostic in 24 (15%), and of these 19 (12.5%) were referred for further investigations (17 NPSG, 1 NPSG and multiple sleep latency test, 1 respiratory study). Three further patients from this group were diagnosed with possible upper airways resistance syndrome and chose treatment with a mandibular advancement splint rather than further investigation. Two patients are awaiting further investigations.

In the 24 patients with non-diagnostic oximetry, average age was 45.6 years (range 25–81 years), and 10 (41.7%) were female. BMI was known in 16 patients and the average was 32.3 kg/m^2 (range 23–62 kg/m^2). The average 4% ODI in this group was 6.9 /h (SD 5.1). In comparison, in the 87 OSA patients, the average age was 47.4 years (range 20–79 years) and 39 (28.7%) were female. BMI was recorded in 61 patients and the average was 35.0 kg/m^2 (range 22.8–63.2 kg/m^2). The average 4% ODI in these were 23.4 /h (SD 25.7).

Conclusion: Nocturnal oximetry is a useful, inexpensive and readily accessible first line investigation in patients with suspected OSA. Only a small proportion of patients required more specialised investigations to confirm or exclude sleep apnoea.

P844

Gender difference in Flow-volume loop in patients with obstructive sleep apnoea/hypopnoea syndrome

M. AL-ABRI, A. AL-KHAROSI, B. JOTHI and M. DIKSHIT

Sultan Qaboos University Hospital, Muscat, OM

Introduction: The pathophysiology of obstructive sleep apnoea/hypopnoea syndrome(OSAHS) is complex and incompletely understood with men are more susceptible for OSAHS compared to women. A narrowed upper airway is commonly seen in patients with OSAHS. A number of parameters derived from the flow volume loops have been studied to evaluate the possible presence of upper airway obstruction, the more promising being FEF50%/FIF50% ratio, FEV1/PEFR ratio(ml/l/min).

Methodology: All patients recruited for the study were diagnosed with obstructive sleep apnea/hypopnea syndrome (OSAHS) after full night polysmnography. Spirometry indices (FEV1, FVC and FEV/FVC) and flow volume curves of the patients were recorded using Medgraphics (Elite Dx, USA) in sitting and supine position. The data were analyzed as whole group and with sub-analysis of aged matched group between men and women.

Results: Fourty-three patients had completed the study (30 men and 13 women). There was no significant difference between the two groups in apnoea/hypopnoea index (AHI)and desaturation index. In the whole group analysis, the study showed significant difference between men and women in standard spirometry indices, FEV1, FVC, and FEV1/FVC ($P < 0.05$) in sitting and supine positions. The data did not show any significant difference between men and women in FEF/FIF50% either in setting and supine position ($P > 0.05$). There was significant difference in FEF/FIF max in supine position ($P = 0.03$) but not in sitting position ($P > 0.05$). In sub-analysis with aged-matched men ($n = 13$) and women ($n = 13$), the results did not show any significant difference in FEF/FIF50% and FEF/FIF max ($P > 0.05$) in both positions. There was also no significant difference in the change Delta) from sitting to supine position in these two parameters ($P > 0.5$) between men and women in either whole group or aged-matched group.

Conclusion: There was no significant difference between men and women in flow-volume parameters.It could be other mechanisms, other than anatomical factor may perhaps contribute to the upper airway obstruction during sleep and that would be the differentiating factor between men and women.

P845

OSA definition, screening and prevention in all ages

A. Y. HESHMAT

ShadyGrove Hospital, Rockville, MA

The primary care physician has grossly under diagnosed Obstructive Sleep Apnea in the general population. More often than not it is specialty making the diagnosis of OSA many years after the initial symptoms have progressed to cause multi-system complications. Therefore the patient's quality of life and cognitive ability could be preserved much longer with early diagnosis and treatment of OSA.

The research data include extensive literature and case studies of the geriatric patient and the complications of OSA. Studies are available that highlight the benefit of CPAP therapy and adherence to the treatment plan. Evidence based data spanning over two decades indicate untreated OSA in the non-demented population causes cognitive impairment, excessive daytime somnolence, and diminished mood thus leading to decreased quality of life. In some instances patients that have been diagnosed with delirium whom are found to have untreated OSA, delirium disappears with CPAP therapy. The frequency of such cases is not known, but the fact that some individuals have dramatic functional and neuropsychometric improvement with CPAP therapy, and the high prevalence of OSA in the elderly is cause for every geriatric physician to be vigilant in the screening for OSA.

Because of the decrease of oxygen saturation and the increase of intracranial pressure during apneic events the elderly patient is at

greater risk for stroke, cardiac arrhythmia, congestive heart failure, and. pulmonary hypertension. Quality of life issues arise, as does depression, risk of falls, and irritability due to daytime somnolence. The importance of early diagnosis of OSA and treatment by the primary care physician are paramount especially in the geriatric population. Many of who already present with decreased quality of life and cognitive impairment caused by OSA.

P846

Correlation of pulmonary function and sleep-disordered breathing parameters in patients with idiopathic pulmonary fibrosis

C. MERMIGKIS, I. BOULOUKAKI, K. ANTONIOU, G. GIANNARAKIS, E. MAUROUDI, V. MONIAKI, N. SIAFAKAS and S. SCHIZA
Sleep Disorders Unit, Heraklion, GR

Objectives: Restrictive pulmonary diseases like Idiopathic Pulmonary Fibrosis (IPF) are characterized by decreased lung volumes that can reduce the upper airway stability and potentially predispose to SDB. Therefore our aim was to correlate pulmonary function testing (PFT) parameters with Apnea-Hypopnea Indices (AHI), overall and during NREM and REM sleep, in newly diagnosed IPF patients.

Methods: Twenty consequent patients (16 males/four females, age 68.5 ± 11 year) with newly diagnosed IPF were included. All had a formal in lab sleep study as well as PFT's before the initiation of any therapy for IPF.

Results: Twelve patients had an AHI above five per hour of sleep indicating underlying SDB. A statistical significant trend was observed between RV and RV/TLC values and REM AHI ($P = 0.07$, r = -0.44 and $P = 0.08$, r = -0.43 respectively). No statistical significant correlations were observed between the other PFT parameters (FEV1%, FVC%, FEV1/FVC, TLC, VC) and AHI indices. DLCO/VA values showed a statistical significant negative correlation with overall AHI ($P = 0.05$, R = -0.50), NREM AHI ($P = 0.04$, r = -0.51) and REM AHI ($P = 0.05$, r = -0.52)

Conclusions: Our results suggest that there is a statistical significant trend between reduced lung volumes and AHI during the vulnerable period of REM sleep. The lack of strong statistical correlations between PFT's and SDB parameters might related to the fact that PFT's routinelly are performed with the patient in the upright and not the supine position.

P847

Respiratory-related and periodic leg movements in patients with obstructive sleep apnoea

I. RUSAKOVA, R. FERRI, C. BASSETTI, I. PISARENCO, D. KUEN, S. FULDA and M. MANCONI
Civic Hospital (EOC) Switzerland, Lugano, CH

Objectives: Leg movements (LMs) are frequent in patients with obstructive sleep apnea syndrome (OSAS). Current giudelines distinguish LMs associated with respiratory events (ResLM) from periodic leg movements (PLM) excluding the former when assessing PLM. The aim of the current study was to describe the time structure and relationship of both types of LMs in patients with OSAS.

Methods: Retrospective chart review of all patients visiting our sleep lab between January 2010 and July 2011, which (1) had undergone full polysomnographic recording, (2) were between 18 to 75 years, (3) had an apnea-hypopnea index (AHI) >20 and oxygen desaturation index >10 with more than half of all apneas being obstructive (4) had >15 LMs/h (leg movements index (LMI)) was performed. We excluded any patient with (1) any medical condition or medication, that could influence LMs or apnea; (2) recordings with artefacts of tibialis anterior or flow for more than 20% of the total sleep time. All leg movements were scored and classifed as respiratory-related, periodic, or isolated LMs according to current WASM-IRLSSG criteria (2006).

Intermovement intervals of LMs were analyzed with distribution mixture analysis. A stepwise linear regression was performed to explore the association of ResLMI to other variables analyzed in this study.

Results: So far, 64 patients were included in this ongoing study (13 M 7 F, 55.81 ± 11.28). Distribution mixture analysis of intermovement intervals (IMI) of all LMs identified 3 classes of LMs which could be distinguished based on their peak frequencies. These were around 5 s, 20 s, and 40 s. The latter class (IMIs ~40 s) could be traced back to the ResLMs, while the 20 s peak corresponds to periodic LMs, also found in patients with restless legs syndrome (RLS). LMs with very short IMIs (~5 s) may be related to wakefulness and arousals.

In the stepwise regression model, both RLS status and AHI were related to ResLMI. Even when controlling for RLS status and AHI, PLM were highly significantly associated with ResLM (incremental R^2 change: 0.35).

Conclusions: Our preliminary results show that ResLMs can be distinguished from periodic LMs based on their time structure (IMI). Importantly, respiratory LMs are found predominantly in patients with periodic LMs suggesting a possible shared trait for increased motor activity during sleep. Irina Rusakova was supported by the ''Swiss Government scholarships for university, fine arts and music schools for foreign students, No: 2011.0632''.

P848

Sleepiness in commercial truck drivers and accident risk - an epidemiological approach

R. CATARINO, J. SPRATLEY, I. CATARINO, N. LUNET and M. PAIS CLEMENTE
Oporto Medical School, Porto, PT

Context: Portugal has one of the highest road-traffic fatality rates in Europe. A clear association between sleep-disordered breathing and traffic accidents has been previously demonstrated.

Objectives: This study aimed to determine the prevalence of excessive daytime sleepiness (EDS) and other sleep disorders symptoms among truck drivers and to identify which individual traits and work habits are associated to increased sleepiness and accident risk.

Methods: We evaluated a sample of 714 truck drivers (244 in a face-to-face interview and 470 with self-administered questionnaires). The questionnaire included socio-demographic data, personal habits, history of previous accidents, the Epworth Sleepiness Scale (ESS) and the Berlin questionnaire.

Results: Twenty percent of drivers had EDS and 29% were at high risk for developing obstructive sleep apnoea syndrome (OSAS). Two hundred sixty-one drivers (36.6%) reported a near-miss accident (42.5% sleep-related) and 264 (37.0%) a driving accident (16.3% sleep-related) in the past 5 years. ESS score ≥11 was a risk factor for both near-miss accidents (OR=3.84, $P < 0.01$) and accidents (OR = 2.25, $P < 0.01$). Antidepressants use was related to accidents (OR = 3.30, $P = 0.03$). We found an association between high Mallampati score (III-IV) and near misses (OR = 1.89, $P = 0.04$).

Conclusion: In this sample of Portuguese truck drivers we observed a high prevalence of EDS and other sleep disorders symptoms. Accidents risk was related to sleepiness and antidepressants use. Identifying drivers at risk for OSAS should be a major priority of Medical-psychological assessment centres, as a public safety policy.

Poster Session - Paediatrics Part II

P849

Antero-posterior changes in the cortical topography during the first three years of life

L. NOVELLI[1], O. BRUNI[1], C. MARZANO[1], E. FINOTTI[2], M. BARUCCA[1] and L. DE GENNARO[1]
[1]University "La Sapienza, Rome, IT, [2]University of Bologna, Rome, IT

Objectives: Sleep EEG frequency bands show striking age-related changes in power and scalp topography. However, most studies have focused on changes occurring during adolescence, which is considered to be a period of important cerebral plasticity and reorganization. In particular, it has been recently reported that slow-wave topography during sleep shows an anterior-posterior gradient. Taking into account that sleep and its electrophysiological counterpart (i.e., EEG) undergo their most important modifications during the early developmental period, the aims of our study were to evaluate the EEG anterior-posterior differences during the first years of life and to analyze the topographic differences in relation to developmental stages.

Methods: Sleep was polygraphically recorded in 29 children aged 0–26 months. A spectral analysis of the sleep EEG was then performed, after a careful rejection of artifact epochs, across the 0.5–25.0 Hz frequency range (frequency resolution = 0.25 Hz). Babies were subdivided into 4 age subgroups: 0–2, 2–4, 4–12, and 12–26 months.

Results: During NREM sleep, a prevalent posterior topography of the delta band was found with no age-related differences. A Group × Region interaction effect was found for the theta band: in the 12–26 months group the theta power greatly increased in all brain areas but with a major representation over the central-frontal scalp areas. This anterior predominance in theta power, discernible from the very early developmental stage, showed a sudden increase and an anteriorization after 12 months of age.

Conclusions: While confirming the posterior distribution of the delta band reported in children of 3 years (Kurth et al., 2011), current results show age-related changes of the theta band that increased in power and showed a posterior-anterior shift. These changes are probably dependent on maturation processes, and suggest that the shift and increase in power of the theta band over the frontal regions might be considered as a marker of normal development.

P850

Childhood narcolepsy with cataplexy is associated with precocious puberty and obesity

F. POLI[1], F. PIZZA[1], E. MIGNOT[2], U. PAGOTTO[1], S. TAHERI[3], E. FINOTTI[1], K. MOGHADAM[1], F. BERNARDI[1], P. PIRAZZOLI[1], A. CICOGNANI[1], L. NOBILI[4], O. BRUNI[5] and G. PLAZZI[1]
[1]University of Bologna, Bologna, IT, [2]University of Stanford, Stanford, CA, [3]University of Birmingham, Birmingham, UK, [4]Niguarda Hospital, Milan, IT, [5]Sapienza University, Rome, IT

Objectives: Childhood narcolepsy with cataplexy (NC) presents specific features that have been partially investigated. We explored the pubertal and metabolic features of childhood NC through a systematic assessment of pubertal staging, body mass index (BMI), and metabolic/endocrine biochemical analyses.

Methods: Forty-three NC children and adolescent, referred to our Sleep Center in Bologna (Italy), were consecutive recruited for a cross-sectional study. Each patient underwent clinical interview, full polysomnographic recordings, cerebrospinal fluid hypocretin-1 measurement, and HLA typing. Height, weight, arterial blood pressure, and Tanner pubertal stage were evaluated. Blood was withdrawn for lipid and glucose profiling. When altered pubertal development was clinically suspected, plasma concentration of hypothalamo-pituitary-gonadal axis hormones were determined.

Results: NC children showed a dramatically higher prevalence of precocious puberty (17%) and overweight/obesity (74%) than the general pediatric population (0.015% and 36%, respectively). Additionally, isolated signs of accelerated pubertal development (thelarche, pubic hair, advanced bone age) were also present (41%). Overweight/obese NC children displayed lower levels of high density lipoprotein cholesterol and higher levels of C-reactive protein when compared to normal weight NC children. NC symptoms, pubertal signs appearance, and body weight gain developed in close temporal sequence.

Conclusion: NC occurring during prepubertal age is associated with precocious puberty and overweight/obesity, suggesting an extended hypothalamic dysfunction. The severity of these co-morbidities and the potential related risks require a multidisciplinary diagnosis and a tailored therapeutic management. We thanks the Italian Narcolepsy And Hypersomniacs Association (AIN) and the nEUroped European project (PHEA).

P851

Influence of prenatal smoking exposure on autonomic nervous activity in sleeping pre-term neonates

E. STÉPHAN-BLANCHARD[1], F. TELLIEZ[1], A. LÉKÉ[2], S. DELANAUD[1], K. CHARDON[1] and V. BACH[1]
[1]Laboratoire PériTox EA4285-UMI01 INERIS, Amiens, FR, [2]Neonatal and Paediatric Intensive Care Unit, Amiens, FR

Background: Prenatal smoking exposure disrupts the development of the central nervous system in neonates and could lead to disturbances in the control of autonomous functions necessary to maintain their homeostasis.

Objectives: Here, we have evaluated the influence of in utero exposure to smoking on autonomic nervous system (ANS) activity in sleeping preterm neonates.

Methods: Overnight polysomnography (EEG, ECG, eye and body movements) was performed at thermoneutrality in preterm neonates (postconceptional age: 33.9 ± 6.0 week, study weight: 1.94 ± 0.49 kg) born to non-smoking (control group, $n = 18$) or smoking (smoking group, $n = 16$, mean consumption: 14 ± 5 cig/day) mothers during pregnancy. Spectral analysis of heart rate variability was used to evaluate ANS activity. Absolute and normalized values of low-frequency (LF) and high-frequency (HF) band powers, as well as the sympathovagal balance (LF/HF ratio) were assessed during active (AS) and quiet (QS) sleep stages.

Results: Heart rate was not modified by prenatal smoking exposure. In both sleep stages, absolute and normalized HF values were significantly lower in the smoking group than in the control group (AS: $P = 0.002$ and $P = 0.001$, respectively; QS: $P = 0.004$ and $P = 0.022$, respectively). Inversely, normalized LF power and the LF/HF ratio were significantly higher in the smoking group than in the control group (AS: $P = 0.001$ and $P = 0.002$, respectively; QS: $P = 0.022$ and $P = 0.006$, respectively).

Discussion: Our results point out a shift in the vagal-sympathetic balance with a decrease in the vagal tone in preterm neonates exposed to maternal smoking during pregnancy. This effect does not depend on sleep stages. The present observations suggest an altered maturation of ANS in these infants, whose development is classically characterized by a progressive increase in vagal activity. These findings raise the question of the repercussions of these ANS disturbances – at what is a critical stage in development – on these infants' vulnerability.

P852

Do pre-term neonates sleep better in incubators controlled with air or skin temperature?

P. DÉCIMA[1], E. STÉPHAN-BLANCHARD[1], L. DÉGRUGILLIERS[2], S. DELANAUD[1], A. LÉKÉ[2], P. TOURNEUX[2], L. GHYSELEN[2], G. KONGOLO[2], G. RAMADAN-GHOSTINE[2], F. MOREAU[2], S. GOUDGIL[2], C. FONTAINE[2], Y. MOUSSA[2], M. BISSUEL[2], C. DEGUINES[2], V. BACH[1] and J.-P. LIBERT[1]

[1]Laboratoire PériTox EA4285-UMI01 INERIS, Amiens, FR, [2]Neonatal and Intensive Care Unit, Amiens, FR

Objectives: Survival of preterm neonates increased when they are nursed at thermoneutrality. Heat power of closed incubators can be controlled from: skin servocontrol (SSC) or air temperature control (ATC). In the literature, comparison of the performance of SSC and ATC has led to questionable data. Some of them showed that SSC increases vasoconstriction, O2 consumption and apneas, but no study was performed on sleep despite its tight interaction with thermoregulatory processes and its importance for preterm neonates. The study aimed at comparing the influence of SSC and ATC on sleep structure and stability.

Patients and methods: Two groups of eight healthy preterm neonates, undergoing routine intensive care, nursed for 7 days in closed incubators using SSC (gestational age: 30.4 ± 0.4 week, birth weight: 1420 ± 259 g) or ATC (gestational age: 30.1 ± 1.3 week, birth weight: 1370 ± 298 g) have been compared. Twelve hour overnight polysomnography was performed at the 6th night of life (N6). Sleep was visually analyzed for stability and structure using total and average durations, percentages and frequencies of active (AS), quiet (QS), indeterminate (IS) sleep stages and wakefulness after sleep onset (WASO) episodes.

Results: No significant difference was found between ATC and SSC groups at N6 for any of the sleep parameters studied. However, total, mean and longest durations of all sleep stages as well as the percentage of QS tended to increase in ATC group (i.e. QStotal = 148 ± 40 versus 118 ± 27 min, QSmean=14 ± 3 versus 12 ± 3 min, QSlonguest = 28 ± 11 versus 21 ± 4 min and QS% = 23 ± 5 versus 20 ± 5%, for ATC versus SSC respectively) and global sleep stage change frequency decreased in ATC as compared to SSC (4.5 ± 0.8 versus 5.2 ± 0.7 h-1, respectively).

Conclusion: The present preliminary study showed that sleep-wake organization and stability tended to be better in ATC compared to SSC during N6 without reaching significance. Increasing the number of infants in each group is required to analyze the influence of incubators' regulation on sleeping neonates. Further investigations need to be carried out on other parameters related to physiology such as arousals and cardiac function.

Support: NR-TECSAN Project (08–006).

P853

Gastroesophageal reflux disease diagnosis in infants previously affected by apparent life-threatening events: 24-h pH monitoring versus anamnestic questionnaire

A. VIGO and S. NOCE

Centro SIDS Regione Piemonte, Torino, IT

Introduction: Paediatric gastroesophageal reflux disease (GERD) is common in infants and children and it's considered one of the most relevant triggers of Apparent Life Threatening Event (ALTE) in infants. Diagnosis of GERD is often based on symptoms presentation. Kleinman (1) reviewed psychometric characteristics and approaches to validation of currently available paediatric GERD questionnaires and demonstrated that the Infant GER questionnaire (I-GER Q) is a reliable, valid and clinically responsive measure of infant GERD symptoms. However, some clinical trials obtained perplexing results of using the I-GERQ-R for diagnosis (2).

Our study evaluated the validity of I-GER Q as a diagnostic questionnaire for GERD in a population of infants affected by previous ALTE comparing questionnaires with pH monitoring results.

Methods: An observational, cross-sectional study was conducted. Two hundred sixty-two infants (median age 10 weeks) affected by previous ALTE underwent 24 h pH monitoring (Ph-day, Memphis). Caregivers of all infants were submitted to I-GERQ. The comparison between ph monitoring results and questionnaire included:

1. Study of correlations between pH-index>5, number of reflux >5 and >15 s and I-GER Q score 2. Association between pH index>5, proximal reflux events and I-GERQ score ≥7.

Results: 1. Correlation between pH-index>5 and I-GER Q score resulted -0.107 (very close to 0). Correlation between number of reflux >5 and >15 s and I-GER Q score was no found.

2. Among 79 patients diagnosed as normal according to the I-GERQ, 22 (22.7%) had a pathological pH index. Among 183 patients diagnosed as pathological according to the I-GERQ, 22 (12%) had a pathological pH index.

Conclusion: The comparison between I-GER Q and pH monitoring results demonstrates that I-GER Q is not a valid instrument to diagnosis GERD in infants affected by previous ALTE.

References:

1. Kleinman et al. The infant gastroesophageal reflux questionnaire revised: development and validation as an evaluative instrument. Curr Gastroenterol Rep. 2006 Jun; 8(3):230–6.
2. Orenstein SR. Symptoms and Reflux in Infants: Infant Gastroesophageal Reflux Questionnaire Revised (I-GERQ-R)-Utility for Symptom Tracking and Diagnosis. Curr Gastroenterol Rep. 2010 Sep 22. [Epub ahead of print]

P854

Effect of regular lights-off time on paediatric sleep health

H. VAHER and M. VELDI

Tartu University Clinic, Tartu, EE

Objective: This study investigates the relation between regular lights off time and pediatric sleep health.

Methods: The Pediatric Sleep Questionnaire for Parents (PSQ) packet was mailed to 1065 families of children aged 8–9 years who were second grade students in Tartu City and County, Estonia. Questionnaires for 763 students/families were returned; response rate of 71.6%. Seven hundred three were properly completed and could be used. Fourty-eighty per cent were female and 52% male. The study was approved by the Tartu University Review Committee

on Human Research; all data was coded for privacy. The Statistica 10 software package was used to analyze the data.

Results: Three hundred forty-six parents said they did not have a regular lights out time for their children (49.2%); 357 (50.8%) did. Ten sleep health variables were significantly ($P < 0.05$) related to lights out regularity. Extra activities in bed besides sleeping occurred in 229 (66.2%) cases of no regular (NRL) lights out and 176 (49.3%) of regular lights out (YRL), $P = 0.0001$. Snoring occurred in 205 (59.3%) of NRL cases and 182 (50.9%) of YRL, $P = 0.03$. Loud snoring occurred in 104 (30.1%) of NRL and 76 (21.3%) of YRL; $P < 0.0072$. Restless sleep was reported in 181 (52.3%) of NRL and 147 (41.2%) of YRL; $P = 0.0031$. Moving to parents bed occurred in 175 (50.6%) of NRL and 144 (40.3%) of YRL; $P = 0.0064$. For moving child to continue breathing, there were 29 (8.4%) for NRL and 16 (4.5%) for YRL; $P = 0.0347$. Frequent difficulties in waking appeared in 64 (18.5%) of NRL and 42 (11.8%) of YRL, $P = 0.0139$. Nightmares occurred in 205 (59.3%) of NRL and 185 (51.8%) of YRL, $P = 0.0476$. Bedtime resistance was found in 100 (28.9%) of NRL and 77 (21.6%) of YRL; $P = 0.0265$. Body rocking occurred in 34 (9.5%) of NRL and 18 (5.0%) of YRL, $P = 0.0154$.

Conclusion: Regular lights-off time has a positive effect on pediatric sleep health. Non-regular lights-out increases the incidence of the related sleep health by an average of 140%. The outliers are nightmares (111%), move child to continue breathing (181%), and body rocking (189%). Given that large numbers of parents practice non-regular sleep times (49.2%), an adjustment to regular lights-off would increase pediatric sleep health.

P855

Usefulness of low dosage melatonin for recording sleep EEG in infants and toddlers

B. GNIDOVEC STRAŽIŠAR and M. PERKOVIC BENEDIK
University Children's Hospital Ljubljana, Ljubljana, SI

Objective: Melatonin has been already succesfully used for sleep EEG recording in uncooperative children. However the dosages used were usually well above the physiologically relevant doses. The aim of our study was therefore to determine the efficacy of low-dose melatonin in obtaining sleep EEG in infants and toddlers.

Methods: Fast-release melatonin was used in 30 unselected uncooperative infants and toddlers reffered to the departement of child neurology for sleep EEG recording. In the first group children recieved 0.1 mg/kg body weight of melatonin orally and in the second group, depending on age, they recieved 1 mg (<1 year of age) or 2.5 mg (1–3 years of age). Both groups were matched to group of 15 infants and toddlers in whom chloral hydrate was used for sleep induction. The main objectives measured were sleep latency and sleep duration.

Results: No difference in the number of children who went to sleep was seen among the groups. Sleep onset latency in the chloral hydrate and melatonin groups were similar (31.1 min ± 13.2 versus 30.3 min ± 12.6 and 23.7 min ± 16.9 respectively, Student paired t-test, $P = 0.89$ and $P = 0.26$ respectively). The same was true for sleep duration (31.1 min ± 17.0 versus 30.1 min ± 33.9 and 27.2 min ± 18.5 respectively, Student paired t-test, $P = 0.94$ and $P = 0.66$ respectively). Two infants vomited after the application of chloral hydrate while in the melatonin groups no significant adverse effects occured.

Conclusion: The study confirmed that low dose fast-release melatonin can be reliably used for obtaining sleep EEG in infants and toddlers. It provides a good alterenative to sleep induction with high dosages of melatonin or chloral hydrate.

P856

The association of socioeconomic status with objective sleep disturbance in normal sleepers from the Penn State Child Cohort: effects of race and gender

S. CALHOUN, A. VGONTZAS, J. FERNANDEZ-MENDOZA, M. BASTA and E. BIXLER
Penn State College of Medicine, Hershey, PA

Objective: Recent research has yielded evidence of the association between obesity, male gender, low socioeconomic status, and minority race on sleep disordered breathing in children. In this study, we investigated the association of objective sleep disturbance with gender, race, and socioeconomic status in a large general population sample of young school age children.

Methods: A random sample of local elementary school children (K-5) was assessed using a two-phased strategy. Three hundred eighty-two preadolescent children (6–12 years) who did not have parent reported insomnia or an apnea/hyponea index ≥1 were selected from a subset of The Penn State Child Cohort ($n = 700$). All children underwent a 9-h polysomnogram, comprehensive neurocognitive testing, detailed medical history, physical examination, and parent completed health, sleep and psychological questionnaires.

Results: Minority race (African American or Hispanic) was significantly associated with increased stage 2 and decreased slow wave sleep (SWS) and low socioeconomic status (SES) with increased sleep latency and stage 2 and decreased total sleep time, sleep efficiency, and% REM sleep. Furthermore, there was a significant race by SES interaction on sleep latency ($P = 0.002$), total sleep time ($P = 0.033$), and sleep efficiency ($P = 0.004$), even after controlling for body mass index, age, and gender. Interestingly, within the minority group, females had less SWS (27% versus 34%) and more stage 2 than males (49.7% versus 42.9%).

Conclusions: These preliminary data suggest that there is a strong association between children of minority race or low SES and objective markers of sleep disturbance. Additionally, minority females had less slow wave sleep than males. Thus, children who live in poor families of minority status are predisposed to impaired sleep that may be associated with vulnerability to cardiometabolic risks.

P857

Sleep duration and its correlates in a Taiwan elementary school

L. CHIA LING
National Taiwan University, Tao-Yuan, TW

Objectives: Sleep plays an important role of the health in the children. The purpose of this study was to estimate sleep duration in Taiwan elementary children, their sleep habits and practices that may affect it.

Methods: This is a cross-sectional, community based study with self-reported sleep questionnaires. Five hundred seventy-five valid questionnaires were analyzed. A questionnaires inquiring about demographical, specific sleep questions and habits.

Results: The study comprised 305 boys (53%) and 270 girls (47%) of grade 4 in elementary school. In sleep behavior, there was 40.5% of children bedtime for the whole group was nine-thirty to ten o'clock in evening on weekdays, there was 3.9% over midnight go to bed, there was 83.6% in the bed within 30 min to fall asleep. The mean sleep duration on weekdays was 8.3 ± 1.22 h and on weekends 9.6 ± 1.92 h, 49.4% were satisfied with their quality of sleep, there was 13.7% feel daytime sleepiness. Times of exercise and sleep quality were significantly related.

Conclusion: The results of this study can provide a high-risk factors affected their quality of sleep, poor quality of sleep at high risk, given appropriate prevention and management.

P858

Prevention of sleep problems in young children in the Netherlands

E. VLASBLOM, B. E. VAN SLEUWEN, M. P. LHOIR and M. M. BOERE-BOONEKAMP
TNO, Leiden, NL

Introduction: In the past few decades young children increasingly sleep less. Persisting sleep problems and a shortage of sleep have a negative influence on the cognitive and emotional development of young children. Furthermore, a consistent relation between a short sleep duration and overweight/obesity has been described for children of all ages.

Methods: In this study we investigate the effect of a primary prevention program of sleeping problems for parents of young infants (0–6 months). Parents are informed by the health nurse about sleep, sleep duration, and the prevention of sleeping problems before their infant is two months old. They also receive a small booklet with written information. The effect of this prevention method on the occurrence of sleep problems and sleep duration on the short and long term (18 months) will be measured in 1200 children and compared with 1200 children who did not receive the preventive information.

Results: Thus far, 1900 children have been included in the study, of which 1176 are in the intervention and 727 are in the control group. The infants' average birth weight was 3504 grams. At baseline the average sleep duration/24 h was 17.1 h and no group differences were observed. Children of twelve months old sleep longer in the intervention group than in the control group, although the difference was not significant (average: 15.4 h). At this age, parents indicate fewer problems in the sleep behaviour of their child, although the difference was not significant. Furthermore, they significantly less often fell asleep in the presence of a parent. Qualitative data of interviews with parents indicate that the preventive information is supportive to parents.

Conclusion: It is important to gain knowledge on the prevalence and prevention of sleeping problems in very young children. The preliminary results indicate a slight benefit of the preventive information, although most outcome measures failed to reach significance. This could be explained by the fact that currently only a small number of children are twelve months old.

This study will yield a method to prevent sleeping problems and to optimize sleep duration in children of 0–18 months.

This project has been funded by ZonMw, The Netherlands Organisation for Health Research and Development.

P859

Psychopathological profile and health-related quality of life in narcolepsy with cataplexy across childhood and adolescence: a case-control study

E. FINOTTI[1], F. POLI[1], F. PIZZA[1], C. FRANCESCHINI[1], O. BRUNI[2] and G. PLAZZI[1]
[1]University of Bologna, Bologna, IT, [2]Sapienza University of Rome, Rome, IT

Objectives: The purpose of our study was to describe the behavioral aspects and quality of life of childhood narcolepsy with cataplexy (NC).

Methods: We performed a case-control study based on self-administered questionnaires in 30 NC hypocretin-deficient patients, 39 epilepsy patients, and 39 healthy controls matched for sex and age.

Results: Our population of children and adolescents with NC showed an increase in internalizing problems in line with previous reports, typically represented by withdrawal and depression symptoms, and somatic complaints. The two patients groups share higher scores than controls for anxiety disorders, attention, social and oppositional-defiant problems. Psychopathological profile in NC were found to be positively correlated with early NC onset, diagnostic delay, nocturnal disturbed sleep, shorter sleep latency and greater number of Sleep Onset REM Periods at Multiple Sleep Latency Test. On the other hand, treatment and disease duration, positively influenced the behavioral evolution. The psychosocial health of pediatric NC also turned out to be worse than in healthy controls, while the physical health showed no significant differences. The internalizing problems adversely affected all areas of the health of NC children, while the duration of disease seemed to improve the functioning at school, suggesting coping strategy.

Conclusions: We found a specific psychopatological profile in a large pediatric NC sample, compared with another neurological chronic disease (epilepsy) and healthy controls. Symptoms of withdrawal, depression and somatic complaints, were specific of NC, and not observed in the two other groups. Effective treatment, and self-awareness of the disease should be promoted in NC children for the positive impact on behaviour and psychosocial health.

P860

Behavioral sleep intervention for adolescents – an effectiveness study

E. J. PAAVONEN, T. HUURRE, O. KIVIRUUSU and T. PARTONEN
National Institute of Health and Welfare, Helsinki, FI

Objectives: The objective of the study was to evaluate the prevalence of sleep disturbances in adolescents and to evaluate the effectiveness of a semi-structured sleep intervention for treatment of sleeping difficulties.

Methods: All students in one high-school aged 16–17 years were screened for short sleep durations, irregular rhythms and clinical symptoms of chronic sleep deprivation. Of the eligible 641 adolescents, 537 (83.8%) participated in the screening phase of the study and 148 of these (23.1%) were willing to participate in the intervention study. The target sample size (>29) was set according to power calculations. The total score for the screening questionnaire was calculated and the 36 most severely symptomatic adolescents were selected to the intervention study. Prior to the intervention, sleep quality was evaluated using an accelometer and a sleep log for 1 week. In addition, the adolescents filled in a questionnaire that evaluated factors that potentially affect sleep quality. The 30-min intervention consisted of individually tailored sleep education, i.e. evaluation of sleep need, circadian typology, and set up of bedtime routines, regular bed-times and wake-up times and avoiding factors that are harmful for sleep (caffeine, alcohol, rigorous exercise, TV, internet and computer games <1 h before bedtime) as well as positive support and motivating. The aim was to lengthen average sleep duration by 1 h. The main outcome variables were sleep duration and sleep quality as evaluated using accelerometers and self-reported sleep quality including the bedtimes and insomnia as well as daytime symptoms, such as tiredness, anxiety and perceived using standardized questionnaires. The follow-up time was 2 weeks.

Results: Sleeping difficulties were prevalent: 39% of the adolescents suffered from chronic lack of sleep, and 40% reported daytime tiredness. More than half (55%) reported irregular diurnal rhythms and 46% slept <7 h/night during the week days. Sleep onset problems were reported by 15%, nocturnal awakenings by 13% and non-restorative sleep by 16% of the adolescents. The intervention improved sleep quality ($P < 0.001$), and reduced perceived stress and anxiety ($P < 0.001$).

Conclusions: Sleep disturbances and chronic lack of sleep are prevalent among adolescents aged 16–17 years of age. A short behavioural sleep intervention can be effective in improving sleep quality and mood among adolescents.

P861

Assessment of autonomic cardiovascular control in critically ill pre-term infants during the first days of life

V. GOLDER, M. HEPPONSTALL, S. YIALLOUROU, A. ODOI and R. HORNE

Monash Institute of Medical Research, Melbourne, AU

Objective: Autonomic cardiovascular function can be assessed non invasively by measuring heart rate (HR) and blood pressure (BP) and calculating autonomic markers – heart rate variability (HRV), blood pressure variability (BPV) and baroreflex sensitivity (BRS). Cross-sectional studies using these techniques to examine autonomic function in preterm infants have shown that HRV, BPV and BRS increase with increasing gestational age (GA) and postnatal age. However, there have been no studies examining the first days after preterm birth which are critical period of cardiovascular instability for infants as the circulation changes from fetal to neonatal configuration. We hypothesised that immaturity of cardiovascular control will manifest as reduced HRV, BPV and BRS, in preterm infants born at younger gestational ages in the first few days after birth. In addition we speculated that impaired cardiovascular control could be used as a marker of circulatory failure such as is manifest as hypotension.

Methods: We recruited 23 preterm infants (11M/12F) who had arterial catheters. Infant were born between 23 and 35 weeks GA (mean 27 ± 0.6 weeks) with birth weights ranging from 512 to 1815 g (mean 887 ± 68 g). Apgar scores ranged from 1 to 8 (median 5) at 1 min and 2–9 (median 6) at 5 min. Infants were studied longitudinally over the first 3 days of life. HRV and BPV were analysed beat to beat in the time domain in 2 min epochs of artifact free data during active sleep. Data were compared with one way ANOVA.

Results: HR and BP variability measures and BRS were not different between the 3 days of study so data were combined. GA was correlated with all HRV indices but not BPV or BRS. Nine babies were given inotropes. Gestational age between the inotrope group and the non inotrope group was not different. SBP was lower in the inotrope group (40.7.5 ± 1.5 versus 47.1 ± 1.5 mmHg, $P < 0.05$). BRS was also lower in the inotrope group (3.8 ± 0.8 versus 6.9 ± 1.6 ms/mmHg) but this was not significant as was HF/LF HRV (5.5 ± 1.3 versus 12.4 ± 2.8, $P < 0.05$).

Conclusions: In the first 3 days after birth, infants receiving inotropes had significantly impaired cardiovascular control compared to those who did not receive treatment,indicating that these infants are at increased vulnerability to circulatory instability. Further studies are required to identify if measures of cardiovascular control can be used clinically to identify infants at risk of hypotension.

P862

Mini-KiSS – effectiveness of a parent sleep training for toddlers and young children

A. A. SCHLARB and I. BRANDHORST

University of Tübingen, Tübingen, DE

Objective: Sleep problems are common in young age. Especially sleep onset problems as well as problems sleeping through the night show high prevalence rates among young children. Most often children suffer from behavioural insomnia. Besides the risk of chronification negative effects on mental development are common. Children with sleep problems often suffer from behaviour problems and show lower learning outcomes. In addition, childhood sleep disorders are correlated with maternal depression, higher maternal stresslevel and lower quality of life. Therefore, we developed a parent training for young children suffering from sleep problems. Mini-KiSS is a multimodal short-term group intervention program for parents of children of 6 months to 4 years of age, consisting of six sessions.

Method: Therapy conditions were treatment group, or a waiting list control group. Till date, 38 parents participated in the study, all children suffered from insomnia. Data of post-measurement, 3 months katamnesis and 6 months after training are available.

Results: The results indicated that Mini-KiSS was more effective in improving sleep problems than waiting list control-condition. Furthermore, Mini-KiSS showed a significant improvement on mothers of the treatment group concerning depressive symptoms. The mothers felt less depressed after treatment and less aggressive as well as lower somatisation symptoms.

Conclusion: Mini-KiSS as a parent treatment was found to be effective in improving sleep problems in young children and depressive symptoms among mothers.

P863

KiSS – learning how to sleep well with Kalimba the leopard: long-term effects of a manualized structured sleep intervention programme for children

A. A. SCHLARB and J. WAGNER

University of Tübingen, Tübingen, DE

Objective: Insomnia in childhood is common among preschool and elementary school children. Till date, structured manualized treatment programs for children suffering from behavioural insomnia are missing. First effects of KiSS showed significant improvements of the KiSS training compared with a control group (Schlarb et al., 2011). Data of mental improvements will be demonstrated.

KiSS is a multimodal group treatment for children 5–10 years suffering from insomnia, behavioural insomnia and nightmares based on cognitive behaviourtherapy and imaginary or hypnotherapy elements.

Method: Therapy conditions were treatment group, or a waiting list control group. Till date, 45 children and their parents participated in the study, all children suffered from behavioural insomnia. Data of post-measurement, 3 months katamnesis and 6 months after training are available.

Results: The results indicated that KiSS was more effective in improving sleep problems than waiting list control-condition. Furthermore, KiSS showed a significant improvement on children of the treatment group concerning mental symptoms. Effects were stable after 3 and 6 months after training.

Conclusion: KiSS as a structured child oriented treatment was found to be effective in improving behavioural insomnia and behaviour symptoms in children.

P864

What parents know about sleep: results of a German community survey

A. A. SCHLARB[1], B. SCHWERDTLE[2] and A. KÜBLER[2]
[1]University of Tübingen, Tübingen, DE, [2]University of Würzburg, Würzburg, DE

Introduction: To prevent sleep disorders in children it is necessary to early recognize sleep problems. But only 18.9% of parents of children with sleep problems ask their pediatrican for help (Blunden et al., 2004). Therefore, it is important to widely provide information about children′s sleep for parents. But what do they already know about healthy and disturbed sleep and sleep behavior? To get an impression about the existing knowledge in Germany, we surveyed parents about children′s sleep in general.

Methods: Knowledge about children′s sleep was recorded in a sample of 377 parents of preschool and school children.

Results: In total parents, correctly answered 69% of the questions, 12% of the questions have been answered wrongly and 19% have been answered with 'I don′t know'. There was a positive correlation between right answers and having a child with a sleep disorder and a negative correlation between the answer 'I don′t know' and having a child with a sleep disorder. Parents with a sleep disorder were more likely to have a child with a sleep disorder. Also, high perceived self-efficacy positively correlated with right answers and negatively correlated with the answer 'I don′t know'. Moreover, there was a negative correlation between high perceived self-efficacy and parents' sleep disorders as well as children′s sleep disorders. High education was positively correlated with correct answers.

Conclusion: Most parents know a lot about sleep in childhood. Parents with information deficits are more likely to have a child with sleep problems.

P865

Night awakenings at 5–8 months of age: prevalence and associations with maternal and infant's characteristics

M. GONÇALVES[1], A. R. COSTA[2], S. CORREIA[2], C. GUILLEMINAULT[3] and H. BARROS[2]
[1]Instituto do Sono, Porto, PT, [2]University of Porto, Porto, PT, [3]Stanford Sleep Medicine Center, Stanford, US

Objectives: To estimate the prevalence of night awakenings in infants with 5–8 months of age and its association with maternal and infant's characteristics.

Methods: A subgroup of 1363 singleton infants from the Portuguese birth cohort, 'Generation XXI, was evaluated at the 6 months follow-up. At birth, interviewers collected data on maternal and pregnancy characteristics, and neonatal data and anthropometry retrieved from medical records. With structured questionnaires, data regarding infant's health and care, particularly sleeping habits, were obtained. Presence of night awakenings was considered if occurring at least three times per week and two or more times per night. Odds ratios (OR) and 95% confidence intervals (95% CI) were estimated using logistic regression.

Results: The prevalence of night awakenings was 26% (24% in girls; 28% in boys, $P = 0.078$), with no significant differences across the age span ($P = 0.718$). In girls, night awakenings were associated with higher maternal age (≥35 versus <25 years: OR = 2.2, 95% CI = 1.2–4.1), family income 1001–1500€/month: OR = 0.5, 95% CI:0.3–0.9), current breastfeeding at request or at fixed schedule (OR = 4.6, 95% CI = 2.9–7.2; OR = 2.3, 95% CI = 1.4–3.8, respectively), sleep all night in parents' bed (OR = 2.4, 95% CI = 1.4–3.9) and need of parental intervention or physical proximity to fall asleep (OR = 2.1, 95% CI = 1.2–3.7; OR = 4.2, 95% CI = 2.3–7.7, respectively), and inversely associated with grandparents or nursery care during day (OR = 0.3, 95% CI = 0.2–0.6; OR = 0.3, 95% CI = 0.1–0.7,respectively). In boys, night awakenings were associated with higher maternal age (≥35 versus <25 years: OR = 1.9, 95% CI = 1.0–3.6), current breastfeeding at request or at fixed schedule (versus never/not currently breastfeeding: OR = 3.4, 95% CI = 2.3–5.2; OR = 2.8, 95% CI = 1.8–4.5, respectively), difficulties in feeding (OR = 2.0, 95% CI = 1.3–3.2) and calming the child when crying (OR = 2.0, 95% CI = 1.1–3.3), move to parents' bed during night or sleep in parents' bed all night (OR = 4.1, 95% CI = 1.6–10.3; OR = 2.0, 95% CI = 1.2–3.4), and need of parental intervention or physical proximity to fall asleep (OR = 1.8, 95% CI = 1.1–3.0; OR = 3.8, 95% CI = 2.2–6.7, respectively).

Conclusion: At a mean of 6 month of age, gender, falling asleep and sleep habits, and feeding habits during the night, are significantly related to awakenings from sleep.

P866

The relationship between sleep slow oscillation and cognitive performance in children

O. BRUNI[1], M. KOHLER[2], L. NOVELLI[1], D. KENNEDY[3], K. LUSHINGTON[2], J. MARTIN[4] and R. FERRI[5]
[1]University 'La Sapienza', Rome, IT, [2]University of South Australia, Adelaide, AU, [3]University of Adelaide, Adelaide, AU, [4]Respiratory and Sleep Medicine, Women's and Children's Hospital, Adelaide, AU, [5]Oasi Institute for Research on Mental Retardation and Brain Aging, Troina, IT

Objectives: Based on recent reports of the involvement of cyclic alternating pattern (CAP) in cognitive functioning in young adults (Ferri et al., 2008; Aricò et al., 2010), the aims of this study was to evaluate the association between CAP and cognitive function in order to test the hypothesis that CAP rate during the night correlates with cognitive performances in children.

Methods: Forty-two healthy children aged 3–12 years underwent standard polysomnography and neurocognitive assessment. The neurocognitive tests were the Stanford Binet Intelligence Scale (5th edition) and a Neuropsychological Developmental Assessment (NEPSY). Sleep scoring and CAP analysis were performed following the standard criteria (AASM, 2007; Terzano et al. 2001). Correlation and regression analysis were performed between CAP parameters and neurocognitive tasks scores were assessed.

Results: Fluid reasoning ability was positively associated with CAP rate, particularly during SWS and with A1 total index and A1 index in SWS. Regression analysis, controlling for age and SES, showed that CAP rate in SWS and A1 index in SWS were significant predictors of nonverbal fluid reasoning, explaining 24% and 22% of the variance in test scores, respectively.

Conclusion: These results confirm our initial hypothesis that CAP A1 is related to better cognitive functioning, whereas A3 is associated with worse cognitive functioning. This data supports the idea that slow oscillations on the EEG during sleep play an important role on cognitive processes.

P867

The relationship between sleep duration and inflammatory markers in Korean adolescents

Y. J. LEE[1], J. K. SEOG[2], I.-H. CHO[1] and L. WEONJEONG[3]
[1]Gachon Medical School Gil Hospital, Incheon, KR, [2]Seoul National University, Seoul, KR, [3]Ewha Woman's University, Seoul, KR

Purpose: Insufficient sleep has been known to cause an increase in inflammation responses. Current study aimed to assess the relation of sleep duration to inflammatory markers in Korean adolescents.

Methods: One hundred six adolescents (male: 26, female: 80, mean age 17.1 ± 0.8) participated in the present study. Sleep variables were measured by actigraph on their nondominant wrist (Mini–Mitter Co.). Plasma interleukin-6 (IL-6), interleukin-1 beta (IL-1 β), tumor necrosis factor-alpha (TNF-α), and leptin level were measured by ELISA. Depressed mood was assessed by Beck Depression Inventory (BDI). Partial correlation analysis with controlling for confounding variables was conducted. SPSS version 17.0 was used for statistical analysis.

Results: For all participants, mean total sleep time (TST) in weekday was 5.9 ± 1.2 h, and mean TST in weekend was 8.7 ± 1.8 h. Mean time in bed (TIB) in weekday was 6.2 ± 1.7 h, and mean TIB in weekday was 8.7 ± 1.7 h. After controlling for age, gender, body mass index (BMI) and BDI score, plasma IL-6 level was positively correlated with TIB and TST in weekend ($r = 0.275$, $P = 0.018$; $r = 0.269$, $P = 0.021$, respectively). TST in week day was inversely correlated with plasma leptin level ($r = -0.260$, $P = 0.025$). There were no significant relations of sleep variables to IL-1 β or TNF-α.

Conclusion: Current results suggest that insufficient sleep indicated by longer sleep duration during weekend could be associated with an increased inflammation in adolescents. In addition, sleep duration during adolescence might be related to obesity.

P868

Sleep and body mass index in Italian children and adolescents: a self-report study

M. MARTONI, M. FABBRI, A. ERBACCI, L. TONETTI, A. SPINELLI and V. NATALE
University of Bologna, Bologna, IT

Introduction: An association between short sleep duration and increased adiposity in children and adolescents has been observed, while in adults the data are more controversy. In these studies the individual sleep need has not been usually considered. We put forward the hypothesis that the individual sleep need could act as moderator between total sleep time and body mass index (BMI). The present pilot study examine this hypothesis. To this aim we collected body mass index (BMI) in children and adolescent, and sleep duration during schooldays, during weekend, and the ideal sleep duration as possible expression of sleep need.

Method: Seven hundred and forty-one students ($n = 394$, age range 9–12 years; $n = 347$, age range 13–22) reported their sleep onset and rise times during school days and weekend; students were also requested to refer ideal sleep onset and rise times. These times allowed us to determine school days, weekend and ideal sleep durations. The height and weight of all participants were also measured in order to calculate BMI. According to BMI cut-offs (Cole et al., 2000, 2007) the children and adolescents were classified as underweight (7.15%), normal weight (69.64%), overweight (18.89%) and obese (4.32%).

Results: Analysis was conducted on two BMI groups: normal weight and overweight (obese were included in this last group). An analysis of variance (ANOVA) with the BMI group (normal weight versus overweight) and Age group (children versus adolescents) as between subjects factors, and Sleep condition (school, weekend, ideal) as within subject factor was performed on mean sleep duration. The ANOVA showed a significant effect of Sleep condition, reflecting a linear increase of sleep duration from school days to ideal condition. The Sleep condition interacted with Age group, suggesting a small amount of sleep in adolescence compared to childhood. In children group we found a significant triple interaction indicating that normal weight and overweight differed for the ideal sleep duration.

Conclusion: Both in children and adolescents the sleep need is greater than the actual sleep, and such difference is larger in adolescent group. However the ideal sleep seemed modulate BMI only in children group. It possible that these results derived from social and biological Zeitgeber changes (masking effect). Longitudinal studies and the use of objective measures of sleep will be necessary to further study our hypotheses.

P869

Clinical characteristics of restless legs syndrome in children

Y. INOUE, Y. KOMADA and N. FURUDATE
Tokyo Medical University, Tokyo, JP

Objectives: Restless legs syndrome (RLS) is a pathological condition mainly appears in adulthood, but a considerable number of children suffer from the disorder. Some reports have indicated that RLS in children may cause attention deficit hyperactivity (ADHD) like symptom. However, the relationship between ADHD like symptoms and symptomatic characteristics of child RLS as well as the treatment strategy for child RLS has not been clarified. Considering these issues, we made a study on the clinical characteristics of child RLS and the outcome for both RLS symptom and its related daytime dysfunction after treatments mainly with iron administration.

Methods: Consecutive 25 child RLS patients (M:F = 6:19, mean age at the investigation: 12.3 years old) who had regularly taken treatment drugs for the disorder for more than 3 months were subjected in this study. Before starting treatment, baseline information of the patients including demographic variables, symptomatic measures, serum ferritin levels, polysomnographic variables, ADHD symptom measure (ADHD-RS-IV) and quality of life (QOL) measure were assessed. The ADHD-RS-IV scores and QOL scores were also obtained from 28 control children without having any sleep disorders or psychiatric disorders (M:F = 10:18, 13.2 years old). In the RLS affected children, the symptom, ADHD-RS-IV score and QOL score were reevaluated after the treatments (iron alone = 8, clonazepam and iron = 9, pramipexole and iron = 6, clonazepam alone = 2) on RLS.

Results: The ADHD-RS-IV score and QOL score of the child RLS patients before treatment were significantly worse than the scores of the controls, and both of these scores were significantly correlated with the daily duration of RLS symptom. Before treatment, serum ferritin levels were lower than 50 ng/ml in 22 patients (88%), and the RLS symptom completely disappeared with iron alone, iron plus clonazepam or iron plus pramipexole in 14 patients (56%). After the treatment, both ADHD-RS-IV score and QOL score of the patients were clearly improved.

Conclusion: Our result suggested that RLS affected children may have deteriorated QOL and ADHD like symptom, and that these daytime dysfunction may appear along with the prolongation of daily duration of RLS symptom. Of note, iron deficiency seems to play a important part of the occurrence of the disorder, and iron supplementation should be considered as one of the candidate for the first line treatment for child RLS.

P870

Sleep problems associated with psychological stress among children and mothers in low-dose radiation area of Fukushima

M. TAKAHARA, M. TOMINAGA, R. TAKAYA and Y. TSUTSUI
Fukushima University, Fukushima, JP

After the Great East Japan Earthquake on March 11, 2011, Fukushima has been facing a very serious threat of radioactive materials especially in the coast area. However, also inland, families including small children are still suffering from psychological stress, although there were less physical damages by the earthquake itself. Human-made catastrophes involving toxic exposures that have the potential to harm population health, especially radiation exposure, have an even more severe and relentless psychological impact than natural disasters, in that it will have non-transient effect. The purpose of this study was to examine psychological stress and associated sleep problems among elementary schools, kindergartens and nursery schools in Fukushima using questionnaire.

The survey was conducted in June, 2011. About 1300 parents (most of them were mothers) in Fukushima city and Koriyama city have fulfilled computer-scoring questionnaire; both cities are in Fukushima prefecture and contaminated by low-dose radioactive materials. The questionnaire included selected items of children's stress responses, parents' stress responses, children's sleep habits questionnaire (CSHQ; Owens et al., 2000) and defensive behaviors from radiation. Parental stress scores were highly correlated with children's stress behavior scores, especially distraction and difficulty in concentrating. Children's stress responses score were moderately correlated with CSHQ score and parents' stress score. Children's sleep problem scores were high in sleep anxiety and daytime sleepiness. It is suggested that parents' stress were substantially associated with children's mental and physical condition in Fukushima.

P871

Sleep-wake cycle disturbances in children with attention deficit hyperactivity disorder – preliminary results

T. ADAMOWICZ[1], T ANACLETO[1], L. SIMOES[1], M CORDEIRO[2], A. C. FARIAS[2] and F. LOUZADA[1]
[1]Federal University of Parana, Curitiba, BR, [2]Pele Pequeno Principe Institute, Curitiba, BR

Objectives: The objective of this study was to compare sleep-wake cycle patterns of boys with Attention Deficit/Hyperactivity Disorder (ADHD) to healthy controls.

Methods: Nine boys diagnosed with ADHD according to DSM-IV, mean age 8.78 years (0.67), were compared to 11 healthy boys, mean age 9 (0.63) years. All the children were students from public schools of Curitiba, Southern Brazil. For both groups, exclusion criteria were IQ < 70 and current usage of stimulant medication. During seven consecutive days, boys wore actigraphs and their parents filled sleep logs. Rest/activity parameters (L5, M10 and RA – relative amplitude) were also analyzed. L5 is the sequence of the five least active hours in the 24-h average activity profile; M10 is the sequence of the ten most active hours in the 24-h average activity profile; RA is a proportional measure, giving a ratio of activity during L5 to activity during M10. Data of both groups were compared by means Student's t-test. A P value <0.05 was considered statistically significant. Dependent variables were sleep onset, offset, duration and efficiency, L5, M10 and RA.

Results: Boys with ADHD showed shorter sleep duration [433.8 (65.6) × 513.4 (23.5); t(18) = 3.76; $P = 0.001$] and shorter sleep efficiency [86.1 (5.5) × 95.8 (2.7)%; t(18) = 5.2; $P < 0.001$] than controls. There was no difference when sleep onset [11:28 pm (53 min) × 10:33 pm (68 min) × t(18) = -1.94; $P = 0.07$; ADHD × controls] and offset [7:52 am (72 min) × 7:33 am (62 min); t(18) = -0.65; $P = 0.52$; ADHD × controls] were compared. On activity parameters analysis, it was detected higher L5 values on ADHD group [11.02 (2.13) × 7.85 (1.88); t(18) = -3.5; $P = 0.002$], indicating greater nocturnal activity. For the RA, the ADHD group had lower values than the control group [0.91 (0.03) × 0.93 (0.02); t(18) = 2.6; $P = 0.018$]. There was no difference between groups on M10 analysis [232.3 (43.77) × 236.1 (36.4); t(18) = 0.22; $P = 0.83$; ADHD × controls, respectively].

Conclusion: In our sample, ADHD boys showed sleep/wake cycle disturbances when compared to healthy boys, including a reduction of RA, which suggest a reduction of the strength of circadian rhythms in these patients.

P872

Does sleep insufficiency impact executive function and academic performance among high school students?

E. SHILOH and M. COHEN-ZION
The Academic College of Tel Aviv-Jaffa, Tel Aviv-Jaffa, IL

Objectives: Among westernized societies, it is recognized that the adolescent's main 'occupation' is that of a student, i.e. to learn. High school students spend on average 30–35 h/week in class and an additional 4–5 h/week doing homework. Thus, being a student is a full-time job, requiring significant, physical, psychological, and cognitive energies. Sleep is a vital necessity for optimal levels of cognitive function, including attention, learning, memory, and higher order executive functions and inevitably has significant influence on academic functioning during adolescence. As part of a larger study exploring the functional consequences of inadequate sleep on teens in Israel, we examined the possible links between sleep loss, daytime sleepiness, executive functions and school performance.

Methods: One hundred and seventy-three high school students [mean age = 16.2 (±0.8); 103 F] were administered the Hebrew versions of the School Sleep Habit Survey, which includes a measure of academic performance, and the Behavior Rating Inventory of Executive Function – Self Report.

Results: Teens reported a mean weekday total sleep time (TST) of 7.0 h (±1.1), with increasing age and female gender being associated with less sleep ($P < 0.01$ and $P < 0.001$, respectively) and more daytime sleepiness ($P < 0.05$ and < 0.001, respectively). Multiple linear regressions indicated less sleep and increased sleepiness were also associated with higher global executive function scores (i.e. lower ability), and reduced performance on indices of meta-cognition and behavioral regulation (all $P < 0.001$). After adjusting for age and gender, these predictors explained 24.6% of the variance in global executive function ($P < 0.001$). In addition, lower TST was associated with lower math grades ($P < 0.05$) while greater sleepiness was associated with lower English grades ($P < 0.05$) and both were associated with problematic sleep-related behavior (e.g. truancy, falling asleep in class; $P < 0.001$) and lower average grades ($P < 0.05$).

Conclusions: The sleep loss and sleepiness seen in this sample of Israeli high school students is consistent with worldwide data. Furthermore, lack of adequate sleep and associated sleepiness may have a vast effect on higher executive functioning, essential for successful academic performance. These findings suggest a clear need for increasing awareness and education on the consequences of sleep insufficiency on adolescents' academic functioning.

Poster Session – Assessment and Consequences of Sleepiness

P873

Sleepiness and motor vehicle accidents in Portuguese drivers

M. GONÇALVES[1], A. R. PERALTA[2], J. MONTEIRO FERREIRA[3] and C. GUILLEMINAULT[4]
[1]Instituto do Sono, Porto, PT, [2]Santa Maria Hospital, Lisbon, PT, [3]Centro de Estudos de Doenças Respiratórias e Alérgicas, Coimbra, PT, [4]Stanford University Sleep Disorders Clinic, Stanford, US

Objective: The aim of this study was to evaluate the prevalence of sleepiness while driving and sleep related accidents in a representative sample of Portuguese drivers.

Methods: Nine hundred Portuguese drivers representative of the habitual driver population were investigated by phone interview. Structured questionnaires included demographic variables, questions about the occurrence of sleep related car accidents or near misses and sleepiness while driving and episodes of falling asleep at the wheel within the last year, were applied. Pittsburg Sleep Quality Index (PSQI), Berlin questionnaire, Epworth Sleepiness Scale (ESS) were also performed. We considered a new variable 'sleepy driving' defined as having experiencing sleepiness or fallen asleep at the wheel during the previous year. Prevalence comparisons between groups were made using chi-square statistics ($P < 0.010$).

Results: Mean [standard deviation (SD)] age was 42.0 (14.8) and a mean BMI of 25.4 (4.0). ESS mean was 5.4 (3.8), PSQI mean of 4.89 (3.1) and 10% had high risk of OSAS. In this sample, 23.1% of the sample recalled at least one time of drowsy driving within the last year and 3.1% fell asleep at the wheel. In addition, 1.6% reported a near miss accident due to sleepiness within the last year and 0.7% recalled an accident due to sleepiness during the same period.

Sleepy driving was more frequently reported in younger age groups ($P < 0.001$), subjects driving longer distances ($P < 0.001$), higher socio-economic status ($P < 0.001$), higher educational levels ($P < 0.001$), ESS score >9 ($P < 0.001$), <6 h of sleep ($P < 0.001$), high risk of sleep apnea ($P = 0.005$), higher amount of caffeinated beverages ($P = 0.005$). Twenty-one percent of the subjects experiencing a sleep related near miss and 14% of subjects having episodes of falling asleep at the wheel also had a sleep related car accident. Only 1% of subjects never reporting near misses and 1% of subject that never falling asleep at the wheel reported sleep related accidents ($P = 0.001$ and $P = 0.003$ respectively).

Conclusion: Sleepiness while driving and near misses accidents are frequent among a representative sample of Portuguese habitual drivers. Although the self-reported sleep related car accidents is substantial, it is probably under-evaluated as drivers who died or have serious injuries are underrepresented. This high prevalence, also found in other population based studies, calls for the need to implement better educational measures.

This study was performed with the help of the Portuguese Sleep Association and suported by educational grants from Colunex, Praxair and Volkswagen.

P874

Excessive sleepiness and sleep disorders in professional pilots of commercial aviation

C. CHAUFTON[1], S. ROYANT-PAROLA[2], P. DOIREAU[3], P.-E. BERTRAN[3], M. MONTEIL[4], J.-F. PARIS[5], A. LEPOYVRE[5], I. FOURNEL[6] and D. LÉGER[7]
[1]APHP – Hôtel-Dieu, Paris, FR, [2]Clinique du Château, Garches, FR, [3]CEMPN – HIA Robert Picqué, Bordeaux, FR, [4]CEMPN – HIA Sainte-Anne, Toulon, FR, [5]CEMA Air France, Roissy, FR, [6]Hôpital du Bocage, Dijon, FR, [7]University Paris Descartes, Paris, FR

Objectives: Excessive sleepiness due to shift work and/or jetlag can impair psychomotor performance for pilots in an operational environment where safety plays a vital role. Furthermore, this risk can be caused and/or intensified by sleep disorders. The main objective of this study is to assess the prevalence of excessive sleepiness, chronic insomnia, obstructive sleep apnea syndrome and restless legs syndrome affecting professional pilots of commercial aviation.

Methods: Six hundred and twelve pilots completed a questionnaire on socio-demographic characteristics, work conditions, sleep habits, excessive sleepiness, sleep disorders, indicators of occupational health and flight safety. These datasets were collected during a fitness test carried out in three aeromedical centres.

Results: Of 25.9% of pilots encounter excessive sleepiness between flight duties. 23.5% admit that they have fallen asleep in the cockpit involuntarily; 7.6% confess to similar experiences with their captain/co-pilot simultaneously. 16.7% suffer from chronic insomnia. Obstructive sleep apnea syndrome is suspected in 5.9% of subjects questioned. Restless legs syndrome is suspected in 10.6% of cases. Factors associated with chronic insomnia are evening typology, non-smoking, and the number of hours (≥600) spent flying per year. Chronic insomnia is associated with a significant risk of excessive sleepiness between flight duties, use of hypnotics, absenteeism, wish to change sectors or airlines, and involuntary sleep episodes in the cockpit. Only 0.68% of pilots report using hypnotics on a daily basis.

Conclusion: Data from our survey will help occupational physicians and medical examiners working with airline pilots to prevent excessive sleepiness related to sleep deprivation and to establish screening for sleep disorders. However, in spite of our results, risk management in commercial aviation seems satisfactory, since flying remains the safest means of long-distance transportation for users.

P875

Pilot study on attitudes toward fatigue and daytime sleepiness in taxi drivers

I. MUNTEANU[1], D. IVASCU[2] and F. MIHALTAN[1]
[1]National Institute of Pneumology 'Marius Nasta' Bucharest, Bucharest, RO, [2]Newmedics Clinic Bucharest, Bucharest, RO

The adverse effect of fatigue on human diving performance is a well-known experience to most of us. 'The subjective experience of fatigue involves conflict between the desire to rest and the inclination to continue driving to their planned destination' (Brown definition 1994).

Objective: (i) identify key demographic and work/rest patterns, and (ii) collect information on drivers' attitudes towards fatigue and propensity for daytime sleepiness on taxi drivers. The study is

important because it is the first study on divers fatigue made in Romania.

Material and methods: The date were collected from a 5–10 min questioner which contain demographic data, Fatigue Severity Scale and Epworth Sleepiness Scale. The questioners were directly distribute to taxi drivers from three large taxi companies from Bucharest.

Results: Hundred questioners were collect from 400 divers; 94% men and 6%women; average age37.79 ± 9.89 years; driving experience7.67 ± 4.55 years. They work in shifts: 7.1% only in day, 63.6% in night and 29.3% in alternative. The work years on night shift were 3.9 ± 3.86 with 8 ± 4.3 h per night. The drivers for the night shifts report the highest value of FSS and ESS (16.07 ± 5.87; 5.06 ± 4.21) but similar with the alternative shifts (15.27 ± 5.18; 5.34 ± 3.97). ESS scores generally increased co-linearly with driver age and years and were correlated with their ratings of how often fatigue was a problem for themselves.

Limits and conclusions: Young population, majority working in night shift. Future work might also be directed towards obtaining larger representative samples and to educate the road-using public regarding the effects and dangers of fatigue.

P876

Considerations on the degree of fatigue and sleepiness in health workers

I. MUNTEANU[1], D. IVASCU[2] and F. MIHALTAN[1]

[1]National Institute of Pneumology, Bucharest, RO, [2]Newmedics Clinic Bucharest, Bucharest, RO

Introduction: Individuals working nights and rotating shifts rarely obtain optimal amounts of sleep. Studies suggest that average sleep durations have decreased from 9 h in 1910 to as little as 6.9 h on work days in 2002. Research findings and published literature reviews of fatigue and sleepiness in medical personnel have not established a consensus on the effects or levels of fatigue or sleepiness.

Objective: We decided to study fatigability and sleepiness among female nursing personnel working a shift schedule, in comparison with day nurses, in 'Marius Nasta' Institute of Pneumology. The study population was composed of 84 female certified nurses working shifts and 19 working days only. All participants completed a self-report sleep questionnaire encompassing (i) demographic data, (ii) sleep survey, and (iii) tirednesss.

Results: Nurses from the day shift are older 44.42 ± 8.72 years, Statistical analysis was performed using the Pearson correlation test. Significant correlation was found between fatigability, sleepiness and age of subjects and years working in night shift. The correlation was also significant for <7.42 + 1.43 h of sleep/day. No sleep disorders were reported by 19.8% of shift workers versus 76.5% of day workers.

Conclusions: The present small study conclude that women doesn't recognize fatigability and sleepiness and because they have a family to support, they can not allow to be tired.

P877

Sleepiness and the risk of car crash: a case-control study

G. KECKLUND[1], A. ANUND[2], M. RODLING WAHLSTRÖM[3], P. PHILIP[4] and T. ÅKERSTEDT[1]

[1]Stress Research Institute, Stockholm, SE, [2]VTI, Linköping, SE, [3]Umeå University, Umeå, SE, [4]University of Bordeaux, Bordeaux, FR

Objectives: The aim of the present study was to carry out a case-control study and examine the relationship between acute and chronic sleepiness characteristics, including disturbed sleep and other factors that may contribute to driver sleepiness, with the risk of crashes in which the driver was admitted to hospital.

Methods: The selection of cases (n = 408, response rate = 68%) included all drivers that were admitted to hospital (emergency unit) as a result of a car crash. Truck drivers, taxi drivers and emergency vehicles were excluded from the study. The control group (n = 2308, response rate: 95%) comprised a random sample of car drivers that were stopped by the Police. The selection of controls was based on the crash spots and the time of the crash. The data collection included a six-page survey that was filled in by the drivers at the hospital or at the Police stop.

Results: The most common crashes were single-vehicle crashes (n = 120) and rear end crashes (n = 91). Sixty-three percent of the crashes occurred on motorways and highways, and the peak crash time was between 12.00 and 18.00 h (n = 185 crashes). The comparison between the cases and the controls demonstrated several significant differences. The cases included more females (47% versus 34% for the controls, $P < 0.001$), younger drivers (mean ± SD, age: 37 years ± 15 versus 46 ± 15, $P < 0.001$) and more shift workers (28% versus 22%, $P < 0.02$). The case group also reported a higher frequency of falling asleep before the crash (for the control group the question referred to 'before the police stop'); 3.5% versus 0.1% for the controls ($P < 0.001$). A logistic regression (MLR) analysis showed four significant predictors of crash risk: falling asleep before crash (odds ratio = 106, 95% CI = 18.6–607.9), young age (≤ 25 years, OR = 3.4, 95% CI = 2.4–4.7), sleep apnea symptoms (OR = 2.1, 95% CI = 1.2–3.5) and poor self-rated health (OR = 1.9, 95% CI = 1.2–3.1). The MLR analysis was adjusted for gender, socioeconomic status, time of day, sleep complaints and alcohol/drug intake. Approximately 20% of the crashes involved acute sleepiness or behaviors related to sleepy driving (such as being awake > 16 h, and <6 h of sleep).

Conclusion: The results showed that acute severe sleepiness (measured as 'falling asleep at the wheel') was the strongest discriminating variable between the cases and controls. The chronic sleep problems and sleepiness measures showed few groups differences, although the case-group had a higher prevalence of sleep apnea symptoms.

P878

Heart rate variability analysis for prediction of sleep onset in car drivers

M. MALCANGI and S. SMIRNE

Università degli Studi di Milano, Milan, IT

Introduction: Falling asleep at the wheel is a cause of many traffic accidents. Monitoring of the driver's physiological state to detect early the propensity to sleep onset could be an effective method to prevent sleep in car drivers. Electrocardiogram (ECG) carries good information about the physiological status of a subject through the variability of the heart rate (HRV). Capturing ECG with non-invasive method enables the monitoring of driver physiological status in the vehicle environment [1]. ECG seems to be more acceptable by drivers than EEG or pupil evaluation. Sleep is a physiological state characterized by variations in the activity of autonomic nervous system as shown by heart rate (HR) and its variability. The power spectral density (PSD) of heart rate changes from wakefulness to sleep [2] following changes in the level of activity of sympathetic and parasympathetic branches of autonomic nervous system [3]. During wakefulness PSD shows high density of low frequency (LF) related to high sympathetic

activity, while during sleep there is high density of high frequency (HF) mainly related to increased parasympathetic activity.

Method: The aim of our study is to identify parameters able to predict the onset of falling asleep. Firstly we have considered the balance of low frequency versus high frequency in PSD. A set of experiments demonstrates that, when a person tries to resist falling asleep, the LF/HF ratio of PSD computed from the HRV signal increases significantly a few minutes before becoming significantly lower during sleep state. Like a reaction to falling asleep, it causes high activity of the sympathetic system while the parasympathetic system decreases its activity: we can call this phenomenon a micro arousal. There are several methods for performing predictions. We use fuzzy decision logic to model the oncoming onset of sleep. The whole system consists of a signal acquisition and preprocessing subsystem, a feature extraction subsystem, and a fuzzy logic decision module to predict.

References:

1. Dorfman Furman, G., et al. Early detection of falling asleep at the wheel: a heart rate variability approach. Computers Cardiol 2008, 35: 1109–1112.
2. Manis, G., et.al. Prediction techniques and HRV analysis. MEDICON 2004, July 31–Aug 5, Naples, Italy, 2004.
3. Tohara, T., et al. Time frequency analysis of biological signal during sleep, SICE Annual Conference 2007, Kagawa University, Japan, 1925–1929, 2007.

P879

Sleep disease in professional drivers: a pilot study in bus drivers

M. MAESTRI[1], F. COSENTINO[1], E. DI COSCIO[1], E. IACOPINI[1], L. CARNICELLI[1], R. BUSELLI[2], S. GARBARINO[2], A. CRISTAUDO[2] and E. BONANNI[1]

[1]Neurological Clinics, Pisa, IT, [2]Department of Endocrinology and Metabolism, Orthopedics and Traumatology, Occupational Medicine, Pisa, IT

Objectives: The relationship between sleep disorders and increase in the risk of car accidents is well known and in professional drivers, obstructive sleep apnea syndrome increases its probability up to four times. Aim of this pilot study was to evaluate the incidence of excessive daytime sleepiness and obstructive sleep apnea syndrome (OSAS) in a group of bus drivers and to evaluate the use of screening scales to distinguish subjects at risk.

Methods: Three hundred and sixty-one bus drivers (353 M, mean age 41 ± 8.03 years) underwent a complete clinical evaluation, including Berlin Questionnaire on OSAS, Epworth Sleepiness Scale (ESS) and screening questionnaire of the Italian Association of Sleep Medicine.

Results: According to the questionnaire, 73 (20.2%) subjects reported snoring, while 10 (2.8%) apneas during sleep. Sleepiness was reported by 29 subjects (8%). According to the questionnaires, 31 subjects were at risk of sleep disorders. In 19 cases, the use of standard questionnaire (ESS and Berlin questionnaire versus AIMS screening questionnaire) were in agreement, while in other 10 cases these results differ.

Conclusions: In our experiences, the incidence of OSAS and pathological sleepiness was not different in this group of bus driver when compared to general populations. The AIMS questionnaire could help to distinguish population at risk. However, these subjects should undergo a complete clinical and polysomnographic evaluation both with a clinical (and preventive) purpose and as further evaluation of the value of this scale.

P880

Differences in the level of sleepiness measured by the different items of the Epworth sleepiness scale: a comparison to the Multiple sleep latency test

M. ULANDER[1], A. BROSTRÖM[2], K. ÅRESTEDT[3] and E. SVANBORG[4]

[1]Linköping University, Linkoping, SE, [2]School of Health Sciences, Jönköping, SE, [3]Linnaeus University, Kalmar, SE, [4]Institution of Clinical and Experimental Medicine, Linkoping, SE

Objectives: Both the Epworth Sleepiness Scale (ESS) and the Multiple Sleep Latency Test (MSLT) measure daytime sleepiness, but correlations are weak. The objective was to examine the ESS items one by one to assess to which degree they are associated to MSLT mean sleep latencies.

Methods: MSLT and ESS data from 154 consecutive sleep clinic patients (71 males, mean age ± SD 31.9 ± 16.8 years) were collected. ANOVA was used to examine significant differences in sleep latencies between subjects with different scores on each item. The mean sleep latencies for patients scoring 1 or 2 on each item were calculated as a measure of the degree of sleepiness measured by each item.

Results: For all items, subjects with higher ESS scores had shorter sleep latencies ($P < 0.001$). The mean sleep latency among subjects scoring 1 or 2 on item 5 was 11.3 mins, while the mean sleep latency among subjects scoring 1 or 2 on items 6 and 8 were 6.5 and 7.0 mins, respectively.

Conclusion: In general, higher ESS scores on individual items corresponded to shorter mean sleep latencies. Respondents scoring 1 or 2 on items 6 and 8 are sleepier than respondents scoring 1 or 2 on items 5, which might indicate that items 6 and 8 measure a higher degree of sleepiness than item 5. This is in line with previous research based on item response theory (IRT). This study adds to previous knowledge as item difficulty has been assessed by independent means rather than by overall ESS score, as in IRT models.

P881

Is maintenance of wakefulnesstest and behavioural index a useful synergy for the evaluation of sleepiness?

S. BAIARDI, A. POINI, F. PIZZA, S. MONDINI and F. CIRIGNOTTA

University of Bologna, Bologna, IT

Introduction: The current gold standard for the assessment of the ability to maintain wakefulness is the Maintenance of Wakefulness Test (MWT) but it is limited by normative data and the correlation with other sleepiness measures. We hypothesized that the video analysis of patients' behavior during MWT, focused on eyelid drops (ED), could improve the sensitivity of the test.

Method: We studied 12 men with severe OSAS (AHI = 54.4 ± 12.08/h), mean age 55.75 ± 6.4 years. Each patient underwent four MWT sessions according to the International Guidelines with the addition of video recording.

We divided patients into three groups according to mean sleep latency (SL) at MWT: pathologic (<8', $n = 4$), borderline (8'–30', $n = 4$), and normal (>30', $n = 4$).

We evaluated the eyelid drops equal to or longer than 2 s. The Behavioral Sleepiness Index (BSI) was defined as the mean number of seconds with eyelid closure per epoch at first, fifth and tenth min in

each MWT. Behavioral Sleep Onset (BSO) was defined as the first epoch with a BSI longer than 15 s.
We evaluated the relationship between BSI and BSO with the SL in each MWT (Spearman test), and compared the mean BSO with the mean SL-MWT in each patient (Wilcoxon test).
Results: There was a inverse ratio between BSI and SL-MWT at 1, 5, 10 min in each MWT (r = -0.505, $P = 0.000$; r = -0.718, $P = 0.000$; r = -0.552, $P = 0.004$), whereas BSO was directly related to SL-MWT in each MWT (r = 0.793, $P = 0.000$). Each patient's mean BSO (14.63 ± 14.68) was significantly lower than the mean SL-MWT (21.35 ± 15.31; $P = 0.003$) and this finding was consistent for all three groups of patients.
Conclusion: Video monitoring of eyelid drops can improve the sensitivity of MWT in detecting drowsy patients. Clinically, this could be particularly useful in borderline patients.

P882

Maintaining alertness in the face of monotony – normative data on a 60-min sustained attention task based on the Mackworth clock

R. POPP[1], H. DANKER-HOPFE[2], E. LORETZ[3], J. ZEITLHOFER[3], P. GEISLER[1] and C. SAUTER[2]
[1]Sleep Disorders Center, Regensburg, DE, [2]Charité University Hospitals, Berlin, DE, [3]University Clinic of Neurology, Vienna, AT
Objectives: The aim of the present multi-centre study was to obtain normative data on a 60-min sustained attention task using a computerised Mackworth Clock Test. Reference data was collected in a large adult sample of healthy subjects in the age range of 20–79 years. Furthermore, we analysed potential influences of sex, age, time-on-task and time-of-day on test performance.
Methods: In total, 234 healthy subjects (116 females, 118 males) between the age of 20 and 79 years participated in the test procedures either in the morning or in the afternoon (129 subjects versus 105 subjects). The sample was age stratified with at least 20 females and males per decade (only in the age group of 70–79 years there were no more than nine females and 16 males). Exclusion criteria comprised the presence of sleep disorders (including irregular sleep-wake patterns or shift-work), psychiatric disorders and chronic illness associated with impaired vigilance. The task was a monotonous sustained attention test based on a computerised version of the 'Mackworth Clock' with a total duration of 60 min.
Results: In all performance parameters, there was no significant difference between female and male subjects (all $P > 0.495$) or between the morning and the afternoon test session (reaction times: $P = 0.159$; false reactions: $P = 0.450$; correct reactions: $P = 0.345$). In contrast to missing sex or time-of-day effects, statistical analysis demonstrated a significant age effect on speed ($P < 0.001$) resulting in an increase of correct reaction times from the youngest to the oldest group. For performance accuracy, Jonckheere-Terpstra Test also showed a significant trend for age indicating an increase in false reactions ($P < 0.001$) and a decrease of correct reactions ($P < 0.001$) with increasing age. Concerning time-on-task, there was a significant overall deterioration in correct reactions and speed during the course of the test. Major vigilance decrement could already be observed during the first half of the test.
Discussion: Our study presents age-related normative data in form of percentile reference charts on sustained performance in healthy adults. The normative data base can serve as a useful source to assess vigilance impairments in patients with hypersomnia. The test proofed to be highly sensitive to vigilance decrements, even after a short time on task. There was an overall age effect on all performance measures, resulting in a decline in sustained attention performance with increasing age.

P883

Sleepiness and sleep literacy in high school teachers

T. REBELO-PINTO, H. REBELO-PINTO and T. PAIVA
CENC, Lisbon, PT
Objectives: The bad sleep hygiene and sleep habits of high school Portuguese children have been proved by several authors. One of the goals of the Sleep-Schools Project is to develop Educational programs in schools, contributing to reverse this worrying situation. This goal implies adequate integrations and participation of teachers, therefore their sleep literacy and daytime sleepiness was evaluated during awareness and teacher training sessions of the Sleep-Schools Project.
Methods: Prior to educational sessions, we evaluated sleepiness using Epworth Sleepiness Scale – ESS. Also, teachers answered a questionnaire on basic concepts of sleep and sleep hygiene (true or false and multiple choice items). In some cases, we were able to compare results before and after teachers training sessions.
Results: One hundred and five teachers (82% female) were evaluated in different types of sessions. The ESS was abnormal in more than 50% of them. The questionnaire on basic concepts of sleep showed that teachers have several myths about sleep (68% of wrong answers in the true or false items) and that their sleep literacy improved significantly after receiving a training session from the Sleep-Schools Project.
Conclusions: The excessive daytime sleepiness in Portuguese school teachers is far above the data on the general population, which may indicate that this is a risk profession for sleep problems. Furthermore, the low sleep literacy in this population raises an important target of sleep education strategies. Finally, the improvements observed after a training session on sleep mechanisms and sleep education support the need to involve teachers in sleep education.

P884

Total sleep deprivation: courses of mood, sleepiness, and occurrence of intermittent sleep episodes in healthy persons and depressed patients

M. H. WIEGAND, C. POHL, M. WASMAIER, S. HUDJETZ and P. WOLF
Technical University of Munich, Munich, DE
Introduction: Sleep deprivation has very different clinical effects in healthy persons and depressed patients. In the present study, we tried to assess and analyze these differences. In a former study of our group, we saw a close relationship between the occurrence of intermittent sleep episodes during the 'sleep deprivation' period and a low response rate in depressed patients.
Patients and methods: Sleeping and waking were monitored continuously in 36 depressed inpatients and 24 healthy controls using a portable device. Mood and sleepiness were self-rated in short intervals. We analyzed the differences between patients and controls, as well as between depressed responders and nonresponders to this treatment. In addition to conventional statistics, we used time series analysis for the assessment of levels and trends of mood, sleepiness and occurrence of sleep episodes in both groups.
Results: The clinically observed divergent courses of mood in depressed patients (rising trend) and healthy controls (declining

trend) were confirmed. The physiological oscillations of sleepiness and mood over the 40 h sleep deprivation period were similar in both groups. There were more intermittent naps in depressed patients than in healthy controls. During the sleep deprivation night and on the day after, patients as well as controls rated their mood worse when the rating was preceded by a nap. There is a continuous negative correlation between mood and sleepiness in both groups; in healthy persons, this correlation is clearly higher (-0.70) than in depressed patients (-0.40).

Conclusions: The opposite effect of sleep deprivation on mood in depresed patients as compared with healthy controls could be confirmed. After an intermittent nap, healthy persons exhibited a mood worsening comparable to depressed patients; thus, this appears not to be an effect specific to depression. The parallel course of mood and sleepiness oscillations during the 40 h of sleep deprivation in both groups points to an independence of ultradian rhythms from mechanisms involved in the pathophysiology of depression. Healthy persons exhibited a clearly higher negative correlation between mood and sleepiness than did depressed patients; in the latter, sleep deprivation seems to activate mood-improving mechanisms which counteract the 'depressiogenic' action of increased sleepiness.

Poster Session – Narcolepsy and Other Hypersomnias

P885

Event-related potentials in narcolepsy-cataplexy and controls to humorous rewarding pictures

A. MENSEN[1], R. PORYAZOVA[2], N. ZOLLINGER[2], F. BISLIMI[2], G. HUEGLI[2], L. BADEL[1], C. R. BAUMANN[2] and R. KHATAMI[1]
[1]Clinic Barmelweid, Barmelweid, CH, [2]University Hospital Zurich, Zurich, CH

Introduction: A defining feature of narcolepsy with cataplexy (NC) is loss of muscle tone induced by emotionally charged events, especially humorous ones. Humour engages the mesolimbic reward network which is compromised in NC during reward processing. Here we examined whether NC-patients and healthy controls show a different neurophysiological response to humour as a task reward.

Methods: Participants completed a simple time estimation task while observing a non-humorous picture. If the estimation was within a certain timeframe (online adjusted), subjects received positive feedback in that the observed picture altered slightly to become humorous, otherwise, the picture was horizontally flipped.

Electroencephalography (EEG) was measured in eight NC-patients and eight healthy matched controls from 125 scalp sites in a geodesic array. Event-related potentials were created 200 ms prior to picture change until 800 ms post-event.

Statistical differences, for all channels and time points, in the ERPs were analysed using a threshold-free cluster-enhancement (TFCE), followed by a non-parametric permutation test for main effects of group and feedback as well as their interaction.

Results: Group differences peaked around 170 ms, but did not reach significance (peak F-value = 25.83). Reward feedback showed multiple significant peaks at posterior sites around 150, 280 and 380 (peak F-value = 40.61). Peak interaction of both variables occurred around 350 ms, but did also not reach significance (peak F-value = 30.52), in this conservative test.

Conclusion: Clear overall differences were found in both groups ERP between rewarding humorous pictures and their neutral counterpoint. Furthermore, there are clues which point to possible group differences between NC-patients and controls in their feedback responses.

P886

Clinical phenotype of patients with narcolepsy with cataplexy, cerebellar ataxia, deafness and neuropathy associated to DNMT1 gene mutation

K. KAVEH MOGHADAM[1], F. PIZZA[1], F. POLI[1], C. FRANCESCHINI[1], C. TONON[1], V. CARELLI[1], R. LODI[1], M. SERI[1], J. WINKELMANN[2], E. MIGNOT[3] and G. PLAZZI[1]
[1]University of Bologna, Bologna, IT, [2]Technical University Munich, Munich, DE, [3]Stanford University School of Medicine, Palo Alto, CA

Objectives: To describe the phenotype of kindreds of two patients (pts) suffering from Autosomal Dominant Cerebellar Ataxia, Deafness and Narcolepsy with Cataplexy (NC), recently associated with DNA methyltransferase 1 (DNMT1) gene mutations.

Methods: Clinical assessment based on history, neurological examination, neurophysiological testing, neuroimaging and genetic analysis was performed in two male probands (pt 1 and 2), and two daughters of pt 1.

Results: Both probands suffer from excessive daytime sleepiness (EDS), cataplexy and deafness from the age of 42/43 years; few years later they slowly developed a mixed, mainly cerebellar, ataxia and a lower limbs oedema. No neuropathic symptoms were reported. Pt 1 (57 years) then developed mood disturbances, reduced visual acuity and, in the last years, asymmetrical mild rigidity, resting and postural tremor, retropulsion with lateral trunk flexion, urinary and erectile complaints. Familial history was unremarkable. His two daughters did not report any neurological nor sleep complaint and their examination was normal. Pt 2 (47 years) has no offspring. His father suffered from depression, EDS with narcoleptic features, deafness and ataxic gait confirmed by a previous hospitalization, and died at the age of 52 years. Testing disclosed on both probands a reduced sleep latency (SL) with multiple sleep onset REM period (SOREMPs), motor overactivity in sleep with periodic limb movements and REM sleep behavior disturbance, optic and axonal sensory neuropathy, increased cerebrospinal (CSF) Tau protein concentration. CSF Hypocretin-1 concentration was 123 and 93 pg/ml in pt 1 and 2 respecticvely. The younger daughter (23 years) of Pt.1, had a normal SL at MSLT, with one SOREMP, whereas the elder (28 years) had a normal SL with two SOREMPs.

Cerebral neuroimaging detected neurodegeneration with spread cerebral and cerebellar morphologic and metabolic alterations on both pts, more severe for Pt.1. Pt.1's daughters showed a normal morphological pattern with initial metabolic alterations. Genetic analysis disclosed two close point mutation on DNMT1 gene: p.Ala570Val on Pt.1 and his two daughters and p.Gly605Ala mutation on Pt.2.

Conclusion: Mutation on DNMT1 gene can be responsible for a slow-progressive neurodegenerative disease with middle-age clinical onset, characterized by an initial manifestation of NC and deafness followed by a multisystemic involvement.

P887

Quantification of electroencephalography across the sleep onset period: a pilot study of young narcoleptic patients

H. B. SHIN[1] and J. W. KIM[2]
[1]Komoki sleep center, Seoul, KR, [2]The University of Sydney, Sydney, AU

Objectives: Electroencephalography (EEG) is commonly used to monitor active changes in brain activity across sleep onset period (SOP). Quantification of the brain activity is important, especially for narcoleptic patients, to reduce risks associated with excessive sleepiness (e.g. drowsy driving). It is thus our main objective to demonstrate and compare several EEG quantification tools, and discuss their potential applications in clinical settings.

Methods: The standard multiple sleep latency tests (MSLT) were performed to 35 young narcoleptic patients. Four-channel EEGs (C3/A2, F3/A2, O1/A2 and O2/A1) were systematically examined to remove epochs with substantial amount of non-neurogenic artefact. Spectral power (delta band: 0.5–4.5 Hz; alpha band 8–12 Hz) and scaling exponent of the detrended fluctuation analysis (DFA SE) were calculated for each 5 s epoch EEG segment at each electrode. For each individual, the measures were averaged over three distinct time intervals: (i) before SOP (BSO), (ii) at SOP and (iii) after SOP (ASO), 2 min each. The averaged measures were then statistically compared using the t-test. Spatial correlations between electrodes

across the SOP were also investigated by a 'synchrony' measure (eigenvalue spectra) based on matrix theories.

Results: The current study involved 35 young narcoleptic patients (M/F: 18/17; Age: 18.8 ± 4.1 years; Sleep onset latency: 2.5 ± 1.3 min; REM sleep onset latency: 6.0 ± 3.4 min). Channel-averaged DFA SE increased across the SOP (BSO: 0.78 ± 0.09; SOP: 0.93 ± 0.07; ASO: 1.05 ± 0.07; $P < 0.01$ for BSO versus SOP, SOP versus ASO), while the alpha power decreased (BSO: 55.6 ± 31.3 uV^2; SOP: 26.4 ± 14.5 uV^2; ASO: 14.8 ± 8.8 uV^2). The delta power is strongest at BSO, 85.0 ± 47.1 uV^2 (c.f., 71.2 ± 25.5 uV^2 for SOP and 77.3 ± 26.8 uV^2 for ASO). We also found a trend of decreasing spatial synchrony in EEG waves across the SOP (BSO: 48.1 ± 82.3; SOP 37.1 ± 29.9; ASO 32.2 ± 19.7), but the differences were not statistically significant ($P > 0.1$).

Conclusion: The active changes in the brain across the SOP were characterised by increased DFA SE and reduced alpha spectral power. The seemingly inconsistent result with delta power may in part be explained by eye-movement artefact that were typically 0.5–2 Hz overlapping the delta band. The spatial synchrony measure could be improved if a higher-density EEG recording system was applied.

P888

Severity of symptoms, disability and quality of life in narcolepsy and other hypersomnias

A. WIERZBICKA, A. WICHNIAK, K. CZASAK, I. MUSINSKA, T. JAKUBCZYK, L. WOLKOW, E. WALINIOWSKA, A. SEK and W. JERNAJCZYK

Institute of Psychiatry and Neurology, Warsaw, PL

Objectives: Excessive daytime sleepiness as a core symptom of narcolepsy and other hypersomnias affects professional and social functioning of the patients. Aim of the study was to evaluate clinical symptoms severity, disability level and health-related quality of life in patients with narcolepsy and other hypersomnias.

Methods: The analysis was performed in 106 patients (mean age 36.1 ± 14.2, 46F/60M) referred to the Institute of Psychiatry and Neurology with suspected diagnosis of narcolepsy. Assessment included: clinical symptoms, results of diagnostic examinations (polysomnography, Multiple Sleep Latency Test, psychomotor tests, neuroimaging), Epworth Sleepiness Scale (ESS), Narcolepsy score, 36-Item Short Form Survey (SF-36), Clinical Global Impression of Severity scale (CGI-S), Beck Depression Inventory (BDI), Sheehan disability scale.

Results: On the basis of clinical features and results of neurophysiological examinations diagnosis of narcolepsy was established in 70 patients (54 with cataplexy), 36 patients were diagnosed with other types of hypersomnia (nonorganic, idiopathic, sleep apnea). Patients with narcolepsy did not differ from subjects with other hypersomnias with respect to gender, age or age at the onset of the disorder. Patients with narcolepsy showed more severe symptoms than patients with other hypersomnias in ESS (19.3 ± 2.9 versus 17.1 ± 3.3; $P < 0.001$) and CGI (4.4 ± 0.9 versus 3.3 ± 0.7; $P < 0.0001$). The results of Sheehan disability scale were higher in narcolepstic patients than in the group with other hypersomnias, especially in learning abilities and functioning in work ($P < 0.005$). Results in all domains of SF-36 were similar in both groups of patients and were lower in comparison to the normative data with exception of physical functioning.

Conclusions: Hypersomnias have profound impact on general daytime functioning, disability level and quality of life. The disability and clinical symptoms severity were more pronounced in patients with narcolepsy than in other types of hypersomnia.

P889

Long-term stimulant use in narcoleptics is not associated with an increased prevalence of hypertension and psychiatric disturbances

J. HUTCHINSON[1], I. MORRISON[2] and R. L. RIHA[1]

[1]University of Edinburgh, Edinburgh, UK, [2]Ninewells Hospital, Dundee, UK

Objectives: The primary aim of this study was to establish the prevalence of hypertension and psychiatric side-effects among stimulant-treated narcoleptics. The secondary aim was to determine if there were any predictors of these potential complications.

Method: Of 110 narcoleptics registered at our department, 29 responded to a questionnaire that focused on their current drug profile, side-effects and known risk factors for hypertension. Their responses were used alongside past sleep study information to determine if any variables were significant in predicting the development of hypertension and psychiatric disturbance. Standard statistical analysis was undertaken using SPSS (v.17; Chicago, IL, USA).

Results: Only the Epworth Sleepiness Scale was significantly associated with the development of hypertension in the study group (OR = 0.52; 95% CI:0.3–0.93, $P = 0.03$) and in the cohort overall (OR = 0.51; 95% CI:0.29–0.91, $P = 0.02$), explaining 60% of the variance. Significant but low correlations were found between hypertension and BMI (r = -0.33, $P = 0.01$), sleep apnoea (r = 0.38, $P < 0.01$) and AHI (r = -0.29 $P = 0.01$). No significant association was found between stimulant use and psychiatric side-effects or illness.

Conclusion: The results from this study mirror past findings that stimulants do not play a significant role in the development of cardiovascular and psychiatric pathology unless given in high doses; not seen in our cohort. The association between sleepiness and hypertension has been previously documented in the context of other sleep disorders but never within narcoleptics. This novel finding forms the basis of ongoing research.

P890

Delay of gratification in individuals with narcolepsy

P.-A. BEITINGER, M.-E. BEITINGER, R. WEHRLE and A. STEIGER

Max Planck Institute of Psychiatry, Munich, DE

Objectives: Orexins are involved in the regulation of food intake and sleep. Narcolepsy is characterized by a central orexin deficiency. Studies report an increased body weight in narcolepsy. The inability to delay gratification is related to obesity. This study investigates the delay of gratification in patients with narcolepsy.

Methods: Forteen patients organized in the German Narcolepsy Self-help Group (DNG e. V.) with polysomnographically verified narcolepsy (F/M 9/5: mean age 43.4 ± 18 years; mean BMI 26.0 ± 4.8 kg/m^2) were included in the study. We designed a board game to assess the delay of gratification. On designated fields patients had to decide whether they choose an immediate small gratification consisting of a small piece of sweetie or whether they continue playing and get double of the amount in the end of the game. The outcome measure is the percentage of decisions in favor of delay. The percentage was calculated for the total game and for the three thirds of the fields. The sleepiness was assed with the Karolinska Sleepiness Scale (KSS) before and after the game. Forteen control subjects were individually matched for gender, age and BMI (mean age 44.1 ± 17 years; mean BMI 25.5 ± 4.1 kg/m^2).

Results: The percentage of decisions in favor of delaying did not differ between patients with narcolepsy (87 ± 21%) and individually

matched controls (82 ± 16%, $P = 0.42$). The percentage of decisions in favor of delayed gratification across the time hardly increased little in the narcoleptic group (81%, 85%, 92%) across the three thirds. It showed a steep increase in the control group (66%, 86%, 93%). KSS dropped or remained stable in all but one narcoleptic individuals.

Conclusion: These preliminary results suggest no obvious peculiarities concerning the delay of gratification in narcoleptic patients. Subtle differences in favor of stronger inhibition may be possible. Remarkably the decisions made induced preferentially the intake of a higher amount of sweeties. The board game paradigm emerged as valuable tool that takes into account the sleepiness of narcoleptic patients. Investigating a larger sample will help control for the large standard deviation.

P891

Narcolepsy-cataplexy associated with hereditary multiple exostoses

E. CALVO[1], J. L. VICARIO[2], J. SUELA[3], M. TAFTI[4], R. DEL RÍO VILLEGAS[5] and R. PERAITA-ADRADOS[1]

[1]University Hospital Gregorio Marañón, Madrid, ES, [2]Blood Center of the Community of Madrid, Madrid, ES, [3]NIMGenetics, Madrid, ES, [4]University of Lausanne, Lausanne, CH, [5]University Hospital La Paz, Madrid, ES

Background: Hereditary multiple exostoses (HME) has thus far been linked with mutations in three genes: EXT1 on chromosome 8q24.1, EXT2 on 11p13, and EXT3 on the short arm of Chromosome 19 (though the exact location is not yet determined). It is thought that normal chondrocyte proliferation and differentiation is affected, leading to abnormal bone growth. A case of periodic hypersomnia with multiple exostoses has been previously reported [1].

Case Report: A 48-year-old man with HME and familial narcolepsy-cataplexy, inherited by his mother, was referred due to sleep episodes since the age of 44 and severe catapleptic attacks two years later. He presented obesity (BMI 35.1 kg/m^2) and multiple osteochondromas causing deformity of the forearm, pelvis, knees and irritation of tendon and muscles. Neurological examination including EEG and cranial CT was normal. PSG showed disturbed nocturnal sleep and a mean sleep latency at MSLT of 3.5 min with two SOREMPs. HLA genotyping revealed DRB1*15:01-DQB1*06:02. Genetic study for HME did not show any mutation in the implicated genes but six non pathogenic polymorphisms have been detected. Patient's unique sister with the same HLA genotype is clinically unaffected.

Conclusion: To our knowledge this is the first report of a familial case of NC associated with autosomal dominant HME. Future assessment should include a genetic work-up including exome sequencing to identify a potential pathogenic mutation.

Reference:

1. Reimão, R., Diament, A. Periodic hypersomnia, congenital ectodermal disorders and multiple exostoses. Arq Neuropsiquiatr 1989, 47(1): 76–9.

P892

Proof of hypocretin deficiency development during onset of human narcolepsy with cataplexy

A. SAVVIDOU[1], S. KNUDSEN[2], M. OLSSON-ENGMAN[1], S. GAMMELTOFT[3], P. J. JENNUM[2] and L. PALM[4]

[1]Paediatric Department, Karlskrona, SE, [2]Danish Center for Sleep Medicine, Glostrup, DK, [3]Department of Clinical Biochemistry, Glostrup, DK, [4]Section for Paediatric Neurology, Department of Paediatrics, Malmö, SE

Background: In animal models destruction of hypothalamic hypocretinergic neurons results in the onset of a phenotype very similar to human narcolepsy – a sleep disorder associated with severe hypocretin deficiency. Although hypothesized, this temporal and causal association has never been proven in humans due to lack of pre-disease cerebrospinal fluid (CSF) samples. We here present the first human narcolepsy case with parallel development of hypocretin deficiency and disease onset.

Methods and results: In December 2010 a 10-year-old Swedish boy was diagnosed with narcolepsy with cataplexy. Except for CSF confirmed (and treated) neuroborreliosis in June 2009, he was previously healthy. He had been H1N1-vaccinated (Pandemrix) in November 2009 and February 2010. Approximately 15 days after the second vaccination, he developed excessive daytime sleepiness. Cataplexy emerged in September 2010. He also experienced disrupted night sleep and hypnagogic/pompic hallucinations and gained weight of 12 kg. His neurological examination, brain MRI and routine blood and CSF parameters were normal. The MSLT mean sleep latency was 5.2 min with sleep onset REM periods (SOREMPS) in 4/5 naps. He was HLA DQB1*0602-positive. Fortunately, CSF obtained during the episode of neuroborreliosis had been saved (frozen), enabling comparison of CSF hypocretin-1 levels pre- and post narcolepsy onset. The CSF hcrt-1 level was normal (318 μg/ml) before narcolepsy onset but dropped to <10 pg/ml after disease onset.

Discussion: Here we confirm for the first time that hypocretin deficiency indeed develops in parallel to disease onset in human narcolepsy with cataplexy, supportive of a causal association.

P893

Anti–aquaporin 4 (AQP4) antibody induce secondary narcolepsy or hypersomnia

T. KANBAYASHI[1], Y. SAGAWA[1], Y. KIKUCHI[1], J. TOKUNAGA[2], W. ITO[3], M. SATO[4], K. YAGISAWA[1], A. NARUMI[5], K. TSUKAMOTO[6], Y. HAYASHI[7], H. KUBOTA[1], E. NARITA[2], S. KURATA[2], R. AIZAWA[8], S. UEMURA-ITO[1], Y. WADA[9], J. ARII[10] and T. SHIMIZU[1]

[1]Akita University, Akita, JP, [2]Akita Prefectural Center of Rehabilitation and Psychiatric Medicine, Akita, JP, [3]South Carolina University, Columbia, US, [4]Stanford University, Palo Alto, US, [5]Imamura Hospital, Akita, JP, [6]Kaiseikai Hospital, Akita, JP, [7]Kita Mental Clinic, Nagoya, JP, [8]Aino University, Takatsuki, JP, [9]Han-nan Hospital, Sakai, JP, [10]Chiba Rosai Hospital, Ichihara, JP

Objectives: Narcolepsy is a chronic sleep disorder, characterized by EDS, cataplexy, and other REM sleep abnormalities. The idiopathic form of narcolepsy with cataplexy is highly associated with a deficiency in a hypothalamic neuropeptide, hypocretin/orexin. Narcolepsy also occurs during the course of various neurological conditions (i.e. symptomatic narcolepsy or narcolepsy due to medical conditions). A recent meta-analysis indicated that 10 out of 116 symptomatic cases of narcolepsy are associated with multiple sclerosis, a disease of autoimmune demyelination. Symptomatic narcoleptic cases consist of heterogeneous disease conditions, but the hypocretin systems are often impaired in these narcolepsy/EDS cases.

Methods: Seven Japanese patients whose diagnoses were neuromyelitis optica (NMO) related disorder and who were exhibiting EDS. Lesions on magnetic resonance imaging, cerebrospinal fluid hypocretin-1 levels, and serum anti–aquaporin 4 (AQP4 = NMO) antibody titer were examined.

Results: Bilateral and symmetrical hypothalamic lesions associated with marked or moderate hypocretin deficiency were found in all seven cases. Four of these patients met the ICSD two narcolepsy criteria.

Conclusion: Since AQP4 is highly expressed in the hypothalamic periventricular regions, an immune attack on AQP4 may be partially responsible for the bilateral and hypothalamic lesions and hypocretin deficiency in narcolepsy/EDS associated with autoimmune demyelinating diseases. Gaining the basic knowledge of symptomatic narcolepsy in immune mediated conditions will be not only useful for selecting the most appropriate treatment and predicting the prognosis of the disease but also for understanding the etiological mechanism of narcolepsy.

P894

Clinical and polysomnographical characterisation of REM sleep motor dysregulation in narcolepsy-cataplexy

M. VICENTE-RASOAMALALA[1], S. SCHOLZ[2], I. JAUSSENT[2], S. BAYARD[2], V. COCHEN DE COCK[2] and Y. DAUVILLIERS[2]
[1]Hospital Vall d'Hebron, Barcelona, ES, [2]Hospital Gui-de-Chauliac, Montpellier, FR

Objective: The regulation of the motor component in REM sleep is impaired in narcolepsy-cataplexy (NC). REM sleep behaviour disorder (RBD) is also frequent in NC but seems less severe than in idiopathic RBD (iRBD). The purpose of our study was to evaluate the frequency of the clinical RBD in patients with NC and to characterize the motor component in REM sleep in NC in comparison to 10 patients with iRBD and to 40 normal controls.

Patients and methods: Of the 107 NC (62 males, 45 females; age ranged 5–83 years), 10 iRBD and 40 normal controls, free of drugs for at least 15 days were included. All of them had a polysomnographic recording and underwent a structured clinical interview on RBD but also on demographical and clinical conditions related to NC or iRBD. Tonic and phasic motor activities were quantified in REM sleep in the submentalis muscle. Rapid eye movements density (REMs) and periodic limb movements index during wakefulness (PLMw) and sleep (PLMs) were also analyzed.

Results: Forty-seven of the 107 patients (43.9%) reported a clinical RBD, including 52.9% with a frequency between one and five episodes per week, 29.4% with almost daily episodes and 17.6% with rare episodes. Ten patients with NC (38.5%) presented violent behaviours during RBD episodes. Comparing narcoleptic patients with RBD to those without, we found that mean age was higher in the former group as it was for the presence of hypnagogic hallucinations. Twelve patients with NC (25.5%) presented an increase of REM tonic activity >20%. Tonic and phasic motor REM activities were higher in NC compared to normal control group but lower compared to iRBD. Patients with NC and clinical RBD had higher tonic and phasic motor activities in REM sleep, higher waketime after sleep onset, more PLMw, PLMs and PLMs associated with microarousals, but without any difference for REMs density.

Conclusion: Clinical RBD is reported in almost half of patients with narcolepsy with cataplexy. REM sleep motor dyscontrol was seen more prominently in narcoleptic patients compared to normal controls but to a lesser extent than in patients with iRBD. Finally, we demonstrate the presence of higher abnormalities in REM sleep motor regulation in patients with narcolepsy-cataplexy with RBD compared to patients with NC without RBD.

P895

Episodic memory in narcolepsy with cataplexy

S. BAYARD[1], M. LANGENIER CROISIER[1], M.-C. GELY-NARGEOT[2] and Y. DAUVILLIERS[1]
[1]Hospital Gui-de-Chauliac, Montpellier, FR, [2]University of Montpellier, Montpellier, FR

Objective: Performances of episodic memory functioning in patients with narcolepsy-cataplexy are still subjects to controversy. Furthermore, there is still uncertainty regarding which components of episodic memory processes (i.e. retrieval, encoding, or retention) are affected. We have therefore prospectively investigated verbal memory and learning in a sample of drug naïve patients with narcolepsy-cataplexy (NC) in comparison to controls.

Methods: Thirty-five drug-free patients with NC and 52 controls matched on sex, age, and estimated intellectual level were included. All participants underwent a standardized interview, completed questionnaires, and neuropsychological tests. The California Verbal Learning Test was used to assess verbal memory. All patients underwent a polysomnography followed by multiple sleep latency tests (MSLT), with memory evaluation performed the same day between MSLT sessions.

Results: Patients with narcolepsy-cataplexy performed significantly worse than controls on free recall, cued recall as well as on recognition memory, even after controlling for depressive symptoms being higher in patients. No interaction was found between episodic memory performances and demographical data, severity of the condition, and sleep variables including subjective and objective daytime sleepiness. No difference was observed regarding the learning slope and the semantic clustering learning strategy. Proactive interference and recall intrusions were larger among patients with narcolepsy-cataplexy compared to controls. However, no between-group difference was found in retention after having controlled for encoding.

Conclusion: This study shows an episodic memory impairment in drug-free patients with narcolepsy-cataplexy, with a clear deficit in encoding without any problem in retention or retrieval. Further studies are needed to explore whether medications that promote wakefulness can improve the memory processing in narcolepsy-cataplexy.

P896

Cerebrospinal fluid cytokine levels in narcolepsy with cataplexy patients close to onset

B. KORNUM[1], O. GOLDENBERGER[2], P. JENNUM[3] and E. MIGNOT[1]
[1]Stanford Center for Sleep Sciences, Palo Alto, US, [2]Stanford University, Palo Alto, US, [3]Danish Center for Sleep Medicine, Glostrup, DK

Objectives: Narcolepsy with cataplexy (NC) is caused by a loss of hypothalamic hypocretin producing neurons. Autoimmunity due to environmental triggers e.g. infections is considered the most likely pathogenesis, recently highlighted by increased numbers of NC cases after H1N1-vaccination/infection.

We here report an analysis of cerebrospinal fluid (CSF) cytokine levels in NC patients close to onset.

Methods: CSF samples were collected in a clinical setting when the patient had the first sleep examination. CSF cytokine levels from nine patients and nine controls were analyzed using a 51-plex Luminex platform. The dataset was tested using SAxCyB (Significance Analysis of xMap Cytokine Beads) statistics. Relevant hits were then tested using ELISA in a larger independent cohort (30 patients,

and 15 age matched controls). The patients were all within 9 months of cataplexy onset, 100% were DQB1*06:02 positive, and all had CSF hypocretin < 110 pg/ml. The controls were matched for age, 53% were DQB1*06:02 positive, and all had CSF hypocretin >110 pg/ml.

Results: Our Luminex data showed a significant increase in CSF IL-1B, CCL2, CCL4, leptin, LIF, and PAI-1 in NC patients close to disease onset. No tested cytokines were significantly decreased. We further saw that CCL5 was significantly increased in the NC patients closest to onset of the disease. We confirmed the finding of increased CCL4 in CSF from patients close to onset, but while CCL5 was indeed high in a subgroup of patients, there was no significant difference from the control group.

Conclusion: Here we show that CCL4 is significantly increased in CSF from NC patients close to onset. CCL4/MIP-1B is a strong chemotaxic factor for lymphocytes, and so is CCL2 and CCL5. This strongly suggests a immune mediated pathogenesis in NC. We further show that the general marker of inflammation IL-1B is higher. Leptin, LIF, and PAI-1 are all involved in metabolism and obesity, and levels of all three correlate with body mass index. Leptin has previously been shown to be increased in CSF from NC patients. We suggest that the changes in these are secondary to the metabolic disturbances in NC. Overall our finding shows an increase in inflammatory markers in CSF close to narcolepsy with cataplexy onset. This supports the autoimmune hypothesis of NC.

We thank the patients and their families for contributing samples. Funded by MH080957-03 and the Danish Medical Council 09-066348/FSS.

P897

Prevalence of frequent vivid dreams and nightmares in narcolepsy with cataplexy and narcolepsy without cataplexy

J. PISKO, J. BUSKOVA and S. NEVSIMALOVA
General Teaching Hospital, Prague, CZ

Objectives: Vivid oneiric activity is ascribed mostly to rapid eye movement (REM) sleep, but its physiology is still not fully understood. Narcolepsy with cataplexy (NC) and narcolepsy without cataplexy (NWC) belong to disorders with disruption of REM sleep, but differ in various clinical and pathophysiological aspects. Several studies indicate that narcolepsy in general presents with high incidence of vivid dreams. Our objectives were to assess oneiric activity in both Nc and Nwc and to search for factors that might be related to vivid dreams.

Methods: Medical history of 118 narcoleptics (62 men, 56 women, 86 with Nc, 32 with Nwc, mean age 41.6) was retrospectively analyzed. Oneiric activity was divided into five categories: (i) low/no recall of dreams; (ii) mundane dreams; (iii) sensually vivid but emotionally neutral dreams; (iv) non-frightening dreams with emotional charge; (v) nightmares. Dreams were considered as frequent when their occurrence was reported as more than once a week. These categories were statistically correlated to other clinical aspects, such as age, gender, body mass index, age at the onset, presence of other symptoms (cataplexy, hypnagogic hallucinations, sleep paralysis, REM sleep behavior disorder and others) and data obtained from polysomnography and multiple sleep latency test (MSLT).

Results: Of the 76 patients (64.4%) reported highly vivid mental activity during sleep. Vivid dreams slightly prevailed in women (45 women versus 31 males) and were present in all patients younger than 15 years (10 subjects). Thirty-five 35 patients (29.7%) reported frequent nightmares. Neither presence of other narcolepsy-related symptoms nor data from polysomnography and MSLT differed significantly between individuals with various types of oneiric activity.

Conclusion: Both NC and NWC present with frequent vivid dreams. Occurrence of nightmares seems increased in these patients, with estimated prevalence of frequent nigthmares in general population as high as 5%. Our data suggest that besides basic pathophysiology, other factors such as environmental and psychological aspects might underlie these phenomena. Further studies will be dedicated to these assumed differences between narcoleptics with and without vivid dreams.

P898

H1N1 influenza vaccination narcolepsy among Swedish children

E. M. SVANBORG and M. ULANDER
Linköping University, Linköping, SE

Introduction: In the fall of 2009 5.3 million Swedes from 6 months of age (approximately 60% of the population) were vaccinated against the H1N1 influenza with Pandemrix® (GlaxoSmithKline, containing AS03 adjuvant. Early in 2010 there were case reports which indicated a connection between severe childhood narcolepsy and this vaccination.

Methods: Our clinic is responsible for neurophysiological testing of 660 000 persons. The Swedish neurophysiological clinics were asked by the government to report all MSLT-diagnosed cases (average sleep latency < 8 min and at least two SOREM-episodes) during 2009 and 2010. We added the years 2007, 2008 and 2011, also comparing the number of referrals and the age distribution of positive cases.

Results: During 2007, 2008 and 2009 26, 20 and 34 MSLT-investigations were performed, which yilded 3 + 2 + 3 cases with definite findings and 3 + 1+ 3 borderline cases. No patient was <10 years old, three were between 10 and 20 years 2010: 26 recordings were performed, 11 with typical findings and two borderline. Two children under 10 years had positive findings and four between 10 and 20 years 2011: 52 recordings were performed, 23 with typical findings. Seven of these were children under age 10, and 13 between 10 and 20 years.

Conclusion: There was a dramatic increase in narcolepsy diagnosis among youngsters <20 years old during 2010 and 2011. Especially disturbing was the finding of children under the age of 10, never previously seen at our laboratory. In 89% of the cases <25 years of age the symptoms had started after the influenza vaccination. This was the case in only two of the adults.

P899

Post influenza A/H1N1 hypersomnolence: report of two cases

D. W. KANG[1], T. W. KIM[1], S. C. HONG[1] and S. Y. SUH[2]
[1]The Catholic University of Korea, Suwon, KR, [2]Stanford University, Stanford, US

Introduction: The cause of narcolepsy is likely autoimmune based on the HLA association. Besides the relationship of narcolepsy to a specific HLA antigen, infections are probably a significant environmental trigger for narcolepsy. In Feb, 2010, two cases following H1N1 infection were reported after onset of epidemic Influenza A/H1N1 infection.

Case Presentation: We present two patients who complained for excessive daytime sleepiness after Influenza A/H1N1 infection. First case, 'Ms. A', is a 42 year old woman who experienced excessive

daytime sleepiness and cataplexy precipitated by anger 10 days after the remission of suspected acute Influenza A/H1N1 infection. Her 16-year-old daughter was diagnosed as narcolepsy 7 years ago. HLA-DQB1*0602 was negative. The diagnosis of narcolepsy with cataplexy was confirmed following extensive investigations including polysomnography and multiple sleep latency test (MSLT). She showed 2.1 min of Mean sleep latency and her SOREMp was 2. Second case, 'Mr. B', is a 16 year old male adolescent who had Influenza A/H1N1 confirmed by RT-PCR. Three months after his recovery, the patient developed monthly hypersomnolent attack with 5 days of mean duration. He was also accompanied by a sudden episode of cataplexy, memory loss and hyperphagia. Polysomnographic recordings inbetween attacks showed relatively normal sleep structure. Two SOREMPs appeared and sleep latency was 5.8 min in MSLT. These findings provide support for association of Influenza A/H1N1 infection with hypersomnolence.

Discussion: Mechanisms in which Influenza A/H1N1 infection trigger narcolepsy are suggested by superantigen stimulation of dormant autoreactive T-cell clones and increased brain inflammation or blood brain penetration. The limitation of this study is that Ms. A and Mr. B refused brain imaging study which could rule out neuroanatomical abnormalities. The cases reported here showed their temporal link between infection and disease onset and unusual clinical presentation. Additive case reports and further examination of a possible link between Influenza A/H1N1 infection and narcolepsy are strongly needed.

P900

Early IVIG treatment has no effect on post-H1N1 narcolepsy phenotype or hypocretin deficiency

S. KNUDSEN[1], B. BIERING-SØRENSEN[2], B. KORNUM[3], E. R. PETERSEN[1], J. D. IBSEN[1], S. GAMMELTOFT[4], E. MIGNOT[3] and P. J. JENNUM[1]

[1]Danish Center for Sleep Medicine, Glostrup, DK, [2]Department of Neurology, Glostrup, DK, [3]Center for Sleep Sciences and Department of Psychiatry, Stanford, US, [4]Department of Clinical Biochemistry, Glostrup, DK

Background: Narcolepsy with cataplexy (NC) is caused by a loss of hypothalamic hypocretin producing neurons. Autoimmunity due to environmental triggers e.g. infections is considered the most likely pathogenesis, recently highlighted by increased numbers of NC cases after H1N1-vaccination/infection. IVIG treatment has previously normalized hypocretin-1 levels in an early treated French spontanous NC case. We here present the first post-H1N1 vaccination NC case treated with a similar IVIG protocol.

Methods and results: In 2009 and in late October 2010 a 21 year old Danish (Caucasian/Asian) man received H1N1-vaccination (Pandemrix; Influvac). January 2011 he developed extreme sleepiness, severe cataplexy triggered by laughter, REM sleep behaviour, but no sleep paralysis or hypnagogic hallucinations. MSLT showed a sleep latency of 2.1 min and SOREMPs in 4/5 naps. CSF hcrt-1 was < 10 pg/ml. He carried the predisposing HLA-DQB1*0301-allelle, but was DQB1*0602-negative. Serum was streptolysin (ASO) positive (200 IU). Mid February 2011 (19 days after disease onset), we treated him with one series of IVIG 1 g/kg/day for 2 days. Post IVIG, he reported a reduction of cataplectic attacks and sleepiness, however, he still had visible severe cataplexy. CSF hcrt-1 remained < 10 pg/ml and the sleep investigations remained abnormal.

Conclusion: Early IVIG treatment normalized neither the phenotype nor the CSF hypocretin-1 levels in this Danish post-H1N1-vaccination NC patient. This could indicate either a different pathogenesis in spontaneous and post-H1N1 narcolepsy or – perhaps more likely – identical mechanisms, but a more fullblown post-H1N1 NC-phenotype and more abrupt loss of hypocretinergic neurons due to pre-immunization, rendering the IVIG-treatment ineffective.

P901

Anti-NMDA-receptor antibody detected in encephalitis, schizophrenia, and narcolepsy with psychotic features

T. KANBAYASHI[1], K. TSUTSUI[1], K. TANAKA[2], S. BOKU[3], W. ITO[4], A. IMANISHI[5], H. SUDA[1], J. TAKAHASHI[1], Y. INOMATA[6], M. TAKESHIMA[1], M. KOSAKA[7], K. YAEGASHI[8], W. YUASA[1], A. MORI[1], S. NISHINO[9], Y. TAKAHASHI[1] and T. SHIMIZU[1]

[1]Akita University, Akita, JP, [2]Kanazawa Medical University, Kanazawa, JP, [3]Hokkaido University, Sapporo, JP, [4]South Carolina University, Columbia, US, [5]Kumamoto University, Kumamoto, JP, [6]Akita Prefectural Center of Rehabilitation and Psychiatric Medicine, Akita, JP, [7]Akita City Hospital, Akita, JP, [8]Nakadori General Hospital, Akita, JP, [9]Stanford University, Palo Alto, US

Recently, causative roles of encephalitis (EN) in major psychiatric features have been emphasized. These symptoms are often in young females with ovarian teratomas with good responses to tumor surgery and immunotherapy, and with autoantibodies to the NMDA receptor (NMDAR).

We have experienced 10 these patients (pts) with various psychiatric and sleep symptoms. These pts exhibited three distinct clinical pictures, and we believe that the report of our cases will bring further discussions on the autoimmune-mediated atypical psychosis.

The first three cases had typical clinical pictures of anti-NMDAR EN, beginning with psychiatric symptoms, and then seizures and disturbances of consciousness occurring. In order to examine the specificity of the anti-NMDAR Ab involvements, we also examined the Ab in other psychotic pts with hypersomnia. Narcolepsy (NA) with severe psychosis was included, because auto-Ab (Ma2, AQP4) mediated mechanisms are suspected in some secondary NA cases. We found that three narcolepsy pts (among five), who had severe psychotic symptoms, were positive for the Ab. These cases were hypocretin deficient, but no significant neurological signs were noted. Antipsychotics and modified electro-convulsion treatment (mECT) were required to manage the psychotic symptoms. In addition, we also found four Ab positive pts with schizophrenia among 51 pts examined. The neurological symptoms were mild in these cases, and mECT was effective for three cases.

Our results showed a high incidence of anti-NMDAR Ab positivity in a broader range of psychiatric disorders, including narcolepsy and schizophrenia pts. Although the causative relationship between anti-NMDAR Ab positivity and psychiatric symptoms in these pts are not known, they exhibit unique demographic and clinical characteristics: Eight are female, and ovarian tumors are associated with 2 pts. Most of their symptoms are resistant to the pharmacological treatments, but responded relatively well to mECT.

P902

Kleine–Levin syndrome: case report

L. ROSCA[1], D. TODEA[2], A. HERESCU[1] and A. COMAN[1]

[1]Clinical Hospital of Pneumology Leon Daniello, Cluj Napoca, RO, [2]University of Medicine and Pharmacy Iuliu Hatieganu Cluj Napoca, Cluj Napoca, RO)

Kleine–Levin syndrome (KLS) is a rare disease characterized by recurrent episodes of hypersomnia and, to various degrees, behavio-

ural or cognitive disturbances, compulsive eating behaviour and hypersexuality The disease predominantly affects adolescent males. Although no population-based studies reporting on KLS prevalence are available, it is generally considered an exceptionally rare disease.

We want to present a case of a patient, 17 years old, who had a lot of upper airway infections during his childhood. From April 2009 until May 2010 he presented nine episodes of hypersomnia, always after an upper airway infection. The mean duration of the episodes was 12 days. During these episodes the patient had some behavior changes. The blood samples (hematology and biochemy) were in normal ranges. The magnet resonance imaging of the brain was normal. The polysomnography revealed a respiratory disturbance index of 2.1, and at the multiple sleep latency test the average sleep latency was 00:01:30, during one episode of hypersomnia. After clinical and paraclinical examination, we established the diagnose of Primary Kleine Levin Syndrome. The particularity of the case was the large number of episodes of hypersomnia, the long duration of them in a short time (13 months) and also the poor quality of life for this patient during this time.

P903

Pitolisant, an inverse agonist of the histamine H3 receptor: an alternative stimulant for narcolepsy-cataplexy in teenagers with refractory sleepiness

C. O. INOCENTE[1], I. ARNULF[2], H. BASTUJI[1], A. THIBAULT-STOLL[3], A. RAOUX[4], R. REIMÃO[5], J.-S. LIN[1] and P. FRANCO[1]

[1]University of Lyon, Lyon, FR, [2]Hospital Pitié-Salpêtrière, Paris, FR, [3]Clinique Sainte Barbe, Strasbourg, FR, [4]Hôpital Femme Mère Enfant, Lyon, FR, [5]University of São Paulo Medical School, São Paulo, BR

Objectives: Narcolepsy is a rare disabling sleep disorder characterized by excessive daytime sleepiness and cataplexy (sudden loss of muscle tone). Drugs such as pitolisant, which block histamine H3 autoreceptors, constitute a newly identified class of stimulants because they increase brain histamine and enhance wakefulness in animal and human adult narcolepsy.

Methods: We report our experience with the off-label use of Pitolisant in four teenagers with narcolepsy/cataplexy with severe daytime sleepiness, refractory to available treatments (modafinil, methylphenidate, mazindol, sodium oxybate, and D-amphetamine).

Results: All teenagers developed their disease during childhood (11.3–2.4 years; 50% boys) and were 17.3–0.8 years old at the time of pitolisant therapy. Pitolisant treatment was increased from 10 to 30 mg ($n = 1$) and 40 mg ($n = 3$). The adapted Epworth Sleepiness Score decreased from 14.3 T 1.1 to 9.5 to 2.9 ($P = 0.03$) with pitolisant alone to 7 T 3.4 when combined with mazindol ($n = 1$), methylphenidate ($n = 1$), or sodium oxybate plus modafinil ($n = 1$). Mean sleep onset latency increased from 31 T 14 to 36 to 8 min ($P = 0.21$) on the maintenance of wakefulness test. The severity and frequency of cataplexy were slightly improved. Adverse effects were minor (insomnia, headache, hot flushes, leg pain, and hallucinations) and transitory, except for insomnia, which persisted in two teenagers. The benefit was maintained after a mean of 13 months.

Conclusions: Pitolisant could constitute an acceptable alternative for the treatment of refractory sleepiness in teenagers with narcolepsy.

P904

Daytime sleepiness: national survey of the Institut National du Sommeil. Journée du Sommeil®, France, 2011

D. LÉGER[1], A. LOPEZ[1], F. FAUGERON[1], J. ADRIEN[1], F. BECK[2], A. BRION[1], C. GRONFIER[1], J. KRIEGER[1], A. MUZET[1], P. PHILIP[1], M.-F. VECCHIERINI[1] and J. PAQUEREAU[1]

[1]Institut National du Sommeil et de la Vigilance, Paris, FR, [2]INPES, Saint Denis, FR

Goal: assessing sleepiness France in order to better identifying causes and consequences and enhance French awareness on sleepiness at the wheel and in their daily lives.

Method: Telephone call survey, made in January 2011 on a 1012 subjects from 18 to 60 years old representative of the French national adults population. Questionnaire was built by the scientific committee of the INSV and included: sociodemographic data, work schedules, familial structure, detailed sleep and nap schedules and sleepiness assessed by the Epworth sleepiness scale (ESS).

Results: 19% of French had an ESS score >/11et 3 > 16.7% of the sleepy subjects reported unvaincing episodes of sleepiness during daytime. However only 20% of the sleepy French have talked about it to their doctors. Daily transportation time (DTT) was shown as a contributor of sleepiness. It was on average 80 min per day in the general group. Eighteen percent had a DTT above 2 h. Subjects with an ESS > 16 had an average DTT of 3 h per day ($P < 0.001$ compared to the non sleepy). They also reported a significant highly mileage per day. Twelve percent of the drivers confessed that they had to stop for sleeping while driving at least once in the last 12 months. Three percent said they have slept at the wheel at least once in the last 12 months. Thirty-one percent of French adults reported sleeping an average 6 h or less. Forty-three percent of those who said they were sleepy at least three times a week and 56% of those who reported sleepy driving weres short sleepers (an average 6 h or less). Thirty-five percent of shift workers had an ESS > 15.

On average French spent 2 h and 37 min on evening to watch TV or DVD videos. The average time spent on the web was 99 min during working days and 70 min on week-ends.

P905

Improving differential symptomatic diagnosis of fatigue and sleepiness related conditions

O. MAIRESSE[1] and D. NEU[2]

[1]CHU Brugmann/Royal Military Academy, Brussels, BE, [2]CHU Brugmann, Brussels, BE

Objective: Semiological, semantic and phenomenological confusion about fatigue and sleepiness persist in clinical practice. Distinguishing between both constructs is of great importance for the treatment of sleep disorders in which both conditions can overlap. The purpose of this study is to offer an add-on to existing sleepiness and fatigue scales which quantifies this level of overlap.

Method: Of 51 drug-free individuals (M age 47 ± 13 years, 23 females) without fatigue or sleepiness complaints, with either one of them or both, or with non-restorative sleep complaints were admitted to our sleep lab for a two-night PSG. Symptom intensities of fatigue and sleepiness were assessed by means of the Fatigue Severity Scale (FSS) and the Epworth Sleepiness Scale (ESS). Psychometric quality of both scales was assessed by means of Rasch Analysis. In order to quantify the overlap between both scales, Rasch-calibrated person measures were equated by means of common person linking (CPL).

Results: Rating scale diagnostics showed that response categories overlapped or were insufficiently spaced in both scales. Rescaled

instruments showed good fit of the data to the model, as evidenced by good person reliability (ESS: 0.80; FSS: 0.82) and good item reliability (ESS: 0.96; FSS: 0.82). Rasch measures and fit statistics show good construct validity and undimensionality [INFIT and OUTFIT < 2 on all but one item (FSS)]. Unidimensional measurement is further supported by Rasch Factor Analysis (eigenvalues of 2nd dimension: ESS: 1.8 and FSS: 2.1). Common person linking showed 62.7% overlap of sleepiness and fatigue person measures and the failure of traditional cut-off scores to determine correct therapeutic group adherence.

Conclusion: Both the ESS and the FSS are adequate, unidimensional linear instruments to measure sleepiness and fatigue respectively, considering proper calibration. A concordance diagram was created cross-plotting raw scale sores and calibrated measures, and displaying margins wherein both constructs overlap. This diagram allows clinicians to determine which condition significantly prevails over the other allowing for a more precise diagnosis.

P906

Behaviourally induced insufficient sleep syndrome

E. WERTH[1], N. MICHAEL[2], C. L. BASSETTI[3] and C. R. BAUMANN[1]
[1]University Hospital Zürich, Zurich, CH, [2]Rheinburg-Klinik, Walzenhausen, CH, [3]University Hospital Berne, Berne, CH

Objectives: When an individual chronically fails to obtain the amount of sleep required to maintain normal levels of alertness and wakefulness and no other cause for these daytime complains can be found, the diagnosis of behaviourally induced insufficient sleep syndrome (BIISS) is made. Its significance is mostly unappreciated by the patient. Actually, some patients may develop secondary symptoms which may even become the main focused complains and often serve to obscure the primary cause of the difficulties.

Methods: With this retrospective study, we aimed at a better and controlled description of patients diagnosed with BIISS. We extended the diagnostic criteria for BIISS and identified 47 consecutive patients with this syndrome in our Center of Sleep Disorders. We applied actigraphy recordings, polysomnography and multiple sleep latency tests and compared the findings with 19 age- and sex-matched healthy controls.

Results: Mean age of the BIISS patient was 40 ± 12 years (mean ± SD). Age of BIISS onset was bimodal distributed with a first peak occurring at age 20–25 years a second peak present at age 40–45 years. Only 30% were females. Mean ESS was 14.1 ± 3.6. Patients mostly complain symptoms of excessive daytime sleepiness; however, many individuals reported other symptoms as sleep attacks without general daytime sleepiness, fatigue, sleep drunkenness, concentration and attention deficits or cognitive impairment. Actigraphy revealed mean sleep duration of 6.6 ± 0.8 h during week days and of 7.9 ± 1.2 h during weekends or holidays. Compared to actigraphy recordings, BIISS patients but not controls overestimated their sleep length when they filled out a sleep questionnaire. Total sleep times per 24 h measured by actigraphy were similar in BIISS patients and in controls. Polysomnography recordings did not reveal markers distinguishing BIISS from healthy controls. On multiple sleep latency tests, eight patients (17%) had narcolepsy-like findings.

Conclusion: The results of this case series indicate[1] that there are a noticeable large number of patients who were not aware that their sleep duration was insufficient and (2) our results confirm the challenge of a correct diagnosis of BIISS, with a significant overlap of critical findings with controls and with patients with narcolepsy.

P907

Aspects of daytime sleepiness in patients with hypersomnia

N. IZURIETA HIDALGO, C. JARA, R. POPP and P. GEISLER
University of Regensburg, Regensburg, DE

Objectives: Excessive daytime sleepiness (EDS) is the core symptom of patients with hypersomnia. It is a multidimensional concept, and its aspects can vary across specific diagnostic groups. The aim of this study was to compare established methods for the assessment of EDS (ESS for subjective sleepiness, a sustained attention task (SAT) for psychomotor performance, MSLT for physiological sleep propensity) in patients with narcolepsy with cataplexy (NC+), narcolepsy without cataplexy (NC-), idiopathic hypersomnia (IH), behaviourally induced insufficient sleep syndrome (BIISS) and obstructive sleep apnea syndrome (OSAS).

Methods: We included 243 unmedicated patients (mean age 33.3 years., 113 females) who fulfilled the criteria for the above mentioned diagnoses, and 36 normal controls (CON). All had a 5-session MSLT (30 min version), ESS and a 25 min SAT (Macworth-Clock). Subjects were selected from a larger pool to obtain age matched groups. The resulting groups were: NC+ n = 44/mean age (years) 33.0; NC- n = 41/29.4; IH n = 51/32.0; BIISS n = 36/34.6; OSAS n = 35/39.3; CON n = 36/31.7 (no significant age difference).

Results: Mean sleep latency in MSLT was significantly shorter in NC+ and NC- than in all other groups, which did not differ significantly. Rate of sleep onset REM periods (SOREM) was higher in NC+ than in NC- (3.3 versus 2.6), and in both narcolepsy groups higher than in all other groups. Impairment score in SAT was higher in NC+, NC-, IH and OSAS than in BIISS and CON. In ESS, all patients groups scored higher than CON, with NC+, NC-, IH and OSAS still higher than BIISS (P < 0.01).

Conclusion: The diagnostic groups show different patterns of impairment in the dimensions of EDS in a hierarchical order. Subjective sleepiness (ESS) is increased in all patient groups (in BIISS to a lesser extent than in the other patient groups), while psychomotor performance (SAT) is not affected in the BIISS group. Physiological sleep propensity (MSLT sleep latency) is affected mainly in narcolepsy; it separates these patients from all other groups. Number of SOREMs in the MSLT should not be considered in this context, because this variable is used to define groups (NC- versus IH).

P908

Determinants and mediators of subjective versus objective sleepiness in healthy controls and apnoeics

I. KRITIKOU, S. PEJOVIC, A. VGONTZAS, J. FERNANDEZ-MENDOZA, M. BASTA and E. BIXLER
Penn State College of Medicine, Hershey, US

Objective: Daytime sleepiness, the most frequent complaint in a sleep clinic, is measured both subjectively and objectively. However the association of these two methods of assessment is inconsistent. The aim of this study was to assess the factors that influence objective versus subjective sleepiness and to examine the association of these two methods with IL-6, a sleepiness mediating cytokine.

Methods: One-hundred and twenty-four non-diabetic healthy controls and sleep apneics participated in the study (83 males, age: 51.28 ± 8.97 year, BMI: 29.62 ± 4.61 kg/m^2, 46.8% obese, 45.2% sleep apneics) underwent polysomnography in the sleep lab for four nights. Apnea/hypopnea index (AHI) was assessed and mean objective total sleep time (TST) was calculated as the average of

TST of nights two and three. Abdominal adiposity was measured using Computed Tomography at the L3 lumbar level and blood samples were drawn every hour for the assessment of Interleukin-6 (IL-6) levels. Subjective sleepiness was assessed with the Epworth Sleepiness Scale (ESS), objective sleepiness with the Multiple Sleep Latency Test (MSLT; six naps on the 4th day). The Beck Depression Inventory-II (BDI-II) was used to evaluate depressive symptomatology.

Results: In multiple linear regression models after controlling for confounders, ESS score was independently and significantly associated with depression ($\beta = 0.24$, $P = 0.007$), visceral adiposity ($\beta = 0.24$, $P = 0.04$) and AHI ($\beta = 0.19$, $P = 0.05$). Mean MSLT values were associated with nighttime total sleep time ($\beta = -0.29$, $P = 0.01$) and sleep latency ($\beta = 0.34$, $P < 0.01$). Finally mean IL-6 values were significantly and independently associated with MSLT ($\beta = -0.22$, $P = 0.02$) but not with total ESS score ($\beta = 0.05$, $P = 0.60$).

Conclusions: It appears that subjective sleepiness is primarily determined by depression and metabolic factors, whereas objective sleepiness by an individual 'trait' most likely genetically determined. Moreover, objective sleepiness appears to have a stronger association with IL-6 levels compared to subjective sleepiness. These preliminary findings suggest that subjective versus objective methods measure different aspects of sleepiness/fatigue in humans.

P909

Daytime continuous polysomnography predicts MSLT results in hypersomnias of central origin

F. PIZZA[1], K. MOGHADAM[1], S. VANDI[1], S. DETTO[1], F. POLI[1], E. MIGNOT[2], R. FERRI[3] and G. PLAZZI[1]

[1]University of Bologna, Bologna, IT, [2]Stanford University, Palo Alto, US, [3]Oasi Institute for Research on Mental Retardation and Brain Aging, Troina, IT

Objective: To investigate spontaneous daytime sleep at 24 h continuous polysomnography (PSG) in hypersomnias of central origin.

Methods: Daytime PSG features were compared to multiple sleep latency test (MSLT) data in 100 consecutive patients presenting with excessive daytime sleepiness and with a final diagnosis of narcolepsy with cataplexy/hypocretin deficiency ($n = 39$), narcolepsy without cataplexy ($n = 7$), idiopathic hypersomnia ($n = 21$), and 'hypersomnia' with normal sleep latency at MSLT ($n = 33$).

Results: Daytime sleep time was significantly higher in narcolepsy-cataplexy but similar in the other groups. Receiver operating characteristics (ROC) curves showed that the number of naps during daytime PSG predicted a mean sleep latency ≤ 8 min at MSLT with an area under the curve of 0.68 ± 0.05 ($P < 0.005$). The number of daytime sleep-onset REM periods (SOREMPs) in spontaneous naps strikingly predicted the scheduled occurrence of two or more SOREMPs at MSLT, with an area under the ROC curve of 0.93 ± 0.03 ($P < 10–12$). One spontaneous SOREMP during daytime had a sensitivity of 96% with specificity of 75%, whereas two SOREMPs had a sensitivity of 75%, with a specificity of 95% for a pathological REM sleep propensity.

Conclusions: The features of spontaneous daytime sleep correlate with MSLT findings. Notably, the occurrence of multiple spontaneous SOREMPs during daytime clearly identified patients with narcolepsy, as well as during the MSLT.

P910

Daytime hypersomnolence due to sleep-disordered breathing is not associated with excessive yawning

S. DUMITRU[1], S. GYFTOPOULOS[1], I. XAZAPIS[1], A. CHRONOPOULOU[1], P. DEMERTZIS[1] and E. KOSMAS[2]

[1]Chest Diseases Hospital 'Sotiria', Athens, GR, [2]Metropolitan General Hospital, Voula, GR

It has been suggested that sleep apnea may have an adaptive benefit, the reduction of nocturnal respiratory heat loss. On the other hand, there is a growing body of evidence that yawning may be a thermoregulatory mechanism and it represents an adaptation to conditions that increase body/brain temperature, such as sleep deprivation. Since sleep apnea and yawning are thermoregulatory mechanisms functioning towards opposite directions, we hypothesized that excessive daytime sleepiness due to sleep apnea is not characterized by excessive yawning. We have studied 85 subjects with excessive daytime hypersomnolence (Epworth scale > 11) who underwent a full night diagnostic polysomnography (PSG). Patients were categorized as sleep apneic when their Apnea-Hypopnea Index (AHI) was >14 events/hour and as non-sleep apneic when their AHI was < 5 events/hour. Before PSG, all patients were asked whether they usually experience bouts of yawning from morning awakening until early evening (6 pm) after an efficient night sleep (>6 h). We discarded 12 subjects with AHI 5–14 events/hour. Fifty two subjects with hypersomnolence were diagnosed to suffer from sleep apnea syndrome [mean (SD); age 47 (13); Epworth scale 16[3]; AHI 51 (22)], while the remaining 21 sleepy subjects [age 44 (17); Epworth scale 17[3]; AHI 2 (1)] had no sleep apnea. Bouts of yawning have been reported by only nine out of the 52 sleepy and apneic patients (17%) and by 18 out of the 21 sleepy and nonapneic patients (86%, $P < 0.001$). It seems that absence of yawning bouts in a sleepy patient may predict the presence of sleep apnea syndrome as a cause for the excessive daytime sleepiness with a sensitivity of 83% and a specificity of 86%. The reason is unclear, however it can be speculated that sleep apnea and yawning, both sharing an adaptive thermoregulatory ability towards opposite directions (heating/cooling respectively), usually do not coexist. Our data suggest that questioning about excessive daytime bouts of yawning should be included in the recording of symptoms when taking medical history from sleepy subjects.

P911

Changes in sleep architecture – specific EEG phenomenons in reflux disease?

W. BÖHNING[1] and E. BRIESE[2]

[1]MZG, Bad Lippspringe, DE, [2]Sleep Centre CHK, Bad Driburg, DE

Reflux disease has a high prevalence. Daytime sleepiness is a key sympton in reflux.

Are there specific changes in EEG for reflux?

Patients and methods: Eleven consecutive patients with daytime sleepiness and suspected sleep apnea. Full polysomnography with simultaneous and time-synchronic longterm pH-probe in the epipharynx.

Results: There is a high coincidence of pathological so-called 'silent' reflux and sleep apnea. Reflux episodes are independant of apnea events. In sleep microstructure there is striking evidence of specific changes in EEG, particular in the form of cyclic alternating pattern with the subtypes A2 and A3.

Conclusion: In sleep apnea patients with persisting daytime sleepiness in spite of effective CPAP-therapy the specific EEG changes

may be indicative for underlying reflux disease. So the specific diagnosis should be taken into account.

P912

Cardiac vagal modulation and baroreflex sensitivity are reduced during wakefulness in patients with narcolepsy-cataplexy

A. SILVANI, D. GRIMALDI, G. BARLETTA, S. BASTIANINI, G. PIERANGELI, G. PLAZZI and P. CORTELLI
Università di Bologna, Bologna, IT

Objectives: Hypocretin/orexin signalling differs between wake-sleep states, is involved in cardiovascular control, and is functionally lost in patients with narcolepsy with cataplexy (NC). Results of investigations on cardiovascular control in NC have been contrasting and often limited to the waking behaviour. We investigated whether control of spontaneous variability of heart period (HP) and systolic blood pressure (SBP) is altered in NC during wakefulness (W), non-rapid-eye-movement sleep (NREMS) and rapid-eye-movement sleep (REMS).

Methods: Polysomnographic recordings and non-invasive blood pressure measurements (Portapres, Finapres Medical Systems) were performed on nine drug-free male NC and nine matched healthy control subjects (CS) in continuous bed rest. The analysis was performed on full-blown episodes ≥5 min of evening W before sleep and of night-time NREMS and REMS. Spontaneous fluctuations of HP and SBP were analysed with an array of techniques (HP variability analysis in the time and frequency domains; SBP versus HP transfer function; sequence technique; SBP versus HP cross-correlation function; coherent averaging of spontaneous SBP surges) yielding complementary information on cardiac autonomic function at different time scales.

Results: We found that SBP variability did not differ significantly between NC and CS in any wake-sleep state. However, during W before sleep, NC showed significantly decreased indexes of vagal HP modulation, cardiac baroreflex sensitivity, and amplitude of cardiac positive-feed-back and feed-forward control compared with CS. These differences were not statistically significant during either NREMS or REMS. Analysis of HP versus SBP cross-correlation functions evidenced a greater negative correlation between HP and subsequent SBP values in NC with respect to CS during NREMS, indicating that the extent to which feed-forward mechanisms explained HP variability was increased in NC.

Conclusion: These results suggest differences in autonomic regulation of spontaneous cardiovascular variability between male NC and CS in NREMS and particularly in W before sleep, when HP fluctuations driven by baroreflex and non-baroreflex (positive feed-back, feed-forward) control mechanisms may be blunted in NC because of reduced cardiac vagal modulation. This provides the rationale for further work investigating the prevalence in real-life conditions and the prognostic significance of these autonomic alterations in NC patients.

P913

Childhood narcolepsy in Finland before and after the 2009–2010 H1N1 pandemic vaccination campaign

M. PARTINEN[1], O. A. SAARENPÄÄ-HEIKKILÄ[2], C. HUBLIN[3], I. JULKUNEN[4] and T. KIRJAVAINEN[5]
[1]Finnish Narcolepsy Research Centre, Helsinki, FI, [2]Tampere University Hospital, Tampere, FI, [3]Finnish Institute of Occupational Health, Helsinki, FI, [4]National Institute for Health and Welfare, Helsinki, FI, [5]Helsinki University Central Hospital, Helsinki, FI

Objectives: Several lines of evidence have shown that the peak age of onset of narcolepsy is around 15 years of age. Onset before age of 10 years has been rare. From the beginning of 2010 an exceptionally large number of Finnish children have been diagnosed with an abrupt onset narcolepsy. Our aim was to find out changes in the incidence and to have information about the clinical picture of narcolepsy.

Methods: All Finnish hospitals and sleep clinics were contacted. The national hospital discharge register from 2002 to 2009 was used as a reference. Two experts reviewed the medical and laboratory records of all cases to verify the diagnosis, and to describe the clinical findings. In doubtful cases a panel of experts made the final decision about the diagnosis.

Findings: During 2002–2009 altogether 335 cases (children and adults) of narcolepsy were diagnosed in Finland. The annual incidence was 0.79 per 100 000 inhabitants (95% confidence interval 0.62–0.96). The incidence in subjects aged <17 year was 0.31 (0.12–0.51)/100 000/year. In 2010, the incidence rose rapidly among children aged <17 year to 5.3/100 000/year (17-fold increase). In 2010 among adults ≥20 years of age the incidence rate remained stable being 0.87/100 000/year. All HLA-typed children were positive for narcolepsy risk allele DQB1*0602/DRB1*15. A Pandemrix vaccination had been given to 50/54 children before (median 42 days) onset of first symptoms. All vaccinated children had abnormal Multiple Sleep Latency Test (mean SL 1.8 ± 1.4 min, mean number of sleep-onset REM-periods 3.8 ± 0.9). In most cases cataplexy started almost simultaneously with EDS. The CSF-hypocretin-1 level was clearly abnormal in all who had had a spinal tap taken ($N = 13$). Psychiatric symptoms were common. Sixty-three percent had a marked weight increase during the first months of the disease onset. Only 10% of newly diagnosed children suffered from an influenza-like illness prior to onset of narcolepsy. After about one year follow-up many children are doing much better but some are still seriously disabled.

Conclusions: The incidence of childhood narcolepsy has dramatically increased after the pandemic vaccination campaign in 2009–2010. There is an association with the Pandemrix vaccination. We are investigating different genetic and environmental factors that may be involved in the pathogenesis of this type of narcolepsy. We consider it very unlikely that the onset of narcolepsy in our patients was associated with microbial infections.

MP is a consultant for UCB Pharma, Bioprojet, and Leiras. He has received honoraries for lecturing and travel grants from Cephalon, Glaxo Smith Kline,
Leiras, MSD, and Servier. He has been involved in clinical trials on narcolepsy and other sleep disorders supported by Actelion, Bioprojet, MSD, Pfizer and UCB Pharma. He is Chairman of the Board of the Helsinki Sleep Clinic, and member of the Board in the Finnish Sleep Sleep Research Society. CH has received honoraries for lecturing from UCB Pharma, and he is a Member of the Board in the Finnish Narcolepsy Association. OSH has received honoraries for lecturing from Janssen-Cilag and UCB Pharma. IJ and TK have nothing to declare.

Poster Session – Physiology of Sleep Deprivation

P914

Longitudinal analysis of the homeostatic response to sleep deprivation in adolescents

L. TAROKH[1], M. CARSKADON[2] and P. ACHERMANN[1]
[1]University of Zurich, Zurich, CH, [2]EP Bradley Sleep Research Lab, Providence, US

Objectives: To date only one study has examined the effects of sleep deprivation on the sleep EEG during adolescence. In this cross-sectional study by Jenni et al. (SLEEP, 2005), the increase in slow-wave activity (SWA) following sleep deprivation was greater in mature as compared to pre/early pubertal adolescents. In the current study we examine the response to sleep deprivation in a longitudinal sample of postpubertal adolescents.

Methods: Polysomnography was recorded in seven teens (three females) when they were ages 15/16 (initial) and again 2 years later (follow-up) after approximately 14 h of wakefulness (baseline) and after approximately 32 h of wakefulness (recovery). Non-rapid eye movement (NREM) sleep spectra were calculated for the first cycle for derivation C3/A2 and power in five frequency bands was calculated: delta (0.6–4.8 Hz), theta (5–8.4 Hz), alpha (8.6–10.8 Hz), and sigma (11–16 Hz). A repeated measures ANOVA with factors assessment (initial versus follow-up) and condition (baseline versus recovery) was used to examine spectral power in each band.

Results: Delta ($F_{1,6} = 12.36$; $P = 0.013$) and theta ($F_{1,6} = 18.53$; $P = 0.005$) power significantly declined between assessments independent of condition (main effect: assessment). In addition, power was greater on recovery compared to baseline nights independent of assessment (main effect: condition) in the delta ($F_{1,6} = 25.93$; $P = 0.002$) and theta ($F_{1,6} = 32.05$; $P = 0.001$) bands. There was no interaction between assessment and condition.

Conclusion: Similar to previous studies, we observed a maturational decline in NREM sleep EEG power on baseline and recovery nights. On the other hand, the compensatory increase in delta and theta power following sleep deprivation did not change from mid to late adolescence. We plan to examine this issue in a larger group of mid-older adolescents and in younger adolescents.

Support: This work was supported by the National Institute of Mental Health (Grant MH076969 to MAC.) and Swiss National Science Foundation (Grant 320030-130766 to PA).

P915

Effect of 92 h awake: experimental insomnia

J. SCHEPER, R. VAN DEN BOSSCHE and A. W. DE WEERD
SEIN, Zwolle-Groningen, Zwolle, NL

Objectives: The aim of the present study was to follow a 33 years old healthy male during 92 h. of sleep deprivation (SD) and his recovering period after SD. This endeavor was meant to break the world record bartending for the Guinness Book of Records and raising money for the ALS foundation. He was allowed to sleep for 5 min for every hour he stayed awake. In fact he preferred to have four periods of 30 min sleep over the whole period.

Methods: During this 4 days and nights he was continuously video monitored and observed by two persons who registered all activity. Moreover we recorded the wake and sleep EEG together with polysgraphy, adding up to limited PSG, using Embletta X100 Embla Remlogic. This included electrode positions F4 and O2 referenced to M1, one EOG channel and two sub mental EMG channels. Awake activity and sleep structure were analyzed through visual scoring following the AASM rules. Actigraphy was done as well during the SD and the ensuing 8 days.

Results: In the first two naps he slept only a few minutes; in the last naps sleep started early and N3 sleep was prominent. After 78 h there was some irritability and drowsiness. Micro sleeps were seen when he was still active during dice games. No hallucinations or further deteriorations occurred. After SD in the 13 h and 34 min time in bed, there was 12 h and 52 min recovery sleep: N1 25 min, N2 405 min, N3 219 min, REM 123 min; sleep onset: 1 min. REM latency: 89 min and onset N3 after 8 min. The results of actigraphy gave similar aspects during the SD. In the 8 days after SD his normal sleep/wake rhythm reoccurred.

Analysis and conclusions: This PSG recording of an unique prolonged SD was possible under these special rules and circumstances. The patterns after SD indicated that N3 sleep recovered earlier than REM sleep suggesting that N3 sleep is most important. This is in accordance with previous findings.

P916

Neurophysiologic evaluation of sleep-wake alteration resulted from different sleep stage interventions

L. MAISURADZE[1], N. LORTKIPANIDZE[1], N. ONIANI[1] and T. ONIANI[2]
[1]Ilia State University, Tbilisi, GE, [2]Georgian National Academy of Sciences, Tbilisi, GE

Objectives: The purpose of this study was to estimate, from the neurophysiologic perspective, sleep-wake alteration due to direct and indirect paradoxical sleep (PS) interventions that make possible to consider the relationship between sleep-wakefulness cycle (SWC) stages.

Methods: Eight mature cats chronically implanted with electrodes were recorded for 24-h SWC during baseline (B), PS interruption (PSI) at the inception of rapid eye movements and recovery (PR), and deep-slow- wave-sleep (DS) interruption (DSI) at the inception of first ponto-geniculo-occipital waves (PGO) and recovery (DR). Intervention conditions were administered in the course order PSI and DSI to one group of animals and vice versa to another one; experiments were separated by a week intermission of complete SWC. Total amount and duration of individual episodes of SWC phases, their latency and percent ratio were compared with baseline. The duration of pre-PS stage of DS was calculated to identify the time needed for the transitions of DS to PS (Tt).

Results: PSI tended to gradual increase of PS entrances; an occasional rise of prolonged episode of wakefulness was followed by the lengthening of Tt with subsequent increase of the PS latency. Accordingly, delay of PS onset was characteristic for this condition. In the percentage ratio of SWC states, the most part was taken by wakefulness. In the initial hours of PR, there was an immediate large increase of PS and marked decrease of wakefulness. During DSI the PS episodes did not appear in the SWC. The number of DSI was less than PSI. An increase of the DS episode prior to PGO appearance was detected when the animal spent more time in waking state. There was prominent increase in total waking time in parallel of the DS percent decrease and lack of PS. DR was generally characterized by a reduced DS latency, increased latency between DS onset and subsequent PS episodes, and slightly longer PS periods. In DR,

the values of slow-wave-sleep (SS) stage parameters were increased relative to baseline, whilst waking amount was reduced. PS compensation following DSI condition tended to be delayed till a certain amount of DS was occurred.

Conclusion: The DSI design was successful in the term to prevent even PS appearance in the SWC; PS was reduced by 100%. Our findings demonstrate that PS propensity is gradually formed during SS; PS onset depends on the prior sleep-waking history; prolonged waking state is able to prevent increased PS propensity.

P917

Sleep deprivation affects cortical excitability

M. GORGONI[1], F. FERLAZZO[1], F. MORONI[2], S. DONARELLI[1], A. DATRI[1], S. FANELLI[1], I. GIZZI TORRIGLIA[1], G. LAURI[1], S. SDOIA[1], M. FERRARA[3], C. MARZANO[1], P. M. ROSSINI[4] and L. DE GENNARO[1]

[1]University of Rome, Rome, IT, [2]University of Bologna, Bologna, IT, [3]University of L`Aquila, L`Aquila, IT, [4]Catholic University of Rome, Rome, IT

Objectives: Sleep deprivation (SD) has degrading effects on alertness and cognitive performance that suggests the existence of alterations in the state of cortical circuits. Animal studies point to an increase of cortical excitability during prolonged wakefulness, while human studies found conflicting results. Only a recent experiment showed a clear increase of cortical excitability, as estimated by TMS-evoked potentials (TEPs) after SD. In the present study, we used full-scalp electroencephalography (EEG) and somatosensory evoked potentials (SEPs) recordings, with the aim to assess the effects of SD on cortical excitability.

Methods: During 40 h of prolonged wakefulness, 16 healthy subjects participated in four experimental sessions (11.00 am and 11.00 pm of the 1st and 2nd day) in the following sequence: (a) resting EEG; (ii) SEPs recordings. The amplitude of N20-P25 complex, N20 and P25 components were considered the principal dependent variables.

Results: Analyses of resting EEG show a net increase, after SD, of delta and theta activity. SD induces a progressive increase of the P25 amplitude in somatosensory cortex. This finding is confirmed by the scalp maps of the statistical comparisons between After-SD and Before-SD SEPs recordings, which show a voltage increase in posterior areas and a voltage decrease in anterior areas after SD in correspondence of the time window between 24 and 27 ms (around P25 component). These changes in SEPs topography after SD are also negatively correlated with theta EEG activity in the left temporal region.

Conclusion: Results confirm that delta and theta activity are the principal EEG markers of sleepiness during prolonged wakefulness. SD induces a net increase of cortical excitability. Modifications of SEPs topography after SD seem to be modulated by the underlying EEG background activity.

P918

The role of alpha1 adrenoceptor activation during sleep deprivation in the subsequent sleep rebound

Z. LELKES, I. HAJDÚ and B. BODOSI

University of Szeged, Szeged, HU

Objectives: We have reported that administration of an alpha1-adrenergic agonist, methoxamine, at the onset of sleep deprivation (SD) enhanced the subsequent non-REM sleep (NREMS) rebound. In order to elucidate the role of alpha1-adrenergic receptor activation in the rebound sleep we studied the effects of prazosin (PRZ), an alpha1-adrenergic antagonist, administered at the onset of SD, on the subsequent sleep rebound.

Methods: Male Sprague-Dawley rats ($n = 7$) with implanted EEG electrodes were injected intraperitoneally with distilled water (DW) on the baseline day, and with DW or 1 mg/kg prazosin (PRZ) on the subsequent SD day. On the SD day after the injection the animals were sleep deprived by gentle handling for 6 h. The sleep-wake activity was recorded for 12 h postinjection on both days. On the following week the same experimental schedule was repeated again, but those rats, which received PRZ on the SD day of the previous week, were treated with DW only, and those ones, which received only distilled water on the week before, were treated with PRZ at the onset of SD.

Results: PRZ treatment resulted in a tendency to a decrease in NREMS rebound. REM sleep (REMS) rebound was suppressed by PRZ.

Conclusion: Previously we have reported that stimulation of alpha1-adrenergic receptors during SD enhances NREMS rebound. In our present study the blockade of these receptors induced only a tendency to a decrease in NREMS rebound. Thus activation of alpha1-adrenergic receptors may contribute to the mechanism of NREMS rebound, but this contribution is very limited and not essential. The finding that PRZ suppresses REMS rebound is in line with our previous report, which emphasizes the role of alpha1-adrenergic receptors in the REMS rebound.

P919

Effects of 29 h sleep deprivation on local cold tolerance in humans

F. SAUVET[1], C. BOURRILHON[1], Y. BESNARD[1], P. VAN BEERS[1], A. ALONSO[1], J.-M. COTTET-EMARD[2], G. SAVOUREY[1] and J.-C. LAUNAY[1]

[1]Institut de recherche biomédicale des armées, Brétigny sur Orge, FR, [2]CHU Croix Rousse, Lyon, FR

To study the effects of a 29-h total sleep deprivation (TSD) on local cold tolerance, 10 healthy men immersed their right hand for 30 min in a 5°C water bath (CWI) after a 30-min rest period in a thermoneutral environment (Control), after a normal night (NN) and after a 29-h TSD. CWI was followed by a 30-min passive rewarming (Recovery). Finger 2 and 4 skin temperatures (Tfi2, Tfi4) and finger two cutaneous vascular conductance (CVC) were monitored to study cold-induced vasodilation (CIVD). Rectal temperature (Tre), mean skin temperature (Tsk), heart rate (HR) and blood pressure (BP) were also measured. Blood samples were collected at the end of the Control, at the lower and at the first maximal Tfi2 values during CWI and at Recovery. Tfi2, Tfi4 and CVC did not differ after TSD at Control, whereas they were reduced during CWI (-2.6 ± 0.7°C for Tfi2; -2 ± 0.8°C for Tfi4, -79 ± 25% for relative CVC, $P < 0.05$) as during Recovery (-4.9 ± 1.9°C for Tfi2, -2.6 ± 1.8°C for Tfi4, -70 ± 22% for relative CVC, $P < 0.05$). After TSD, the lower CVC values appeared earlier during CWI (-59 ± 19.6 s, $P < 0.05$). After TSD at Control and CWI, plasma endothelin levels were higher and negatively correlated with Tfi2, Tfi4 and CVC. However, no effect of TSD was found on the number and amplitude of CIVD and in Tre, HR, BP and catecholamines, for all periods. We concluded that TSD induced thermal and vascular changes in the hand which impair the local cold tolerance, suggesting that TSD increases the risk of local cold injuries.

P920

Can sleep inertia decrease postural stability?

P. FORSMAN, A. TIETÄVÄINEN and E. HÆGGSTRÖM
University of Helsinki, Helsinki, FI

Objectives: Postural stability (PS) affects everyday functioning and research shows that both the circadian and the homeostatic processes influence PS. Hence, PS may be a marker of fatigue from time of day and time awake. The effect of sleep inertia on PS has not been reported previously. Here we investigated the effects of a 4-h night-time sleep opportunity on PS.

Methods: $N = 12$ healthy adults (ages 21–38 years; 2F) participated in two randomized counterbalanced laboratory conditions separated by 1 week. We checked with sleep logs that all subjects slept 7–9 h during the two nights preceding each condition. In condition 1, the subjects were kept awake for 36 h (from 6:00 until 18:00 the next day). In condition 2, the subjects were kept awake for 18 h (from 6:00 to 00:05), allowed a 4-h sleep opportunity (between 00:05 and 03:55), and kept awake for another 14 h (from 03:55 to 18:00), totaling to 36 h. In both conditions, we tested PS every 2 h: from 08:00 to 00:00 on day 1 (session 1); from 04:00 to 18:00 on day 2 (session 2). We tested PS with a force platform on which the subject stood (no shoes, feet together, arms folded, gaze forward). The platform sampled body center of pressure (COP) excursions for 30 s at 32 Hz. We scored PS as the area of the 95% confidence ellipse enclosing the COP. A larger area indicates decreased PS.

Results: Mixed-effects ANOVA on the data points recorded at 00:00 (the last test in session 1) and at 04:00 (the first test in session 2) revealed a significant interaction of condition by time point ($F_{1, 33} = 5.45$, $P = 0.026$) with decreased PS after the sleep opportunity given in condition 2. However, there was no interaction of condition by session (all data points in sessions 1 and 2 now collapsed within sessions and subjects), although there was a significant main effect of session ($F_{1,391} = 10.59$, $P = 0.001$) with decreased PS in session 2.

Conclusion: The sleep opportunity given in condition two induced a short-term decrease in PS. It appears that sleep inertia, along with time of day and time awake may affect balance. This supports earlier research suggesting that PS is a marker of fatigue from sleep pressure. For future research it poses the question whether sleep inertia might be an additional risk factor in slips, trips, and falls in persons with diagnosed balance deficits.

P921

Empirical evidence for robust parameters separating electroencephalograms from awake and sleep-deprived subjects

G. DORFFNER[1], G. KOENIG[2], S. HANKE[2], G. KLOESCH[1], E. LORETZ[3], W. MAYR[1] and J. ZEITLHOFER[1]
[1]Medical University of Vienna, Vienna, AT, [2]Austrian Institute of Technology GmbH, Vienna, AT, [3]The Siesta Group Schlafanalyse GmbH, Vienna, AT

Objectives: To objectively quantify daytime vigilance and sleepiness on a long-term, all-day basis it is crucial to identify electrophysiological biomarkers holding the necessary information. To reach this aim we analyze Electroencephalogram (EEG)-based parameters, which are able to separate EEG data from subjects after sleep-deprivation from data after normal sleep. Such parameters can be used in a model describing and predicting diurnal vigilance and sleepiness.

Methods: We conducted an exploratory study under real-world conditions including 26 healthy female and male subjects. For two 24 h periods we recorded six EEG channels, two EOG channels and two EMG channels using a mobile recording system, along with hourly subjective sleepiness ratings and reaction times. The sessions consisted of a night and the following day under a sleep-deprived and a normal-sleep control condition. The two sessions were embedded in 14-days of recording actigraphy and subjective sleep quality ratings.

We derived 62 features from the recorded data, with a focus on EEG-based values, such as relative and absolute frequency band powers, band ratios, complexity and entropy measures, and measures capturing EEG events such as alpha events or sleep spindles during wakefulness. We also used various types of EEG artefacts as EEG features.

We scaled the features' timelines relative to the subject's circadian phase and the time of waking up, thus covering circadian and homeostatic properties of the features.

Using statistical means such as the paired t-test and k-fold cross validation we analyzed the EEG-based features. We tested the features' ability to distinguish between the two conditions of the study by using a model-based error estimation.

Results: Our successful results show, that several of the described features robustly separate sleep-deprived data from data after normal sleep. Good examples for robust separating features are the relative delta-band power (t-test statistic 5.92, $P < 0.0000$) or the $(\theta + \alpha)/\beta$-band ratio (t-test statistic 4.37, $P = 0.0005$). These features can serve as descriptive and predictive biomarkers for diurnal vigilance and sleepiness in the EEG during daytime.

Conclusion: Our findings are an important step towards the aim of objectively describing diurnal vigilance and sleepiness based on EEG-signals. They contribute to a better understanding of the representation of attentive processes in the EEG.

This work was funded by the Austrian Research Promotion Agency FFG (827 600), the governement of Lower Austria, and the European Commission (EFRD WST3-T-81/015-2008).

Georg Dorffner is the CEO of The Siesta Group GmbH and a part-time employee of Philips-Respironics.

P922

Experimental acute sleep restriction in adolescents. A pilot study

G. BADER[1], M. G. JOHANSSON[2], R. HAMAAMIN[2] and D. SVILAR[2]
[1]SDS kliniken, Gothenburg, SE, [2]Polhems Gymnasiet, Gothenburg, SE

Objectives: It is not uncommon that adolescents, during holidays, decrease their sleep time for a few consecutive nights developing an acute sleep restriction (SR).

The purpose of this investigation was to study the impact of controlled SR on cognitive, behavioural, mental and physiological functions as well as the course of the recovery period.

Methods: Twelve healthy college students were followed from Monday 11 am to Thursday 2 am and exposed to supervised sleep restriction consisting of 3 h sleep at 3 am, which meant a total sleep time of 9 h over a period of 88 h. They were followed during the seven following days: the recovery period.

They had to fill questionnaires covering somatic, mental, psychological conditions. They were tested three times a day (11 am, 5 pm and 2 am) for cognitive functions (mathematic MT, picture and word memory, word recognition), attention, reaction time (RT) and balance. Anxiety and depression were scored according to HAD.

Results: Two subjects were asked early on to leave the experiment due to odd behaviour.

Among all the cognitive tests only MT (results and latency) and concentration worsened. Memory and attention tests were not affected. While there was no significant change in the average responses of RT, its spreading increased significantly during the day – but not at night.

Somatic discomfort increased (sickness, headache…). There was progressive increased appetite, consumption of caffeine and sweet. Balance was not affected.

Subjects reported increased stress and delusions as well as mood variability. They felt tired and had difficulties in remaining awake during the day but recovered alertness at night.

At the outset, the first day, 11 subjects had an increased anxiety level. Though there were no changes in the average level of anxiety and depression those with high scores had their values worsened during the test period.

Recovery period to retrieve previous values (sleep latency and duration, waking up time) required at least 4 days. Bedtime did not change the first recovery night and it was not until the second night that the subjects went to bed earlier. However when they tried to go back to usual sleeping time, sleep latency increased.

Conclusions: These healthy adolescents seemed to be more resilient than expected to acute SR with however individual variations. SR had limited but clear behavioural, mental, physiological and cognitive impacts with some circadian character. Recovery period could take at least 4 days.

P923

Time course of ocular indicators of drowsiness, performance and EEG correlates of sleepiness: implications for drowsy driving prevention

S. FTOUNI[1], S. RAHMAN[2], K. CROWLEY[2], C. ANDERSON[2], S. RAJARATNAM[1] and S. LOCKLEY[2]

[1]Monash University, Clayton, AU, [2]Harvard Medical School, Boston, US

Objectives: To assess the associations between the time course of ocular indicators of drowsiness with performance, EEG, and subjective sleepiness over 40 h of acute sleep deprivation, and their accuracy in predicting drowsiness-related performance lapses.

Methods: Ten male participants (mean age ± SD = 23.3 ± 1.57 years) underwent 40 h of continuous wakefulness under constant routine (CR) conditions. Participants completed the Karolinska Sleepiness Scale (KSS) and a 10-min auditory psychomotor vigilance task (aPVT) hourly. Ocular variables and waking electroencephalogram (EEG) were recorded continuously throughout the CR. Ocular variables were recorded using the Optalert™ Drowsiness Measurement System (ODMS), which measures eye and eyelid movements using infrared reflectance oculography. The system automatically calculates ocular outcomes, including mean total blink duration, percentage of time with eyes closed, and drowsiness levels (Johns Drowsiness Scale; JDS; range 0–10).

Results: Ocular variables, aPVT reaction times (RT) and lapses, KSS scores and EEG power density in the delta-theta (0.5–5.5 Hz), theta-alpha (5.0–9.0 Hz) and β (13.0–20.0 Hz) ranges remained low during the first approximately 16 h of wakefulness, after which all variables began to increase and peaked after approximately 24 h of wakefulness. Following this peak, ocular variables, and aPVT RT and lapses declined over the remaining hours to levels close to that observed at start of CR, whereas KSS scores and EEG power densities remained high. Similar temporal dynamics between these variables were confirmed by cross-correlational analyses. ROC area under curve (ROC AUC) analysis between aPVT lapses and ocular variables on a per minute basis showed that ocular variables were able to detect drowsiness-related lapses in performance.

Conclusion: Under conditions of acute sleep deprivation, ocular indicators of drowsiness correspond to increasing impairments in performance and detect lapses. These results demonstrate the potential efficacy in the approach of using real-time ocular variables in on-road driving settings to detect drowsiness. Dr Lockley reports that he received two investigator-initiated research grants from the ResMed Foundation and an unrestricted equipment gift from ResMed Inc, in support of the studies described in this article; receiving consulting fees from Apollo Lighting, Naturebright, Sound Oasis, and Wyle Integrated Science and Engineering, and federally funded projects at Brigham and Women's Hospital, Thomas Jefferson University, and Warwick Medical School; lecture fees from Takeda Pharmaceuticals North America, I Slept Great/Euforma, LLC, and Emergency Social Services Association Conference, UK; unrestricted equipment gifts from Philips Lighting and Bionetics Corporation; an unrestricted monetary gift to support research from Swinburne University of Technology, Australia; a fellowship gift from Optalert, Pty Ltd, Melbourne, Australia; advance author payment and royalties from Oxford University Press, and honoraria from Servier Inc for writing an article for Dialogues in Clinical Neuroscience and from AMO Inc, for writing an educational monograph, neither of which refer to the companies' products; honoraria or travel and accommodation support for invited seminars, conference presentations or teaching from the Second International Symposium on the Design of Artificial Environments, Eighth International Conference on Managing Fatigue, American Academy of Sleep Medicine, American Society for Photobiology, Apollo Lighting, Bar Harbor Chamber of Commerce, Bassett Research Institute, Canadian Sleep Society, Committee of Interns and Residents, Coney Island Hospital, FASEB, Harvard University, Illinois Coalition for Responsible Outdoor Lighting, International Graduate School of Neuroscience, Japan National Institute of Occupational Safety and Health, Lightfair, National Research Council Canada, New York Academy of Sciences, North East Sleep Society, Ontario Association of Fire Chiefs, Philips Lighting, Thomas Jefferson University, University of Montreal, University of Tsukuba, University of Vermont College of Medicine, Utica College, Vanda Pharmaceuticals, Velux, Warwick Medical School, Woolcock Institute of Medical Research, and Wyle Integrated Science and Engineering (NASA); investigator-initiated research grants from Respironics Inc, Philips Lighting, Apollo Lighting, and Alcon Inc; and a service agreement and sponsor-initiated research contract from Vanda Pharmaceuticals. Dr Lockley also holds a process patent for the use of short-wavelength light for resetting the human circadian pacemaker and improving alertness and performance which is assigned to the Brigham and Women's Hospital per Hospital policy and has received revenue from a patent on the use of short-wavelength light, which is assigned to the University of Surrey. Dr Lockley has also served as a paid expert witness on behalf of two public bodies on arbitration panels related to sleep, circadian rhythms, and work hours.

Dr Rajaratnam reports that he has served as a consultant through his institution to Vanda Pharmaceuticals, Philips Respironics, EdanSafe, The Australian Workers' Union, and National Transport Commission, and has through his institution received research grants and/or unrestricted educational grants from Vanda Pharmaceuticals, Takeda Pharmaceuticals North America, Philips Lighting, Philips Respironics, Cephalon, and ResMed Foundation, and reimbursements for conference travel expenses from Vanda Pharmaceuticals. His

institution has received equipment donations or other support from Optalert™, Compumedics, and Tyco Healthcare. He has also served as an expert witness and/or consultant to shift work organizations.
Ms Ftouni reports her institution has received equipment donations or other support from Optalert™ and Compumedics.
Dr. Rahman reports the he received research funding from Government of Ontario/Pharmacia Canada Inc./Genesis Research Foundation/OBGYN Graduate Scholarship in Science and Technology at the University of Toronto, Faculty of Medicine and the Frederick Banting and Charles Best Canada Graduate Scholarships Doctoral Award from Canadian Institutes of Health Research. SAR has IP filed for prevention of circadian rhythm disruption by using optical filters. SAR owns shares in ZiircLight Inc.

P924

First night effect evaluated by cardiac autonomic function in young and midlife women

I. VIRTANEN[1], N. KALLEINEN[2], A. URRILA[3], C. LEPPÄNEN[1] and P. POLO-KANTOLA[2]
[1]VSSHP TYKS-SAPA, Turku, FI, [2]Turku University Hospital, Turku, FI, [3]University of Helsinki, Helsinki, FI

Objective: To study first night effect using overnight cardiac autonomic function parameters in young, perimenopausal, and postmenopausal women with no previous sleep laboratory experience.
Methods: We studied postmenopausal women on oral hormone therapy [HT; $n = 10$, aged 64.2 (1.4) years], on transdermal HT [$n = 6$, aged 63.2 (1.0) years], and off HT [$n = 28$, aged 63.9 (0.8) years], perimenopausal women off HT [$n = 17$, aged 47.7 (0.5) years], and young women [$n = 11$, aged 23.1 (0.5) years] using a prospective case-control protocol. Polysomnography (PSG) studies were performed over two consecutive nights. Time and frequency domain and nonlinear heart rate variability (HRV) was assessed overnight from both recordings. Possible first night effect on heart rate variability (HRV) was analysed both separately in all groups and groups combined.
Results: Groups combined, the power law slope was slightly higher ($P = 0.029$) and spectral entropy lower ($P = 0.037$) during the first night recording in sleep laboratory. There was no significant difference between groups in first night effect. In separate analysis of all groups, pNN50 and HF power ($P = 0.016$ and $P = 0.044$, respectively) were lower during the first night in the perimenopausal group, while in postmenopausal women on oral HT, the alpha 1 correlation coefficient of detrended fluctuation analysis was lower ($P = 0.038$) during the first night. Other groups showed no first night effect.
Conclusions: There seems to be a slight decrease in heart rate variability during the first night spent in a sleep laboratory in women. Although this change is small, it implies that the initial stress evoked by laboratory conditions may influence the cardiovascular system as well as sleep architecture especially in older subjects.

P925

Sleep stage independent cardiac autonomic change after 40 h of complete sleep deprivation in women

I. VIRTANEN[1], N. KALLEINEN[2], A. URRILA[3], C. LEPPÄNEN[1] and P. POLO-KANTOLA[2]
[1]VSSHP TYKS-SAPA, Turku, FI, [2]Turku University Hospital, Turku, FI, [3]University of Helsinki, Helsinki, FI

Objective: To study the effect of total sleep deprivation on heart rate variability during sleep in young and postmenopausal women.
Methods: We studied postmenopausal women on oral hormone therapy (HT) [on-HT, $n = 10$, aged 64.2 (1.4) years], postmenopausal women off HT [off-HT, $n = 10$, aged 64.6 (1.4) years] and young women [$n = 11$, aged 23.1 (0.5) years] using a prospective case-control protocol.
Polysomnography (PSG) studies were performed over four nights: an adaptation night, a baseline night, 40 h sleep deprivation, and a recovery night. PSG recordings were scored in 30 s epochs. Time and frequency domain and nonlinear heart rate variability (HRV) was assessed overnight from the baseline and rebound nights. HRV in subject groups were compared at baseline and at recovery, and the effect of sleep deprivation was analysed separately in all groups. The sleep deprivation effect was compared between groups, and the changes in HRV were related to the changes in sleep stages after sleep deprivation.
Results: At baseline, young women had higher time and frequency domain and nonlinear HRV than older women, the most marked difference was between young and on-HT women. Furthermore, on-HT women had lower time domain HRV than off-HT women.
After sleep deprivation, frequency domain HRV decreased in young and off-HT women, while in on-HT women only the mean heart rate increased and HRV remained unchanged.
Compared to sleep stages, HRV was higher during nights with less wake and light sleep or more slow wave sleep. At rebound, more REM sleep decreased HRV. Sleep deprivation effects on HRV did not correlate to sleep stage changes after sleep deprivation.
Conclusions: Decreased HRV has previously been associated with an increased risk of cardiovascular morbidity and mortality and overall mortality. The risk of acute myocardial infarction is increased both in men and women sleeping 5 h or less per night, and overall mortality is significantly increased in short sleepers. The HRV changes seen in our study may at least partly explain the increased cardiovascular morbidity and overall mortality associated with sleep loss.
The low baseline HRV in on-HT women was similar to the decreased recovery night HRV in off-HT women. It is possible that in such low HRV levels no further decrease is possible. In women over 60, HT is known to increase cardiovascular morbidity and mortality, and these results may provide a pathophysiological explanation for this connection.

P926

Neutrophil counts: an immune sensor of sleep debt?

B. FARAUT[1], K. ZOUAOUI BOUDJELTIA[2] and M. KERKHOFS[2]
[1]University Paris Descartes, Paris, FR, [2]Université Libre de Bruxelles, Montigny-le-Tilleul, BE

Objectives: The interactions between sleep and neuroendocrino-immune systems may offer insight into why sleep restriction has been linked to negative cardiovascular outcomes. Sleep and its slow-wave sleep (SWS) component are expected to enforce during nighttime sleep the low-release phase of catecholamine and cortisol (both inducers of neutrophil vascular mobilization). Our aim was to analyze the neutrophil and myeloperoxidase (MPO) responses to several degrees of sleep restriction and recovery.
Methods: Young healthy men were investigated under continuous EEG polysomnography and performed distinct sleep restriction and recovery protocols: (i) chronic moderate ($n = 9$): three baseline nights of 8-h sleep/five sleep-restricted nights of 5-h sleep/three recovery nights of 8-h sleep; (ii) chronic severe ($n = 8$): one baseline night of 8-h sleep/three sleep-restricted nights of 4-h sleep/one recovery night

of 8-h sleep; (iii) acute: one baseline night of 8-h sleep/one sleep-restricted night of 2-h sleep/one recovery night of 8-h sleep (n = 12), or a 30-min nap in addition to one recovery night of 8-h sleep (n = 10), or a 10-h extended recovery night (n = 9).
Blood was sampled at 7 am and saliva taken at several time points of the day depending on conditions.
Results:
Sleep restriction measures: After one night of 2-h sleep, neutrophil and MPO levels are significantly increased over baseline but not after one night of 5-h sleep. After three nights of 4 h-sleep, neutrophil counts are significantly higher but not after three and fiove nights of 5 h-sleep although a tendency to increase is observed.
Sleep recovery measures: After one night of 2-h sleep, neither neutrophils nor MPO are normalized to baseline values after 8-h sleep recovery. However, with additional sleep i.e. nap or extended recovery sleep, neutrophil counts returned nearly to baseline. A drop in cortisol was observed immediately after the nap rich in SWS. After five nights of 5 h-sleep, peaks in MPO, SWS and insulin-growth factor-1 (a potent neutrophil degranulation enhancer) were measured.
Conclusions: Neutrophil level appears sensitive to the intensities of sleep restriction and sleep recovery and is potentially a sensor reflecting the stress response to sleep loss. Increased neutrophil count is considered as a cardiovascular risk factor, possibly through their ability to release pro- oxidant molecule such as MPO. A more finely tuned dynamic of neutrophil level and degranulation responses to sleep manipulations is required.

P927

Interaction betweeen REM sleep homeostasis and sleep deprivation induced by modafinil

D. ESPINOZA and A. OCAMPO
Universidad de Chile, Santiago de Chile, CL

Objectives: Sleep deprivation is following by an immediately sleep rebound. This makes it possible total recuperation of rapid eye movement (REM) sleep time in rat. We are interested to evaluate whether sleep deprivation induced by modafinil (MOD) affects compensatory responses in selected REM sleep deprivation rats.
Methods: Rats were implanted to record electroencephalographic and muscle activities. A peritoneal cannula was implanted for drug administration. Six male Sprague Dawley rats were housed at constant temperature and under a controlled light-dark cycle (12:12) in isolation chambers. After two base-line days each rat was infunded with MOD 100 mg/kg to fifth light-on hour. We created two conditions in no consecutive experimental days: whit and whitout previous REM sleep deprivation (Privation and no-privation conditions).
Results: MOD caused a wakefulness period of 3 h in two conditions, allowed by a sleep period whit predominance of non rapid eye movement (NREM) sleep. Total REM sleep time did not show significative differences in two conditions. We observed an increase of duration of REM sleep episodes in privation condicion, whit special increase in large episodes (82%).
Conclusion: Modafinil Impairs occurrence of inmediatily REM sleep rebound despite homeostatic pressure induced during selective deprivation. FONDECYT 1100245.

P928

Selective paradoxical sleep deprivation in mice using a new unsupervised automatic method

S. ARTHAUD, P.-A. LIBOUREL, D. GERVASONI, P. FORT and P.-H. LUPPI
Centre de Recherche en Neurosciences de Lyon, Lyon, FR

An increase in PS quantities always follows paradoxical sleep (PS) selective deprivation (PSD), a process named PS homeostasis. PS deprivation has long been used in rats to study the neuronal networks and mechanisms responsible for PS genesis and homeostatic regulation. However, in the recent years, mice are increasingly used to take advantage of the optogenetic method or transgenic models. It is therefore of particular interest to develop sleep deprivation and hypersomnia methods in this species. Here, we describe the adaptation to mice of two deprivation methods: the flowerpot and a new automatic method.
Mice were implanted with two muscle (EMG) and three cortical (EEG) electrodes for polygraphic recordings. After habituation and baseline recordings, platform PSD mice (n = 12) were put in a barrel with two platforms (2.6 cm diameter) surrounded by water. After 48 h, they were put back in their home cage for 3 h of PS recovery. For automatic PSD, mice remained in their home barrel. A real-time detection and quantification of wake, SWS and PS via an adaptive algorithm analyzing EEG/EMG signals was performed. As soon as PS was detected, a TTL pulse was applied to a mechanical device that moved the barrel floor. The stimulation was applied during 24 h (n = 6) or 48 h (n = 3) and followed by 3 h of PS recovery.
During PSD, quantities of residual PS were identical for platform and automatic PSD (1.6% for both versus 6.7% PS in baseline). The latency to the first PS episode was 241 min for platform PSD and 20 min for automatic PSD. SWS quantities during PSD were 31% for platform and 44% for automatic PSD (versus 40% in baseline). At the onset of PSR, the latency to PS was 105 min for platform and 6 min for automatic PSD. Over the 3 h of PSR, the PS amount was 16% after 48 h of platform PSD, 19% after 24 h of automatic PSD and 16% after 48 h of automatic PSD (versus 8% in baseline).
In summary, platform and automatic deprivation methods both induced during PSD and PSR similar decreases and increases in PS quantities. However, PS latency was much longer and SWS quantities were more decreased with the platform than with the automatic method clearly indicating that automatic PSD is less stressful (no handling, less hostile environment, absence of water) than the platform method. In summary, our results indicate that automatic PSD is a suitable, easy to use and more ethical method for performing PSD in mice than the platform method.
This work has received institutional financial support from Agence Nationale de la Recherche (ANR SleepNet), CNRS, INSERM, Claude Bernard University, PRES University of Lyon, and Lyon Science Transfert.

P929

Unsupervised paradoxical sleep deprivation using real-time sleep scoring in rats: a new alternative to the 'flower pot' technique

P.-A. LIBOUREL, S. JÉGO, F. BRISCHOUX, J. NIGRI, S. ARTHAUD, P. FORT, P.-H. LUPPI and D. GERVASONI
Centre de Recherche en Neurosciences de Lyon, Lyon, FR

Paradoxical sleep (PS) deprivation (PSD) in rats is classically performed with the 'inverted flower pot' method. Once placed on one or several platforms surrounded by water animals refrain from

entering PS, and present a PS hypersomnia (rebound) when placed back in their home cage. In the first hours of deprivation this method also suppresses SWS; hence it cannot be used for short selective PSD. As a non-stressful alternative, manual deprivations are possible but involve an operator who constantly scrutinizes the sleep recordings and gently wake the animal up. To overcome these limitations, we introduce an approach based on a real-time detection of PS coupled to a new mechanical device to awaken the animal. Our adaptative algorithm identifies PS from EEG and EMG signals (98% specificity), and on each PS occurrence a stimulus is applied to a device placed underneath the cage that briskly lifts the cage floor up and then let it return to its initial level. This new method was used in three paradigms, a 6-h PSD with a comparison between automated and gentle handling methods, a 72-h PSD with a comparison between 'inverted flower pot' and automated methods, and a 48 h automated PSD.

In the 6-h PSD paradigm, both gentle handling and automated methods efficiently suppressed PS (<3% of residual PS, corresponding to the epochs used for PS detection), and subsequently elicited similar increases in PS amounts: 22.9 ± 1.4% versus 24.6 ± 2.3% respectively over 120 min. Another group of animals went through a 72 h PSD using the flower pot method and, 2 weeks later, through a 72 h-PSD with our new device. During deprivation, PS residual amounts were slightly higher with the automated method and on average below 3%. During the 150 min recovery period PS amounts were less after the unsupervised PSD (23.3 ± 3.3% versus 41.2 ± 5.1%; $n = 6$). Finally, when reducing PSD duration to 48 h ($n = 6$), a marked reduction in PS residual amounts (0.8 ± 0.2%) and an increased PS rebound were observed (25.8 ± 1.5% over 150 min). SWS amounts were not or only marginally affected in all paradigms. A smaller rebound with the automated PSD compared to the flower pot might primarily result from a lower stress level and to a less extent from residual PS bouts. Altogether, our results show that our online scoring approach can efficiently overcome the drawbacks of manual detection when performing short PSD, and constitutes a valuable alternative to both gentle handling and the flower pot method for selective PSD.

This work has received institutional financial support from Agence Nationale de la Recherche (ANR SleepNet), CNRS, INSERM, Claude Bernard University, PRES University of Lyon, and Lyon Science Transfert.

P930

Sleep pressure and circadian process do not modulate pseudoneglect effects

R. SCHMITZ[1], V. GABEL[2], P. PEIGNEUX[1], M. MAIRE[2], C. F. REICHERT[2], C. CAJOCHEN[2], C. SCHMIDT[2] and A. U. VIOLA[2]
[1]*Université Libre, Brussels, BE,* [2]*University of Basel, Basel, CH*

Objectives: A slight but consistent right visual field pseudoneglect [i.e. a leftward attentional bias (LWB)] is observed within the healthy population. Right hemispheric (RH) dominance in alertness regulation is usually supposed to explain this phenomenon. It has been shown using a greyscales (GS) task that sleep deprivation (SD) induces a rightward shift in attention abolishing this LWB at 05:00 but not at 09:00 (Schmitz et al. 2011 Neuropsychologia) suggesting a possible circadian modulation of laterality bias in the GS. Here we aimed at replicating this effect in a controlled setting using a constant routine protocol (CRP).

Method: Following a baseline night, thirteen healthy right-handed volunteers (nine males; mean age = 23.4 ± 1.5 years) were kept awake during 40 h under constant routine conditions (CR) to assess endogenous circadian phase and amplitude while controlling the confounding effects of light-dark and behavioral cycles. During the CR period, the GS was administered 16 times from 9:00 am on Day 1 to 10:30 pm on Day 2. The GS task consisted in six types of rectangles (height 79 pixels; width 320, 400, 480, 560, 640 or 720 pixels). Each rectangle was darker on its left or right side (for a total of 72 stimuli), changed by increments of 80 pixels in density from black on one side to white on the other. Each trial (72/session) consisted in one upper and one lower GS arranged in such a way that they were left-right reversals of one another. Participants had to decide which one of the two stimuli was the darkest. Unbeknownst to them, the two stimuli within each trial were equiluminescent. A leftward bias was computed as the proportion of responses for darker GS on their left side according to their position (top or bottom).

Results: A two ways repeated measures ANOVA on the leftward bias score with factors Session (Session 1 to Session 16) and Position (Top versus Bottom) failed to revealed a significant effect of Session ($P > 0.98$). The effect of Position was highly significant ($P < 0.001$), with a leftward bias for the top position only (71.7 ± 4.9% versus 38.1 ± 7.8%).

Conclusion: Under CR, a total night of SD failed to reduce the LWB indicating that circadian effect does not modulate this attentional effect under well controlled conditions. Since the vestibular system is known to modulate the LWB, the effect of position might be explained by the participants' supine posture during the CR.

P931

Influence of sleep homeostasis and circadian rhythm on waking EEG oscillations during a constant routine

V. MUTO[1], C. MEYER[1], M. JASPAR[1], A. SHAFFII-LE BOURDIEC[1], C. KUSSE[1], A. FORET[1], G. VANDEWALLE[1], F. COLLETTE[1], S. ARCHER[2], D.-J. DIJK[2] and P. MAQUET[1]
[1]*University of Liège, Liège, BE,* [2]*University of Surrey, Guildford, UK*

Waking EEG oscillations are known to be modulated by both homeostatic sleep pressure and circadian rhythms. Here, we tested whether the individual vulnerability to sleep loss predicted by the PERIOD3 gene polymorphism influences these modulations.

Thirty-five healthy young volunteers (age19–26; 17 females) were recruited based on the PER3 polymorphism. From a sample of about 400 screened volunteers, twelve 5/5 and 23 4/4 homozygotes, matched for age, sex, level of education at the group level participated in this study. Waking EEG was recorded during 23 sessions distributed during a 42-h constant routine at F3, Fz, F4, C3, Cz, C4, Pz, O1, O2. Data reported here pertain to 60-s periods during which participants were asked to try to suppress blinks while fixating a circle displayed on a screen placed at approximately 75 cm. After re-referencing to mean mastoids, recordings were scored using Rechtschaffen criteria. Artifacts were manually rejected. EEG power was computed on Cz, using 2-s windows, overlapping by 1 s and the pwelch function in MATLAB (7.5.0). A linear mixed model tested for the effect of sleep homeostasis (modeled as a linearly increasing factor) and circadian oscillation (modeled as a 24-h period sine wave), on alpha EEG power.

Preliminary data showed that alpha power tended to be modulated by circadian oscillation ($F_{1,385} = 3.05$, $P = 0.0815$). There was a significant sleep homeostat by group interaction ($F_{1,385} = 4.32$, $P = 0.0383$). The circadian by group interaction tended to be significant ($F_{1,385} = 2.98$, $P = 0.0854$).

These results confirm that waking alpha EEG power is modulated by circadian factors. However, they also indicate that alpha power is also under the combined influence of PER3 polymorphism and sleep homeostasis.

The three first authors equally contribute to the present work.

P932

Influence of sleep homeostasis and circadian rhythm on executive discriminative ability during a constant routine

M. JASPAR[1], C. MEYER[1], V. MUTO[1], A. SHAFFII-LE BOURDIEC[1], C. KUSSE[1], G. VANDEWALLE[1], F. COLLETTE[1], S. ARCHER[2], D.-J. DIJK[2] and P. MAQUET[1]

[1]University of Liège, Liège, BE, [2]University of Surrey, UK, Guildford, UK

Maintaining optimal performance during a working memory task requires not only to detect target items (i.e. hits, in contrast to misses) but also to discard fillers (i.e. correct rejection, in contrast to false alarms). Following the signal detection theory, the ability to discriminate target from non-target stimuli is estimated by d prime (d') and criterion (cr). Here we assessed whether d' and cr were modulated by the raising need for sleep and the oscillating circadian signal during a 42-h constant routine while participants performed 13 sessions of auditory 3-back task. We also tested whether the individual vulnerability to sleep loss predicted by the PERIOD3 gene polymorphism would influence this cognitive modulation imposed by sleep/wake regulation.

Thirty-five healthy young volunteers (age19–26; 17 females) were recruited based on the PER3 polymorphism. From a sample of about 400 screened volunteers, twelve 5/5 and 23 4/4 homozygotes, matched for age, sex, level of education at the group level participated in this study. A linear mixed model tested for the effect of sleep homeostasis (modeled as a linearly increasing factor) and circadian oscillation (modeled as a 24-h period sine wave), on d' and c'.

Preliminary results show that there was a significant effect of sleep homeostasis ($F_{1,404} = 129.31$, $P < 0.0001$) and circadian oscillation ($F_{1,404} = 40.49$, $P < 0.0001$) on d'. There was no significant group effect but the group by sleep homeostasis interaction tended to be significant ($F_{1,404} = 3.22$, $P = 0.0734$). The criterion was also significantly modulated by homeostatic ($F_{1,404} = 13.03$, $P = 0.0003$) and circadian ($F_{1,404} = 4.78$, $P < 0.0294$) factors, without any group effect or interaction.

These results show that both sleep need and circadian factors influence signal detection and decision making in conditions of constant routine. In particular, the decision criterion, which is known to be altered by sleep loss, seems also modulated by circadian factors. Finally, the modulation of d' by sleep homeostasis seems also influenced by the individual vulnerability to sleep loss predicted by PER3 polymorphism.

The first three authors equally contribute to the present work.

P933

Implication of Per1 and Per2 genes in sleep architecture and homeostasis

F. LA SPADA, Y. EMMENEGGER and P. FRANKEN

University of Lausanne, Lausanne, CH

Circadian rhythms give time context to most behavioral, physiological, and biochemical processes. At the molecular level circadian rhythms are a property of interlocking transcriptional feedback loops involving the core clock genes Npas2, Clock, Bmal1, Cry1, Cry2, Per1, and Per2, among others. These genes seem, however, also involved in sleep homeostasis because mice lacking clock genes display altered sleep homeostasis and the brain expression of clock genes, especially that of Per2, increase in function of time-spent-awake [1]. Surprisingly, Per2 mutants (Per2m/m) mice largely preserve their homeostatic sleep regulation [2,3].

We therefore assessed sleep homeostasis in Per2 null-mutant (Per2-/-) mice, together with Per1 mutants (Per1m/m) mice and their double mutant offspring.

In 50% of the Per2-/- mice, locomotor activity patterns became arrhythmic immediately after release into constant dark (DD) conditions. The remaining mice displayed free-running rhythms of an extreme short period (22.6 h) compared to wild-type (WT) controls (23.7 h). Also Per1m/m mice have shorter circadian periods (23.3 h) while all double mutants are arrhythmic in DD. As previously described for Per2m/m mice [2], in Per2-/- mice activity onset was advanced under light-dark conditions. Moreover, in the dark period, Per2-/- and double mutant mice slept more than WT mice. We then analyzed the effects of 6 h sleep deprivation (SD). The increase in EEG delta power after SD in Per2-/- and Per1m/m mice did not differ from WT, while this increase was smaller in double mutant mice ($P < 0.05$). Over the 1st 6 h of recovery sleep Per2-/- mice did recover 32 min less of the NREM sleep lost during SD as compared to WT ($P < 0.03$, $n = 7$/genotype) and this difference was maintained throughout the subsequent dark period. Preliminary results indicate that also for double mutants recovery of NREM sleep was less efficient, while in Per1m/m mice no differences were observed.

In conclusion, we found that although several aspects of sleep and circadian rhythms are shared between Per2-/- and Per2m/m mice, the circadian phenotype is more severe and that the inability to adequately compensate for NREM sleep lost during recovery from SD is unique to the Per2-/- genotype. The data further underscore the involved of clock genes in sleep homeostasis.

1. Franken, P., Dijk, DJ. Eur J Neurosci 2009.
2. Kopp, C., et al. Eur J Neurosci 2002.
3. Shiromani, P. J., et al. Am J Physiol Regul Integr Comp Physiol 2004.

P934

Circadian modulation of sleep latencies in the rat

R. YASENKOV[1], J. H. MEIJER[2] and T. DEBOER[2]

[1]University of Surrey, Guildford, UK, [2]Leiden University Medical Center, Leiden, NL

Objectives: Sleep latency, sleep duration, and sleep efficiency are among the main characteristics of sleep quality in humans. In different sleep deprivation protocols, NREM and REM sleep latencies demonstrate a robust circadian pattern. It is unknown whether other mammals also show circadian modulation in sleep latency. We have previously found that repeated 2 h sleep deprivations alternated with 2 h rest, redistribute sleep over 24 h in the rat. Noteworthy, NREM sleep remains circadian modulation under this protocol, whereas REM sleep does not. The latter suggests that, in contrast to humans, the circadian control over REM sleep is weak in the rat. Here, we apply the same protocol to investigate circadian modulation of sleep latencies in the rat.

Methods: EEG and EMG recordings were performed in freely moving rats ($n = 8$) exposed to constant dark conditions. Starting at the onset of subjective day (CT 0), twelve 2 h-periods of sleep deprivation (SD) were alternated with twelve 2 h-periods of rest (48 h). At the onset of the 2 h rest periods of the second day, NREM and REM sleep latency were determined applying definitions similar to those of humans:

NREM sleep latency – the time between release from SD and the first consolidated NREM sleep episode lasting ≥30 s; REM sleep latency – the time between the first consolidated NREM sleep episode after release from the SD and a subsequent REM sleep episode lasting ≥30 s.

Results: NREM sleep latency showed minor variation across the six periods of rest. The latency to enter REM sleep showed a gradual but significant shortening in the course of the subjective day (from more than 20–10 min), followed by an abrupt increase at the start of the subjective night (>20 min). In the middle of the subjective night REM sleep latency decreased again to values comparable to those found at the end of the subjective day. At the end of the subjective night REM sleep latency increased again to approximately 20 min. As a result, REM sleep latency showed a complex bimodal circadian pattern ($P < 0.05$, Duncan after ANOVA).

Conclusion: The biomodal modulation in REM sleep latency can be caused by the changes in monoamines level and brain temperature, and may be related to the nocturnality of the rat. The absence of a circadian modulation in NREM sleep latency, and the presence of a bimodal circadian pattern of REM sleep latency are further indications for key differences in circadian sleep regulation between humans and the rat.

This research was supported by the Netherlands Organization for Scientific Research (NWO, grant 818.02.016, TD

Poster Session – Circadian Rhythmus

P935

Circadian rhythm and team performance in the last 10 seasons of the Volleyball World League

M. R. SILVA[1] and H. H. SILVA[2]
[1]*University Fernando Pessoa, Oporto, PT,* [2]*Portuguese Volleyball Federation, Oporto, PT*

Introduction: The rapid transition across time zones known as jet lag syndrome leads to desynchronization of endogenous biological clock and can cause transient negative effects on athletic performance.

Objectives: The main purpose of this study was to evaluate the final result of the performance of elite volleyball teams, according to an anthropometric profile and country of origin during the most important international championship in volleyball, the World League.

Methods: Of the 30 400 athletes were analyzed according to anthropometric data: weight and height [body mass index was calculated as weight (kg)/height^2 (m)] and team result. It was explored the significance of performing at different circadian times in the World League from the 2001 to 2011 seasons. Logistic regression analysis of win-loss records relative to anthropometric profile, point spreads and home-field advantage was examined. The significance level was 5% ($P < 0.05$). Data was analyzed using SPSS, version 18.0.

Results: West teams won more often ($P < 0.05$) than East teams. West teams were performing significantly ($P < 0.05$) better. This advantage enhanced home-field advantage for West teams and eliminated the beneficial effects of home-field advantage for East teams during the majority of the seasons.

Conclusion: These results show a circadian advantage of the West teams; they imply the need of future optimization of sleep and sport training and performance in elite athletes.

P936

Availability of electricity influences sleep of rubber tappers living in the Amazon

S. VASCONCELOS[1], A. LOWDEN[2], D. J. SKENE[3], F. FISCHER[1] and C. MORENO[1]
[1]*University of São Paulo, São Paulo, BR,* [2]*Stockholm University, Stockholm, SE,* [3]*University of Surrey, Guildford, UK*

Objectives: To compare sleep parameters of a group of rubber tappers living in an Amazon Extractive Reserve, during work and leisure, with or without electricity at home. Previous studies have demonstrated a phase delay in circadian timing caused by artificial light exposure in the evening. Our principal hypothesis was that rubber tappers without electricity at home would have an advanced sleep onset during the work week and at weekends.

Methods: A cross-sectional study with 257 rubber tappers (43.1 ± SE 0.93 years), work time ranging from 3:00–4:00 to 15:00–17:00 h, from Monday to Friday, with 2 days-off, was conducted. 91.4% were male; 72.4% had no eletricity at home. Participants completed questionnaires on sociodemographic characteristics, lifestyle, work conditions, morbidities, light exposure and the Munich Chronotype Questionnaire (MCTQ).

Results: Reported natural light exposure was 5.9 ± SE 0.17 h during the work week and 3.6 ± SE 0.16 h on weekends. Mean sleep duration was 472.5 ± SE 5.73 min and 518 ± SE 6.82 min on the work week and weekends, respectively ($P = 0.00$). Those who had no electricity at home slept significantly longer during the work week (478.7 ± SE 6.92 min) than those who had electricity (456.1 ± SE 9.86 min, $P = 0.04$). There were no differences in sleep duration between the groups on weekends. Timing of sleep onset on work days and weekends was significantly later ($P < 0.01$) for the workers with electric lighting at home (work days, 20:52 ± SE 0.13 h; weekends 20:56 ± SE 0.15 h) than those without electricity (work days 20:18 ± SE 0.89 h; 20:28 ± SE 0.09 h). Mean midsleep on work days was significantly earlier than on weekends (00:17 ± SE 0.13 h and 00:48 ± SE 0.12 h, $P = 0.000$) for the whole population. Midsleep was delayed on weekends for those who had electricity (01:14 ± SE 0.11 h) compared to those without (00:39 ± SE 0.15 h, $P = 0.005$).

Conclusion: Our results show that electricity and the availability of artificial light influences both timing and duration of sleep. An advanced sleep onset on work days and weekends and longer sleep duration on work days was observed for those who had no electricity at home.

Support: FAPESP-UniS; CNPq; FUNTAC.

P937

Effects of age, sleep duration and midsleep time on satisfaction with leisure time of rubber tappers living in the Amazon

S. VASCONCELOS[1], A. LOWDEN[2], D. J. SKENE[3], F. FISCHER[1], E. MARQUEZE[1] and C. MORENO[1]
[1]*University of São Paulo, São Paulo, BR,* [2]*Stockholm University, Stockholm, SE,* [3]*Unversity of Surrey, Guildford, UK*

Objectives: To evaluate the effects of age, sleep duration and time of midsleep on satisfaction with leisure time. A secondary aim was to examine the correlation between the satisfaction with leisure time and diurnal preference. It has been postulated that discrepancies between social and biological timing are reflected in shift workers' well-being, which may impact on satisfaction with leisure time.

Methods: A cross-sectional study with 257 rubber tappers (91.4% male, 43.1 ± SEM 0.93 years), work time ranging from 3:00–4:00 to 15:00–17:00 h, from Monday to Friday, with 2 days-off, was conducted. Participants completed questionnaires on sociodemographic characteristics, Diurnal Preference Scale, Munich Chronotype Questionnaire (MCTQ), and satisfaction with leisure time, accessed by VAS (visual analogue scale).

Results: Sleep duration was shorter for younger workers ($n = 14$, 17–21 years, 467 ± 27 min) than older workers ($n = 45$, 22–30 years, 483 ± 13 min; $n = 190$; 31 years or more, 471 ± 7 min) on the work week. By contrast, on weekends the older workers slept less: 17–21 years, 563 ± 29 min, 22–30 years, 538 ± 16 min, and 31 years or more, 511 ± 8 min. Midsleep was delayed on weekends for young workers (01:30 ± 0.3 h) compared to older workers (00:13 ± 0.5 h). Satisfaction with leisure time decreased with morning preference ($P = 0.03$; Spearman test). Factorial ANOVA showed an effect of midsleep ($P = 0.02$) and sleep duration ($P = 0.05$) on satisfaction with leisure time during the work week. Interaction effects were found between age and sleep duration ($P = 0.04$); age and midsleep ($P = 0.05$); age, midsleep and sleep duration ($P = 0.04$).

Conclusion: Our results show that shorter sleepers and evening types were more satisfied with leisure time. It is possible that timing,

length and satisfaction with leisure, especially on work days, are dependent on diurnal preference and sleep need.

Support: FAPESP-UniS; CNPq; FUNTAC.

P938

Sleep and fatigue in bridge officers working 6 h on and 6 h off – a simulator study

A. DAHLGREN[1], W. VAN LEEUWEN[2], A. KIRCHER[3], M. LÜTZHÖFT[3], M. BARNETT[4], G. KECKLUND[2] and T. ÅKERSTEDT[2]

[1]KTH Royal Institute of Technology, Stockholm, SE, [2]Stockholm University, Stockholm, SE, [3]Chalmers University of Technology, Gothenburg, SE, [4]Warsash Maritime Academy, Warsash, UK

Objective: Fatigue at sea is a hot topic, with reports of seafarers falling asleep on watch. The present study examined fatigue and sleep in bridge officers during a simulated voyage using subjective and objective measures.

Method: Ninteen seafarers participated in a simulator study for 7 days (mean age 34 ± 12, 18 men) working 6 h on followed by 6 h off. They were randomly assigned to the 00–06/12–18 (n = 9) or the 06–12/18–00 (n = 10) watch team. Watches were spent in a bridge simulator and all participants sailed the same voyage in the English Channel and North Sea. Participants rated sleepiness (Karolinska Sleepiness Scale – KSS, 1–9 very sleepy) and stress (1–9 high stress) every hour. Before and after each watch a 5 min Psychomotor Vigilance Test (PVT) was performed. Polysomnographic (PSG) recordings were made during six watches and sleep was defined as minimum of 20 s of 4–12 Hz waves. Sleep duration during free-watches was recorded in a diary. One free-watch was disturbed at the beginning or end of the week (counterbalanced between and within watch teams) by simulating administrative overtime work. The watch after the interrupted free-watch was compared with a similar watch without previous disruption.

Results: PSG recordings showed that 50% of participants fell asleep on watch with the watch 00–06 being most affected but sleep also occurred during day watches. Elevated levels of sleepiness were observed during the 1st watch as compared to the 2nd watch (KSS 4.6 ± 0.2 versus 4.0 ± 0.2; $F_{1,13}$ = 15.2, P < 0.01). From the beginning to the end of the watch sleepiness levels increased (from 3.7 ± 0.2 to 5.1 ± 0.3; $F_{3.66,47.60}$ = 15.3, P < 0.001), and performance on the PVT declined with longer reaction times (from 274 ± 10 to 296 ± 12 ms; $F_{1,15}$ = 13.2, P < 0.01) and more lapses (from 1.3 ± 0.5 to 2.7 ± 1.0; $F_{1,15}$ = 6.3, P < 0.05). There were usually two sleep episodes per 24 h (mean total sleep time = 368 ± 23 min). After the interrupted free-watch participants reported greater levels of sleepiness (6.7 ± 0.4 versus 4.6 ± 0.3; $F_{1,16}$ = 75.3, P < 0.001), slower reaction times (339 ± 27 versus 289 ± 18 ms; $F_{1,17}$ = 11.5, P < 0.01) and more stress (4.0 ± 0.5 versus 2.9 ± 0.2; $F_{1,16}$ = 5.5, P < 0.05), but there were no differences in PSG measured sleep episodes.

Conclusion: Homeostatic and circadian processes contributed to many participants falling asleep on watch. The results highlight greater fatigue related risks on the 1st watch, at the end of a watch and as a result of interrupted free-watches.

P939

Sleep and sleepiness while on watch in a simulated '4 h on/8 h off' maritime watch system

W. M. A. VAN LEEUWEN[1], A. KIRCHER[2], A. DAHLGREN[3], M. LÜTZHÖFT[2], M. BARNETT[4], G. KECKLUND[1] and T. ÅKERSTEDT[1]

[1]Stockholm University, Stockholm, SE, [2]Chalmers University of Technology, Gothenburg, SE, [3]KTH Royal Institute of Technology, Stockholm, SE, [4]Warsash Maritime Academy, Warsash, UK

Objective: Ships are operated 24/7, introducing seafarer fatigue as a hazard to safety at sea. Severe sleepiness has been documented as a direct or contributing factor in many maritime accidents. This study investigates sleep and sleepiness in a simulated 4 h on/8 h off watch system as well as the effects of a single free watch disturbance, simulating a condition of low demanding overtime work.

Method: Thirty bridge officers (age 30 ± 6 years; 29 men) participated in five parallel bridge simulations during two separate experimental weeks. The three watch teams started respectively with the 00–04, the 04–08, and the 08–12 watch on an identical voyage in the North Sea and English Channel. The free watch disturbance was counterbalanced, taking place between day 2 and 3 or day 5 and 6. Participants rated their sleepiness every hour (Karolinska Sleepiness Scale) and carried out a 5-min psychomotor vigilance test (PVT) at the start and end of every watch. In addition, polysomnography (PSG) was recorded during six watches in the first and the second half of the week.

Results: Sleepiness was higher during the first (mean ± SD, 4.0 ± 0.2) compared to the second (3.3 ± 0.2) watch of the day ($F_{1,24}$ = 18.0, P < 0.001). In addition, sleepiness increased with hours on watch ($F_{2.8,67.1}$ = 12.2, P < 0.001), peaking at the end of watch (4.1 ± 0.2). The free watch disturbance increased sleepiness profoundly ($F_{1,26}$ = 67.8, P < 0.001): from 4.2 ± 0.2 to 6.5 ± 0.3. PVT reaction times were slower during the first (290 ± 6 ms) compared to the second (280 ± 6 ms) watch of the day ($F_{1,25}$ = 29.1, P < 0.001) as well as at the end of the watch (289 ± 6 ms) compared to the start (281 ± 6 ms; $F_{1,25}$ = 15.7, P = 0.001). The free watch disturbance increased reaction times ($F_{1,26}$ = 17.2, P < 0.001) from 283 ± 5 to 306 ± 7 ms. Similar effects were observed for PVT lapses. Seventy percent of all participants slept during at least one of the PSG watches. Sleep on watch was most abundant in the team working 00–04 (80% of participants sleeping). The team working 04–08 reported a shorter average daily sleep duration (416 ± 19 min) than the other two teams (457 ± 16 and 459 ± 24 min respectively).

Conclusion: This study reveals that – within a 4 h on/8 h off shift system – subjective and objective sleepiness peak during the night and early morning watches, coinciding with a time frame in which relatively many maritime accidents occur. In addition, we showed that overtime work strongly increases sleepiness. Finally, a striking amount of participants experienced sleep whilst on duty.

P940

The effects of a 6 h on/6 h off maritime watch system on sleep and sleepiness using bridge and engine room simulators

W. M. A. VAN LEEUWEN[1], C. PEKCAN[2], M. BARNETT[2], D. GATFIELD[2], M. LÜTZHÖFT[3], G. KECKLUND[1] and T. ÅKERSTEDT[1]

[1]Stockholm University, Stockholm, SE, [2]Warsash Maritime Academy, Warsash, UK, [3]Chalmers University of Technology, Gothenburg, SE

Objective: Fatigue at sea – where ships have to be operated on a 24/7 basis – is a safety issue that has hardly been studied before and needs thorough investigation. This study investigates sleep and sleepiness both on the bridge and in the engine room during a 1-week simulated voyage through the North Sea and English Channel on a 6 h on, 6 h off regime.

Method: Twenty bridge officers [aged 31 ± 9 (mean ± SD) years] and 20 engineers (aged 32 ± 8 years) participated in paired bridge and engine room simulators on a 1 week voyage through the North Sea and English channel whilst being on a 6 h on 6 h off regime. Participants rated their sleepiness every hour (Karolinska Sleepiness Scale, KSS) and carried out a 5-min psychomotor vigilance test (PVT) at the start and the end of every watch. In addition, a work diary was filled in at the end of every watch and polysomnography (PSG) was recorded during four watches in the first and the second half of the week.

Results: On both the bridge ($F_{2.5,\ 39.8} = 4.9$, $P = 0.008$) and in the engine room ($F_{4.4,\ 69.6} = 4.4$, $P = 0.003$), sleepiness increased during the course of the week. Sleepiness was also higher during the first watch of the day compared to the second watch, both at the bridge ($F_{1,16} = 7.8$, $P = 0.013$) as well as in the engine room ($F_{1,16} = 25.7$, $P < 0.001$). Sleepiness increased with hours on watch, reaching 4.8 ± 0.3 on the bridge ($F_{1.8,\ 29.1} = 29.2$, $P < 0.001$) and 4.5 ± 0.3 in the engine room ($F_{1.8,28.9} = 16.7$, $P < 0.001$). PVT performance was only affected in the engine room, reaction times were slower $F_{1,15} = 15.3$, $P = 0.001$) and lapses more frequent $F_{1,15} = 8.5$, $P = 0.011$) during the second watch of the day. Watches with the highest proportion of participants falling asleep were 18:00–00:00 (>20%) and 00:00–06:00 (20%) on the bridge and 00:00–06:00 and 06:00–12:00 in the engine room (both > 20%). Overall mean daily sleep duration was 400 ± 17 min.

Conclusion: This study shows that in a 6 h on 6 h off maritime watch regime, sleepiness peaks during the end of night and early morning watches. This is consistent with the timing during which many maritime incidents and accidents at sea occur. In addition, a considerable amount of watch keepers fell asleep on watch. Furthermore, this study shows that sleepiness may increase with time at sea.

P941

The influence of feeding method on a mother's daily rhythm and on the development of her infant's circadian rest-activity rhythm

S. KIKUCHI[1], K. NISHIHARA[2], H. ETO[3], S. HORIUCHI[4] and Y. HOSHI[1]

[1]Tokyo Metropolitan Institute of Medical Science, Tokyo, JP, [2]The Institute for Science of Labour, Kawasaki, JP, [3]Nagasaki University, Nagasaki, JP, [4]St. Luke's Birth Clinic, Tokyo, JP

Objectives: An infant's circadian sleep-wake rhythm is established during the first 3 months after birth. It is crucial to identify how entrainment factors contribute to the process of an infant's obtaining circadian sleep-wake rhythm. Our previous study [1] suggested that feeding method, that is, breast feeding alone or breast feeding mixed with formula feeding, may be part of maternal influence. The present study was conducted to see the influence of feeding method on the mother's daily rhythm and on the development of her infant's circadian rest-activity rhythm.

Methods: The subjects were 24 healthy primiparas and their vaginally-born, full-term infants. Written informed consent was obtained from each subject prior to the study. All the mothers hoped to exclusively breast feed, but as time went by, seven of the 24 began mixed feeding. In all cases, the feeding amounts and intervals were irregular, depending on demand. Actigraphic recordings for the pairs were made over 3–5 consecutive days during the 2nd–3rd, 6th, and 12th week. Using autocorrelograms, we examined circadian rest-activity rhythm during each examination week. We looked at the amplitude of the 24-h peaks of the mean autocorrelogram for each pair and the significance of the feeding method, using a one-way, repeated-measure ANOVA.

Results: At the 2nd–3rd week, a 24-h peak on the infants' autocorrelograms was observed and circadian rest-activity rhythm had already started, but there was no significant difference between feeding methods. At the 6th week, the mean values of the autocorrelograms at 24 h for the breast-feeding pairs were significantly higher than those for the mixed-feeding ones. At the 12th week, the infants' rest-activity rhythm was established independently of the feeding method, but the autocorrelograms at 24-h for the mixed-feeding mothers were significantly smaller than those for the breast-feeding mothers. As the amplitude on an autocorrelogram at 24-h rises with the regularity of the circadian rhythm, the regularity of the rhythms of the mixed-feeding mothers was weak compared with the breast-feeding mothers'.

Conclusion: The regularity of the rhythms of the breast-fed infants became significantly stronger than that of the mixed-fed infants. The breast-feeding mothers' entrainment factors seemed to be stronger than those of the mixed-feeding mothers.

Refernce:

1. Nishihara, K., et al. Chronobiol Int 2012; 29(3): 363–370.

P942

Delayed sleep phase disorder circadian period length

L. LACK, G. MICIC, A. DE BRUYN, H. WRIGHT and N. LOVATO

Flinders University, Adelaide, AU

Objectives: Delayed Sleep Phase Disorder (DSPD) is defined as an abnormally late sleep period (e.g. 3 am – 12 noon). DSPD is prevalent in the adolescent and young adult population and is associated with significant morbidity. Attempts to establish an earlier sleep period usually fail. DSPD is presumed to be caused by a delayed circadian rhythm. However, the difficulty advancing the sleep period to an earlier time and the strong tendency in DSPD to phase delay may arise from a longer endogenous circadian rhythm period length, tau. The study aimed to measure tau in DSPD in comparison with normally entrained good sleepers.

Methods: Six DSPD participants and seven normal sleeping controls had period lengths determined from a three-day laboratory ultradian routine. One hour 'days' (40 min wake alternating with 20 min sleep opportunities) were carried out in a time free, constant bed rest, dim light conditions. Core body temperature was measured every 20 min from an ingested capsule and averaged hourly. Best fit, two component (24 h plus 12 h harmonic) cosine curves were derived for each participant over the 78 h protocol. The 24 h

component was allowed to vary to achieve the best fit to the 78 h of data and derive the best estimate of tau.
Results: Both groups had longer than 24-h core body temperature tau with the good sleepers at 24.6 (0.27) hours and significantly longer ($P < 0.01$) at 25.2 (0.47) hours for the DSPD participants.
Conclusions: The longer DSPD core body temperature tau found in this study is consistent with the only previous but sparse data on DSPD. An abnormally long circadian tau is most likely to be a cause of DSPD and make it particularly difficult to shift to an earlier, more conventional sleep time. Successful treatment of DSPD would, therefore, require aggressive and persistent chronobiologic therapy with a combination of early evening melatonin and morning bright light.
Supported by a research grant from Flinders University, South Australia.

P943

Gender differences in the associations between self-reported short sleep duration and obesity risk: the Tromsø study

M. T. JOHNSEN, R. WYNN and T. BRATLID
Faculty of Health Sciences, Tromsø, NO

Background: Prior studies have suggested that sleep duration is a major risk factor for mortality and morbidity of a large variety of diseases and that it is associated with body mass index (BMI) and central obesity. The aim of this study was to examine the gender differences in the association between sleep length and body composition measures for people living in this sub-arctic region.
Methods: The cross sectional population Tromsø Study was conducted in Tromsø, North Norway, at 69.4° North. The study included entire birth cohorts and random samples of the population aged 30–87 years. Data was collected continuously from 1 October 2007 to the end of December 2008 except July. Of the 8032 persons completed questionnaires including sleep habits. Height, weight, waist- and hip circumference were measured, as well as non-fasting blood samples. Body mass index (BMI) was calculated as weight in kilograms (kg) divided by the square of height in meters. Waist-to-hip ratio (WHR) was calculated as waist circumference divided by hip circumference. Overweight was defined as BMI 25–29.9 kg/m^2, obesity class I as BMI 30–34.9 kg/m^2 and obesity class II+III as BMI 35 kg/m^2 or more. Abdominal obesity was defined as waist circumference over 101 cm for men and 87 cm for women.
Results: More than 60% of the population had BMI 25 kg/m^2 or more, and more men were found in the overweight and obesity groups. The optimal sleep time regarding body composition was found to be 7–8.9 h, and this was used as the reference group. We found a decrease in BMI for the reference group compared to the short sleepers which corresponded to an average weight loss of 2 kg for a moderate sleeping person who was 170 cm high. We also found that short sleepers (<6 h) had 50% increased risk of being in the obese group compared to moderate sleepers (7–8.9 h). Among short sleeping men, the risk of abdominal obesity was 50% higher, and the risk of having BMI 25 kg/m^2 or more was almost two times higher compared to moderate sleepers. We found no significant differences in female body composition between short and moderate sleepers, except for women aged 40–49 years, where the odds of having BMI 30 or more were 2.3 times higher among short sleepers.
Conclusions: An inverse relationship between sleep duration and BMI was found for both genders. Associations between short sleep duration, and both abdominal obesity risk and BMI 25 kg/m^2 or more was found only for men after controlling for confounders.
This was not an industry supported study. The authors have no conflicts of interest.

P944

A role for PERIOD3 in sleep/wake rhythms: photic responses in humanised knock-in mice and gene expression correlates of PER3 expression

D. R. VAN DER VEEN, D.-J. DIJK and S. N. ARCHER
University of Surrey, Guildford, UK

Objectives: Previously, we reported a light-dependant phenotype in circadian regulation in PER3 knockout (Per3-/-) mice. These mice also showed altered sleep architecture and elevated activity levels in the second half of the dark period. In humans, a polymorphism in PER3 has been associated with diurnal preference, sleep homeostasis, and cognitive decline in response to sleep loss. We generated humanised knock-in (KI) mice expressing two variants of the human polymorphism and investigated activity patterns in response to different photoperiods. We also further investigated gene expression profiles of Per3-/- and KI mice during an ultradian light exposure paradigm.
Methods: Male and female C57Bl/6 mice, expressing either the 4- or 5- repeat of the human variable number tandem repeat in PER3 (Per34/4 and Per35/5) were exposed to short (8 h), intermediate (12 h) and long (16 h) photoperiods, as well as constant light. Transitions between the conditions were mixed between animals, such that the response to a new photoperiod could be analysed, taking into account different light-histories. Behavioural activity was recorded as running wheel revolutions. In addition, we subjected Per3-/- and KI mice to an ultradian light-dark cycle (3.5 h L–3.5 h D) and analysed whole genome RNA expression at CT 16, in an ultradian light episode.
Results: Significant differences between male and female activity were seen. Female mice showed more activity in the second half of the dark period, and overall 24-h activity levels were more than 1.5-fold higher in females. These differences were seen in all genotypes. In constant darkness, both male and female Per34/4 mice showed increased activity in the second half of the dark period, compared to WT and Per35/5 mice. The behavioural responses to photoperiods were diverse, with KI mice appearing to adjust more rapidly to a new photoperiod. Whole genome RNA expression in Per3-/-and KI mice was altered compared to WT mice, and similar pathways were affected in both Per3-/-and KI mice.
Conclusion: Here we show behavioural data on a novel humanised mouse model of PER3. In mice, this polymorphism associates with altered activity, especially in the transition between photic conditions. We also observed a consistent difference between male and female activity. This emphasizes the need to not only use transgenic mice but also to include both sexes in animal models of human conditions.
Research funded by the BBSRC (BB/F022883/1 and BB/E003672/1).

P945

Effects of genotype and chronotype on time use on work and rest days

J. A. GROEGER[1], C. A. FINNAN[1], S. ZOELLER[1], K. M. MCGREGOR[2] and S. N. ARCHER[2]
[1]University College Cork, Cork, IE, [2]University of Surrey, Guilford, UK

Objective: A variable number tandem repeat (VNTR) polymorphism in PERIOD3 (rs57875989) is associated with extreme diurnal

preference and various health outcomes. Under sleep challenge it predicts individual vulnerability of cognitive functioning. However little is known about how different PER3 genotypes manage work and rest activity outside the laboratory. This study aimed to assess joint and separate effects of chronotype and PER3 genotype self-reported activities of daily living.

Methods: Five hundred adult, University-based subjects completed multiple chronotype measures and reported daily activity across two recent Rest and Work days, using a customized 15-min epoch time use diary, which had various activity categories. Participants were genotyped with respect to the PER3 polymorphism.

Results: Compliance was excellent. An 'other' category for activity was used infrequently, suggesting activities identified were sufficiently comprehensive to describe daily activity. The data's validity was assured from the fact that expected differences in patterns of activity across Work and Rest days were significant. On Rest days significantly more time was spent on sleep, exercise, hobbies, errands, caring, relaxing, socializing, while on Work days significantly more time was spent on activities related to classes, study, travel, employment, breaks from work, religion. Work and Rest days were similar in the amount of time devoted to personal body care and eating/drinking. PER3 genotype effects, independent of chronotype, were observed in main effects relation to breaks from work (PER5/5 < PER34/4 = PER34/5) and exercising (PER34/4 > PER34/5 > PER35/5). Work-Rest day balance differed across genotypes in relation to other activities. PER34/4 spend more time exercising on Rest days, and significantly less time studying and doing errands. Study time allocation differed substantially across genotypes, with PER5/5 studying least on Work days and PER34/4 significantly more. PER35/5 compensated for this by studying significantly more on Rest days. Heterozygotes studied allocated similar amounts of time to study on both days.

Conclusion: Independent of chronotype, PER3 genotypes differ in amount and timing of activities on Work and Rest days. These daily activity patterns suggest that there are phenotypic differences in daily activity, which result in less rest and exercise, perhaps compromising recuperation and health among PER3 homozygotes with the long allele VNTR polymorphism.

This research was supported by grants from the Science Foundation Ireland (SFI 09/RFP/NES2520).

P946

Chronic partial sleep deprivation in morning- and evening-oriented individuals – subjective estimations, performance, and neural activity (fMRI) in a visual attention task

H. OGINSKA, E. BELDZIK, A. DOMAGALIK, M. FAFROWICZ and T. MAREK

Jagiellonian University, Krakow, PL

Objectives: The study was aimed to trace the consequences of chronic partial sleep restriction in morning- and evening-oriented individuals, as distinguished by a behavioural preferences questionnaire (Chronotype Questionnaire, Oginska, 2011).

Methods: The analysis comprised performance of a saccadic task (oculography), self-assessments (Karolinska Sleepiness Scale and estimations of subjective effort), and neuroimaging data collected with fMRI registrations simultaneous with saccadometry. Eight morning- and eight evening-oriented healthy female volunteers were studied in full rest state and in chronic sleep deficit condition (1 week of sleep restriction, by 3 h daily), in a counterbalanced order. The measurements were taking place four times during the day: at 10:00, 14:00, 18:00, and 22:00. Visual attention task consisted in quickly moving attention and sight to a stimulus appearing randomly on the left- or right side of the central fixation point, and preceded with a congruent or an incongruent cue.

Results: In sleep deficit condition morning types reported higher levels of sleepiness at evening hours ($P = 0.042$) and greater effort needed to perform the task ($P = 0.026$). There were no significant differences between M- and E-types in the percentage of correct reactions in rested wakefulness (RW) and sleep deprivation (SD), but in SD, M-types showed more omissions in the evening. The activations of brain structures involved in correct saccadic reactions exhibited characteristic diurnal patterns (repeated-measures GLM; interaction effect of time-of-day × chronotype; $F_{3,39} = 6.58$; $P = 0.001$) – decreasing for morning types (NIR *post-hoc* for 22:00 versus other times; $P < 0.05$) and stable for evening-oriented subjects (NIR *post-hoc* n.s.). Moreover, *post-hoc* tests revealed significantly lower activations in M-types versus E-types in the last session ($P = 0.039$).

Conclusions: Evening chronotype used to be regarded as a marker of emotional vulnerability, and sleep loss is supposed to augment the stress response. The results reported here showed that evening orientation might be advantageous, as far as the tolerance for long working hours is concerned, in terms of performance level and subjective effort. Diurnal patterns of neural activations in M and E types are in line with the theoretical model of sleep/wake regulation by homeostatic and circadian factors. The fMRI registrations may be considered as a validation of the self-estimated behavioural chronotypes.

P947

Towards quantitative sleepiness phenotypes

O. MAIRESSE[1], E. DE VALCK[2], A. CORTOOS[2], D. NEU[3], N. PATTYN[1] and J. HOFMANS[2]

[1]Royal Military Academy, Brussels, BE, [2]Vrije Universiteit Brussel, Brussels, BE, [3]CHU Brugmann, Brussels, BE

Objectives: Subjective sleepiness is likely the organism's first indication of the detrimental effects of prolonging wakefulness. As individuals largely differ in their vulnerability to sleep loss, accounting for individual differences in subjective sleepiness is of crucial importance when considering safety critical operations. The purpose of this study is to precisely quantify the determinants of inter-individual variability in daytime sleepiness to capture its phenotypic richness.

Methods: Twenty-three volunteers (11 females; M age = 30.41, SD = 10.26) enrolled in a 36 h constant routine. Sleepiness was assessed 2-hourly by means of VASs and of the Karolinska Drowsiness Test. Circadian rhythmicity was assessed through salivary cortisol. Subjective sleepiness data were subjected to a functional principal component analysis (fPCA).

Results:

Approximately 80% of the total variance is accounted for by three functional components: component S (50.28%), component C (18.40%) and component D (10.09%). High (low) scores on component S raise (lower) the mean sleepiness profile. Individuals with high (low) scores on component C display more (less) rhythmic variability in their sleepiness profiles, as characterized by a higher (lower) peak-to-through amplitude. Participants with high (low) scores on component D show higher (lower) than average levels of subjective sleepiness during morning hours and a buildup of wake effort occurring later (earlier) than low (high) scorers. Component S

scores were related to self-reported habitual sleep times (r = 0.58, $P < 0.05$) and mean EEG delta power during the KDT (r = 0.46, $P < 0.05$). Participants with higher (lower) than average component C scores showed a significant higher (lower) amplitude in cortisol profiles [t(20)= -2.164, $P < 0.05$]. Finally, the circadian phase of cortisol occurs significantly later (earlier) in participants with higher (lower) than average scores on component D [t(20)= 1.77, $P < 0.05$].
Conclusion: It is concluded that component S represents the responsiveness of the sleep homeostat and its initial level, whereas component C is related to circadian strength and component D to diurnal preference. Our results show that the major modes of variations in sleepiness profiles mirror well-known sleep regulatory processes and allow for the specification of sleepiness phenotypes on a precise quantitative basis. These results have promising implications for further research relating sleepiness phenotypes to genetic factors.

P948

Chronotype and the relation between taste threshold for saltiness and salivary concentration of sodium ions

T. MORITA[1], T. WAKAMURA[2] and J. WATERHOUSE[3]
[1]Fukuoka Women's University, Fukuoka-city, JP, [2]Kyoto University, Kyoto-city, JP, [3]Liverpool John Moores University, Liverpool, UK

While many studies have focused on diet in terms of nutritional intake, there are few studies on rhythms associated with dietary intake, especially the role of environmental lighting. However, the recent concept of Chrononutrition considers relationships between the biological clock and nutritional intake. Our own studies on the relationship between taste thresholds, biological rhythmicity and environmental lighting revealed that taste thresholds showed diurnal variations in saltiness and sweetness dependent upon chronotype. Thus, the thresholds peaked in the early morning with morning-types and in the early evening with evening-types. This result suggests the possibility that taste thresholds vary according to the body's physiological conditions. In order to investigate this possibility and examine rhythmic variation in the threshold for saltiness, we have recorded salt concentration in the body (as reflected in salivary concentration of Na+ ions) and investigated the relationship between this and taste threshold in subjects of different chronotypes [as assessed by a Morningness-Eveningness Questionnaire (MEQ)].
Ten female students were enrolled as the subjects in the study. Subjects were divided into two groups; morning-types whose MEQ score were 46–53, and evening-types whose MEQ score were 39–44. While living their normal daily lifestyle and under uniform dietary conditions, their thresholds for saltiness were measured and their saliva was collected six times (08:30, 10:30, 13:00, 14:30, 16:30 and 18:00 h) during the course of a waking day. For the taste threshold test, the subjects sipped a series of 10 NaCl solutions (increasing regularly in strength from 0.008 to 0.017 M) in order to establish their threshold for saltiness. Saliva samples were collected before measurement of the taste threshold and later analysed for Na+ concentration. The threshold for saltiness in the morning-types tended to decline, and in the evening-types subjects tended to increase, from the early morning to the evening. Furthermore, there was a direct relationship between the Na^+ ion concentration and the saltiness threshold in the group as a whole ($P = 0.08$), a tendency that was more marked in morning-types ($P = 0.04$). From this result, the existence of a mechanism of increasing sensitivity to salt taste, to encourage intake when the Na+ concentration in the body is low or deficient, can be inferred.

P949

Eveningness predisposes to depression, type 2 diabetes and arterial hypertension

I. MERIKANTO, T. LAHTI, E. KRONHOLM, M. PELTONEN, T. LAATIKAINEN, E. VARTIAINEN, H. PUOLIJOKI, M. VANHALA and T. PARTONEN
National Institute of Health and Welfare, Helsinki, FI

Objectives: Different chronotypes may have different susceptibility to depression, cardiovascular diseases and type 2 diabetes. In most previous studies Evening-types has been associated with stronger likelihood for health problems as well as for depressive symptoms and major depression than other chronotypes. Morning-types on the other hand have been associated with less likelihood for depressive symptoms or major depression as compared to other chronotypes. Association between chronotype and susceptibility to type 2 diabetes and a range of cardiovascular diseases has not to our knowledge been studied before. In our study we clarify if chronotype is associated with different susceptibility to these illnesses.
Methods: Our study is based on a large sample of the general Finnish adult population aged 25–74 years. Data in this study comes from the National FINRISK Study 2007 Survey consisting a set of self-report questionnaires and a health examination ($N = 7162$). Laboratory measurements regarding carbohydrate and lipid metabolism were performed as a follow-up research for part of the participants ($n = 4589$). Chronotype was assessed based on six items from the original Horne-Östberg Morningness-Eveningness Questionnaire (MEQ). Depression was assessed with four self-reported items. Our results show that Evening-types self-report more depressive symptoms and have more diagnosed depression. Binary logistic regression, chi-squared tests and general linear models were used in the data analysis.
Results: Our results show that Evening-types self-report significantly more depressive symptoms, both among women ($\chi^2 = 67.9$, df = 2, $P < 0.0001$) and men ($\chi^2 = 47.1$, df = 2, $P < 0.0001$), and have more diagnosed depression ($\chi^2 = 67.9$, df = 2, $P < 0.0001$) as compared to Morning-types. These results were especially clear among women. Evening-types also have significantly higher susceptibility to type 2 diabetes (OR = 2.7, $P < 0.0001$) and arterial hypertension (OR = 1.3, $P < 0.05$) than Morning-types.
Conclusion: Eveningness seems to predispose individuals to health problems, such as depression, type 2 diabetes and arterial hypertension. Morningness on the other hand might protect from these illnesses.

P950

circadian clock gene polymorphisms and Morningness-Eveningness in Korean Adults

J. H. LEE[1], S. J. KIM[2], J. F. DUFFY[3], T. H. JUNG[1] and I. B. SUH[1]
[1]Kangwon National University Hospital, Chunchon, KR, [2]Hyosung Hospital, Cheongju, KR, [3]Harvard Medical School, Boston, US

Objectives: Diurnal preference refers to individual differences in preferred sleep-wake timing, and one source of such variation is the circadian timing system. Mutations in circadian 'clock' genes can alter circadian period, and polymorphisms in clock genes have been reported to be associated with diurnal preference and/or sleep timing. However, not all such reports have been replicated, and racial/ethnic differences in study populations have been suggested as a contributing factor. We examined the association of previously reported clock gene polymorphisms with diurnal preference in a group of Koreans.

Methods: Two thousands eleven subjects age 18 years or older were recruited from visitors to the National Museum in Chunchon City from 2010 to 2011. Standard scores on the MEQ were used to categorize subjects as morning type (MT), neither type (NT) and evening type (ET). In 63 MT and 37 ET subjects, nine previously reported single nucleotide polymorphisms (SNPs) in eight clock genes (CLOCK, PER1/2/3, CK1 epsilon CK1 delta CRY1/2) were analyzed by DNA sequencing up to 677 bp. Based on these analyses, three previously reported SNPs (PER1 C2485T, PER2 A2221G, and CRY1 G2790T) and two newly detected SNPs (PER1 G2475T and PER3 G2767A) were further pursued as candidate alleles for morning or evening preference. Among 425 participants who had provided their DNA as a part of the study, 62 MT (age = 43.7 ± 12.2, M:F = 23:39) subjects with the highest MEQ scores, 62 ET (age = 29.2 ± 8.1, M:F = 20:42) subjects with the lowest MEQ scores, along with 62 NT (age = 35.2 ± 9.5, M:F = 23:39) subjects were selected for genotyping. The five candidate SNPs were analyzed by SNaPshot assay.

Results: The genotypes and allele frequencies in three of the SNPs (PER1 C2485T, PER1 G2475T, PER2 A2221G) were significantly different between the MT, NT, and ET groups (χ^2 test, $P < 0.05$). In PER1 G2475T, the MT group had a significantly higher T allele frequency (0.12) compared to the ET group (0.03; χ^2 test, $P = 0.017$, OR = 4.26). In CRY1 G2790T, the MT group had a significantly higher T allele frequency (0.82) than the ET group (0.70; χ^2 test, $P = 0.041$, OR = 1.88).

Conclusion: Newly detected PER1 2475T allele and previously reported CRY1 2790T allele were associated with the morning preference in Korean adults. Whether PER1 G2475T is specific to ethnic Koreans remains to be tested in other populations.

P951

Association of the VNTR in the PER3 gene to the entrainment process in different latitudes in Brazil

M. PEDRAZZOLI

Universidade de São Paulo, São Paulo, BR

Per3 gene is a component of the circadian molecular mechanism. Its function is not completely understood. One of the hypotheses is that Per3 gene may be involved in light synchronization mechanism. The aim of this project was investigate the association between the VNTR in Per3 gene and circadian rhythmicity dependent of the photophase duration in different light/dark cycle regimens.

Subjects from two locations in Brazil with different latitudes were selected (Natal, 5° and São Paulo, 23°) based on their genotype relative to VNTR. The experiment was carried out in two different seasons of the year to allow to investigate entrainment according photophase variation. We have studied rest/activity cycle and wrist temperature cycle in day-to-day life conditions We found a phase delay in the circadian parameters analyzed [beginning and end of activity, markers of activity (M10) and temperature (M6)] in the PER35/5 group from Natal on November, when compared to São Paulo.

These data show that it is possible to associate Per3 gene with the phase adjustments derived from specific characteristics of light/dark cycle in different latitudes.

P951A

Seventy percent of totally blind people with sleep complaints are not entrained to the 24 h day

M. A. DRESSMAN[1], L. LICAMELE[1], J. FEENEY[1], C. LAVEDAN[1], S. W. LOCKLEY[2] and M. H. POLYMEROPOULOS[1]

[1]Vanda Pharmaceuticals Inc., Washington, US, [2]Harvard Medical School, Boston, US

Introduction: Non-24-h disorder (Non-24) is a serious chronic circadian rhythm disorder with no available treatment. Tasimelteon, a circadian regulator, is a dual MT1/2 receptor agonist being developed as a potential therapeutic for Non-24. The inability to entrain the circadian pacemaker to the 24-h day is definitional of the disorder and constitutes a reliable method for diagnosis and assessment of treatment efficacy. Here we describe the circadian period distribution in a large cohort of self-reported, totally blind individuals with sleep-wake complaints.

Methods: Data were collected during screening for the SET study, an ongoing multicenter, double-masked, placebo-controlled investigation of the Safety and Efficacy of Tasimelteon to treat Non-24. Circadian phase was determined by measuring the major urinary metabolite of melatonin, 6-sulphatoxymelatonin (aMT6s). Urine sample were collected for 48 h/week for at least 4 weeks in 4–8 hourly episodes. aMT6s was measured by a Liquid Chromatography-Mass Spectrometry/Mass Spectrometry. aMT6s excretion rate (ng/h) was plotted against the midpoint of each collection episode and fitted with a cosine function to determine the rhythm peak (acrophase) times. Circadian period (tau) was calculated using weighted linear regression of the serial acrophase times.

Results: Circadian period was calculated for 143 participants. Non-24 was diagnosed in 70% of subjects with tau (T) ranging from 24.08 to 25.34 h (95% Confidence Interval did not cross 24.0) with a median of 24.45 h. Approximately 30% of subjects were entrained to the h day.

Conclusion: The SET trial is the largest study of circadian rhythms in totally blind individuals to date and supports previous reports of a high prevalence of non-entrained circadian rhythms in this population. The difficulty Non-24 patients experience engaging with the 24-h society is a major additional burden. The high prevalence of Non-24 in the totally blind calls for increased education of health care professionals, including primary care physicians, sleep specialists, ophthalmologists, psychologists and psychiatrists, and the visually impaired community and associated service organizations, about the link between total visual blindness and Non-24.

P951B

Pleiomorphic expression of non-24-h disorder in the totally blind

L. LICAMELE[1], M. A. DRESSMAN[1], J. FEENEY[1], C. LAVEDAN[1], M. H. POLYMEROPOULOS[1] and S. W. LOCKLEY[2]

[1]Vanda Pharmaceuticals Inc., Washington, US, [2]Harvard Medical School, Boston, US

Introduction: Non-24-h disorder (Non-24) is a serious chronic disorder that is highly prevalent among the totally blind. Patients suffering from Non-24 are unable to synchronize their endogenous circadian rhythms to the 24-h day due to a lack of light input to the circadian pacemaker. Patients with Non-24 suffer from a variety of behavioral symptoms particularly disruption of the sleep-wake cycle and the daily rhythm in sleepiness.

The traditional clinical expectation is that patients with this disorder will express an aberrant non-24-h sleep-wake cycle with ‘a pattern of

sleep and wake times that typically delays each day with a period longer than 24 h' (ICSD-2). This description does not represent the symptoms experienced by most patients, however. Given that most patients attempt to keep their sleep-wake cycle aligned with the 24-h day in order to attend school, work, and social activities, a clear non-24-h sleep-wake cycle is usually not apparent even when a non-24-h period in strongly endogenous rhythms such as melatonin is confirmed.

Methods: In the present study, we categorize the prevalence of different sleep-wake phenotypes observed with varying degrees of cyclic night-time sleep and daytime napping rhythmicity to demonstrate the pleiomorphic expression of the sleep-wake cycle disruption in Non-24. Data from more than 100 non-entrained totally blind patients have been collected from the screening phase of the SET study, study, an ongoing multicenter, double-masked, placebo-controlled investigation of the Safety and Efficacy of Tasimelteon to treat Non-24. During screening, their individual non-24-h circadian period is calculated from the timing of the urinary 6-sulphatoxymelatonin rhythm assessed weekly over 4 weeks. Nighttime and daytime sleep episodes are reported daily.

Results: Examination of individual sleep data demonstrates that the pattern and severity of the sleep and sleepiness symptoms vary significantly from person to person. Participants with confirmed Non-24 were categorized into four pre-defined sleep subtypes. Less than 5% of individuals matched the traditional textbook definition of Non-24 (Subtype IV) with a clearly non-24-h sleep period.

Conclusion: The heterogeneity of the sleep-wake symptoms highlights the complexity in evaluating Non-24 solely on the basis of sleep parameters, underscoring the need to confirm a diagnosis of Non-24 using an endogenous circadian marker such as the melatonin rhythm.

P951C

Sleep impairment in totally blind individuals with non-24 h disorder

R. TORRES[1], L. LICAMELE[1], C. LAVEDAN[1], E. SCHREFFLER[1], J. FEENEY[1], M. A. DRESSMAN[1], S. W. LOCKLEY[2] and M. H. POLYMEROPOULOS[1]

[1]Vanda Pharmaceuticals Inc., Washington, US, [2]Harvard Medical School, Boston, US

Introduction: Non-24-h Disorder (Non-24) is highly prevalent in individuals with no light perception. Non-24 results when individuals are unable to synchronize their circadian pacemaker to the 24 h day, which reverts to its endogenous non-24-h period. Symptoms include cyclic sleep-wake complaints characterized by episodes of good sleep, followed by poor nighttime sleep, and excessive daytime naps, followed by good sleep and so on in a repetitive, life-long cycle. In the SET study, we assessed the magnitude of sleep impairment in blind individuals with Non-24.

Methods: Data were collected during SET study screening, an ongoing multicenter, double-masked, placebo-controlled, parallel study to investigate the Safety and Efficacy of Tasimelteon to treat Non-24. Participants were asked to maintain a fixed 9 hour sleep episode of their choice and to complete a nighttime sleep and daytime nap diary for a minimum of 6 weeks. Non-24 diagnosis was made by measuring circadian phase utilizing the major urinary melatonin metabolite, 6-sulphatoxymelatonin (aMT6s). 48 hour urine samples were collected for 4 weeks in 4–8 hourly episodes. aMT6s was measured by Liquid Chromatography-Mass Spectrometry/Mass Spectrometry. aMT6s excretion rate was plotted against the midpoint of each collection episode and fitted with a cosine function to determine the rhythm peak times. Circadian period was calculated using weighted linear regression of the serial peak times. Average subjective total nighttime sleep for the quartile of nights with the worst sleep was compared between individuals with Non-24 and the entrained totally blind participants. Similar analyses were conducted for daytime naps.

Results: A total of 161 visually blind individuals with self-reported sleep problems were analysed (n = 107 Non-24 and n = 54 entrained). Total nighttime sleep was, on average, 53 min/night ($P = 0.003$) shorter and daytime sleep duration was 48 min/day longer in Non-24 individuals compared to entrained patients ($P = 0.0027$).

Conclusion: Sleep patterns vary in relation to circadian phase among totally blind individuals with Non-24. Overall, nighttime sleep is decreased and daytime sleep is increased when their endogenous circadian rhythm is out-of-phase with the 24-h light-dark cycle. The resulting chronic sleep deprivation may lead to impairment in daily functioning, alertness, mood, social interactions, school and work performance, and increase the risk for accidents.

Poster Session – Positive Airway Pressure Therapies

P952

Clinical impact of adaptive servoventilation compared to other ventilatory modes in patients with complex sleep apnoea, central sleep apnoea or Cheyne-Stokes respiration

S. CORREIA[1], V. MARTINS[2], L. SOUSA[2], J. MOITA[2], F. TEIXEIRA[2] and J. MOUTINHO[2]

[1]ULS-Guarda, Guarda, PT, [2]HG-CHUC, Coimbra, PT

Introduction: Adaptive servoventilation (ASV) is a recent ventilatory mode, directed to Central Sleep Apnea (CSA), Complex sleep apnea (CompSA) or Cheyne-Stokes Respiration (CSR) resolution. Other forms of noninvasive positive pressure ventilation (NPPV) may be used to treat these patients, but may be insufficient.

Objectives: The aim of our study is to compare the clinical impact (in terms of symptoms, apnea hypopnea index, compliance, cardiac function and cardiovascular events) of ASV with other forms of NPPV in treating patients with CompSA, CSA and CSR.

Methods: Medical data of all the patients who underwent polysomnography to titrate ASV, were evaluated. Demographic, clinical and polysomonographic data were obtained. All patients had a minimal time of treatment and follow-up of 6 months.

Results: ASV titration was performed in 34 patients: 31 male with a mean age of 68 ± 8.5 years and BMI of 30 ± 4.6 kg/m^2. Fifty-eight percent present a CompSA, 26.5% a CSA/CSR, 8.8% a CSA 5.9% an OSA with CSR. Heart failure was present in 20.6% of cases and other cardiovascular disease in 88%. The median diagnostic AHI was 46 ± 22 events per hour.

Fifteen patients were treated with NPPV, 17 with ASV and 2 patients were lost in follow up and didn't receive any kind of ventilation. In both groups (NPPV versus ASV) there were no statistical difference in terms of age (mean 71 years ± 6 versus 66 ± 10), sex (88% male versus 93%) and sleep apnea severity (AHI 44 ± 18 versus 21 ± 25). Most of patients present a CompSA (53% in ASV group versus 67% in NPPV group) or a CSA/CSR (29.4% in ASV group versus 20% in NPPV). After ASV titration, the mean follow up was 25 ± 14 months. Both groups (ASV versus NPPV) were similar in terms of compliance (77 ± 23% versus88 ± 14%) and in terms of Epworth sleepiness scale score (6 ± 5 versus 7 ± 5).

There was a statistical difference in terms of residual AHI: mean AHI was 4 ± 3 in ASV group and 9 ± 3 in NPPV group (P = 0.005).

We found no differences in terms of Left ventricular fractional shortening (ASV 33 ± 10% versus NPPV 32 ± 10%). There was no difference in terms of non-fatal cardiovascular events (three events in each group) whereas 2 fatal cardiovascular events occurred only in the NPPV group (sudden death).

Conclusions: ASV is an effective treatment in patients with CompSA, CSA/CSR significantly decreasing residual AHI. In both groups, compliance rate was high and sleepiness improved. It is clinically relevant that the 2 patients who died of sudden death were treated with NPPV.

P953

Prognostic impact of sleep-disordered breathing and their treatment

M.-P. DORTHO[1], L. MARGARIT[2], S. GUENDOUZ[2], M. STOÏCA[1], X. DROUOT[2], L. HITTINGER[2] and T. DAMY[2]

[1]AP-HP Hopital Bichat, Paris, FR, [2]AP-HP Hopital Mondor, Paris, FR

Objective: To determine whether sleep-disordered breathing (SDB) severity, patterns, oxymetric variables and their nocturnal ventilation in chronic heart failure (CHF) were associated with adverse CHF outcomes.

Background: SDB are frequent in CHF. The relationships between SDB and outcome in CHF are unknow.

Methods: CHF patients with LVEF≤ 45% were assessed by polygraphy in our CHF clinic between 2001 and 2009. Nocturnal ventilation was started according to SDB severity. Combined endpoint was death, heart tranplant and ventricular assit device implant.

Results: Of the 384 CHF were included and 82% were men. Their mean (SD) age and LVEF were respectively 59 ± 13 and 29 ± 9% and. Obstructive sleep apnoea (OSA), central sleep apnoea (CSA) and Cheyne-stockes respiration (CSR) prevalences were 62%, 26% and 29%. Primary endpoint was observed in 31%. Mean (SD) follow-up for survivors was 47 ± 25 months. Moderate (5/h ≤ AHI < 20 /h) and severe SDB (AHI ≥ 20/h), OSA and CSA had a similar bad prognostic compared to patients without SDB (respectively $P = 0.036$; $P = 0.003$). Thirty-one percent of the SDB patients were treated with nocturnal ventilation. Treated SDB had a better outcome than untreated severe SDB after adjustement for cofounding factors [$P = 0.031$; HR: 0.56; 95% CI (0.33-0.95)]. Subgroup analysis including only OSA showed a similar result after adjustement [$P = 0.017$; HR: 0.40; 95% CI (0.19-0.95)]. In multivariate cox analysis including all the oxymetry variables, only CSR and minimal oxyhemoglobin saturation predicted adverse outcomes in all CHF patients untreated for SDB but not AHI.

Conclusion: In CHF, SDB is associated with a poor prognosis wathever the SDB patterns and nocturnal ventilation is associated with a better outcome. Between 2009 and 2012, MPO has been membre of scientific committee, principal investigator or co-investigator for research projects funded by ResMed, Philips et Bioprojet; has been speaker in symposia funded by Vitalaire, Philips, IPSEN and has received travel grant from Orkyn' & UCB.

P954

The impact of Servo-assisted CPAP on Cheynes-Stokes respiration

K. WALDRON and D. PRICE

Liverpool Heart and Chest Hospital, Liverpool, UK

Background: Patient A is a 70 year old male, height 158 cm and weight 127 kg who was referred to the Obstructive Sleep Apnoea (OSA) screening clinic at the Liverpool Heart and Chest Hospital due to his loud snoring and witnessed apnoeic episodes. He presented with excessive daytime somnolence the severity of which was assessed using an Epworth Sleepiness Scale Questionnaire (18/24). A limited overnight sleep study was completed which, after analysis, showed a significant Apnoea Hypopnoea Index (AHI) of 63/h with a high number of periodic apnoeic episodes due to central respiratory dysfunction. A diagnosis of nocturnal cheyne stokes respiration (CSR) secondary to heart failure was made.

Intervention: Continuous Positive Airways Pressure (CPAP) therapy was prescribed in the interim, which was tolerated but failed to address the CSR. It was therefore decided that before Non-Invasive Ventilation be considered Servo-Assisted Bi-Level Positive Airways Pressure (BiPapAuto-SV) may prove to be effective. Patient A was given a weeks trial on BiPapAuto-SV

Results: Once established on the BiPapAuto-SV therapy overnight oximetry was performed. This indicated that the CSR was successfully controlled and there were no further significant desaturations. Morning blood gases undertaken following treatment were also within acceptable levels. ESS performed the following day was significantly reduced to 3/24 (normal < 11)

Conclusions: Following the treatment Patient A was discharged from hospital within 1 week.

Follow up out-patient appointments in clinic revealed:

1. Significant weight loss
2. Increased mobility
3. ESS continued to be reduced
4. Quality of life improved.

The use of BiPapAuto-SV to treat CSR in patients with heart failure is now becoming widely recognised as a viable treatment option.

P955

Prevalence of complex sleep-disordered breathing in a sleep laboratory population of OSAS patients treated with CPAP

L. MARGARIT[1], C. PHILIPPE[2], M. STOÏCA[1], X. DROUOT[3], A. BOKAR-THIRÉ[1] and M.-P. DORTHO[1]

[1]Hôpital Bichat – Claude Bernard, Paris, FR, [2]Hôpital Tenon, Paris, FR, [3]Hôpital Henri Mondor, Créteil, FR

Background: Sleep-disordered breathing (SDB), has been described in the last years. The first prevalence of this syndrom pointed out was 15%.

Objective: The aim of our study is to define this prevalence in a french cohort of patients treated for obstructive sleep apnea syndrome (OSAS), with continuous positive airway pressure (CPAP). We sought to characterize the residual SAS and to identify clinical characteristics of CompSAS.

Methods: The study consisted of retrospective analysis of a cohort of patients addressed to two French sleep centres for SAS suspicion between 2006 and 2007. Patients were included if their diagnostic polysomnography (PSG) or polygraphy (PG) revealed an obstructive SAS which required CPAP treatment. We excluded OSAS which part of the obstructive events was <80% and OSAS not treated with CPAP.

Results: Files of 1004 consecutive patients were examined. Among them, 696 had a mild to moderate SAS and CPAP was not considered (279 mild, 417 moderate), 308 had a severe SAS. Among the later, 7 denied CPAP and 14 were lost to follow-up. CPAP efficacy was checked 5.14 ± 3.21 months after treatment initiation. Among these 287 patients on CPAP, 53 patients presented a residual SAS (IAH > 10/h), all but 1 had obstructive respiratory events, which only required pressure adaptation. Among these 52 patients with residual obstructive events. Two patients presented short episodes of Cheyne-Stokes respiration, not present during the initial diagnosis either, but the overall AHI was <5/h. All together the prevalence was found 0.35% (one out of 287).

Conclusion: CompSAS prevalence in a long term follow-up seems lower than initially published.

The study was sponsored by ResMed.

P956

Sleep architecture in patients with sleep apnoea syndrome before and at the background of CPAP therapy

A. CHIKADZE[1], I. BURDULADZE[2], L. KHUCHUA[1], T. CHIKADZE[1], M. JIBLADZE[1] and R. SHAKARISHVILI[1]

[1]P.Sarajishvili Institute of Neurology, Tbilisi, GE, [2]Scientific Research Institute of Clinical Medicine, Tbilisi, GE

Objective: The syndrome of sleep apnea appears to be one of the most spread forms of sleep disorders. The goal of the research was to study the peculiarities of sleep architecture in patients with the syndrome of sleep apnea before CPAP therapy and at the background of CPA.

Methods: Total of 17 patients with sleep apnea were examined at the age of 28–65. According to sleep questionnaire ESS and MBI were determined in all the patients. For differential diagnostics of sleep apnea PSG was carried out using Dr. Sagura Medizintechnik P59 polygraph. PSG investigation was performed accompanying by full video synchronized recording. For CPAP therapy CPAP (IPAP) Machine was used.

Results: According to the questionnaire all the patients have a high rate of night sleep disorders. Epworth Sleepness Score (20–22, maximum 24) and body mass index (BMI) overall maximum (31–45 > 31). The patients were characterized by night sleep disorder, loud snore, headache, apathy, the problems of concentration, excess daytime sleep. PSG has shown that the patients with both obstructive sleep apnea (OSA) 14 and central sleep apnea (CSA) 3 are characterized by significant decrease in sleep architecture, which results in full absence of the NREM3 stage of sleep (superficial sleep), the increase of REM stage, frequent EEG and EMG awakenings and defragmentation of sleep as a whole. It should be noted that a separate part of OSA patients (both women and men) was characterized by clearly expressed REM behavioral disorders. Central sleep apnea was characterized by relative low index of snore SI (80–120) and relative high indices of the Sp02 (87–93) in case of obstructive sleep apnea (SI > 200, Sp02-(36–91). At the background of CPAP therapy the first significant effect was received after 2 h resulting in the regulation of respiration and snore index. The progressive increase of Sp02 within the limits of 92–95%. Sleep architecture considerably changed, EEG and EMG awakenings sharply decreased, NREM stages increased, in rare cases NREM3 stage was noted, sleep defragmentation significantly decreased.

Conclusion: Thus, Sleep Apnea (both CSA and OSA) is characterized by significant disorder of sleep atchitecture. At the background of CPAP therapy a significant improvement of sleep architecture and the regulation of symptomocomplex characteristic of sleep apnea take place.

P957

Factors that affect continuous positive airway pressure level during titration of night polisomnography in patients with obstructive sleep apnoea

B. SALEPCI, E. TORUN PARMAKSIZ, N. KIRAL, G. SARAC, S. SENER COMERT, A. FIDAN and B. CAGLAYAN

Sleep breathing disorders, Istanbul, TR

Study objectives: There is no designated pressure level for CPAP (Continuous Positive Airway Pressure), which is accepted globally as the gold standart for treatment of OSAS (Obstructive Sleep Apnea Syndrome) and there are many great factors that affect pressure levels. In our study we aimed to assess factors that affect CPAP pressure levels at titration night stays.

Design: Retrospective analysis.
Settings: Accredited sleep laboratory.
Patients: Five hundred twenty five patients who were diagnosed OSAS between January 2005 and June 2011 and were recommended to use CPAP were included in the study. All the patients were diagnosed OSAS by PSG (polysomnography) conducted at first night stay and their CPAP titrations were made at a second night stay by full night PSG.
Statistical Analysis: Data were entered to SPSS package program. Data were analysed by Spearman Correlation Analysis.
Results: Three hundred and seventy (70.5%) of 525 cases were men; 155 (29.5%) were women. Mean age was 50.48 ± 9.87, BMI (body mass index); 32.29 ± 5.71, ESS (epworth sleepiness scala) score; 10.68 ± 6.06, CPAP pressure level; 10.52 ± 2.18. In first night polysomnography mean AHI (Apnea Hypopnea Index) was 50.15 ± 23.73, Apnea Index (AI); 28.95 ± 24.95, ODI (Oxygen Desaturation Index); 42.72 ± 24.83 min SpO_2% (minimum oxygen saturation%); 75.63 ± 10.96, PLMI (Periodic Leg Movement Index); 19.64 ± 21.30. In terms of correlation with CPAP pressure level following results were achieved: No correlation was found with age or gender. Positive correlation was found with BMI and ESS score. At first night stay PSG positive correlation was found with AHI, AI, ODI and PLMI; negative correlation with min SpO_2%. At titration night PSG positive correlation was found with sleep latency, oro-nasal mask usage and PLMI; negative correlation with sleep efficiency and nasal mask usage.
Conclusion: Although age and gender don't affect CPAP pressure levels designated at titration night; higher BMI and ESS and severe OSAS requires higher levels of CPAP pressure. Bad sleep quality and oro-nasal mask usage also lead to higher levels of CPAP pressure.

P958

Life satisfaction and close relationships in male and female sleep apnoea patients before and after 1 year on CPAP treatment

M. PETERSEN[1], S. BERG[1], B. MIDGREN[2] and E. KRISTENSEN[2]
[1]University of Lund, Lund, SE, [2]University of Copenhagen, Copenhagen, DK

Introduction: The present study investigates life satisfaction and close relationships in male and female patients with Obstructive Sleep Apnea, before and after 1 year of CPAP-treatment.
Material and methods:
Study design: Consecutive inclusion of male (n = 150) and female (n = 46) patients with OSA scheduled for treatment with CPAP. After informed consent the patients were asked to fill out a questionnaire on two different occasions: before start of CPAP-treatment and after 1 year of CPAP-treatment. We selected four questions from LiSat-11; one investigating general satisfaction (life as a whole) and three investigating closeness (Family Life, Partner Relation and Sexual Life). Epworth Sleepiness Scale was used to investigate daytime tiredness.
Results within the groups and between genders are shown.
Results: With respect to life satisfaction (life as a whole) we found no significant difference neither between nor within the groups. When looking at the three questions on closeness (family life, partner relation and sexual life) we found a significant improvement in Sexual Life in the male group after 1 year on CPAP-treatment. No other items showed any significant improvement. In both groups daytime tiredness was reduced after 1 year of CPAP- treatment.
Conclusion: Except for improved sexuality in male patients, no change can be seen in life satisfaction and close relationships in our patients after 1 year of CPAP-treatment. Although no improvement is seen in these items, the results indicate that CPAP-treatment *per se* does not have a negative impact on life satisfaction and close relationships. This is important information to patients who finds CPAP-treatment cumbersome and stigmatizing.

P959

Continuous positive airway pressure side effects: evolution over time and association to treatment dropout

M. ULANDER[1], A. EKEGREN[2], M. SVENSSON JOHANSSON[2], E. SVANBORG[1] and A. BROSTRÖM[2]
[1]Linköping University, Linkoping, SE, [2]School of Health Sciences, Jönköping, SE

Objectives: Continuous Positive Airway Pressure (CPAP) side effects are common, and might influence adherence. While more frequent and severe side effects are associated to lower treatment adherence, the associations are not clear-cut. The aim was to examine CPAP side effects prospectively, and to correlate side effects to treatment adherence.
Methods: Of the 186 consecutive Obstructive Sleep Apnea Syndrome (OSAS) patients planned for CPAP treatment (71% males, median age 51 years, range 20–76) were enrolled and followed prospectively. They completed the Side Effects to CPAP Inventory (SECI) questionnaire after 2 weeks and after 1 year on CPAP. In SECI, the patient is asked to rate the frequency, magnitude and impact on adherence of 15 common CPAP side effects on a five-point Likert-type scale. Patients scoring 4 or 5 on any of the three questions (i.e. frequency, magnitude and effect on adherence) regarding a given side effect were considered to suffer significantly from it. Outcome measure was treatment dropout during the first year.
Results: The most common side effects after 2 weeks were blocked up nose, dry mouth, awakenings, mask pressure and mask leaks. After 1 year, the most common side effects were blocked up nose, dry mouth, irritated bowl, mask pressure and mask leaks. Patients with significant problems from dry mouth, transient deafness, increased number of awakenings, problems exhaling or anxiety after 2 weeks had a significantly higher risk of dropping out during the first year, with relative risks ranging from 1.65 to 2.14. Other side effects were not significantly associated to dropout.
Conclusion: Side effects differ in their association to treatment dropout. Side effects that are associated to treatment dropout are especially important to address and alleviate.

P960

Adherence to treatment with CPAP in a group of patients with obstructive sleep apnoea syndrome

B. JURADO-GAMEZ[1], O. GUGLIELMI[2], I. JURADO-ROBLES[1] and G. BUELA-CASAL[2]
[1]Reina Sofia University Hospital, Cordoba, ES, [2]University of Granada, Granada, ES

Objectives: Identify which variables related to socio-demographic aspects and disease severity are better predictors of adherence to treatment with Continuous Positive Pressure Airway (CPAP) in patients diagnosed with Obstructive Sleep Apnea Syndrome (OSAS).
Method: We selected consecutively 50 patients diagnosed with OSA, who had been given treatment with CPAP (mean ± SD: AHI = 59.7 ± 23.5 events per hour, CPAP = 7.9 ± 0.9 cmH_2O).

Before making the diagnosis with a full night polysomnography, all patients answered a socio-demographic interview that collected information like body mass index, education level, marital status, alcohol consumption, smoking and drug habits, use of medication and other illnesses suffered.

Results: A comparison for the variables studied was made between the group of adherent patients (CPAP < 4 h/night group, mean ± SD: hours of CPAP use = 5.99 ± 1.13) and the non-adherent group (CPAP < 4 h/night, mean ± SD: hours of CPAP use = 1.46 ± 1.42). Patients that showed better adherence had more cardiovascular disease (χ^2 = 4.710, P = 0.030) and had more efficient sleep (t = -3.08, P = 0.003). Linear regression showed a weak and not significant correlation between sleep efficiency and adherence to CPAP treatment (t = 1.803, P = 0.078).

Conclusion: The lack of adherence to CPAP treatment is among the main problems of the doctors who treat patients with OSAS. On average, 20% of patients fail to comply with recommended therapy and do not improve their health. Some studies have tried to find the key factors involved in adherence to treatment. With regard to CPAP, and in line with our results, we have shown a relationship between sleep characteristics, like the amount of slow wave sleep or efficiency, and adherence to CPAP, as well as the presence of other diseases.

P961

Hypertension among patients just diagnosed with obstructive sleep apnoea compared to controls and 2-year change after starting treatment with continuous positive airway pressure

S. GUDMUNDSDOTTIR[1], E. BJORNSDOTTIR[2], E. S. ARNARDOTTIR[1], A. I. PACK[3], B. BENEDIKTSDOTTIR[1] and T. GISLASON[1]
[1]The National University Hospital of Iceland, Reykjavík, IS, [2]University of Iceland, Reykjavík, IS, [3]University of Pennsylvania School of Medicine, Pennsylvania, US

Objectives: The aim of this study was to explore the prevalence of hypertension among patients with obstructive sleep apnoea (OSA), both while untreated and again 2 years after starting CPAP treatment. Hypertension among OSA patients was compared to the prevalence of hypertension in a general population sample.

Methods: The OSA patients (n = 822) were a part of the Icelandic Sleep Apnea Cohort (ISAC). They were newly diagnosed with moderate or severe OSA (665 males, 157 females). The mean (±SD) age was 54.9 ± 7.6 years. Majority were obese with a mean body mass index 33.5 ± 5.7 kg/m^2. The control group consisted of 758 randomly selected subjects from the general population (www.boldcopd.org). Altogether 52.9% were males and they were younger (57.0 ± 11.8 years) and less obese (27.9 ± 4.9 kg/m^2). Two years later, 90% of the patients (n = 742) came for follow up. Subjects were defined as having hypertension if they had been diagnosed by a doctor and were on antihypertensive medication.

Results: At baseline 45.7% of the OSA had hypertension compared 245 (33%) among the 758 controls (P < 0.001). The difference in prevalence was highest when comparing the younger age groups 40–60 years, but similar among the older ones. At the 2 year follow-up altogether 46.2% fulfilled the same criteria on medically treaded doctor diagnosed hypertension. Among the OSA patients those with hypertension were older, more obese, had more severe OSA [apnea hyponea index 50 ± 21.6 compared to 43.3 ± 19.7 (P = 0.01)]. The hypertensive OSA patients were also more likely to have diabetes. The majority (87.7%) of those with hypertension at baseline did also have hypertension at follow up. Hypertension was more likely to improve among those that were using CPAP in the younger ones (P < 0.05). Of those who did not have hypertension at baseline, 11.3% reported at follow up that they had hypertension. Older subjects and non CPAP users were more likely to develop 'new' hypertension. Subjects with hypertension at baseline were more likely to be using CPAP at follow up and hypertension at follow up was consequently more prevalent among CPAP users (51.1% among users and 35.7% among non users, P < 0.0001).

Conclusion: Hypertension is comparatively more common among young OSA patients and with severe OSA and these patients are also more likely to be continuous positive airway pressure (CPAP) users at follow up. Hypertension is more likely to improve among those who are using CPAP and new onset of hypertension is more prevalent among non-users.

P962

Continous positive airway pressure and compliance – a long-term follow-up study: The Icelandic Sleep Apnea Cohort (ISAC)

M. Ó. SIGURGUNNARSDOTTIR[1], E. S. ARNARDOTTIR[1], B. BENEDIKTSDOTTIR[1], E. BJORNSDOTTIR[1], S. JULIUSSON[1], A. I. PACK[2] and T. GISLASON[1]
[1]The National University Hospital of Iceland, Reykjavík, IS, [2]University of Pennsylvania School of Medicine, Philadelphia, US

Objectives: The aim of this study was to estimate in a long-term follow-up study, the main determinants of continuous positive airway pressure (CPAP) usage in a well defined sleep apnea population.

Methods: Patients diagnosed with moderate to severe obstructive sleep apnea (OSA) in Iceland and referred for CPAP treatment to the Landspitali University Hospital from 2005 to 2010 were invited to participate. Altogether 822 OSA patients participated (665 males, 157 females). Two years later they were invited for a follow-up evaluation. Most subjects had CPAP devices with objective registration of daily usage in the last month. CPAP use of other subjects was based on questionnaires. All CPAP users in Iceland are taken care of by the Landspitali and pay a monthly service fee.

Results: Altogether 741 (90%) OSA patients returned for the 2 year follow-up. Of those, n = 475 (64%) were using CPAP and n = 266 were non-users. Of the nonusers, 17% had returned the device within 30 days, and altogether 30% had returned the device within 3 months. Among the 475 CPAP users, n = 363 had objective last month registration. Their average ± SD use per night was 6.2 ± 1.9 h and only n = 47 used CPAP < 4 h/night. At baseline, the users at 2 years had significantly higher BMI (34.1 ± 5.6 versus 32.4 ± 5.6 kg/m^2, P < 0.0001) and a higher apnea hypopnea index (AHI; 48.5 ± 21.0 versus 38.6 ± 17.9 events/h, P < 0.0001). They also reported more sleepiness as measured by the Epworth Sleepiness Scale (ESS, 12.3 ± 5.0 versus 11.3 ± 5.0, P = 0.03). Among those with BMI > 35 kg/m^2 and ESS > 10, altogether 76% were using CPAP at the follow-up visit compared to 44% of those with BMI < 30 and ESS < 10, a significant interaction in logistic regression. Hypertensives on antihypertensive medications at baseline were more likely to use CPAP (72%) at follow-up compared to nonhypertensives (58%), P < 0.001, which remained significant after adjusting for AHI, BMI and sleepiness. No relationship of CPAP compliance to smoking, gender, age diabetes and cardiovascular disease was found.

Conclusion: Two-thirds of moderate to severe OSA patients are regular CPAP users after 2 years and the majority of them have high usage per night. Obesity, OSA severity, hypertension status and sleepiness are all important determinant of long-term compliance.

P963

Comparison of group versus individual patient training in the use of continuous positive airway pressure (CPAP) for sleep apnoea

H. JANEBDAR[1], C. KOSKY[2], R. BROWN[2], I. DUNCAN[2], J. CHAPMAN[2], R. MUZA[2], J. STEIER[2] and A. J. WILLIAMS[2]
[1]King's College London, London, UK, [2]Guy's and St Thomas' NHS Foundation Trust, London, UK

Aim: CPAP is the standard treatment of patients with obstructive sleep apnoea (OSA). Training of patients in the use of CPAP is usually done on an individual basis with the patient and a qualified practitioner. We compared CPAP training delivered to patients in groups with those trained individually. We analysed CPAP compliance, cost of training, patient and staff satisfaction.

Patients and methods: A prospective field study recruited patients with OSA that required CPAP therapy between January 2010 and June 2010 at a busy tertiary referral centre for sleep disorders. Patients were allocated to either individual CPAP or group CPAP training based on patient preference. The content of training was identical in both groups. Individual training (45 min) was delivered by one medical technologist. Group training (90 min) involved 4–6 patients and was delivered by 2 medical technologists. Compliance at 2 weeks and 12 months was assessed by a CPAP data card. CPAP compliance was considered adequate if the average nightly use was greater than 4 h. Patients and staff were asked to complete a satisfaction questionnaire. Costs were based on National Health Service hourly rate for a band 5 medical technologist.

Results: 262 patients with OSA (61 female) were studied, 61 (23.3%) had mild, 80 (30.5%) moderate and 121 (46.2%) had severe OSA. Eighty received individual CPAP training and 182 received group CPAP training. There was no significant difference between either training group in > 4 h/night CPAP compliance at 2 weeks (69% individual trained versus 67% group trained, $P = 0.96$) or at 1 year (69% individual trained versus 57% received group training, $P = 0.08$). No difference in compliance was found when method of training was analysed by severity of OSA (mild $P = 0.68$, moderate $P = 0.57$, severe $P = 0.11$) or patient ethnicity (Black patients $P = 0.55$, Asian patients $P = 0.88$, compared with white patients). Patient satisfaction was similar in both training groups (somewhat satisfied or very satisfied; group 88%, individual 89%, $P = 0.80$). Four staff preferred group training, 4 staff preferred individual training, three had no preference. Group training was cheaper than individual training (£6.00 versus £9.00/patient).

Conclusion: We found no difference in compliance, patient satisfaction or staff preference between individual and group CPAP training. In a highly frequented sleep service, it was more cost effective to deliver group CPAP patient training.

P964

Clinical feasibility of an auto-adjusting bi-level PAP device for the treatment of obstructive sleep apnoea

B. OKTAY[1], N ALTINTAS[2], H. FIRAT[3] and P. STROLLO[2]
[1]Mardin devlet hastanesi, Mardin, TR, [2]University of pittsburgh, Pittsburgh, US, [3]Diskapi hastanesi, Ankara, TR

Bacground: Bi-Level positive airway pressure (BPAP) is an effective alternative to continuous positive airway pressure (CPAP) in patients with obstructive sleep apnea (OSA) who could not tolerate CPAP. An automatically titrating BPAP device has recently been developed, BPAP Auto® with BiFlex™ (BPAPauto). The primary aim of this study was to examine the performance of this new device during attended polysomnography (PSG).

Methods: This was a prospective case series study. Participants with OSA currently using CPAP or BPAP therapy were recruited from the University of Pittsburgh Medical Center Sleep Medicine Center where they had been evaluated for OSA. Patients who met all criteria for participation and provided consent were asked to undergo in-lab PSG study with BPAPauto.

Results: A total of 27 participants met the criteria and were enrolled the study. Thirteen of the 27 participants currently had been using CPAP and 14 were on BPAP treatment. All participants received BPAPauto therapy during an attended PSG. Sleep and respiratory data were examined. The mean apnea hypopnea index (AHI) was found 2.2 ± 2.5 events per hour. SaO_2 (oxygen saturation) was 94.0 ± 1.8. The mean inspiratory positive airway pressure (IPAP) abolish respiratory events was 14.1 ± 3.4 cmH_2O and that of expiratory positive airway pressure (EPAP) was 10.7 ± 3.9 cmH_2O.

Conclusions: BPAPauto is able to establish an appropriate Bi-Level PAP and control oxygen saturation without excessive disruption of sleep. Further studies using randomized control design are needed to examine potential roles and advantages of BPAPauto for treatment of OSA.

P965

CPAP treatment for acute mountain sickness

P. L. JOHNSON[1], C. C. JOHNSON[1], P. POUDYAL[2], N. REGMI[2], M. WALMSLEY[2] and B. BASNYAT[2]
[1]University of Sydney, Sydney, AU, [2]Himalayan Rescue Association, Kathmandu, NP

Acute Mountain Sickness (AMS) is very common at altitudes ≥3000 m and there are few treatment options, particularly in the field where electricity availability is limited, and medical assistance or oxygen are unavailable or difficult to access.

Positive airway pressure has been used to treat AMS at White Mountain (3800 m in California). We hypothesised that CPAP could be used under field conditions by using a small rechargeable battery for power, and tested this at 3900 m in the Nepal Himalaya in five subjects. CPAP effectively eliminated AMS symptoms in this group and maintained higher sleeping oxygen saturation (SaO_2). We then trialled CPAP at Pheriche (4200 m in the Nepal Himalaya) on 17 trekkers who had developed AMS.

Trekkers with symptoms of AMS were recruited. All subjects had been taking acetazolamide for at least the previous 24 h. The Lake Louise questionnaire for AMS was administered before and after overnight CPAP use and SaO_2 was recorded continuously overnight. CPAP was also applied for 15–20 min at the time of recruitment, and SaO_2 and AMS symptoms monitored during this time.

During the 15–20 min use of CPAP at the time of recruitment, SaO_2 rose from a mean of 84.3 ± 4.9–89.1 ± 3.4% ($P = 0.003$) and headache was reduced or eliminated in all subjects. Following overnight CPAP use the Lake Louise AMS score was significantly lower: 6.1 ± 3 versus 1.6 ± 1 ($P < 0.0001$).

CPAP appears to be a useful treatment for AMS when used for either a short time during wakefulness or during sleep. AMS is known to be associated with lower sleeping SaO_2 and this may be the mechanism

for improved AMS symptoms after overnight use of CPAP. However, improvement in SaO_2 and headache during short duration use of CPAP may be due to increased partial pressure of oxygen from positive airway pressure resulting in 'artificial descent to a lower altitude'. Due to the portability of the CPAP machine and rechargeable battery i.e. <3 kg, and the availability of solar power to recharge the battery, there are potential uses for this treatment method in field conditions where serious high altitude illness occurs in areas with limited treatment options.

P966

Mild and moderate sleep apnoea: continuous positive airway pressure treatment revisited

M. TESTA, R. A. VELLUTI and M. PEDEMONTE
Facultad de Medicina CLAEH, Punta del Este, UY

Introduction: Continuous positive airway pressure (CPAP) is the indicate treatment for moderate and severe obstructive sleep apnea-hypopnea syndrome (OSAHS). However there is no consensus about the CPAP indication in mild apneas. This study takes consideration not only the apnea-hypopnea index (AHI) but also health-related quality of life, changes in the sleep architecture and patient evolution when they are not treated by CPAP.

Methods: Forty-six patients were studied with split-night protocol (78% males, 22% females; average age 56 years old). The technician diagnoses sleep stages online and the first part of the study finish when patient pass through all sleep stages at least one time: slow wave sleep (SWS or Stages N1, N2, N3) and rapid eyes movements sleep (REM or Stage R) spending about 4 h in each part. Based on AHI, 29 patients suffered mild and 17 moderate apneas. The second part of the study 'CPAP titration' was done manually according to the patient tolerance. Percentages of sleep stages were compared between the first and the second part of the study. Two Epworth Somnolence Scales (ESS) were done in each patient: the first one at the recording night and the other 1 year later (approximately). Half of patients were treated by CPAP and the other half do not.

Results: All patients treated by CPAP improved the diurnal hypersomnia, passing from 17 to 6 in the ESS average (statistically significant $\leq$ 0.001) while patients without CPAP treatment maintaining or increasing the hypersomnia and their symptoms, except two of them that thinned. During the second part of the study, in spite of the uncomfortable situation provokes by CPAP titration, sleep architecture shows increment in Stage N3 and Stage R triplicates is percentage, in comparison with the corresponding periods in the first part of the study.

Discussion and conclusions1. The split-night study is a satisfactory way to evaluate OSAHS and CPAP titration, under the continuous supervision of trained technician able to diagnose sleep stages and to fix the adequate airway pressure manually.

2. Patients suffering milder degrees of OSAHS improve the day-time sleepiness and health-related quality of life when is treated by CPAP while most of them -without CPAP treatment- worse their symptoms.

3. The sleep architecture restoration is one of the most important consequences of the CPAP treatment to re-establish the circadian physiology.

P967

Serum adiponectin levels in obstructive sleep apnoea patients, the effect of continuous positive airway pressure therapy and the relation of serum adiponectin to selected anthropometric parameters of obesity

M. HOBZOVA[1], D. STEJSKAL[2], E. SOVOVA[1], V. KOLEK[1] and J. ZAPLETALOVA[1]
[1]University Hospital Palacky University, Olomouc, CZ, [2]Palacky University, Olomouc, CZ

Objectives: Obstructive sleep apnoea (OSA) is the most frequent sleep breathing disorder. The most important risk factor for OSA is obesity. Adiponectin, having antiinflammatory, cardioprotective, antiatherogenic, anorectic and antidiabetic effects, is produced by adipose cells. The study aimed to find the effect of continuous positive airway pressure (CPAP) therapy on serum adiponectin levels and the relation of obesity in OSA patients to adiponectin.

Subjects and methods: 159 OSA patients (137 males) with a mean age of 53.9 ± 10.3 years, were divided into two groups. The CPAP treated group – 82 patients (71 males) and the control (untreated) group – 77 patients (66 males). Anthropometric (body mass index - BMI, waist circumference, total body fat percentage), clinical and laboratory investigations were carried out and repeated after 1 year. The data were statistically analyzed and after 1 year were compared to changes in the studied parameters between the groups.

Results: There were no significant differences in sex ($P = 0.648$), age ($P = 0.848$) or adiponectin levels ($P = 0.483$) between the two groups. Serum adiponectin decreased after 1 year in the CPAP group (8.0 mg/l; 6.7 mg/l; $P < 0.001$), and in the control group (8.0 mg/l; 7.9 mg/l; $P = 0.168$). Comparison of statistical significance of the difference between the two groups showed that the difference in the decrease was not significant ($P = 0.399$). There was no significant correlation between adiponectin and OSA severity in both groups initially ($P = 0.684$; $P = 0.639$) and after 1 year ($P = 0.483$; $P = 0.951$). Changes in BMI in the treated and the control group (35.8; 35.3; $P = 0.107$ versus 31.7; 32.5; $P = 0.065$)-comparison of the significance of the difference between the two groups ($P = 0.167$), in total body fat percentage (35.5; 36.7; $P = 0.111$ versus 33.9; 33.5; $P = 0.249$) – comparison of the significance of the difference between the two groups ($P = 0.908$), in waist circumference [117.0; 117.0; $P = 0.001$ versus 113.0; 110.5; $P = 0.450$)] – comparison of the significance of the difference between the two groups ($P = 0.225$). None of the obesity parameters are changed by CPAP therapy. The correlation between obesity parameters and serum adiponectin levels was not statistically significant in any of the measurements in both groups.

Conclusion: The study showed no correlation between adiponectin and OSA severity and obesity parameters. CPAP therapy has not have an impact on adiponectin levels and obesity parameters.

P968

There is no difference in the adherence of continuous positive airway pressure (CPAP) therapy for obstructive sleep apnoea syndrome among the auto-adjusting CPAP machines

H. YAEGASHI
HIRO Sleep and Respiratory Clinic, Matsumoto, JP

Objectives: Many continuous positive airway pressure (CPAP) machines are prescribed for the patients with obstructive sleep apnea syndrome (OSAS). There is numerous research between

machine design and patient's adherence, but there are few studies about adherence among auto adjusting CPAP (APAP) machines.

Methods: Eighty-eight consecutive CPAP first time participant Japanese adult patients, who were primarily diagnosed as OSAS by in-laboratory full-night polysomnography at the Matsumoto Kyoritsu Hospital and who were prescribed APAP machines at our clinic from January 2009 to December 2010, were enrolled in this retrospective study. The patients were moderate to severe OSAS on the apnea-hyperpnoea index (AHI) of more than 20 events per hour. One patient changed to another APAP machine, and three patients changed clinics within a year from starting APAP, were excluded. All patients were randomized to one of two APAP machine groups: S8 AutoSet Spirit II (AS) of ResMed or M series REMstar Auto with A-Flex (REM) of Phillips Respironics GK. In both groups the prescribed pressure was decided empirically by the physician. In the REM group, a mild pressure-relief function (A-Flex level 1) was used. Adherence measures were set down for the mean daily APAP use time, percentage of days on which APAP was used, percentage of days on which APAP was used for >4 h, and a respiratory disturbance index (RDI) during APAP use. This data was obtained by using the following software ResScan of ResMed or EncorePro and EncorePro2 of Phillips Respironics GK at 1, 3, 6, 12 month intervals after starting APAP.

Results: Fifty patients (45 men) were randomized to the AS group and 34 (30 men) were randomized to the REM group. At the 12 month visit, 40 (36 men) out of the AS group (80.0%) and 27 (25 men) out of the REM group (79.4%) were continuing APAP treatment ($P = 0.83$), and mean daily APAP use was 4.6 ± 2.0 versus 4.5 ± 1.9 h (AS versus REM, mean ± SD; $P = 0.43$), percentage of days on which APAP was used was 82.9 ± 25.6 versus 83.9 ± 20.1% ($P = 0.53$), percentage of days on which APAP was used for > 4 h was 74.0 ± 26.2 versus 65.5 ± 28.4% ($P = 0.17$), and the RDI was 4.4 ± 2.4 versus 3.9 ± 1.8 events per hour ($P = 0.46$). There were no statistical differences in these adherence measures between AS and REM at the specified intervals.

Conclusion: There were no significant differences in adherence to APAP treatment within a year between AS and REM, and mild pressure-relief function did not influence APAP adherence.

P969

CPAP therapy in idiopathic pulmonary fibrosis patients with obstructive sleep apnoea

C. MERMIGKIS, I. BOULOUKAKI, K. ANTONIOU, G. GIANNARAKIS, D. MERMIGKIS, E. KALLERGIS, N. SIAFAKAS and S. SCHIZA
Sleep Disorders Unit, Heraklion, GR

Objectives: Recent literature shows an increased incidence of Obstructive sleep apnea (OSA) in patients with IPF. On the other hand there are no published studies related to CPAP treatment in this patient group. Our aim was to assess CPAP effectiveness and adherence in sleep and overall quality of life parameters in IPF patients with OSA.

Methods: Twelve patients (10 males and two females, age 68.7 ± 11 years) with newly diagnosed IPF and moderate to severe OSA, confirmed by overnight attended polysomnography, were included. CPAP therapy was initiated after a formal in lab CPAP titration study. The patients completed the Epworth Sleepiness Scale (ESS), the Pittsburgh Sleep Quality Index (PSQI), the Functional Outcomes in Sleep Questionnaire (FOSQ), the Fatigue Severity Scale (FSS), the SF-36 quality of life questionnaire and the Beck Depression scale (BDS) before and 1, 3, 6 months after CPAP therapy.

Results: Statistical significant improvement was observed in the FOSQ (12.9 ± 3.1 versus 14.7 ± 2.6 versus 15.8 ± 2.1 versus 16.9 ± 1.9 at CPAP initiation and after 1, 3 and 6 months respectively, $P = 0.02$). Improvement, although not statistical significant, was noted in ESS score (10.1 ± 5.7 versus 7.6 ± 4.9 versus 7.5 ± 5.3 versus 7.7 ± 5.2, $P = 0.65$), PSQI (11.8 ± 3.8 versus 11.1 ± 4.3 versus 9.4 ± 4.8 versus 8.6 ± 5.2, $P = 0.41$), FSS (40 ± 10.8 versus 34.8 ± 8.5 versus 33.3 ± 10.3 versus 33.4 ± 10.9, $P = 0.43$), SF-36 (63.4 ± 13.2 versus 68.9 ± 13.5 versus 72.1 ± 12.9 versus 74.4 ± 11.3, $P = 0.31$) and BDS (12.3 ± 4.3 versus 10.7 ± 4.3 versus 9.9 ± 4.2 versus 9.6 ± 4.5, $P = 0.53$). All patients had intense follow up by our CPAP Clinic. Two patients experienced difficulties in CPAP acceptance and stopped usage after the first month. Heated humidification was added in all patients in order to improve compliance.

Conclusions: Effective CPAP treatment, with intense follow up by the CPAP clinic, in IPF patients with OSA, results in a significant improvement in daily living activities based on the FOSQ namely a OSA specific follow up questionnaire. Improvement was also noted based on other questionnaires assessing quality of life even though in a not statistical significant manner, probably related to the multifactorial influences of IPF in physical and mental health.

P970

Acceptance and compliance to CPAP therapy in a group of Armenians with obstructive sleep apnoea

M. PETROSYAN
St. Nerses the Great Medical Center, Yerevan, AM

Objectives: To assess CPAP acceptance and compliance among Armenian patients with obstructive sleep apnea (OSA). This is the first experience of long term CPAP therapy and first study analyzing CPAP acceptance and compliance in Armenia.

Methods: OSA was diagnosed by portable monitoring system with recording of nasal flow, snoring, saturation and heart rate. Sixty two patients, 54 men and eight women (mean age 49.7 ± 12.0 years) with apnea/hypopnea index (AHI) more than 15 were offered CPAP therapy. For long-term CPAP therapy patients had to cover the device acquisition cost out of their own pocket. A card embedded in the CPAP device electronically recorded compliance. Mann–Withney U-test, chi-square test and binary logistic regression were applied.

Results: Thirty-one patients (50%), 30 men and 1 woman agreed to have CPAP pressure titration trial. Sixteen males (29.6%) accepted CPAP therapy and presently are on long-term CPAP therapy with mean duration of 13.6 ± 12.6 months and mean compliance of 81.2 ± 3.5%. There was no significant difference between the age, BMI, clinical symptoms, presence of comorbidity, marital status, income and education level between acceptors and refusers. Severe OSA was noticed with both the acceptors and refusers. However those who accepted long-term CPAP therapy had significantly higher AHI (61.7 ± 25.2 versus 44.4 ± 28.1 $P < 0.001$), ODI (58.7 ± 25.2 versus 42.0 ± 25.6 $P < 0.001$) and ESS (20.5 ± 4.3 versus 12.5 ± 8.1 $P < 0.01$). Binary logistic regression analysis revealed that the significant predictors for CPAP acceptance were excessive daytime sleepiness (OR 1.3, 95% CI 1.04–1.58, $P < 0.01$) and CPAP therapy awareness (OR 14.2, 95% CI 1.92–219.1, $P < 0.05$). All the studied female completely denied CPAP therapy.

Conclusion: The study revealed low acceptance and high compliance to CPAP therapy among Armenian patients with OSA. Excessive daytime sleepiness and CPAP therapy awareness were the only significant predictors of CPAP acceptance.

P971

Modification of nasal stuffiness and mouth dryness with CPAP therapy

A. BACHOUR, J. WÖRLIN, L. PETMAN, A. HILDEN and H. R. KREIVI
Helsinki University Hospital, Helsinki, FI

Objectives: Nasal symptoms are common during continuous positive airway pressure (CPAP) therapy. Nevertheless, it remains unclear whether the therapy itself increases these symptoms. We evaluated nasal symptoms before and within few days from CPAP initiation.

Methods: We included 583 consecutive obstructive sleep apnoea patients scheduled for CPAP initiation. Patients filled in a visual analogue questionnaire (0 = no symptoms, 100 = severe symptoms) enquiring about nose stuffiness, mouth dryness and rhinorrhea prior and few days after CPAP initiation. Heated humidification was added to the treatment if the patient had any nasal symptoms or he/she used nasal steroids. Temporary use of decongestant was allowed, when needed.

Results: Heated humidification was used by 451 patients (77%). A total of 542 patients (93%) did not use decongestant and of them 127 (23%) had no humidification, while 415 (77%) patients had. In the no humidification group, the nasal stuffiness and the rhinorrhea scores increased significantly with CPAP (13 ± 17 versus 20 ± 24, $P = 0.001$ and 6 ± 11 versus 16 ± 24, $P < 0.001$, respectively). Meanwhile, the mouth dryness score did not change significantly (30 ± 32 versus 28 ± 30, $P = 0.51$). Within the humidification group, the nasal stuffiness and the mouth dryness scores decreased significantly ($P < 0.001$) with CPAP (34 ± 25 versus 28 ± 26 and 47 ± 33 versus 30 ± 29, respectively). Rhinorrhea score did not change (18 ± 23 versus 18 ± 24, $P = 0.57$).

Conclusions: The use of heated humidification with CPAP reverses the tendency of nasal stuffiness to increase during CPAP treatment.

P972

Cutaneous capnography measurement and BPAP titration

L. FUKS, D. SHITRIT, O. FRUCHTER, Y. RAVIV, D. ROSENGARTEN, V. RUSSANOV, N. ABDELRAMAN and M. R KRAMER
Rabin medical center, Jerusalem, IL

Objectives: Bi-level positive airway pressure (BPAP) titration is indicated for many patients in different settings. The test can be performed overnight in a sleep lab or in a day care facility under proper supervision. Among carbon dioxide retainer patients, BPAP titration includes measurement of arterial blood carbon dioxide levels before and after the titration. This painful procedure requires at least two arterial punctures. This study aimed to review the data on BPAP titration using cutaneous carbon dioxide tension ($PcCO_2$) measurements.

Methods: We retrospectively analyzed the files of 35 patients who underwent BPAP titration with $PcCO_2$ tension measurements in our facility, from January 2009 until January 2011. Baseline and optimal $PcCO_2$ were recorded, as well as gender, age, and primary disease. We also noted the inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP) set to the patient needs.

Results: The mean $PcCO_2$ was 59 mmHg before and 44 mmHg after BPAP titration. The mean PO_2 increased from 85 to 97 mmHg. The mean IPAP was 12 cmH_2O and the mean EPAP was 5 cmH_2O. There were no significant differences between baseline PO_2 and $PcCO_2$ when arterial blood gas and transcutaneous measurements were compared. During the titration, all patients indicated that they understood that the device is important in lowering $PcCO_2$ levels and that they were happy to avoid repeated arterial punctures. Three months after the titration, 70% of the patients were using the BPAP with high compliance.

Conclusion: BPAP titration with $PcCO_2$ measurement and no arterial blood sampling is feasible and can contribute to high compliance among CO_2 retainers.

P973

Non-adherence with CPAP therapy for OSAS is associated with mask air leak

M. MESHKAT, J. EBNER, O. BURGHUBER and A. VALIPOUR
Otto-Wagner Hospital, Vienna, AT

Aims: We hypothesized that patients with obstructive sleep apnea syndrome (OSAS) and poor adherence to CPAP therapy have greater levels of mask air leak.

Methods: We studied 63 patients (age 55 ± 11 years, BMI 36 ± 7 kg/m^2, AHI 48 ± 30/h, ESS 11 ± 5) who received fixed or auto-adjusted CPAP treatment for OSAS. All patients underwent a standardized educational session and mask fitting by experienced staff. Treatment adherence, residual sleep disordered breathing, and data on mask leakage were obtained approximately 6 months after CPAP initiation.

Results: Overall, mean ± standard deviation days of CPAP use was 176 ± 82 days, percentage of days with CPAP usage 84 ± 18%, and percentage of days with at least 4 h CPAP use/night 71 ± 24%. There was a significant inverse relationship between CPAP adherence using Kribbs criteria and average time spent with mask leak per night (r = -0.362, $P < 0.01$). Patients with good adherence ($n = 42$), defined as CPAP use >4 h per night on at least 5 days per week, were compared with those who used their device less frequently ($n = 21$). Patients with poor CPAP adherence had significantly higher average mask leakage flow (39 ± 8 l/min versus 34 ± 6 l/min, $P < 0.01$) and higher time spent with mask leakage per night (7.7 ± 10 min/night versus 3.7 ± 6 min/night, $P < 0.05$). There were no significant differences between residual AHI or therapeutic CPAP pressure between groups.

Conclusion: We demonstrated significant differences in quantity and quality of air leak between non-adherent and adherent patients with CPAP for OSAS.

P974

Pathway-dependent difference in the treatment outcome of obstructive Sleep apnoea in Korea

C.-H. YUN[1], E.-K. BAE[2], J. LEE[1], K.-H. HONG[1] and S.-H. PARK[1]
[1]*Seoul National University Bundang Hospital, Seongnam, KR,*
[2]*Inha University Hospital, Incheon, KR*

Objectives: In Korea there are no laws or ordinances to tabulate the official process of the education and accreditation for the medical professionals who provide medical services to patients with obstructive sleep apnea (OSA). Furthermore the Korean National Health Insurance does not cover the polysomnography (PSG) and continuous positive airway pressure (PAP) therapy. This study is a single center study to document the current status of OSA management and explore the presence of differences in clinical outcomes depending on the management pathway.

Methods: We consecutively included adults who presented with typical OSA symptoms to one tertiary care center. There were two management pathways. In pathway-1, the evaluation of OSA and PAP titration was done through in-laboratory full night PSG, and the

fixed-level PAP therapy was a main type of intervention. In pathway-2, in-laboratory PSG or portable studies were adopted and the types of intervention included upper airway surgery and auto-titrating PAP therapy at home. We compared the acceptance rate of diagnostic tests and intervention, and adherence to CPAP therapy between two pathways.

Results: Total 305 subjects (77.7% male, 44.2 ± 14.1 years old) visited during the designated period. One hundred fifty three subjects (50.2%) were managed through pathway-1 and 152 (49.8%) through pathway-2. Acceptance rate of diagnostic test was 99.3% in pathway-1 and 89.5% in pathway-2 ($P < 0.001$). Treatment was recommended to 190 subjects (87.2%) of 218 OSA subjects. Surgery was performed in 23 (10.6%) and PAP therapy in 167 (76.1%). Acceptance and adherence of PAP therapy was significantly lower in pathway-2 than pathway-1 (19.7% versus 82.6%, $P < 0.001$; 41.7% versus 81.9%; $P = 0.006$).

Conclusions: There was a significant difference in the respect of acceptance of diagnostic test and PAP therapy, and adherence to PAP therapy. The results of previous studies from other countries that documented comparable efficacy between various management pathways cannot be directly applied to Korea.

P975

Efficacy of auto-Trilevel positive airway ventilation on patients with both obese hypoventilation and obstructive sleep apnoea syndromes

X. ZHANG and F. YAO

Nanjing Medical University, Nanjing, CN

Objectives: To observe the efficacy of auto-Trilevel positive airway pressure (auto-Trilevel PAP) ventilation in patients with both obese hypoventilation syndrome (OHS) and obstructive sleep apnea syndromes (OSAS) by comparison of fixed bilevel positive airway pressure (BiPAP) ventilation.

Methods: seventen patients with both OHS and OSAS were recruited. Three different ventilation modes issued by the ventilators (SOMNOvent auto-S; Weinmann Inc, Germany) were used for 8 h per night with each mode at each night and two nights' interval with on treatment In mode one, the EPAP issued by BiPAP was titrated as the minimal positive pressure for disappearance of snoring. The same inspiratory positive airway pressure (IPAP) titrated by $PaCO_2$ in mode 1 was used in mode 2 and 3 as well. However, the EPAP issued by BiPAP in mode 2 was 3 cmH_2O higher than that in mode 1. In mode 3 with auto-Trilevel PAP, the beginning of EPAP was set the same as that in mode 1 while the end of EPAP (EEPAP) was automatically adjusted to elevate based on upper airway patency condition.

Results: Compared with the parameters before ventilation therapies, there was a significant decrease in nocturnal AHI, arousal index, morning $PaCO_2$ and daytime ESS, but a significant increase in nocturnal mini SpO_2 and sleep efficiency caused by all three modes of ventilation (all $P < 0.05$). Comparison among three modes demonstrated that with the same IPAP, the mode 3 could result in the lowest arousal index, daytime ESS and the highest sleep efficiency. Compared with mode 1, there was a statistically lower AHI but higher mini SpO_2 and $PaCO_2$ in mode 2 (all $P < 0.05$). Compared with mode 1, there was a lower AHI, higher mini SpO_2 (all $P < 0.05$), but no significant difference in $PaCO_2$ in mode 3. Compared with mode 2, in mode 3 there was a significant lower $PaCO_2$ ($P < 0.05$), but no significant difference in AHI and mini SpO_2.

Conclusions: Auto-Trilevel PAP ventilation is superior over fixed BiPAP ventilaiton for treatment of OHS with coexisting OSAS, since this novel therapy can achieve a higher efficacy in simultaneous removal of residual apnea hypopnea events, correction of hypercapnia, and a higher sleep quality and lower daytime sleepiness.

P976

Comparison between CPAP pressure with PSG and anthropometric parameters

A. MOZAFARI[1], Z. AFRAKHTEH[2], S. FAZAELI[1] and M. REZAIE[1]

[1]Islamic Azad University, Qom, IR, [2]University of Medical Science, Qom, IR

Background: obstructive sleep apnea (OSA) is a preventive, prevalent major health hazard with serious health consequences including excessive daytime sleepiness, cognitive disturbances and depression, hypertension, and cardiovascular and cerebrovascular disease. SAHS is a disorder affecting 2 to 4% of the adult population. Standard practice for CPAP treatment in SAHS requires pressure titration during PSG.

Aim: aim of this study is whether there is relationship between PSG and anthropometric parameters with CPAP pressure and which of them are more related.

Methods: We included 60 patients with SAHS requiring CPAP treatment. CPAP titration was done accordance to AASM protocol. Comparison among CPAP with PSG and anthropometric parameter was performed and analyze with Pearson correlation coefficient and chi-square and if it was required, checked by fisher's exact test in SPSS version 18 software.

Results: Out of 72 patients with OSA there were 60 cases with inclusion criteria. Of these, mean age was 57.8 ± 12.7, male frequency 60%, BMI 35 ± 7.2, AHI 38.5 ± 22.7, mean Arousal Index (AI) 28.4 ± 17.6 and mean CPAP of 13 ± 4.1. There were significant relationship among CPAP pressure with AHI > 15 ($P = 0.022$), CPAP pressure with arousal index ($P = 0.009$), CPAP pressure with BMI ($P = 0.040$), CPAP pressure with ESS > 16 ($P = 0.016$) and CPAP pressure with O_2 desaturation index (ODI)>10 ($P = 0.028$). although other parameter weren't significant correlation.

Conclusion: in according to this data, we found out significant correlation among CPAP with arousal index, AHI > 15, ESS > 16 and ODI > 10. Other parameter like age, sex, neck size, hadn't relationship.

P977

Validation of a device for telemonitoring continuous positive airway pressure treatment: Bench test

V. ISETTA[1], G. CARLOS[2], D. NAVAJAS[1] and R. FARRÉ[1]

[1]University of Barcelona, Barcelona, ES, [2]Air Liquide, Jouy en Josas, FR

Introduction: Patient's compliance is crucial for the effectiveness of continuous positive airway pressure (CPAP) treatment of obstructive sleep apnea syndrome (OSAS). Unfortunately, up to 50% of patients withdraw CPAP because of treatment constraints. Continuously patient's CPAP compliance monitoring at home would be useful to early detect underuse and to properly address possible problems. Existing CPAP devices monitor patient's compliance by using different algorithms, and only few of them offer continuous telemonitoring. Air Liquide developed a telemonitoring prototype device compatible with all CPAP devices.

Aim: To validate this new monitoring device of CPAP treatment in a bench test.

Methods: The device was specially designed to record CPAP usage and treatment efficiency parameters, such as the residual number of apneas and hypopneas. These parameters were recorded as mean values over 15–min consecutive periods. The monitoring device was plugged at the CPAP device outlet, prior to the tubing of a model simulating an OSAS patient (Rigau et al. Chest 2006; 130: 350–61). The device performance was tested in 30 test scenarios, simulating 30 sleep periods of treatment in patients, lasting 4 h each. These simulated breathings consisted of realistic patterns built from a library of actual events (e.g. normal breathing, apneas, hypopneas, flow limitations) selected from real OSAS patients' polysomonographic recordings. The data was also telemetrically sent to a server to test the GPRS communication functionality of the device. The simulated patients were treated with 3 different currently available devices for automatic CPAP treatment (S9 Autoset – Resmed, Remstar Auto – Respironics, Goodknight 420E – Puritan Bennett).

Results: The difference between the treatment duration estimated by the device and actual values was never higher than 2 min AHI estimated by the device, 5.6 ± 5.9 (mean ± SD), was not significantly different from actual values, 6.2 ± 7.1, ($P = 0.631$) and they showed a very good correlation $R^2 = 0.97$. All data sent via GPRS were successfully received.

Conclusion: The prototype evaluated in this bench study showed an excellent performance in estimating the duration of the CPAP treatment and in detecting residual respiratory events in simulated OSAS patients. These results have to be confirmed on patients.

This research was partially supported by Airliquide.

P978

Assessment of exercise capacity following continuous positive airway pressure therapy in patients with obstructive sleep apnoea/hypopnoea syndrome using the incremental shuttle walk test (ISWT)

T. AUNG, C. BILLINGS, S. RENSHAW and S. BIANCHI
Sheffield Teaching Hospitals, Sheffield, UK

Patients with Obstructive Sleep Apnoea/Hypopnoea Syndrome (OSA) have reduced exercise capacity compared to matched controls and have impaired cardiovascular responses to exercise. We evaluated the effect of continuous positive airway pressure (CPAP) therapy in patients with moderate to severe OSA monitoring the effect on exercise capacity and cardio-pulmonary responses to exercise using the Incremental Shuttle Walk Test (ISWT).

Thirty eights subjects were included in the study. Twenty-two patients were CPAP compliant (utilized CPAP for at least 4 h/night on average; CPAP-C), 9 were partially compliant (used CPAP < 4 h/night; CPAP-PC). Seven patients were CPAP intolerant (CPAP-I). All subjects underwent ISWT, anthropometric measurements and completed quality of life questionnaires prior to CPAP therapy. Repeat measures were at 2, 12 and 26 weeks after initial assessment. CPAP-I patients were reviewed only at 26 weeks.

CPAP-C subjects increased walking distance within 2 weeks and improved exercise performance over the 26 week period by 110.0 ± 27.5 m ($P = 0.001$). Improvement in exercise capacity was identified in the CPAP-PC group after 12 weeks (mean increase of 56.7 ± 21.6 m, $P = 0.03$). No significant change in walking distance was noted in the CPAP-I group over the 26 wk assessment period. A significant reduction in resting diastolic blood pressure was noted in CPAP-C patients (82.9 ± 2.7 mmHg at baseline versus 76.0 ± 2.5 mmHg at 26 weeks of CPAP therapy; $P = 0.014$) and in absolute values of diastolic blood pressure 3 min post-exercise (84.9 ± 2.0 mmHg at baseline versus 78.7 ± 2.0 mmHg at 26 weeks; $P = 0.004$). Statistically significant improvement in peak exercise heart rate was noted in the CPAP-C subjects (128.3 ± 6.0 bpm at baseline versus 137.9 ± 6.1 bpm at 26 weeks; $P = 0.03$) and in the CPAP-PC group (112.9 ± 4.6 bpm at baseline versus 126.4 ± 6.5 bpm at baseline; $P = 0.036$). More rapid recovery from peak heart rate following cessation of exercise was noted in the CPAP-C group (heart rate recovery at 2 min post exercise 38.0 ± 3.7 bpm at baseline versus 50.5 ± 3.6 bpm at 26 weeks of CPAP; $P = 0.009$).

Conclusion: CPAP therapy in patients with at least moderately severe OSA results in increased exercise capacity and improvement in cardiovascular responses to exercise. The ISWT is safe, tolerable and sensitive to change in the evaluation of exercise capacity in patients with OSA. This study provides support for the use of the ISWT in the evaluation of patients with OSA and suggests that improved exercise ability may be translated into clinical benefit through exercise programmes.

P979

An outcome evaluation of a local respiratory support service

L. DALE and D. BROCKLEBANK
Worcestershire Acute NHS Trust, Worcester, UK

Introduction: Despite its international use, domiciliary nocturnal non-invasive ventilation (NIV) for the management of chronic hypercapnic respiratory failure remains inconsistent and limited. This study tested the hypothesis that a local domiciliary nocturnal NIV for chronic hypercapnic respiratory failure patients was a worthwhile long-term intervention, by reducing hospital admissions and changing daytime blood gases. The physiological impact on the patients and reduction in hospital admissions were audited before and after initiation of domiciliary nocturnal non-invasive ventilation.

Methods: This study was a retrospective service evaluation of twenty patients who had commenced domiciliary nocturnal NIV for longer than 4 weeks and continued for up to 3 years. Case note analysis of daytime capillary blood gases (CBGs) pre and post-commencement of domiciliary nocturnal NIV in addition to exploration of hospital case notes to determine reasons for and numbers of hospital admissions 1 year pre and post-commencement of domiciliary nocturnal NIV were included. An Encore Pro database was also utilised to download the smartcard taken from the patients NIV machine. The patient's therapeutic history and compliance to therapy data was accurately assessed and recorded. Exacerbations treated in the community were not recorded.

Results: Domiciliary nocturnal NIV with mean inspiratory/expiratory pressures (IPAP/EPAP) of 21 ± 2/9 ± 2 cmH_2O and mean pressure support (PS) of 12 ± 2 cmH_2O led to statistically significant improvements in daytime blood gases and hospitalisation rates. A statistically significant increase in daytime PaO_2 values $P < 0.001$ and a decrease in daytime $PaCO_2$ values $P < 0.001$ was observed following domiciliary nocturnal NIV. A significant reduction in hospital admissions for cardio respiratory conditions in the year following domiciliary nocturnal NIV $P < 0.005$ was detected.

Conclusion: High intensity domiciliary nocturnal NIV (HI-NIV) improves daytime CBGs and reduces hospital admissions for a group of patients with chronic hypoventilation secondary to COPD, OHS ± OSA, OL and kyphoscoliosis. A small general hospital can provide a worthwhile long term domiciliary NIV service for local patients.

P980

The effect of CPAP on blood pressure and cardiac output during the apnoea-cycle in patients with obstructive sleep apnoea

K. E. SCHREUDER[1], J. J. SCHREUDER[2] and A. W. DE WEERD[1]
[1]SEIN Zwolle, Zwolle, NL, [2]CD-Leycom, Zoetermeer, NL

Objectives: The obstructive sleep apnea syndrome (OSAS) is seen as a cause of a considerate amount of cardiovascular restraint and blood pressure elevation during daytime. The purpose of CPAP treatment in OSAS is to stabilise upper airway during sleep, which results in restoring normal ventilation (respiratory rate, $PaCO_2$ and PaO_2), stabilising heart rate and sleep. The positive airway splint prevents upper airway resistance to occur during sleep, which has a direct positive effect on (night-time) hypertension, as is shown by several authors during continuous non-invasive blood pressure registrations. The immediate effects CPAP has on pre- and afterload, stroke volume and cardiac output during titration are not precisely understood.

Methods: To evaluate cardiovascular effects of OSAS and the immediate effects CPAP has on cardiac output (CO) and blood pressure changes during sleep, we registered 5 patients with severe OSAS by continuous blood pressure measurement with the pulse contour method undergoing a CPAP titration procedure under full Polysomnography. Blood pressure has been continuously registered on the finger arteries of the left hand by means of two finger cuffs adjusted on the middle phalanx of dig. II and III, which were alternatively inflated every 20 min (portapres, TNO-biomedical Instrumentation, Academic Medical Centre, Amsterdam). Beat to beat analyses of blood pressure was performed using the pulse contour method and aortic modelflow to calculate CO. Finger artery blood pressure was registered during wake (A) and sleep in the first 1½ h to evaluate OSAS (B). CPAP titration was performed during the second half of the night, until optimal pressure was reached (C).

Results: The five measured patients had a body mass-index between 27 and 37.8, an awake systolic and diastolic blood pressure between 150/90 and 160/108 mmHg and severe OSAS (an apnea-hypopnea-index between 50 and 88/h). During apnea cycles relative changes in diastolic/Systolic Blood pressure (mmHg) and cardiac output (CO = HMV = l/min) during NREM1,2 sleep (B) varied from 90% at 4/10 of the apnea cycle to 120% at the end of the cycle. With adequate CPAP (C) the immediate effect on diastolic and systolic blood pressure and cardiac output gave normalisation around 100% with respiratory variation of + and -5% to values measured during awake at baseline measurement (A).

Conclusion: Immediate effect of CPAP results in normalisation of blood pressure and cardiac output to awake values.

P981

Effects of a group-based educational programme on adherence to CPAP treatment in obstructive sleep apnoea

A. BROSTRÖM[1], B. FRIDLUND[2], M. ULANDER[1], O. SUNNERGREN[3], E. SVANBORG[1] and P. NILSEN[4]
[1]Department of Clinical Neurophysiology, Linköping, SE, [2]Jönköping University, Jönköping, SE, [3]County Hospital Ryhov, Jönköping, SE, [4]Linköping University, Linköping, SE

Objective: Continuous positive airway pressure (CPAP) treatment of obstructive sleep apnea (OSA) has a low long-term adherence. Educational interventions are few and sparsely described regarding content, pedagogical approach and the participants' perceptions. The aims were to: (i) describe adherence to CPAP treatment, (ii) knowledge about OSA/CPAP, as well as three OSA patients' perceptions of participating in a group-based program using problem-based learning (PBL) for CPAP initiation.

Intervention: The PBL based educational program used elements from theories and models concerning motivation and habits. Tutorial groups consisting of 4–8 patients met at six sessions during 6-months.

Method: A sequential explanatory mixed method design was used on 25 strategically selected patients. Quantitative data regarding (i) clinical variables, (ii) OSA severity, (iii) CPAP use, and (iv) knowledge were collected at baseline, after 2 weeks and 6 months. Qualitative data regarding patients' perceptions of participation were collected after 6 months by semi-structured interviews using a phenomenographic approach.

Results: The majority of the 25 participants (mean age 59.6 years, range 49–65) were married, had an educational level of 12 years or more and were overweight or obese (mean BMI 30.5 kg/m^2, range 21.9–48.1). Mild, moderate and severe OSA was seen among 8%, 56% and 36% of the patients, respectively. Seventy-two percent of the patients were adherent to CPAP-treatment (use > 4 h/night) both after 2 weeks and 6 months. A total of 9 patients (36%) decreased and 15 (60%) of the patients increased their CPAP use/night during the follow up. All patients improved their baseline knowledge about OSA and CPAP after 2 weeks and sustained it after 6 months. Anxiety and fear, as well as difficulties and needs were motivational factors for participation. Patients described: difficulties of behavioural change; an awareness that improvements do not occur immediately; a realization of the importance of both technical and emotional support; and the need for a healthier lifestyle.

Conclusion and practice implications: A group-based program using a PBL approach seems to facilitate both adaptive and developmental learning and result in acceptable CPAP adherence levels. Pedagogic personnel, using research-based knowledge regarding CPAP adherence, as well as knowledge regarding behavioural theories are of importance to improve CPAP-adherence.

P982

The role of BIPAP ventilation on NT-pro-BNP, isoprostanes and free fatty acids in heart failure patients with OSA

R. CHERNEVA, O. GEORGIEV, D. PETROVA, A. CAKOVA and V. MITEV
University Hospital, Sofia, BG

Background: Obstructive sleep apnea (OSA) is present in 15% of adult patients and is strongly associated with the incidence and poor outcome of heart failure. Treatment of OSA with positive pressure is supposed to reverse its cardiovascular consequences. The therapeutic outcome of BiPAP therapy is still elusive.

Aim: To determine the effects of 3-month BiPAP non-invasive ventilation on plasma NT – pro-BNP and FFA levels as well as on urine isoprostanes in patietns with mild heart failure and OSA.

Methods: Thirty patients with OSA and mild chronic heart failure (EF 45–55%) participated in the study. Twenty patients were on BiPAP for 3 months in addition to the standard pharmacological therapy. Ten patients remained only on pharmacological treatment. Ejection fraction, NT pro-BNP and FFA plasma levels were compared before and after treatment. Quality of life was measured with Minnnesota quality of life questionnaire. Physical activity was determined with 6-min walking test. FFA (WAKO assay) and NT pro-BNP plasma levels (COBAS) were measured. Levels of urine isoprostanes were

determined by mass spectrometry (Cayman) and normalized to creatinine.

Results: Ejection fraction improved in up to 3%. NT-pro BNP and FFA did not change during the follow-up in patients with pharmacological therapy only (NT-pro-BNP – 24.7/17.4 pg/ml; FFA – 0.25/0.27 mM) In patients on BiPAP NT-pro-BNP decreased significantly (NT-pro-BNP – 60.3/13.8 pg/ml; FFA – 0.25/0.27 mM. There was a tendency for an increase in the free fatty acid palsma levels FFA – 0.135/0.350mM. Quality of life and physical activity improved significantly after BiPAP treatment. Urine isoprostanes decreased in patients on BiPAP therapy isoprostane/creatinine ratio derecreased from 0.142 to 0.094 after 3 months' therapy.

Conclusion: BiPAP therapy significantly improves physical activity, quality of life and prognosis of heart failure patients with OSA in addition to the standard pharmacological treatment.

Poster Session – Treatment of Insomnia and Insomnia Associated with Psychiatric Disorders

P983

Who wants treatment for their sleeping difficulties?

J.-E. BROMAN[1], L. MALLON[2] and J. HETTA[3]
[1]*Dept Psychiatry Uppsala University, Uppsala, SE,* [2]*Psychiatry, Uppsala University, Uppsala, SE,* [3]*Karolinska Institutet, Stockholm, SE*

Introduction: Sleeping difficulties are common, with approximately 10% fulfilling a diagnosis of insomnia, and about 20% in population studies reporting different sleeping problems. The objective of the present study was to examine how many that want treatment regarding their sleeping difficulty.

Methods: A sample of 1550 subjects living in Sweden, aged 18–84 years of age and proportionally stratified for sex was selected for a telephone interview. The interview was completed by 1128 subjects (72.8%). Sleep initiation problems (DIS) were assessed by asking 'How often have you had difficulties falling asleep during the last month?' to be answered on a five point scale (1 = never or less than once a month; 2 = less than once a week; 3 = 1–2 times per week; 4 = 3–5 times per week; 5 = daily or almost daily). Sleep maintenance problems were assessed by asking 'How many times do you wake up during the night?' to be answered on a five point scale (1 = never; 2 = once; 3 = twice; 4 = 3–4 times; 5 = at least 5 times) Other symptoms were ranked on similar five point measures. A need for treatment (NFT) was answered categoricially by yes or no.

Results: Of the women (W) 14.3% stated that they wanted treatment for their sleeping difficulties, compared to men (M), 10.2% ($p < 0.05$). In a logistic regression analysis with this item (NFT) as dependent variable and DIS, EMA, AW and fatigue during daytime (FDD) as independends, some sex differences were shown: women had the highest odds ratio (OR) for DIS (11.7, CI 6.2–21.6), whereas men had the highest OR for FDD (OR 16.3, CI 67.0–44.5). Reported sleep latency for W was 65 min and for M 45.6 min, reported average TST was for M 6.1 h and for W 5.8 h. Experience of stress during daytime affecting sleep was more common in W v. M, 50% v. 33%.

Conclusion: More women than men want help for their sleeping difficulties, and women regard initiation of sleep as the most important symptom whereas men consider daytime fatigue as a major complaint.

P984

Efficacy of light therapy in insomnia: a systematic review

J. CHAMBE, A. WIESER, U. KILIC, C. SCHRODER, A. GHOBADI, E. RUPPERT and P. BOURGIN
University hospital of Strasbourg, Strasbourg, FR

Objectives: Given the prevalence of insomnia and the limitations of hypnotics use, there is a need for alternative therapeutics to improve the management of insomniac patients. Bright light therapy may represent such an innovative treatment but its efficacy remains to be clarified. Our goal was to evaluate the effectiveness of light therapy in primary insomnia in adult populations through a systematic review. Secondary objectives included the determination of predictive factors of light therapy efficiency (specific indications, conditions of light administration, acceptance in general practice).

Methods: We systematically evaluated available data on the efficacy of light therapy in insomnia based on medline, Cismed and Ovid databases search. Selection criterias of the publications were the following: clinical trials with light therapy intervention, adult population of patients complaining of chronic insomnia. Reports including phase shift of circadian rhythm and severe dementia were excluded.

Results: We identified 25 reports which met our predefined selection criteria. Most of the studies were limited by small sample size (mainly < 30 patients) and elderly population. Light intensity was high, above 5000 lux in most of the studies. The 8 studies with morning light intervention noticed an expected phase advance with improvement of sleep latency or wake after sleep onset (WASO). The few trials based on day light intervention, yielded to objective improvement on WASO and nocturnal agitation. In the studies designed on evening bright light intervention ($n = 12$) most of the patients also displayed a phase advance that was improved by the treatment. Finally, considering all three kind of interventions (morning, day evening) the most common improvement were observed on WASO, sleep efficiency, sleep quality and mood even though the evaluation criteria were different. Acceptance of treatment and side effects were rarely evaluated.

Conclusion: The available data show a trend toward an improvement of sleep quality and suggest that light therapy could represent an adjuvant treatment in primary insomnia. However, the efficacy of light therapy in insomnia still requires a proof of concept and needs to be further established before use in primary care. Further evaluations should take into account the characterization of insomnia (onset, maintenance or early awakening), should control for lighting parameters and timing as well as associated conditions.

P985

JuSt – improving sleep during adolescence – long-term effects of a multimodal treatment

A. A. SCHLARB and V. MILICEVIC
University of Tübingen, Tübingen, DE

Objective: Between 20% of adolescents are suffering from insomnia. This study examines the long-term outcome of the age-oriented treatment program for adolescents (JuSt-treatment). Previous results showed that the treatment was well accepted by the adolescents and their parents and led to a significant reduction in sleep problems, such as sleep onset, sleep efficacy, sleep duration (Schlarb et al., 2011).

Method: Thirty-one adolescents and their parents participated in a psychological short-term treatment comprising six sessions.

Results: Long-term outcomes report that the significant changes concerning sleep parameters as sleep efficacy, total sleep time, sleep onset latency, disorders of initiating and maintaining sleep, daytime sleepiness, and inappropriate sleep hygiene remained stable after 3 months.

Conclusion: Randomized controlled studies are needed.

P986

Efficacy of an online CBT coaching programme for insomnia

E. NAUJOKAT[1], S. DEVOT[2], P. SAINI[2] and V. CASTRONOVO[3]
[1]*Philips Consumer Lifestyle, Eindhoven, NL,* [2]*Philips Research, Eindhoven, NL,* [3]*San Raffaele Hospital, Milan, IT*

Objectives: The main objective of the study was to explore the efficacy of an online Cognitive Behavioural Therapy for Insomnia (CBT-I) programme.

Methods: A web-based system was developed consisting of an actigraph (Actiwatch, Philips Respironics), a personal webpage, and the protocol-based coaching of a sleep expert. The webpage first presented assessment questionnaires to identify the nature and severity of insomnia as well as the behavioural and cognitive factors associated to it. Moreover, it allowed viewing the sleep efficiency (SE) and total sleep time measured by the Actiwatch, filling in a sleep diary, reading weekly modules with standard components of CBT-I (including sleep restriction, stimulus control, sleep hygiene, cognitive restructuring, and relapse prevention – sequenced according to the specific needs of the participant), goal setting and reporting on daytime functioning and adherence to these goals. Participants received coaching by weekly progress reports and other messages (reminders, motivation).

Participants were recruited via an online questionnaire. They had to indicate at least mild insomnia symptoms (Insomnia Severity Index ISI > 7). Pregnancy, shift work, sleep disorders, chronic pain and/or psychiatric conditions were excluded. The screening was followed by a telephone interview checking on motivation and practical aspects (e.g. holidays during testing period).

The treatment group (N = 25, 18 females, mean age 38.1) engaged in the online coaching programme for 7 weeks on average. The control group with no treatment (N = 24, 16 females, mean age 38) completed a sleep diary for 2 eeks at the beginning and the end of the intervention period. Analyses of variance were conducted on ISI and standard sleep parameters from the sleep diary before and after treatment.

Results: Thirty-seven participants (23 treatment, 14 control) were included in the analyses.

In the treatment group the ISI significantly improved from 14.2 to 8.4 (CI 95% for mean difference [4.11, 7.46], $P < 0.001$) but did not change for the control group [10.8–11.3, CI 95% (-1.45, 0.45)]. Participants of the online coaching also achieved significant increases in SE from 76.1% to 84.7% (CI 95% for mean difference [-11.4, -5.1], $P < 0.001$).

Conclusion: Participants who received the online coaching programme significantly improved their sleep, whereas sleep in the control group did not change. This study confirms that online delivery might improve the accessibility of CBT-I.

P987

Suvorexant, an orexin receptor antagonist, in preventing symptom return in patients with insomnia after 1 year of treatment: a randomised, double-blind, placebo-controlled study

W. J. HERRING[1], E. SNYDER[1], E. PARADIS[1], J. HUTZELMANN[1], M.-C. LIU[1], D. SNAVELY[1], J. WALSH[2], A. KRYSTAL[3], T. ROTH[4] and D. MICHELSON[1]

[1]Merck, Whitehouse Station, US, [2]St. Luke's Hospital, Chesterfield, US, [3]Duke University Hospital, Durham, US, [4]Henry Ford Hospital, Detroit, US

Objectives: Suvorexant is an orexin receptor antagonist being developed for treatment of insomnia. Results from a 1 year Phase 3 trial in patients with primary insomnia demonstrated suvorexant to be generally safe, well-tolerated and effective with no evidence of significant rebound/withdrawal following discontinuation. Here we report results from the randomized-discontinuation phase that took place immediately after the 1 year trial. The aim was to evaluate whether after 1 year of effective treatment, patients required continued suvorexant to maintain symptom control. This is the first placebo-controlled insomnia relapse trial.

Methods: Patients with primary insomnia who had previously completed a 1 year double-blind placebo-controlled trial of suvorexant (40 mg for patients 18–64 years and 30 mg for patients ≥65 years) were re-randomized into a double-blind, placebo-controlled, parallel-group, 2 month discontinuation phase. Patients assigned to suvorexant during the 1 year treatment phase were either continued on their previous dose of suvorexant (suv/suv) or switched to placebo (suv/pbo) for an additional 2 months. Two sets of responders were evaluated for relapse: (i) those whose 1 year Insomnia Severity Index (ISI) score indicated no/subthreshold insomnia (ISI score ≤ 14), and (ii) those whose subjective total sleep time (sTST) had improved by >20% at 1 year compared to baseline. Relapse for these two sets of responders was defined as: (i) a return to moderate/severe insomnia (ISI > 14), and (ii) a worsening back to within 20% of baseline sTST.

Results: A total of 322 patients who took suvorexant during the treatment phase continued into the randomized-discontinuation phase (suv/suv = 156, suv/pbo = 166). The risk for relapse at the end of 2 months was greater in the suv/pbo group compared to the suv/suv group. For ISI responders (N = 267), the hazard ratio was 0.617 (95% CI: 0.378, 1.007, P = 0.053). For sTST responders (N = 148), the hazard ratio was 0.551 (95% CI: 0.365, 0.832, P = 0.005). Reductions in sTST were apparent within 1 week. The proportions of patients reporting ≥1 adverse event over 2 months was similar in both groups: suv/suv = 22.4%, suv/pbo = 22.9%.

Conclusions: Among patients whose insomnia responded to suvorexant as evidenced at 1 year, discontinuing treatment was associated with a return of symptoms that began soon after discontinuation and persisted. No safety concerns emerged with stopping suvorexant after 1 year of treatment.

Support: Merck

P988

Efficacy and safety of suvorexant, an orexin receptor antagonist, in patients with primary insomnia: a 3-month phase 3 trial (trial #2)

N. IVGY-MAY[1], H. LEIBENSPERGER[1], S. FROMAN[1], J. HUTZELMANN[1], D. SNAVELY[1], E. SNYDER[1], K. LIU[1], J. WALSH[2], T. ROTH[3], D. MICHELSON[1] and W. J. HERRING[1]

[1]Merck, Whitehouse Station, US, [2]St. Luke's Hospital, Chesterfield, US, [3]Henry Ford Hospital, Detroit, US

Objectives: Suvorexant is a potent orexin receptor antagonist being developed for the treatment of insomnia. Suvorexant was effective and well-tolerated in a 4-week study in patients with primary insomnia. Here we report results from one of two 3-month Phase 3 trials.

Methods: This trial (Trial #2) was a randomized, double-blind, placebo-controlled, parallel-group, 3-month trial in non-elderly (18–64 years) and elderly (≥65 years) patients with primary insomnia. The core treatment phase was followed by a 1-week double-blind run-out period to assess withdrawal/rebound. Two doses were evaluated in each age group: (i) 40 mg for non-elderly patients and 30 mg for elderly patients, and (ii) 20 mg for non-elderly patients and 15 mg for elderly patients. The elderly dose adjustments were made to match non-elderly exposures. Efficacy was assessed at week 1, month 1, and month 3 by patient-reported outcomes (PRO) of subjective total-sleep-time (sTST), time-to-sleep-onset (sTSO), and wake-time-after-sleep-onset (sWASO), and at night 1, month 1, and month 3 by polysomnographic (PSG) endpoints of Latency-to-onset-of-Persistent-Sleep (LPS) and Wakefulness-After-persistent-Sleep-Onset (WASO).

Results: A total of 1009 patients were treated (40/30 mg = 387, 20/15 mg = 239, placebo = 383). Suvorexant 40/30 mg was significantly superior to placebo on all PRO and PSG endpoints at night 1/week 1, month 1 and month 3, except for LPS at month 3. Differences from placebo in change from baseline at Month 3 for suvorexant 40/30 mg were: sTST = 25.1 min, sTSO = -13.2 min, sWASO = -8.9 min, LPS = -3.6 min (not significant), WASO = -29.4 min. The magnitude of effect of suvorexant 20/15 mg compared to placebo was generally smaller than that of suvorexant 40/30 mg. Differences from placebo in change from baseline at Month 3 for suvorexant 20/15 mg were: sTST = 22.1 min, sTSO = -7.6 min, sWASO = -7.7 min, LPS = -0.3 min, WASO = -31.1 min. All doses of suvorexant were generally well-tolerated, with low treatment phase rates of discontinuation due to adverse events: 4.8% for 40/30 mg, 4.2% for 20/15 mg, and 4.4% for placebo. Overall, no clinically important rebound or withdrawal was observed following suvorexant discontinuation.

Conclusions: In this Phase 3 trial, suvorexant improved sleep onset and maintenance over 3 months of nightly treatment, without clinically important rebound or withdrawal effects following discontinuation.

Support: Merck.

P989

Effects of online and group administered cognitive behavioural therapy for insomnia on sleep, chronic sleep reduction and behavioural problems in adolescents: a pilot study

E. DE BRUIN, A. M. MEIJER, F. J. OORT and S. M. BÖGELS
University of Amsterdam, Amsterdam, NL

Objectives: Literature shows a high prevalence of insomnia in adolescents. Cognitive behavioural therapy for insomnia (CBT-i) is proven effective in adults. Adolescents are not inclined to seek help for their sleep problems. We developed a CBT-i protocol of 6 weekly consults and compared results from an internet ($N = 13$) and group-treatment ($N = 7$). We expected improvements in sleep variables, chronic sleep reduction and behavioural measures after treatment for both groups.

Methods: After screening and interviewing for other primary psychological or medical disorders and drug-use interfering with sleep, subjects were included by convenience. At baseline and directly after the last consult measurements were obtained from wrist-actigraphy for a 7 day period registering sleep onset latency (SOL), wake after sleep onset (WASO), total sleep time (TST) and sleep efficiency (SE), and from questionnaires for chronic sleep reduction (CSR) and behavioural measures from the Youth Self Report questionnaire (YSR).

Results: Mixed model analysis showed a significant decrease of SOL after treatment for both groups ($F_{1,\ 186.79} = 35.76$, $P < 0.01$) although at baseline SOL in the internet condition was significantly lower compared to the group condition ($F_{1,\ 25.92} = 27.92$, $P < 0.01$). There was also a significant improvement of sleep efficiency for both groups ($F_{1,\ 178.85} = 24.89$, $P < 0.01$) with a significant interaction for treatment and condition showing more improvement for the group condition ($F_{1,\ 180.27} = 6.84$, $P < 0.05$). There was no significant effect on WASO and TST for either group. The total scores on CSR and YSR improved significantly for both groups ($F_{1,\ 493.64} = 20.11$, $P < 0.001$ and $F_{1,\ 335.73} = 12.32$, $P < 0.01$ respectively).

Conclusion: Internet and group administered CBT-i is effective for improvement of sleep, chronic sleep reduction and secondary behavioural problems in adolescents. SOL decreased and SE improved. TST did not increase which we attribute to restriction of time in bed that still is applied after the last consult. Differences in SOL before treatment could be caused by holidays during baseline for the internet condition. Further studies with a larger sample, a waiting list control group and long term follow up are needed.

P990

Effects of an Internet-based cognitive behaviour treatment for insomnia: preliminary results

C. BAGLIONI[1], G. BATTAGLIESE[2], F. DELIA[2], D. RIEMANN[1], C. LOMBARDO[2] and C. VIOLANI[2]
[1]University of Freiburg Medical Center, Freiburg, DE, [2]Sapienza University of Rome, Rome, IT

Objectives: Insomnia is one of the most prevalent health complaint with significant health and psychological consequences and recent studies have shown that it is a risk factor for other psychiatric disorders (Baglioni et al., 2011). Despite Cognitive-Behaviour Treatment for Insomnia (CBT-I) is one of the most effective treatment for insomnia, its availability is limited. The Internet could represent a key conduit for delivering this intervention and increase its availability. The aim of this study was to examine the effectiveness of an Internet-based CBT-I on ameliorating self-reported symptoms and emotional states.

Methods: Until now, 10 patients (8 female and 2 male; mean age: 32, 30; SD: 9.02), with an insomnia diagnose according to DSM-IV criteria were assigned to either a CBT-I (TR: 5 patients) or a waiting-list (WL: five patients). Sleep parameters and positive and negative emotional states were measured through sleep diaries filled in during the week preceding the treatment and the week following the end of the treatment were compared.

Results: Preliminary results showed that the CBT-I group at post-treatment showed reduced sleep-onset latency (SOL) and wake-after-sleep onset (WASO), and increased sleep-efficacy index (SEI) both as compared to the WL group and as compared to the pre-treatment.

Moreover, the group that received the treatment at post-treatment report reduced negative emotions in the morning as compared to both the WL group and the pre-treatment.

Conclusion: Preliminary results suggest that internet-delivered CBT-I is effective on both nocturnal (sleep parameters) and daytime (negative emotions) symptoms of insomnia.

P991

Does Mindfulness therapy reduce sleep worry in insomnia patients? A pilot study

M. SERNEE, M. HOUNIET-DE GIER and G. KERKHOF
MCH Hospital, The Hague, NL

Study objectives: To explore the effect of a three-session Mindfulness training with Acceptance and Commitment Therapy (ACT)-interventions on sleep worry in patients suffering from psychophysiological insomnia.

Design: Within-subject study.

Setting: specialized sleep treatment centre.

Methods: Sixteen patients (mean age 49 years, 11 female, five male) all meeting the ICSD-2 criteria of psychophysiological insomnia, took part in a 6 weeks Mindfulness/ACT treatment, involving three group sessions in which patients were trained in the basics of meditation. ACT metaphors and stories where used to help patients understand contra productive intentions. The treatment consisted of

three sessions with specific goals: session 1 increasing patient's self-awareness (thoughts, feelings and bodily sensations) and teaching the basics of meditation; session 2 increasing patient's understanding of the paradox of resisting unpleasant sensations, reducing their interference with sleep; and session 3 increasing the acceptance of negative sensations or experiences and how to endure them. Patients where asked to practice daily with meditation exercises. All subjects filled in a Dutch translation of the Anxiety Preoccupation about Sleep Questionnaire (APSQ) twice, i.e. at baseline and within 4 weeks after treatment. They where also asked to fill in an evaluation form after the treatment.

Results: as compared to baseline, APSQ's total score was significantly decreased after treatment ($P < 0.01$). Simultaneously with their Mindfulness treatment, seven patients were treated with cognitive behavioural therapy for insomnia. After exclusion of these subjects, the Mindfulness effect remained significant ($P < 0.05$). All patients evaluated the Mindfulness treatment positively.

Conclusions: The results of this pilot study indicate that patients with psychophysiological insomnia may profit from a limited number of Mindfulness/ACT sessions in reducing their anxiety and preoccupation with sleep. Mindfulness suggests itself as an additional treatment to the standard cognitive behavioural therapy for insomnia.

P992

Effects of individualised acupuncture on sleep latency, anxiety and depression among hospitalised psychiatric patients

I. HAIMOV[1], B. BLOCH[2], A. RESHEF[2], L. VADAS[1] and I. KREMER[2]
[1]Yezreel Academic College, Emeak Yezreel, IL, [2]Ha'emek Medical Center, Afula, IL

Objectives: Insomnia is the most common psychiatric sleep disorder. A growing number of studies have demonstrated that acupuncture has a positive impact on sleep disorders. Yet to the best of our knowledge, no research has examined the impact of acupuncture on hospitalized psychiatric patients. The present study examined the effects of acupuncture on sleep quality and emotional measures among psychiatric ward inpatients.

Methods: Study participants included twenty patients (mean age 42.8 ± 11.9: 8 males, 12 females) hospitalized in the psychiatric ward and exhibiting acute symptoms of schizophrenia, schizoaffective disorder or affective mood disorders. Participants were randomized into three groups: acupuncture therapy, music therapy and no treatment. Acupuncture therapy comprised 16 acupuncture sessions (four times a week for the duration of 4 weeks) given by a qualified therapist, and music therapy comprised 16 40-min sessions during which participants listened to relaxing music. During the entire study period, patient sleep was continuously monitored with a wrist actigraph. Furthermore, at the beginning (no-treatment), middle and end of the study, patients completed a broad spectrum of questionnaires assessing emotional measures.

Results: The analysis revealed a decrease in sleep latency ($F_{2,16} = 4.1$, $P < 0.036$), level of activity during sleep ($F_{2,16} = 7.8$, $P < 0.004$) and depression ($F_{2,9} = 6.9$, $P < 0.015$) over the study period for all three groups. Additionally, the analysis revealed a significant interaction between type of treatment and state anxiety ($F_{2,16} = 5$, $P < 0.045$), indicating greater improvement in anxiety level following acupuncture treatment compared to no treatment.

Conclusion: The results suggest that among psychiatric inpatients acupuncture doesn't have a positive impact on sleep quality and depression; however, acupuncture appears to have a beneficial impact on state anxiety. This exploratory study was limited by the small and heterogeneous sample. Further research is needed to investigate this issue.

P993

Cognition in sleep – a therapeutic intervention in patients with nightmares and post-traumatic stress disorder

B. HOLZINGER[1], G. KLÖSCH[2] and B. SALETU[2]
[1]Institute for Consciousness and Dream Research, Vienna, AT, [2]Medical University Vienna, Vienna, AT

Introduction: The aim of this project was to investigate whether the technique of lucid dreaming leads to a sustainable reduction in nightmare frequency or to a reduction of suffering caused by nightmares in patients diagnosed with PTSD. In addition, we evaluated the efficiency and sustainability of nightmare frequency reduction.

Methods: A total of 31 inpatient (27–59 years old) diagnosed with PTSD suffering from frequent nightmares and anxiety dreams participated a 6-week-training-group in sleep education and lucid dreaming, also called cognition in sleep (one 60 mins session per week with homework). At the beginning, and at the end of the project, all subjects completed various questionnaires, such as SCL-90 R, IES, PSS, SAS, SDS, PSQI, QLI. They kept a sleep and dream diary during the 6 weeks in addition.

Results: The results show that anxiety and depression decreased significantly in the experimental group within the treatment period (anxiety mean score before therapy 46.56 (±9.59), significantly lower at the end of therapy 41.42 (±9.56). Depression also has decreased from a mean score of 50.93 (±8.71) before therapy and 45.08 (±10.92) at the end of therapy. The impairment of quality of life through nightmares in the days affected by nightmares, in the overall quality of life, severity of trauma, daytime sleepiness and sleep quality show only a tendency of improvement (e.g. PSQI at 11.33 (±3.33) before therapy and 8.79 (±3.93) after therapy < 5 = cut off score).

The consequences and complaints stemming from the traumaatizing event(s) even increased, as well as mental health problems (not significant).

Conclusion: The technique of lucid dreaming helps patients with PTSD associated with nightmares and anxiety dreams to reduce anxiety and depression, however might improve the PTSD symptoms within the 6-week-training-course. An additional qualitative analysis and individual evaluation is desirable and in planning.

P994

Effectiveness of cognitive behavioural therapy for insomnia: influence of depressive symptom severity and worrying

A. HAMOEN and E. REDLICH
SEIN, Zwolle, NL

Objectives: Cognitive Behavioural Therapy for Insomnia (CBTi) is a well known, effective treatment of primary insomnia. However, the majority of sleeping problems occur in the presence of another psychiatric disorder. Depression and General Anxiety Disorder (with a main feature of excessive generalised worrying) are disorders that frequently co-occur with insomnia. The purpose of this study is to evaluate whether depressive symptom severity or worrying influences the subjective effectiveness of CBTi.

Methods: Patients with a complaint of insomnia ($N = 124$) received CBTi. At the beginning of the therapy patients completed a sleep evaluation list, the Beck Depression Inventory (BDI-II-NL) and the

Penn State Worry Questionnaire (PSWQ). The evaluation list was again completed after the treatment and 6 months later.
Results: Sleep evaluation scores, subjective sleep onset latency, subjective wake after sleep onset, the strong focus on sleep and the control over sleep all changed in a positive way after CBTi and stayed that way 6 months later for all patient groups. Only the subjective total sleep time did not change after the treatment. High and low BDI scorers did not differ on these measures. For high and low PSWQ scorers, the only difference that appeared was the stronger focus on sleep for worriers at pre-treatment, but after CBTi this difference disappeared.
Conclusion: Results suggest that CBTi improves subjective sleep experiences, regardless of depressive symptom severity or worrying.

P995

Cognitive behavioural therapy for shift workers with chronic insomnia

H. JÄRNEFELT[1], R. LAGERSTEDT[2], S. KAJASTE[3], M. SALLINEN[1], A. SAVOLAINEN[2] and C. HUBLIN[1]
[1]Finnish Institute of Occupational Health, Helsinki, FI, [2]Finnish Broadcasting Company, Helsinki, FI, [3]Private Psychologist, Helsinki, FI
Introduction: Shift work is a challenge when screening and treating chronic insomnia. The aim of this study was to examine the implementation and effectiveness of a cognitive behavioral group intervention for insomnia (CBT-I) among shift workers with chronic insomnia. The treatment was given by occupational health services (OHS). We also studied whether insomnia symptoms and intervention effects differed between work days and days off.
Methods: The study design was a non-randomized group intervention, including a waiting period prior to CBT-I as a control condition. A total of 26 media workers (aged 43.5 ± 8.4 years, 13 women) who worked irregular hours and had non-organic insomnia with features of psychophysiological insomnia participated in the study. The follow-up measurements were conducted three and 6 months post-intervention. The assessment of intervention outcomes were based on sleep diary and actigraphy measurements and questionnaires. Trained OHS nurses led the CBT-I groups.
Results: Nineteen participants completed the study. The post-intervention results showed improvements in self-reported ($P < 0.001$) and actigraphic-based ($P = 0.019$) sleep onset latency, and self-reported sleep efficiency ($P = 0.019$) and sleep quality ($P < 0.001$). In addition, perceived severity of insomnia ($P < 0.001$), sleep-related dysfunctional cognitions ($P < 0.001$), psychiatric and somatic symptoms ($P < 0.001$), and the mental component of the health-related quality of life ($P = 0.004$) showed improvements. The improvements lasted and even strengthened over the follow-ups. The participants slept better on days off than on work days ($P < 0.05$–0.001), but the treatment outcomes were not different for these days.
Conclusions: The results suggest that trained OHS nurses can successfully implement non-pharmacological treatment of insomnia among shift workers with chronic insomnia. Some caution is, however, needed when interpreting the results because of the non-randomized design and small sample size.

P996

A new standardised programme for treating severe forms of insomnnia in a psychiatric inpatient setting

T. CRÖNLEIN, T. WETTER and P. GEISLER
University of Regensburg, Regensburg, DE
Introduction: Insomnia is a very frequent problem among the general population and it is associated with a high socio-economic impact on health care management. Cognitive-behavior-therapists developed programs specifically for insomnia (CBT-I), however they are not available for the majority of insomnia patients. Step-by-step treatment of insomnia as recently proposed by Espie is a new health management perspective to offer treatment for different degrees of insomnia. Treatment offers may range from psychoeducational sessions up to elaborated standardized programs in tertiary inpatient setting for severe forms of insomnia.
Methods: A new standardized CBT-I program for severe forms of insomnia is introduced. Severe insomnia here is defined as not having improved by an outpatient treatment with CBT-I, long-term intake of hypnotics and/or having a comorbid psychiatric disorder. The program is lasting 14 day and is evaluated in a psychiatry ward in the University of Regensburg. Groups consisted of 8 patients. The program comprises polysomnography, bedtime-restriction scheme, stimulus control and relaxation therapy.
Results: Preliminary data show good acceptance and feasibility of the program. Objective and subjective sleep improved and hypnotics could be dismissed within the treatment duration.
Conclusion: Severe forms of insomnia profit from a short inpatient program scheme offering CBT-I.

P997

Transcranial direct current stimulation during sleep in patients with schizophrenia

R. GÖDER, P. C. BAIER, B. BEITH, C. BAECKER, S. L. WEINHOLD, M. SEECK-HIRSCHNER and L. MARSHALL
University Schleswig-Holstein, Kiel, DE
Schizophrenia is a devastating mental disorder with diverse dimensions of symptoms like delusions, hallucinations, affective symptoms and alterations in cognition. Declarative memory deficits are among the most important factors leading to poor functional outcomes in this disorder. Recently it was supposed, that sleep disturbances in patients with schizophrenia might contribute to these memory impairments (Göder et al. 2008, Manoach et al. 2009, Ferrarelli et al. 2010, Lu and Göder 2011). In young healthy subjects it was shown that declarative memory consolidation was enhanced by inducing slow oscillation-like potential fields during sleep (Marshall et al. 2006). In the present study transcranial direct current stimulation (tDCS) was applied to 14 patients with schizophrenia on stable medication with a mean age of 33 years. The main effects of tDCS in comparison to sham stimulation were: An enhancement in declarative memory retention and an increase in mood after sleep. In conclusion, so-tDCS offers an interesting approach for studying the relationship of sleep and memory in psychiatric disorders and could possibly improve disturbed memory processing in patients with schizophrenia.

P998

Improving sleep disorder management through risk assessment in community pharmacies: opinions of general practitioners, pharmacists and pharmacist assistants

K. C. KASHYAP[1], L. M. NISSEN[1], S. SMITH[2] and G. J. KYLE[3]
[1]University of Queensland, Brisbane, AU, [2]Queensland University of Technology, Brisbane, AU, [3]University of Canberra, Brisbane, AU
Objective: To describe opinions, perceptions and barriers of general practitioners (GPs), pharmacists and pharmacist assistants towards sleep disorder management and the potential for improved manage-

ment of sleep through use of an over-the-counter (OTC) community pharmacy sleep disorder risk assessment service.

Method: GPs, pharmacists and pharmacist assistants of varied demographic backgrounds were invited by convenience to participate in a short 10–15 min interview based on their opinions on sleep management. Interviews with participants were conducted face-to-face in Queensland, Australia. Seeding questions common to all groups were used to facilitate discussion. Interviews were recorded digitally and transcribed verbatim. Participants received remuneration in appreciation for their time. Leximancer software was used to qualitatively analyse responses.

Results: A total of 36 participants took part in the semi-structured interviews. Common concepts relating to several themes based on the seeding questions were identified. These included negative themes such as barriers including time and patient/s and positive themes including training, assessment and useful. GPs were generally aware of and respectful towards the valuable contribution of pharmacists in healthcare: 'pharmacists have got a bigger role to play in general medicine…. their roles should be more involved'. However GPs also perceived that patient attitudes and expectations provided barriers to the implementation of optimal OTC sleep management and some were cynical about other health professionals 'stepping over' perceived boundaries within their expected roles. Pharmacists and pharmacy assistants were very interested to extend the role of community pharmacy in the area of OTC sleep management however they also perceived that patient responsiveness towards this service may be a barrier in conjunction with time constraints and workload demands in pharmacy practice.

Conclusion: Community pharmacies are the most accessible primary health care locations for those with sleep problems. Pharmacists and pharmacy assistants are highly trained and there is potential for optimal utilisation of their expertise in the area of OTC sleep management. The results of this research provide unique insight into the views held by GPs, Pharmacists and Assistants across a variety of backgrounds and may aid the development of a sleep risk assessment service for use in community pharmacies.

P999

Supply of non-prescription 'pharmacist-only' doxylamine tablets in Australian community pharmacies: a simulated patient study

K. C. KASHYAP[1], L. M. NISSEN[1], S. SMITH[2] and G. J. KYLE[3]
[1]University of Queensland, Brisbane, AU, [2]Queensland University of Technology, Brisbane, AU, [3]University of Canberra, Canberra, AU

Objective: To assess current practice, when non-prescription pharmacist-only sleep medication is requested in the Australian community pharmacy setting.

Methods: A trained simulated patient visited 50 randomly selected South East Queensland community pharmacies in June 2011. The simulated patient enacted a direct product request scenario of someone with acute insomnia symptoms who wished to purchase a box of doxylamine tablets (Restavit). Results of the encounter were recorded immediately after each visit.

Results: 46 out of the 50 requests for Restavit resulted in supply of the product (92%). Of all requests only 30% were handled entirely by the pharmacist, 38% were handled entirely by an assistant/naturopath/student while the remaining 32% of interactions were initially handled by an assistant/naturopath/student and completed by a pharmacist.

Initial questioning on who the medication is for and whether it has been used before was performed well in almost 100% of all interactions. However questioning on specific sleep symptoms and the cause of the insomnia was undertaken in only 28% of the interactions and questioning on frequency of product use was not undertaken at all.

Questioning on smoking and alcohol intake was not undertaken at all, while questioning on caffeine intake and stress factors was undertaken in only 2% and 14% of interactions respectively. Non-drug management of sleep symptoms was recommended in only 10% of interactions.

Conclusion: In the Australian state of Queensland, the sale of the sedating antihistamine doxylamine is regulated and it is mandatory by law that this product involves direct personal interaction with the pharmacist. Furthermore it is expected that upon initial presentation of sleep requests, staff undertake questioning on sleep specific issues to elicit the underlying causes and need for therapeutic intervention by use of the 'WHAT STOP GO' or similar pharmacy supply protocols.

These results indicate insufficient direct pharmacist interaction in supply of doxylamine as well as suboptimal sleep specific questioning when compared with recommended practice standards.

Further investigation into factors preventing pharmacists' direct involvement in the supply of non-prescription sleep medications may be useful, as well as development of sleep-specific supply protocols and targeted education programs to enhance current practice.

P1000

Is the relationship between circadian preferences and depressive mood dependent on sleep variables and problematic sleepiness?

M. BAKOTIC, B. RADOSEVIC VIDACEK and A. KOSCEC
Institute for Medical Research and Occupational Health, Zagreb, HR

Objective: The objective of this study was to explore the association between morningness-eveningness and the level of depression symptoms in healthy young adults after controlling for variables of sleep quantity, sleep regularity and sleep quality including the perception of problematic sleepiness.

Methods: A sample of 1025 students (643 females) aged 18–24 years., 1st–4th year of study at University of Zagreb completed a modified version of the School Sleep Habits Survey (Wolfson & Carskadon, 1998), which included the Composite Scale of Morningness (CMS) and Depressed Mood Scale (DSM), to assess circadian preferences and depression symptoms in addition to sleep parameters. Hierarchical multiple regression analysis was performed to predict depression scores with one block of demographic variables (gender, year of study), and four blocks of sleep-related variables including: CSM scores, sleep debt (misalignment between preferred sleep duration and weekday sleep duration), indices of sleep irregularity (bedtime and wake-up time irregularity), indices of sleep quality (night waking, premature awakening, difficulty falling asleep, nightmares/bad dreams, general satisfaction with sleep, day dysfunction due to sleepiness).

Results: CSM scores correlated negatively with depression symptoms ($r = 0.115$, $P < 0.001$), implying that higher preference for eveningness was associated with more frequent depressive mood. Hierarchical multiple regression analysis showed that CSM scores were independent predictor of depression after controlling for sleep

debt and indices of sleep regularity. However, when indices of sleep quality were entered into model, CSM scores were no longer significant predictor of depression symptoms. The best predictors of depression symptoms in the final model were subjects' perception of day dysfunction due to sleepiness, experience of nightmares or bad dreams and general satisfaction with sleep.

Conclusion: The association between eveningness preference and depression symptoms in healthy young adults is not related to insufficient sleep or indices of sleep irregularity. Our results indicate that subjects' perception of problematic sleepiness and general satisfaction with sleep could be responsible for the relationship between eveningness and depression symptoms.

Supported by the Croatian Ministry of Science, Education and Sports (022-0222411-2659).

Poster Session – Movement Disorders

P1001

Heritability of sleep bruxism: a polysomnographic study

S. KHOURY[1], M. C. CARRA[2], N. HUYNH[3], G. ROULEAU[2] and G. LAVIGNE[1]

[1]Centre d'études avancées en medecine du sommeil, Montreal, CA, [2]University of Montreal, Montreal, CA, [3]CHU Sainte-Justine, Montreal, CA

Objectives: Sleep bruxism (SB) is a stereotyped movement disorder characterized by tooth grinding and jaw clenching during sleep. Its prevalence in the general population is 8% and tends to decrease with age. In 1966, it was suggested that there is a positive and statistically significant association between bruxism in the subject reported on and a history of bruxism in blood relatives. Later, in the Finnish Twin Cohort, SB was found to have an attributable genetic effect in both gender in up to 53% in a model of genetic and environmental factor. All data presented above is based on questionnaires only and not on an objective and validated diagnostic. Recently, validated diagnostic criteria have been established to confirm the presence of SB. The diagnostic is based on polygraphic sleep recordings, electromyographic recording of jaw muscles along with audio and video. In this study, we want to replicate the genetic share of sleep bruxism using our validated research criteria.

Methods: Of the 111 SB subjects were diagnosed in our sleep laboratory for two nights. SB subjects were selected according to tooth-grinding history (>3 nights/week), without trauma history. SB diagnosis and absence of other sleep disorders were confirmed by two nights of polygraphic recordings. The following polygraphic criteria were used to identify SB subjects: >4 SB episode per hour of sleep, >25 SB bursts per hour of sleep and >1 episode with grinding noise. SB subjects were divided in 2 groups based on afore mentioned criteria: mild SB subjects ($n = 51$) failed in two out of the three criteria and severe SB subjects ($n = 60$) met at least two criteria. All those subjects were questioned about relatives with SB.

Results: 36.7% and 38.5% of mild and severe SB subjects had at least one first degree relative with SB respectively. Seven and 12% of mild and severe SB subjects had at least two first degree relative with SB respectively. Three and 6% of mild and severe SB subjects had at least three first degree relative with SB respectively. The subjects had no relatives or data was missing with SB in 63.3% and 61.6% for mild and severe SB subjects respectively.

Conclusion: Our results are the first to determine the hereditary effect of SB with an objective polygraphic sleep diagnosis. We also confirmed the heritability of SB seen in earlier studies.

P1002

Periodic limb movements during sleep in patients with moderate-severe heart failure

L. KOROSTOVTSEVA, Y. SVIRYAEV, J. SAZONOVA, K. MALIKOV, N. ZVARTAU, A. KOZLENOK, S. KOZLOVA, A. KONRADI and E. SHLYAKHTO

Almazov Federal Heart, Blood and Endocrinology Centre, St Petersburg, RU

Objective: To assess the prevalence of periodic limb movements (PLM) and sleep characteristics depending on PLM presence in patients with congestive heart failure (HF).

Design and methods: Full polysomnography (Embla N7000, MedCare Flaga, Iceland) and PLM scoring (the AASM manual for the scoring of sleep and associated events) were performed in 53 stable HF patients with NYHA functional class III-IV [49 males, 57 ± 9 years, ejection fraction (EF): 28.2 ± 7.3%]. In 42 (79%) subjects HF resulted from coronary artery disease, in 11 (21%) – from cardiomyopathy.

Results: Twenty subjects (38%) demonstrated PLMs with the index 44.8 (CI 95% 35.6–56.3) per hour of sleep compared to 0.9 (CI 95% 1.5–5.0) per hour of sleep in patients without PLMs ($n = 33$). Regarding the PLMs severity the distribution was the following: mild, moderate and severe PLMs were found in 4 (7%), 8 (15%) and 8 (15%) subjects, respectively. Subjects with PLMs were slightly older [60 (CI 95% 55–65) versus 56 (CI 95% 53–58), respectively, $P = 0.08$], and had higher arousal rate [arousal index 18.1 (CI 95% 13.7–21.7) versus 12.2 (CI 95% 10.1–15.8) episodes per hour of sleep, $P = 0.01$]. Other sleep parameters and indices of sleep-breathing disorders were similar in both groups.

Conclusions: PLMs are very common in stable HF patients with NYHA functional class III-IV being found in one third of subjects. Subjects with PLMs have poorer sleep, regarding higher arousal index and more profound sleep fragmentation, but not other sleep parameters. It is unknown whether the presence of PLMs is associated with different outcomes in this group.

In the framework of SICA-HF (SICA-HF is a collaborative project funded by the European Commission under the Seventh Framework Programme (FP7/2007–2013) under grant agreement number 241558 (SICA-HF) and the Russian Ministry of Science and Education within the FTP 'R&D in priority fields of the S&T complex of Russia 2007–2012' under state contract number 02.527.11.0007).

P1003

Hypericin, a cytochrome P450 enzyme system inducer, is a possible treatment for restless legs syndrome

J. C. PEREIRA[1], R. ALVES[2] and M. PRADELLA-HALLINAN[3]

[1]Jundiai Medical School, Sao Paulo, Sao Paulo, BR, [2]University of Sao Paulo, Sao Paulo, BR, [3]Federal University of Sao Paulo, Sao Paulo, BR

Introduction: Some drugs alleviate restless legs syndrome (RLS) symptoms whereas others aggravate them. A study of their pharmacological profile suggests that in first case drugs wane the thyroid axis (TH), and in second, exalt it. One of these diverse effects may be secondary to the diverse actions these drugs have on Cytochrome P450 system (CYP450): The first induce the system (e.g., dopamine agonists), and the second inhibit it (e.g., SSRIs). Recently, we have suggested that RLS pathophysiology is secondary to disequilibrium between TH and dopaminergic system; dopamine modulates TH and so diminishes sensitivity to stimuli felt as RLS unpleasant sensations.

Objective: To show that hypericin is a possible treatment for RLS. The rationale behind the trial was that hypericin, a strong inducer of CYP4503A4 isoform, by increasing TH metabolism could diminish severity of the RLS symptoms.

Methods: Open-label pilot trial with 16 RLS patients (three male; 13 female; medium age 54; medium RLS severity score 23), were treated with hypericin (300 mg daily, during 10 days) and the effects of the treatment were observed.

Results: Hypericin has substantially reduced RLS symptoms severity in 13 of the 16 patients studied.

Conclusion: The results of this trial (and evidence from medical literature) suggest that RLS is a disease whose severity may be alleviated by drugs that increase TH metabolism, and consequently favoring DA in the fragile equilibrium between DA and TH.

P1004

Persistent rhythmic movement disorder in a young adult aggravated after brain traumatic injury: description of a case

K. RAHNAMA, M. VICENTE-RASOAMALALA, S. NÚÑEZ and E. LAÍNEZ

Vall d'Hebron Hospital, Barcelona, ES

Sleep related rhythmic movement disorder (SRMD) is defined as a group of stereotyped and rhythmic repetitive movements involving large muscles usually of the head and neck that typically occur during drowsiness and can be sustained during sleep. The prevalence is high in infants (59%), dropping dramatically to 5% at the age of 5 years. When persisting to older childhood or beyond, it may underlie mental pathology, autism or mental retardation. Few cases in adult persons of normal intelligence have been reported in the literature. Our aim is to present an atypical case of adult head-rolling. We report a 33-year-male with medical history of alcohol and marijuana abuse. Family reports sporadic episodes of head-rolling from infancy. Following a severe traumatic brain injury (TBI) after jumping out from a car, the patient was admitted in our hospital. The initial brain TC showed left frontotemporoalparietal fracture that spreads out to the right parietal lobe with hemorrhagic subdural collection and massive brain swelling. He stayed in ICU for 20 days under high doses of sedative drugs; 10 days after the weaning phase, the patient started showing involuntary head movements. The electroencephalographic recording showed a disorganised low-voltage background activity with mixed frequencies; during drowsiness a high-voltage rhythmic 1 Hz pattern appeared, corresponding to the artifact produced by the stereotyped side-to-side head movement of the patient, that occasionally was accompanied by rhythmic trunk and legs movements.

With the improvement of the brain injury the episodes of head-rolling return to the patient's pre-traumatic frequency.

Although its low prevalence in adults, SRMD should be considered as a part of the differential diagnosis in individuals with abnormal movements, especially if there is a personal or familiar history of sleep movement disorders. We speculate that in the reported case the TBI would be an aggravating factor of the SRMD.

P1005

Restless legs syndrome during pregnancy in Czech women

Z. SRUTKOVA

Charles University, Prague, CZ

Objective: The objective of this study was to identify the prevalence of restless legs syndrome (RLS) among pregnant Czech women, with questionnaire based survey during the third trimester of pregnancy, and to determine risk factors.

Methods: It was a cross-sectional study. We surveyed 276 pregnant women (20–48 years old) who came to the prenatal outpatient clinic to consult an obstetrician at the third trimester (36th–38th week of pregnancy). We used the 3 epidemiological questions to assign RLS status, disease course and frequency of symptoms. Further, we asked for previous pregnancies and comorbidities.

Results: The prevalence of RLS during pregnancy was 28.9% (95% confidence interval from 23.5% to 34.8%) in our sample, among which 62% of the cases started with their symptoms during the current pregnancy. On the other hand 14.9% reported positive family history of RLS. More than half of the patients (66.7%) presented symptoms at least once per week and the largest proportion of them (48.15%) reported onset or major worsening of previous symptoms in the third trimester. We did not observe any differences in prevalence of screened comorbidities between RLS positive and RLS negative pregnant women or any demographic difference between these groups. We also could not confirm higher prevalence of RLS among multiparous women.

Conclusion: RLS during pregnancy is more frequent than in the general population, such that about two thirds of the pregnant women with RLS suffer from the symptoms frequently. It occurs especially in the third trimester.

Supported by grant IGA-NT 12141-3/2010.

P1006

Effects of pregabalin on subjective sleep measures and quality of life in restless legs syndrome: results from a randomised, double-blinded, placebo-controlled, active-comparator, three-way cross-over polysomnography study

R. P. ALLEN[1], D. GARCIA-BORREGUERO[2], J. PATRICK[3], S. DUBRAVA[3], P. BECKER[4], A. LANKFORD[5], C. CHEN[3], L. KNAPP[3] and J. MICELI[3]

[1]Johns Hopkins Sleep Disorders Center, Baltimore, US, [2]Sleep Research Institute, Madrid, ES, [3]Pfizer Global Research and Development, Groton, US, [4]University of Texas Southwestern Medical Center, Dallas, US, [5]Sleep Disorders Center of Georgia, Atlanta, US

Objectives: A recent randomised controlled trial reported significant improvements in polysomnography (PSG) measures with pregabalin compared with placebo and pramipexole in patients with restless legs syndrome (RLS) [reduction in Wake After Sleep Onset (WASO): 27.1 min versus placebo, 26.9 min versus pramipexole]. However, the clinical significance of these PSG improvements depends on documenting similar subjective improvements. We therefore evaluated changes in subjective sleep measures and quality of life (QoL) for pregabalin compared with placebo and pramipexole in this trial.

Methods: This was a randomised, double-blinded, placebo-controlled, crossover trial in participants with moderate-severe idiopathic RLS and associated sleep disturbance (International RLS Study Group Rating Scale ≥ 15; Item 4 ≥ 2). Participants were randomised across 6 treatment orders, each comprising three 4-week periods with evening dosing of pregabalin 300 mg, pramipexole 0.5 mg or placebo. PSG was conducted on 2 consecutive nights at the end of each period. Participants completed the Subjective Sleep Questionnaire (SSQ), and the RLS-Next Day Impact (NDI) and RLS-QoL questionnaires for the week prior to a PSG visit.

Results: Eighty-five participants (mean age 55 years; 65% female) were randomised; data were obtained for 75 on pregabalin, 76 pramipexole and 73 placebo. Subjective measures of sleep maintenance were significantly improved with pregabalin compared with placebo and pramipexole: subjective WASO was reduced by 25.3 min versus placebo and 28.5 min versus pramipexole (both $P < 0.0001$); subjective Total Sleep Time was increased by 30.8 min versus placebo ($P < 0.0001$) and 26.8 min versus pramipexole ($P = 0.0004$); and participants reported fewer awakenings with pregabalin (mean 1.7) versus placebo or pramipexole (2.5 and 2.6; $P < 0.0001$). Subjective sleep latency improved with pregabalin versus placebo (-7.6 min; $P = 0.02$) and was comparable for pregabalin and pramipexole ($P = 0.56$). Pregabalin improved SSQ

quality of sleep score versus placebo and pramipexole (both $P < 0.0001$). RLS-NDI and RLS-QoL scores were also improved with pregabalin versus placebo ($P = 0.04$ and $P = 0.002$), although differences versus pramipexole were not statistically significant.

Conclusion: Pregabalin significantly improved subjective measures of sleep maintenance and quality compared with placebo and pramipexole, consistent with previously reported improvements in PSG measures. Pregabalin was also associated with improvements in RLS-NDI and RLS-QoL compared with placebo.

This study was funded by Pfizer Inc. JP, SD, CC, LK and JM are employees of Pfizer Inc. RPA, DGB, PMB and AL have served as consultants for Pfizer Inc and PMB and AL have acted as investigators for Pfizer Inc. Medical writing support was provided by Elizabeth Harvey PhD, of UBC Scientific Solutions, and funded by Pfizer Inc.

P1007

Restless legs syndrome in dialysis patients and survival

F. CIRIGNOTTA[1], S. MONDINI[1], S. BAIARDI[1], A. BALDI ANTOGNINI[1] and A. SANTORO[2]

[1]University of Bologna, Bologna, IT, [2]S.Orsola-Malpighi Hospital, Bologna, IT

Introduction: Restless Legs Syndrome (RLS) is more prevalent among dialysis patients compared to the general population. Some studies found an increased mortality in dialysis patients with associated RLS, particularly for severe forms of RLS.

Method: In 1996 we studied 128 patients with end-stage kidney disease undergoing hemodialysis; 36 patients (28%) had concomitant RLS: 9 (7%) with RLS symptoms less than once a week; 11 (8.5%) with RLS symptoms more than once a week not disturbing sleep; 16 (12.5%) with RLS symptoms more than once a week with sleep disturbance. Fifteen years later we evaluated the mortality of this population. We excluded from the analysis patients who had suffered of RLS 'in the past' (11 patients, 8.5%).

The Kaplan Maier curves in dialysis patients with or without RLS (control group matched for age) were constructed for all-cause mortality and compared by log-rank test.

Result: The survival analysis disclosed a lower mortality in the group with RLS than in controls ($P = 0.04$). The mortality rate was not influenced by RLS severity ($P = 0.11$) and gender ($P = 0.15$).

Conclusion: Our study has some limitations but suggests that RLS in dialysis patients does not shorten survival. Instead, the survival rate was longer in our sample and we found no relationship between RLS severity and mortality.

P1008

Nocturnal periodic leg movements in spinal cord injury

O. KURKELA[1], A. SALMINEN[1], E. KOSKINEN[2], T. LUOTO[2], V. RIMPILÄ[1], J. ÖHMAN[2] and O. POLO[2]

[1]Unesta Research Centre, Tampere, FI, [2]Tampere University Hospital, Tampere, FI

Objectives: Periodic leg movements (PLM) have been suggested to have their origin in the central nervous system because they can be suppressed by dopaminergic therapy. However, periodic leg movements (PLM) occur also in patients with complete spinal cord injury (SCI), challenging the hypothesis of central origin (Yokota et al. 1991, Telles et al. 2011). In the current study we aimed to confirm these results in a larger patient population and with various degrees of SCI.

Methods: Full polygraphic sleep recording was performed in 32 patients (24 men, eight women) with chronic spinal cord injury. Seven subjects had American Spinal Injury Association (ASIA) class A injury, as 25 were of ASIA classes C–D. Sleep staging was performed, and PLMs were analyzed from each recording according to the WASM scoring criteria. Movements related to breathing events were excluded. PLM indexes were correlated with the ASIA classification of the injury.

Results: PLM was a common finding, present in 14/32 patients. When present, the average PLM-index was 72.5/h. In 11 patients the PLM index was higher than 25/h. In 13 patients with PLM the SCI was ASIA class C–D, as one was ASIA A. The PLM occurred in all sleep stages, including REM sleep and wakefulness. In 4 patients the PLM index exceeded 120/h. In two of these (ASIA class A and C) no heart rate or cortical events were associated with PLM. The PLM in these two patients were never bilateral.

Conclusions: In our patients with SCI the incidence of PLM was higher than previously reported. The results suggest that PLMs do exist in patients of all classes of SCI, including complete lesion (ASIA A). The appearance of PLMs in patients with complete spinal cord lesion does not support central origin of PLM. A peripheral mechanism for PLM is also supported by the absence of cortical and heart rate responses to PLM in some patients.

P1009

Frequent symptoms of restless legs syndrome in obstructive sleep Apnoea: The Icelandic Sleep Apnea Cohort

B. BENEDIKTSDOTTIR[1], E. S. ARNARDOTTIR[1], E. BJÖRNSDOTTIR[1], C. JANSON[2], A. PACK[3] and T. GISLASON[1]

[1]Landspitali University Hospital, Reykjavík, IS, [2]Uppsala University, Uppsala, SE, [3]University of Pennsylvania School of Medine, Philadelphia, US

Objectives: Patients with obstructive sleep apnea (OSA) have in some reports been found to report frequently restless legs syndrome (RLS) symptoms. Most often these reports, however, lack comparative groups. In addition, OSA patients suffer from multiple comorbidities that could also contribute to RLS. It is also unclear how RLS is associated with CPAP treatment. The aim of this study was to estimate the frequency of reported RLS in untreated OSA patients and compare the results to the general population and after CPAP treatment

Materials and methods: The OSA subjects ($n = 822$) were newly diagnosed with moderate or severe OSA (665 males, 157 females). The control subjects ($n = 742$) were randomly chosen Icelanders (394 males, 348 females) who participated in another epidemiological study (Benediktsdottir B et al. 2009). Measurements included a standardized RLS rating scale, questions about sleep and the Epworth Sleepiness scale. The prevalence of RLS was assessed again 2 years after starting CPAP treatment.

Results: Among untreated OSA males 34.74% reported RLS but 12.9% of control males ($P < 0.001$). Altogether 45.5% of untreated OSA females reported RLS but 24.4% of control females ($P = 0.03$). Both among OSA patients and controls those with RLS more commonly reported insomnia, daytime sleepiness, nocturnal sweating, snoring and gastro oesophageal reflux ($P < 0.05$). No relationship was found between RLS age, BMI, hypertension or respiratory diseases in a logistic regression adjusting for the presence of OSA and the other factors mentioned. No relationship was found between RLS and sleep apnea severity. At the 2 year follow-up subjects ($n = 475$) using CPAP reported a decrease in prevalence of RLS from 35.9% to 24.2% ($P < 0.0001$). Those OSA patients not using

CPAP at the 2 year follow-up also reported some decrease in prevalence of OSA from 38.8% to 28.5% ($P = 0.01$).

Conclusions: RLS is significantly more prevalent in OSA patients than in the general population. The prevalence of RLS decreases to similar levels as among controls in CPAP users.

P1010

Clinical severity and sleep disturbance in augmented restless legs syndrome

T. MITTERLING, B. FRAUSCHER, T. FALKENSTETTER, L. EHRMANN, D. GABELIA, V. GSCHLIESSER, E. BRANDAUER and B. HÖGL

Innsbruck Medical University, Innsbruck, AT

Objectives: Augmentation is the most bothersome complication of dopaminergic therapy in restless legs syndrome (RLS). It is characterized by a worsening of symptoms during treatment with a shift to earlier hours in the day, a shorter latency to the occurrence of RLS symptoms at rest and a spread of symptoms to other body parts. Aim of this study was to compare clinical and sleep parameters of augmented versus non-augmented RLS patients.

Methods: 45 consecutive RLS-patients (15 untreated, 15 treated non-augmented, 15 augmented) were recruited for this study. Evaluation of patients contained demographic data, clinical history, RLS-specific scales [International RLS Study Group Rating Scale for RLS (IRLS), RLS-6 scale, clinical global impression (CGI), Structured Interview for the Diagnosis of Augmentation (SIDA), Augmentation Severity Rating Scale (ASRS)] and a video-polysomnographic (PSG) examination.

Results: Augmented RLS patients had longer disease duration than untreated patients [mean ± standard deviation (SD) 21.5 ± 17.2 versus 8.3 ± 5.4 years $P < 0.05$]. Moreover these patients had higher scores in RLS-specific scales than patients without augmentation (mean ± SD augmented versus treated non-augmented versus untreated: IRLS: 29.5 ± 5.8 versus 11.5 ± 9.3 versus 16.9 ± 11; RLS-6: 35.3 ± 11.2 versus 12.4 ± 7.8 versus 20.5 ± 13.2; median range CGI: 6 (4–6) versus 3 (2–5) versus 4 (1–5); ASRS item 4 scores: 3 (1–4) versus 1 (0–3) versus 2 (0–4); all ps < 0.05). Regarding sleep parameters augmented patients had lower percentages of stage N3 compared to treated non-augmented patients (mean ± SD 1 ± 2.2 versus 6.1 ± 6.2; $P < 0.05$), and a tendency towards longer REM sleep latency compared to untreated patients (mean ± SD 116.2 ± 72.4 versus 104.5 ± 95.8 min $P = 0.063$). All other sleep parameters were not different between augmented and non-augmented RLS patients. In addition periodic leg movement indices, during both wakefulness and sleep, did not differ significantly between the three groups (all ps > 0.05).

Conclusion: Our study showed that augmented RLS patients differed clearly from non-augmented RLS patients in disease severity as measured by different severity rating scales, whereas PSG parameters revealed only differences in the amount of N3 sleep, as potential indicator for sleep disturbance.

This study was supported by Österreichische Nationalbank Jubiläumsfonds Projekt 12594 to Birgit Högl.

P1011

Association between mild cognitive impairment and electroencephalographic slowing in idiopathic rapid eye movement sleep behaviour disorder

T. SASAI, Y. KOMADA and Y. INOUE

Tokyo Medical University, Tokyo, JP

Objectives: Mild cognitive impairment (MCI) and electroencephalographic (EEG) slowing have been reported as an common finding of idiopathic REM sleep behavior disorder (iRBD) and alpha-synucleinopathy. The objective of this study is to clarify association between clinical finding or EEG finding and MCI in iRBD.

Methods: Seventeen patients with iRBD (younger iRBD group; <70 years), 18 age and sex-matched control and 14 patients with iRBD (older iRBD group; ≥70 years) were enrolled in this study. We conducted cognitive function test (MMSE and MoCA), nocturnal PSG (n-PSG) and power EEG spectral analysis for all subjects. Among the findings of EEG, REM sleep without atonia (RWA), RBD morbidity and RBD severity using Japanese version of RBD questionnaire (RBDQ-JP), the factors associated with MCI were explored.

Results: The younger iRBD group showed significantly lower scores of MMSE and MoCA compared to controls. Additionally, the patient group had lower alpha power during wakefulness, lower delta power during REM sleep, and lower EEG power in all frequency bands during NREM sleep. In younger iRBD group, MCI was detected in 6/17 (35.2%) patients on MMSE and in 13/17 (76.5%) on MoCA. The older iRBD group showed increased proportion of slow wave sleep (SWS) and decreased EEG frequency during REM sleep as well as worsening of MCI. For all iRBD patients, the score of MoCA negatively correlated with age, proportion of SWS, and delta and power during REM sleep. Multiple regression analysis provided an equation; the score of MoCA = 64.774 ± 0.147*age ± 8.011*log(delta power during REM sleep; $R^2 = 0.508$, $P < 0.01$). Standardised partial regression coefficient for age was -0.535 and that for log(delta power during REM sleep) was -0.491.

Conclusions: Patients with iRBD showed mild cognitive impairment. The MoCA was better screening instrument for the detection of mild cognitive impairment than MMSE. EEG slowing during REM sleep, but not clinical findings of iRBD, was proven to be associated with mild cognitive impairment in iRBD.

Poster Session – Parasomnias

P1012

Slow wave activity and slow oscillations in sleepwalkers and controls before and after sleep deprivation

R. PERRAULT, J. CARRIER, J. MONTPLAISIR and A. ZADRA
University of Montreal, Montreal, CA

Objectives: Several studies have investigated slow wave sleep electroencephalographic parameters, including slow-wave activity (SWA; 0.5–4 Hz), in relation to somnambulism. While most studies show that sleepwalkers have a lower SWA density during the first non-rapid eye movement (NREM) cycle when compared to controls (a finding explained by sleepwalkers' frequent arousals from their first NREM cycle impeding normal SWA buildup), others show that the power density in the delta range is comparable among SW and normal controls or that SW have a higher power density in the slow delta range. We recently examined changes in the amplitude and density of slow wave oscillations (SWO) prior to episodes of somnambulism and found a significant increase in SWO density in the 20 s immediately prior to episode onset. The goal of the present study was to investigate delta (1–4 Hz) and slow delta activity (0.5–1 Hz) as well as SWO density and amplitude in sleepwalkers and controls during both normal sleep as well as recovery sleep following sleep deprivation.

Methods: Ten adult sleepwalkers and 10 sex- and age-matched control subjects were studied in the laboratory. After a screening night, participants were monitored during one night of baseline recording, and one recovery night following 38 h of sleep deprivation.

Results: SWA, delta, slow delta and SWO all showed marked increases during recovery sleep when compared to baseline levels. A fronto-central gradient in the topographic expression of these variables was also found for both groups on both nights. Between group comparisons across nights as well as across individual NREM cycles revealed no significant differences between sleepwalkers and controls on the SWA and SWO parameters.

Conclusion: Our findings reveal no significant differences between sleepwalkers and controls in SWA and SWO parameters at baseline as well as in response to sleep deprivation. Possible explanations for these unexpected results include the relatively small sample size and the heterogeneity of sleepwalkers as a population. In comparison to past studies, the SWS awakenings and sleepwalking episodes recorded from our 10 patients were more equally distributed across the night thus limiting their postulated interference with SWA in early NREM cycles.

Research supported by a grant from the Canadian Institutes for Health Research (CIHR).

P1013

Subjective sleep parameters of patients with non-REM parasomnia

V. HIRSCHER, T. UNBEHAUN, B. FEIGE, C. NISSEN and D. RIEMANN
University Medical Center Freiburg, Freiburg im Breisgau, DE

Objectives: The main objective of this study was to examine the sleep habits and subjective sleep parameters of patients with non-REM parasomnia compared to good sleeper controls. Since several behaviours can trigger parasomnic events, e.g. sleep deprivation, we tested the hypothesis that patients with non-REM parasomnia would demonstrate unfavourable habitual sleep patterns prior to any intervention.

Methods: We examined 19 patients with non-REM parasomnia (somnambulism and/or night terror) and 19 sex- and age-matched good sleeper controls. All participants were investigated with two consecutive nights of polysomnography in the sleep laboratory. Prior to the sleep laboratory study, all participants filled out a sleep diary as well as several sleep questionnaires to measure the subjective total sleep time, the regularity of the sleep-wake rhythm, subjective sleep quality, alcohol consumption and daytime naps.

Results: Patients with non-REM parasomnia did not demonstrate any significant differences in the total sleep time, sleep-wake rhythm, sleep quality, alcohol consumption or daytime naps. Power analyses did not show any relevant group differences in the outcome parameters.

Conclusion: The results indicate that, against our hypothesis, patients with non-REM parasomnia did not demonstrate any significant differences in their sleep habits and subjective sleep parameters. The findings rather suggest that the occurrence of parasomnic events is driven by other, potentially neurobiological factors.

P1014

Adult-onset non-REM parasomnia with hypnopompic hallucinatory pain

L. MANTOAN, S. H. ERIKSSON, A. P. NISBET and M. C. WALKER
Institute of Neurology, London, UK

We report on a 43 year-old woman presenting with nocturnal episodes of pain and screaming during sleep starting at age 30. There was no childhood or family history of parasomnia. The events had gradually become more frequent over the years, occurring in the first half of the night within 2 h of sleep onset. There were no triggers and she had partial amnesia for the events. A diagnosis of adult-onset sleep terrors was made on clinical grounds and confirmed on polysomnography. Seizures and periodic limb movements were excluded as triggering factors. There was some mild sleep disordered breathing (predominantly non-desaturating hypopnoea during rapid eye movement (REM) sleep). Imaging of the brain and spine and neurophysiological investigations ruled out lesions, entrapments or neuropathies as possible causes of pain. Treatment was started with paroxetine, a selective serotonin reuptake inhibitor, and Gabapentin. This is the first report of hypnopompic psychic pain in association with a non-REM parasomnia. We hypothesize that the pain may be analogous to previously reported non-REM parasomnia-associated hypnopompic visual hallucinations and that, as such, it may be arising during arousal of the sensory neocortex as confabulatory response to sub-cortical fight-or-fright arousal stimulus occurring during slow wave sleep.

P1015

High dream complexity in adult sleepwalking

J. BUŠKOVÁ, J. PIŠKO, T. VORLOVÁ, S. DOSTÁLOVÁ, L. PLCHOVÁ and K. ŠONKA
Charles University, Prague, CZ

Objectives: Although NREM sleep dreams are generally considered as being short, less complex and less vivid then REM sleep dreams, there are sporadic descriptions of the mental content associated with

sleepwalking in adults, suggesting complex mental activity preceding the arousal state.

Methods: Fifty one patients referred for sleepwalking (45% men and 55% women; mean age 29.9 ± 9.1 years; age range from 19 to 63 years, with 17.5 ± 14.0 years of age at the onset of parasomnia), underwent structured interview concerning frequency and timing, risk behaviour, predisposing factors and mental content immediately preceding the sleepwalking episodes, thereafter underwent nocturnal video-polysomnography. The mental contents were classified for complexity (Orlinski score) and described using nominal categories according to Hall and Van De Castle.

Results: Sleepwalking episodes occurred more than once a week in 49% of the patients; the precipitating factors were alcohol intake in four cases, sleep deprivation in seven, work and family stress in 12 and moving to another place in fie cases. Sleep apnea was present in seven and periodic limb movements in sleep occurred in five patients. In one patient, episodes started after she failed at high-school graduation. In one case, episode was preceded by threatening behaviour of his drunken neighbour. Six patients had diagnosis of migraine, seven patients suffered from anxiety disorder, one patient from phobia and one was diagnosed with somatization disorder. Violent behaviour was described in 49%. Overall, 43.1% of the patients experienced at least one prolonged, image-scenario resembling real life (e.g. dressing up going to work/cooking or walking the dog/packing for a journey/packing a suitcase to work), 29.4% of patients described coherent and detailed dreams, with the dreamer as an actor (e.g. an effort to hold the falling wardrobe/searching people under the bed/taking a glass of water for a girlfriend/tearing of the chandelier in an effort to escape) while only 27.5% had no clear memory about the dreamlike mentation. These dreamlike mentations were frequently associated with misfortune (45%) and apprehension (79%). 9.8% of patients reported seeing animals during the episode (bugs, snakes, spiders, mice).

Conclusion: High dream complexity with a strong emotional character could occasionally appear as a trigger of sleepwalking episode in adults.

P1016

Spectral electroencephalographic sleep alterations in subjects with frequent nightmares

K. HORVÁTH[1], P. SIMOR[2], F. GOMBOS[2] and R. BÓDIZS[3]

[1]University of Oxford, Oxford, UK, [2]Budapest University of Technology and Economics, Budapest, HU, [3]Semmelweis University, Budapest, HU

Objectives: Idiopathic nightmare disorder, which affects 2–8% of the population, is a distinct diagnostic category in the International Classification of Sleep Disorders (2nd edition) and the Diagnostic and Statistical Manual of Mental Disorders as well. However, the characteristic sleep profile of nightmare subjects (NMs) has rather been under-researched. Our goal is to obtain a comprehensive picture of the sleep of NMs by means of spectral electroencephalographic (EEG) analyses which can provide valuable insights into the underlying pathophysiology.

Methods: Thirty-five university students without any prior history of mental or chronic somatic disease (17 NMs and 18 controls) went through standard two-night polysomnographic examination (with 19 EEG channels) in our sleep laboratory. Psychometric testing was also conducted including the State-Trait Anxiety Inventory (STAI) and the Beck Depression Inventory (BDI). EEG spectra were obtained by using Fast-Fourier Transformation of the second night recordings for rapid-eye movement (REM) and non-rapid eye-movement (NREM) sleep separately. We also computed the spectra of the first 4 sleep cycles distinctly in order to understand better sleep dynamics. To control the individual differences in the amplitude of power spectral density, relative EEG spectra were calculated for 6 frequency bands (delta, theta, alpha, sigma, beta, gamma).

Results: Regarding all night data we compared the two groups by covariance analysis with STAI and BDI as covariates. The nightmare group was characterised by marginally ($P < 0.10$) lower frontal delta (1.25–4 Hz), as well as significantly ($P < 0.05$) higher fronto-central theta (4.25–7.5 Hz) and alpha (7.75–10.25 Hz) NREM activity compared to controls. The separate analysis of sleep cycles revealed that the reduced delta activity is characteristic for the 1st, while the increased theta for the 1st and the 4th sleep periods in NMs. Higher alpha activity was found mainly in the 4th sleep cycle.

Conclusions: Our results provide evidence that NMs, even if they did not experience negative dreams, differ from controls in their sleep EEG spectra, mostly regarding NREM sleep. Lower delta activity indicates disrupted sleep which may be associated with impaired executive functions in NMs, whereas higher alpha activity in the 4th sleep cycle may be the sign of hyperarousal later in the night. Moreover, the covert REM sleep phenomena might explain the higher theta activity in NMs.

The present research was supported by the 2010 Research Grant of the BIAL Foundation (55/10).

P1018

Prevalence of nightmares among Finnish general adult population and veterans of the Second World War, 1972–2007

N. SANDMAN[1], K. VALLI[1], E. KRONHOLM[2], H. M. OLLILA[3], A. REVONSUO[1], T. LAATIKAINEN[3] and T. PAUNIO[3]

[1]University of Turku, Turku, FI, [2]National Institute for Health and Welfare, Turku, FI, [3]National Institute for Health and Welfare, Helsinki, FI

Objectives: The aim of the current study was to investigate nightmare prevalence among the Finnish general adult population and veterans of the Second World War. Specifically, we were interested in how nightmare prevalence is affected by gender and age of the participants, how the prevalence has changed from 1972 to 2007 and how the nightmare prevalence of war veterans differs from that of general population. In addition to nightmares, we also investigated the prevalence of insomnia and anxiety symptoms among the war veterans.

Methods: Data from the Finnish National FINRISK Study were used to estimate nightmare prevalence. FINRISK is a large cross-sectional health survey conducted every 5 years since 1972 and it includes an extensive health and lifestyle questionnaire and physical examination for a random sample of Finnish adults. Our study uses data from eight surveys (1972, 1977, 1982, 1987, 1992, 1997, 2002 and 2007) and includes 69 813 participants aged 25–74 years. The questions about nightmares and insomnia symptoms in FINRISK are self assessment of frequency in the last 30-days. War veterans are identified by direct questions in surveys of 1972 and 1977. For our analysis we used Pearson Chi-Square and the Mantel-Haenszel chi^2 test for linear trend.

Results: The prevalence of frequent nightmares among the study population over all the study years is 3.5% for men and 4.8% for women. However, the gender difference was most profound among young adults and disappeared around 60 years of age. This is

because nightmare frequency increases with age and this increase is stronger in men ($P < 0.0001$).

After controlling for the effect of war, the amount of frequent nightmares has not significantly changed from 1972 to 2007, but the number of people reporting occasional nightmares has increased 20% ($P < 0.0001$).

Of the war veterans, 7% report frequent nightmares while the prevalence of frequent nightmares in the general population in the same samples is significantly less ($P < 0.0001$). Veterans also have more self-reported symptoms of insomnia, depression and anxiety than the general population ($P < 0.0001$).

Conclusion: Nightmare prevalence is significantly affected by age, gender, study year and war experiences in the series of large population surveys of Finnish adults. In addition to nightmares, war veterans also report more insomnia and anxiety symptoms than the general population.

P1019

The prevalence and associated factors with sleep-related eating disorder: results of internet survey for Japanese young adults

Y. KOMADA[1], S. ASAOKA[1], T. SASAI[2] and Y. INOUE[1]

[1]Tokyo Medical University, Tokyo, JP, [2]Neuropsychiatric Research Institute, Tokyo, JP

Objectives: Sleep-related eating disorder (SRED) is a condition with recurrent episodes of involuntary eating and drinking during arousal from sleep resulting in problematic consequences. The prevalence of SRED is unclear among Japanese population. Furthermore, there have been no large population study to elucidate the factors associated with the occurrence of SRED. The aim of this study was to elucidate an estimate of the prevalence in Japanese young adults and to identify the associated factors with SRED.

Methods: This study was approved by the ethics committee of the Neuropsychiatric Research Institute. The anonymous questionnaire survey was conducted over the internet in January 2012 with the cooperation of a research company (Rakuten Research, Inc. Tokyo, Japan), targeting male and female aged 19–25 years throughout Japan. The number of website visits was 3904, and 3613 of them completed their answer (response rate: 92.5%).

The contents of the questionnaire were (i) Demographic variables: age, sex, height, weight, the disease currently being treated, living alone or not, smoking habits, and alcohol consumption. (ii) The Japanese version of the Pittsburgh Sleep Quality Index (PSQI). (iii) The standardized eight-item Short Form Health Survey of the Medical Outcomes Study (SF-8). (iv) The 12-item version of the Center for Epidemiological Studies Depression Scale (CES-D). (v) Japanese version of the Munich Parasomnia Screening (MUPS).

Results: Lifetime prevalence of SRED in the subject population was 7.0%. The percentage of the respondents who answered that they experienced the episode at least once a year, and at least once a month were 3.1% and 1.1%, respectively.

The factors associated with SRED episode at least a year were examined with the aid of a series of logistic regression analyses. The existence of SRED episode was significantly associated with habits of alcohol ingestion (OR = 2.65, 95% CI: 1.36–5.16, $P = 0.004$), PSQI C6 score i.e. sleep medication use (OR = 1.48, 95% CI: 1.06–2.08, $P = 0$ 0.02), and other nocturnal problematic behaviors (sleep enuresis: OR = 6.14, 95% CI: 2.35–16.04, $P = 0.0002$, nocturnal eating syndrome: OR = 8.22, 95% CI: 3.76–18.00, $P < 0$ 0.0001).

Conclusion: The prevalence of SRED among Japanese young adults is comparably high with previous reports. Our results suggest that sleep medication use, drinking habit, and the other nocturnal problematic behavior are associated with occurrence of SRED.

This study was supported by KAKENHI (Grant-in-Aid for Young Scientists).

P1020

How is sexsomnia evaluated legally?

J. HETTA[1] and J.-E. BROMAN[2]

[1]Karolinska Institutet, Stockholm, SE, [2]Uppsala University, Uppsala, SE

Sexsomnia is rather newly described parasomnia, which comes into attention to sleep experts especially when legal considerations are asked for.

Some requirements for a diagnosis have been proposed, for instance inclusion of a polysomnographic recording (hypersynchonized delta, or aiming at find treatable sleep disorders). In court cases PSG is not always possible and not even required, partly because the limited availability and high costs.

The purpose for this presentation is to discuss two aspects of the legal procedure: 1. Can an individual get the diagnosis without having a history of somnambulism and/or other parasomnias?

2. If the accused have had sexsomnia previously and then go to sleep in a room with a naked woman and during the night perform sexsomnia with her, should he then be convicted because he has not abstained from sleeping in a situation that could trigger his sexsomnia.

Three cases will be presented, illustrating these difficult questions.

Conclusion: Our perspective is that a diagnosis can be based on the history and examination of the description of the particular behaviour, especially reports of circumstances in conjunction with the awakening. However, algorithms for proper diagnostic procedures should be developed.

P1021

Heart rate regulation under normal and increased homeostatic pressure in sleepwalkers and controls

G. SCAVONE, P. LANFRANCHI, J. CARRIER, A. A. BARIL, M. DE COURVILLE, V. LAROSE, C. GAUDET, J. MONTPLAISIR and A. ZADRA

Center for Advanced Research in Sleep Medicine (CARSM), Hôpital du Sacré-Coeur de Montréal, Montreal, CA

Objectives: Sleep deprivation followed by recovery sleep during the daytime can facilitate the occurrence of sleepwalking episodes in predisposed patients. Sleeping during the diurnal period is also associated with an activation of the autonomic nervous system (ANS), but this association has never been studied in patients suffering from somnambulism. The goal of the present study was to determine whether sleepwalkers have a higher ANS activation than controls and if this activation is affected by increased homeostatic sleep pressure following sleep deprivation.

Methods: Eight sleepwalkers (6F/2M; 27.2 ± 4.8 years) and 9 controls (7F/2M; 26.3 ± 4.8 years) were recorded in the sleep laboratory during normal baseline sleep and during daytime recovery sleep following 25 h of sleep deprivation. ANS activation was determined according to three temporal cardiac variables; mean and standard deviation of the RR interval (mRR and sdRR) as well as the pNN50. These variables were extracted from multiple 5 min

segments of NREM sleep. Repeated measure ANOVAs were used to assess main and interaction effects.

Results: There was a trend for a group X sleep condition interaction effect for sdRR during stage 2 ($P = 0.06$) with sleepwalkers showing a higher sdRR than controls during normal sleep (60.5 ± 22.2 versus 47.2 ± 9.0 ms) but a lower index during recovery sleep (59.2 ± 17.1 versus 62.9 ± 19.9 ms). A trend for a group X condition interaction effect was also found for mRR in stage 2 ($P = 0.07$) with sleepwalkers showing a lower mRR than controls during normal sleep (948 ± 129 versus 967 ± 156 ms) and recovery sleep (924 ± 130 versus 1014 ± 123 ms). Finally, pNN50 was significantly lower across both groups during baseline stage 2 as compared to recovery stage 2 (13.2 ± 11.1 versus 7.1 ± 10.1 $P < 0.05$). No significant group effect was found for any other variables.

Conclusion: Lowered values for mRR, sdRR and pNN50 are known to be associated with the activation of the ANS. These preliminary results thus suggest a higher level of ANS activation in sleepwalkers' NREM sleep when compared to controls. Both groups, however, show a decrease in ANS activation during daytime recovery sleep. These findings highlight the need to study cardiac ANS functioning in patients with NREM sleep parasomnias and suggest that ANS functioning may play a role in the pathophysiology of somnambulism.

P1022

Frequent neck myoclonus in REM sleep in a patient with vivid dreams and dream-enacting behaviour

M. OTTO, K. SVENDSEN, S. FUCHS and A. HESS
Aarhus University Hospital, Aarhus, DK

Objectives: Neck myoclonus in REM sleep has been reported as a coincidental finding in routine PSG, with an index below 10 per hour REM sleep in many patients (Frauscher et al. 2010). However, the significance of neck myoclonus remains unclear. To date, it is unknown if the phenomenon may be associated with REM sleep parasomnias.

Methods: We report the case of a 26-year old woman, referred for nocturnal hallucinations or a REM parasomnia. During the last 5 years, the patient suffered from vivid dreams with threatening content, sometimes perceived as visual scenic hallucinations, which awoke her. On awakening, she sometimes found herself acting out these dreams. There were no complaints of excessive daytime sleepiness. A treatment with nortriptyline for minor depression was stopped 3 weeks before the polysomnography, with no change in symptoms.

Results: Two night's polysomnography with 19-channel EEG and synchronous video showed frequent neck myoclonus mainly during REM sleep, with an index of 59.8 and 89.9 per hour REM sleep during the first and second night, respectively. Movements were either versive to one side or flexing movements, all with a duration <1 s, measured by the length of the EEG artefact. The EEG showed no epileptic activity. Few epochs showed some EMG activity in the submental and anterior tibial muscles, but no epoch fulfilled criteria for REM sleep behaviour disorder (AASM 2007). The patient did not perceive any vivid dreams or hallucinations during the study nights.

Conclusion: Our case shows an association between a clinically suspected REM sleep behaviour disorder and frequent neck myoclonus in REM sleep, without other signs of abnormal muscle activity in REM sleep. Further studies have to evaluate a potential relation of neck myoclonus with REM sleep parasomnias.

P1023

Cognitive profile in RBD patients – a pilot study

V. STUKOVNIK, A. OZURA, M. TROST, N. ZUPANCIC KRIZNAR and L. DOLENC GROSELJ
University Medical Centre Ljubljana, Ljubljana, SI

Objective: Cognitive impairment is a frequent feature in REM sleep behavior disorder (RBD), a sleep disturbance that is often a preclinical stage of Parkinson's disease or other synucleinopathies. The goal of this pilot study was to determine the extent and profile of cognitive impairment in a sample of Slovenian RBD patients.

Patients and methods: Eight patients (mean age 63.8 ± 11.6; one woman, mean disease duration 37.6 ± 34.9) with polysomnography-confirmed RBD underwent a comprehensive neuropsychological evaluation including tests of executive functions and attention (Digit span, Stroop color word test, TAP – alertness, verbal fluency, Wisconsin card sorting test), memory (California verbal learning test, Rey complex figure test and recognition trial) and visuospatial and visuoperceptual abilities (Benton judgment of line orientation test, Copy of Rey-O figure, Block design – WAIS IV). Cognitive impairment was determined using a standard criteria: performance ≥1.5 standard deviation below the standardized mean, or, depending on norms, percentile range ≤ 8 or t-score ≤ 36

Results: 62% of patients showed a reduced attention span. In addition 50% were impaired in psychomotor speed. Similarly, 50% were prone to interference on the Stroop test, while they were not slowed on reading or naming colors. Only 28% of patients had deficits in long term verbal recall. Delayed visual recall was impaired in 50%. Forty percent of patients show impairment in ability of strategy adaptation on WCST, while none of the patients show impairment in lexical word fluency. Twenty-five percent of patients were impaired on categorical verbal fluency. None of the patients were impaired in the domain of visuo-spatial and visuoperceptual abilities.

Conclusion: The results of this pilot study show a tendency in RBD patients to exhibit cognitive deficit in the domains of attention span, psychomotor speed and visual memory. The small size of our sample prevents us from making definite conclusions. It is important to consider the implication of such potential deficit for everyday functioning. As this is an ongoing study we plan to enlarge our sample, so that more definite conclusions about cognitive impairment in our RBD patients could be made.

P1024

A case of catathrenia – definitely a sleep-related breathing disorder

S. JANKOVIC[1], D. SOKIC[1], N. VOJVODIC[1], A. RISTIC[1], M. KOVACEVIC[1] and V. KOSTIC[2]
[1]Clinic of Neurology, Belgrade, RS, [2]Center for sleep research, Belgrade, RS

We present a rare case of catathrenia in a 37 years old, healthy female patient with a frequent, unremitting episodes of purely expiratory nocturnal groaning (NG) sound appearing several times every night exclusively during sleep. NG first appeared at the age of 21 years and persisted even during pregnancy with the patient unaware of nocturnal sounds.

A full video-polysomnography (v-PSG; digital video/EEG/time/sound synchronized recording with Nicolet One, Viasys Healthcare system) was performed on two consecutive nights from 09 pm to 08 am next morning. v-PSG included: full longitudinal bipolar montage to detect EEG activity with additional recordings from O2/A1, O1A2, C4A1 and

C3A2; right and left electro-oculogram, right and left surface submental EMG and right and left periodic limb movements; thoracic and abdominal respiratory movements; microphone for sound recording; body position; one electrocardiogram derivation (modified V2 lead) and oxygen saturation.

v-PSG of two consecutive nights showed on average 16 episodes of NG sound during NREM sleep. The episodes were initialized by a short awakening, followed by immediate cessation of respiratory movements and nasal airflow (central sleep apnea, CSA) accompanied by a morose sound. The longest NG episode consisted of 40 s CSA and 17 s NG; the shortest consisted of apnea and groaning each lasting 1 s. NG consisted of monotonous vocalization frequently interrupted by 2–3 inhalations with CSA always being longer than NG. On the first night, total duration of 13 NG episodes was 5.81 min. Mean duration of CSAs was 26.83 s, and total and mean duration of a NG was 3.49 min and 16.11 s, respectively. The sound was persistent, frequently discontinuous, of different volume and pitch. We also noticed a high number of CSAs with a pattern similar to catathrenia but with no NG or with only a short initial (up to 1 s) NG sound. In full wakefulness we noticed a high number of CSAs during prolonged periods of pre-sleep placid lying down. No oxygen desaturation was noticed.

In a patient with catathrenia CSA breathing was present both in wakefulness and sleep. However, only in sleep it contained NG. The presence of different disturbed breathing patterns (catathrenia with NG; CSA but without NG vocalization; CSA in full wakefulness) suggest that catathrenia itself is a specific clinical entity with an underlying disturbance of breathing drive both in sleep and wakefulness.

P1025

RBD in narcolepsy as a predictor for Parkinson's disease? Results of a prospective study of narcoleptic patients with RBD

G. MAYER[1], K. KESPER[2], A. TSINTARIS[2], W. OERTEL[2], K. STIASNY-KOLSTER[2] and M. UNGER[2]

[1]Hephata Klinik, Schwalmstadt-Treysa, DE, [2]Philipps University, Marburg, DE

Introduction: There is growing evidence that narcolepsy is caused by autoimmune mechanisms. Some of the literature of the past 10 years on the cause of destruction of hypocretinergic cells in the hypothalamus has raised the question of a neurodegenerative cause. RBD, a precursor of neurodegenerative disease is frequently associated with narcolepsy. Loss of hypocretin in advanced Parkinson's disease supports this hypothesis. So far very few articles have been published about narcolepsy patients with dementia or synucleopathies.

Methods: We studied the narcolepsy patients with RBD that have been studied by Stiasny-Kolster et al. (Brain 2005) 7–8 years later with olfactory tests, MMSE, UPDRS III, polysomnographies and FP-cit SPECT. We also used the REM sleep behavior disorder screening questionnaire.

Patients: Twelve narcoleptic patients with RBD were re-investigated (7M, 5F mean age: 51 ± 7.9 years).

Results: REM sleep behaviour questionnaire: 9.9 ± 3.4 = highly pathological value. MMSE: 29.2 ± 1 = normal range, olfactory threshold: 8.41 ± 5.85, olfactory discrimination: 10.24 ± 3.41, olfactory identification: 11.55 ± 2.11. All olfactory values are pathological. UPDRS III: 2.55 ± 1.41 = normal range, but 7 patients have increased scores compared to 2003, and 3 have developed discrete to manifest signs of PD (tremor, rigidity, falls).

Conclusion: This longitudinal study shows that RBD in patients with narcolepsy is a predictor for development of Parkinson's disease. Parkinson's disease has rarely been found in narcolepsy patients. The finding raises the question if neurodegeneration is a part of an underlying neurodegenerative process in narcolepsy or a result of comorbid RBD.

Investigator initiated study, no financial support.

Poster Session – Sleep and Aging

P1027

Sleep problems: an emerging global epidemic? Findings from the INDEPTH WHO-SAGE study among over 40 000 older adults from eight countries across Africa and Asia

S. STRANGES[1], W. TIGBE[1], F. X. GÓMEZ-OLIVÉ[2], M. THOROGOOD[1] and N.-B. KANDALA[1]

[1]University of Warwick Medical School, Coventry, UK, [2]University of the Witwatersrand, Agincourt, ZA

Objectives: Several studies have reported downward trends in the average duration of sleep and an increasingly higher prevalence of sleep problems across different Western populations. However, the evidence from low-income countries is limited. This study aims to fill this gap by examining the prevalence of sleep problems and associated factors in low-income settings.

Methods: Communitywide samples were taken from eight countries across Africa and Asia participating in the INDEPTH WHO-SAGE multicentre collaboration during 2006–2007. The participating sites included rural populations in Ghana, Tanzania, South Africa, India, Bangladesh, Vietnam and Indonesia, and an urban area in Kenya. The overall sample comprised 24 434 women and 19 501 men, for a total of 43 935 participants, aged 50 years and over. Two measures of sleep quality, over the last 30 days, were assessed alongside a number of socio-demographic variables, measures of quality of life, and co-morbidities.

Results: Overall 16.6% of participants reported severe/extreme nocturnal sleep problems, with a striking variation across the eight populations, ranging from 3.9% (Purworejo, Indonesia, and Nairobi, Kenya) to over 40.0% (Matlab, Bangladesh). There was a consistent pattern of higher prevalence of sleep problems in women and older age groups. In bivariate analyses, lower education, not living in partnership, and poorer self-rated quality of life were consistently associated with higher prevalence of sleep problems ($P < 0.001$). In multivariate logistic regression analyses, limited physical functionality or greater disability and feelings of depression and anxiety were consistently strong, independent correlates of sleep problems, both in women and men, across the eight sites ($P < 0.001$).

Conclusion: A large number of older adults in low-income settings are currently experiencing sleep problems, which emphasises the global dimension of this emerging public health issue. This study corroborates the multifaceted nature of sleep problems, which are strongly linked to poorer general wellbeing and quality of life, and psychiatric co-morbidities.

P1028

Old, tired and over-medicated: age and associated effects on insomnia-related physician-office visits in the United States

M. MOLONEY[1], C. ZIMMER[2] and T. KONRAD[2]

[1]North Carolina State University, Raleigh, US, [2]University of North Carolina, Chapel Hill, US

Objectives: Sleeplessness is increasingly linked to individual and large scale health issues in the United States. While certain risk factors for insomnia and its treatment are well-identified, little is known of how age interacts with other socio-demographic characteristics such as race and sex and how these interactions may in turn predict specific insomnia-related outcomes such as insomnia complaint, diagnosis and prescription of a sleep drug. The objective of this paper is to highlight populations who are at greatest risk for overuse of sedative hypnotics.

Methods: We use the National Ambulatory Medical Care Survey, an annual population-based, nationally representative survey of U.S. office-based physician visits. We examined data from 1993–2007 for adults aged 18 and older. Our dependent variables are: (i) sleeplessness as reason for office visit (ii) diagnosis of insomnia and (iii) prescription of a sedative hypnotic. Independent variables include: age, sex, race, anxiety or depression as reason for office visit, insurance status, physician specialty, amount of time spent with physician in 5 min increments, region of the country and year. We used logistic regression to model our data. We include multiplicative interaction effects of age with all patient characteristics. For those significant in each model we test and interpret the specific effects of the variables conditional on age and the effect of age conditional on its interacting variables.

Results: We found older age, female gender, Caucasian race, mental illness and low socio-economic status to be highly correlated with insomnia diagnosis. Anxiety or depression as reason for office visit interacted significantly with older age.

Conclusion: This paper builds on previous research and explores the socio-demographic factors associated with sleeplessness while highlighting the effects of age on insomnia-related office visit outcomes. Our findings suggest that older adults with mood disorders may be more likely to receive prescriptions for sedative hypnotics. These individuals may have a narrower therapeutic window and thus are at greater risk of falls, cognitive difficulties and accidents. Implications for policy are discussed.

P1029

Effect of age and gender on sleepiness and sleep traits in the general population of Lausanne – HypnoLaus study

G. LUCA[1], D. ANDRIES[2], N. TOBBACK[2], J. HABA-RUBIO[2], R. HEINZER[2] and M. TAFTI[1]

[1]University of Lausanne, Lausanne, CH, [2]University Hospital Lausanne, Lausanne, CH

The purpose of this study was to identify the effects of age and gender on sleepiness, sleep quality and subjective and objective sleep characteristics in a large general population-based sample.

Methods: HypnoLaus is a population-based cross-sectional ongoing study on subjects aged 40–80 years living in Lausanne, Switzerland, extensively evaluated for sleep habits and sleep disorders, but also for cardiovascular risk factors, psychiatric evaluation and genetic profile. Of the 4834 participants filled in to date sleep related questionnaires [Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI)] and full ambulatory polysomnography (PSG) was conducted in 1386 individuals.

Results: In the general population of Lausanne, the prevalence of sleepiness, evaluated by ESS (cut-off point 10) is subject to interaction between age and gender, men showing both a higher prevalence (11.9 versus 9.45%, $P = 0.01$) and severity of sleepiness (6.05 ± 3.7 in men versus 5.22 ± 3.46 in women, $P < 0.001$). Evaluation of sleep quality and sleep disturbances by PSQI (cut off 5) showed also a significant effect of age but only in women (men versus women: 36.95 versus 43.62%, $P < 0.001$). Aging is associated with a decrease in subjective daytime sleepiness and an

increase in self-reported sleep quality, in spite of increase in sleep onset latency and decrease of sleep efficiency. Changes in sleep duration and fragmentation, and in sleep latency are independent of the presence of sleep disorders or environment. Objective sleep variables in relationship with age and gender differ from subjective evaluation only in regards to total sleep time, which is decreasing by age (with up to 33 min difference in favour of younger subjects). In men, aging is associated with increased amount of stage 1 and higher arousal index, independent of body mass index, respiratory or movement events. Surprisingly, no sleepiness correlates could be retained after the analysis of objective sleep parameters.

Conclusion: Our main findings suggest that in spite of alterations in sleep macro- and micro- structures by aging, sleepiness and sleep quality are improving in aging subjects, irrespective of the presence of comorbidities, and daytime functioning is better, but the alterations in sleep quality and quantity are more severe in men compared to women.

Supported by FP7-People, Marie Curie Actions, NINA Project 238665, Swiss National Science Foundation and Center for Investigation and Research in Sleep (CIRS/Lausanne).

P1030

Sleep diagnoses in elderly patients and younger controls visiting an outpatient clinic for epilepsy

C. J. M. VAN BOHEEMEN, K. E. SCHREUDER and A. W. DE WEERD

Department of Clinical Neurophysiology and Sleep Centre SEIN, Zwolle, NL

Objectives: Patients with epilepsy or other episodic signs frequently suffer from various sleep related symptoms, for example, involuntary movements at night-time or sleepiness during daytime. The former may be due to a seizure, but often the diagnosis has to be made by polysomnography (PSG). It is unknown if the outcome of sleep investigations are different in younger or elderly patients with epilepsy or other disorders with an episodic character.

Methods: Young (≥30 and < 40 years old) and elderly (≥ 60 years old) patients who visited the outpatient clinic epileptic disorders as well as the sleep clinic were included in this retrospective study. Results of validated questionnaires on sleep disorders, PSG and actigraphy were studied. The final sleep diagnosis was made according to the International Classification of Sleep Disorders-2.

Results: Nineteen of the 29 elderly patients had epilepsy. Based on history and results of PSG, eight subjects suffered from apnea syndrome (AS), three had RLS, four period limb movement disorder (PLMD), one psychophysiological insomnia (PFI), one insomnia due to severe osteoarthritis, one inadequate sleephygiene (ISH), and one had no sleep disorder. In the 10 elderly without epilepsy three had AS, two had AS combined with REM sleep behaviour disorder (RBD). Of the other five elderly without epilepsy one had RBD, the others hypnic jerks, RLS or PLMD.

In the younger control group (n = 20), ten subjects had epilepsy. Out of those ten subjects five were diagnosed with AS, one had RLS, one paradoxical insomnia, one ISH, one slow wave sleep (SWS) parasomnia, and one did not have a sleep disorder. In the younger patients without epilepsy four had AS, PFI was found in two, one had insomnia due to mental disorder, two suffered from ISH, and one had SWS parasomnia combined with ISH.

Conclusion: Sleep related symptoms in the young and elderly patients (with or without epilepsy) had no epileptic origin. RBD was only found in elderly, and SWS parasomnia only in the younger patients. Apnea syndrome and PLMD was frequently diagnosed in young as well as in older patients, in some cases resulting in motor symptoms during the night. Polysomnography in patients with episodic disorders remains essential to discriminate sleep disorders from seizures.

P1031

Sleep structure and sleep disturbances across lifespan in a general population

W. A. MORAES, D. POYARES, L. BITTENCOURT, M. MELLO and S. TUFIK

University Federal of Sao Paulo, Sao Paulo, BR

Introduction: There is a need of studies evaluating the polysomnographic sleep structure of a representative sample of general population throughout lifespan. The objective of this study was to identify sleep patterns and disturbances across lifespan in the population of the city of Sao Paulo.

Methods: A population-based survey adopting a probabilistic three-stage cluster sample of Sao Paulo was used to represent the population according to gender and age (20–80 years). This sample included 1024 individuals who underwent full polysomnography and structured interviews. One-way ANOVA was performed considering insomnia syndrome and AHI >5 as covariates. Age ranges were set at 5-year intervals.

Results: Total sleep time, REM and SWS percentage, and mean oxygen saturation showed a significant reduction while stage 1 was increased with age ($P < 0.05$). There was a significant late tendency toward increment in PLM index ($P < 0.05$). While insomnia complaints increased progressively across lifespan, insomnia syndrome peaked between 40 and 60 years in both genders ($P < 0.05$). Both genders showed a significant progressive increment in AHI with age ($P < 0.05$).

Conclusion: Not only sleep structure but also total sleep time were subject to continuous change throughout lifespan. Insomnia syndrome showed a different age distribution from insomnia complaints. As expected, OSA increased progressively with age.

P1032

Activity forecast by season and weather? two-year actigraphy in a woman with Alzheimer's disease

A. WAHNSCHAFFE[1], C. STOLL[1], A. RATH[2] and D. KUNZ[3]

[1]Charité University Hospitals, Berlin, DE, [2]Split Fennert Nursing Home, Berlin, DE, [3]German Heart Institute Berlin, Berlin, DE

Objectives: With age the linkage between internal and external clock tends to become weaker and the amplitudes of circadian rhythms flatten. In dementia the decline of circadian power seems to be even more severe and culminates in the clinical problem of nighttime agitation often referred to as the main reason for admission to nursing homes. A positive influence of light interventions on nighttime agitation as reflected in short term actigraphy rhythms was shown in several studies. The current single case report describes 2 years of actigraphy in an 82 year old woman with Alzheimer's Disease (AD) focusing on the impact of season and weather.

Methods: Starting in December 2009 the activity of an 82 year old woman with AD living in a nursing home is continuously monitored by a wrist actigraph. The current case report analyzes the activity data from two consecutive years using the Actiwatch and Sleep Analysis software version 7.3. For explorative analysis the Nonparametric Circadian Rhythm Analysis (NPCRA) as suggested by van Someren et al. (1999) was performed in terms of a rolling 7 day analysis. Day

by day plots of raw data and sequence charts of NPCRA data were visually inspected. Furthermore the NPCRA data was correlated (Pearson) with paralleled regional daily weather data from German Meteorological Service (DWD: Deutscher Wetterdienst).

Results: Visual inspection of plotted raw data shows fluctuations in the day-night-relation of rest and activity. Relative amplitude of activity fluctuates in a seasonal manner recurring in both years. There is a high peak in spring and troughs in midsummer and winter. Degree of cloudiness, sunshine duration and air temperature correlate significantly with intradaily stability and interdaily variability of acitivity data.

Conclusions: The observation of seasonal fluctuation in long term activity data and their association with weather variables in this case should be tested in a bigger sample. An 'activity-forecast' in AD patients by seasonal and meteorological variables could provide compensation techniques for negative influences by artificial lighting and climatisation in the living environment.

Funding support: German ministery of economy FKZ 0319057L.

References:

1. van Someren, E. J., Swaab, D. F., Colenda, C. C., et al. Bright light therapy: improved sensitivity to its effects on res.t-activity rhythms in Alzheimer patients by application of nonparametric methods. Chronobiol Int 1999; 16: 505–518.

P1033

Subjective sleep, cognitive complaints and neuropsychological performances in healthy elderly subjects: the Proof cohort

M. SAINT MARTIN, E. SFORZA, C. THOMAS-ANTÉRION, J.-C. BARTHÉLÉMY and F. ROCHE

CHU and Faculty of Medicine of Saint-Etienne, Saint-Etienne, FR

Objectives: No extensive data are available on the association between sleep duration and sleep quality, sleep complaints and so-called age-related cognitive impairment in the elderly. The aim of this study was to examine whether subjective sleep estimation affects subjective and objective cognitive scores considering the effect of associate factors., such as, depression, anxiety and sleep medication.

Methods: Two hundred seventy-two elderly healthy volunteers aged 74.8 + 1.1 years were examined. All subjects filled in self-assessment questionnaires evaluating cognitive function (Mac Nair scale), anxiety (Goldberg scale), depression (Pichot questionnaire) and subjective sleep quality (Pittsburgh Sleep Quality Index, PSQI). Based on the total PSQI score, subjects were classified as good sleeper (GS, PSQI < 5, $n = 116$) and poor sleeper (PS, PSQI ≥ 5, $n = 156$). All participants underwent an extensive neuropsychological testing including the MMS, the Trail Making Test A & B, the Stroop verbal fluencies, the Benton visual retention test, the Grober and Buschké Selective Reminding Test, and the similarities and code (WAIS-III) test.

Results: The mean scores for subjective complaints were 6.6 ± 3.5 for the PSQI and 27.6 ± 12 for the McNair scale. Although the McNair score was related to the PSQI score, the degree of subjective cognitive complaints was mostly affected by the presence of anxiety and depression. No significant differences for objective cognitive performances were found between GS and PS except for the TMT-A, poor sleepers significantly less efficients. Hypnotics significantly affect the cognitive complaints (McNair) as well as the MMS, the Stroop and the TMT-A scores.

Conclusions: Subjective cognitive complaint depends on the level of anxiety and depression and hypnotic intake without significant effect of sleep quality and sleep duration. Considering objective cognitives scores, no significant differences were found between poor and good sleepers, except for the TMA-A speed. These results suggest that in healthy elderly subjects, subjective sleep quality and duration did not affect significantly subjective and objective cognitives performances, except the attention level, for that the interference of sleep medication should be considered.

P1034

Age-related changes in sleep and its associations with cognitive and emotional functioning in Hong Kong Chinese

J. H. Y. WAN, E. Y. Y. LAU and T. M. C. LEE

The University of Hong Kong, Hong Kong, HK

Objectives: The present study aims to investigate the relationships of sleep with age, cognitive functioning, and emotional functioning in healthy Chinese adults. We hypothesized that deteriorative change in sleep, namely poorer sleep quality, longer sleep latency, and shorter nocturnal sleep duration, would be observed upon normal ageing. Furthermore, we hypothesized that changes in sleep would be associated with cognitive and emotional functioning.

Methods: Forty-three healthy young adults (mean age = 23.30, SD = 1.67) and eighty-nine healthy elderly (mean age = 75.83, SD = 6.61) were recruited from the community and four local elderly community centres, respectively. A set of questionnaires, including the Pittsburgh Sleep Quality Inventory, the Epworth Sleepiness Scale, the Composite Scale of Morningness, and the Depression Anxiety Stress Scale, was used to assess sleep quality, daytime sleepiness, chronotype, and emotional functioning. A battery of neuropsychological tests was administered to examine different domains of cognitive functions.

Results: Present results revealed that the elderly group had shorter nocturnal sleep duration, lower sleep efficiency, and longer sleep latency compared to the young adults. On the other hand, the young adults experienced more daytime sleepiness compared to the elderly. In addition, most of the elderly were morningness type (67.4%), while the majority of the young adults were intermediate type (90.7%). Regarding the sleep-related difference in cognitive functioning, our data suggested that longer sleep latency was associated with poorer response inhibition in the elderly. Several sleep variables were correlated with emotional functioning. In the young adults, longer sleep duration and eveningness were associated with depressive symptoms, while poorer sleep quality and daytime sleepiness were correlated with anxiety symptoms. In the elderly, poor sleep quality was associated with symptoms of depression, anxiety, and stress. Daytime sleepiness was correlated with symptoms of anxiety in the elderly. Shorter sleep duration, longer sleep latency, and lower sleep efficiency were also correlated with depressive symptoms in the elderly.

Conclusions: Our results suggested changes in some aspects of sleep upon normal ageing. Longer sleep latency were associated with poorer executive functioning, namely response inhibition. The elderly also tended to experience more sleep problems in relation to mood states as compared to the young adults.

P1035

Sleep microstrutcure in patients with mild cognitive impairment

L. CARNICELLI[1], M. MAESTRI[1], G. TOGNONI[1], E. DI COSCIO[1], I. GHICOPOULOS[1], E. IACOPINI[1], N. T. CONOMOU[2], P. KTONAS[2], R. FERRI[3] AND E. BONANNI[1]

[1]Neurological Clinic-Department of Neurosciences, Pisa, IT, [2]Department of Psychiatry, Athens, GR, [3]IRCSS Oasi Maria SS, Troina, IT

Objective: Mild cognitive impairment (MCI) indicates an initial state in the process of developing dementia which is considered by some to be an early stage of dementia, especially of Alzheimer type. Only few works have focalized on sleep and its disorders, although recent evidences point out a role for sleep and in particular cyclic alternating pattern (CAP) in cognitive processes. Aim of our study was to evaluate sleep microstructural pattern in MCI patients (compared to normal aging and dementia) and to correlate it with cognitive performance.

Methods: Among 30 patients recruited, 12 subjects (7F, 5M; mean age 73 ± 4) completed the study, undergoing 48 h polysomnographic at home recording. Macrostructural and CAP pattern evaluation was based on standard international scoring criteria. A napping behaviour was found in 4 subjects. According to previous literature findings, sample was thus divided into two subgroups. Results were compared with 14 healthy controls and 20 demented patients, defined by a CDR score of 1 and both age-matched. An ANOVA test, considering the group (MCI versus controls and MCI versus AD, napping versus non napping) as independent variable was used. Macro and microstructural parameters were correlated to the scores obtained at the neuropsychological assessment.

Results: Macrostructural variables showed no statistically significant differences in MCI subjects compared to AD and controls, while a trend of decreasing CAP time and CAP rate in MCI subjects towards healthy controls with an increased number of A3 subtypes in MCI, whereas A1 subtypes appeared diminished. Macro and microstructural variables in napping patients showed reduced nocturnal slow wave sleep and A1 subtype. Correlations between microstructural variables and neuropsychological scores were pointed out.

Conclusions: The relations between sleep and learning have been extensively studied. Correlations between sleep microstructure and neuropsychological examination emphasize the association of A1 subtypes with a better cognitive function, while an increased number of A3 may predict worse performances both in normal subjects and in children with developing diseases. Sleeping alterations in MCI subjects, regarding both sleep parameters and sleep/wake cycle, may help in the differential diagnosis of cognitive impaired conditions and may be useful to define a prognosis for cognitive functioning.

P1036

Age-related differences in grey-matter intensity are correlated with memory consolidation and sleep spindles

F. ASSELIN[1], S. FOGEL[1], G. ALBOUY[1], C. VIEN[1], B. KING[1], R. HOGE[1], S. JBABDI[2], H. BENALI[3], A. KARNI[4], P. MAQUET[5], J. CARRIER[1] and J. DOYON[1]

[1]University of Montreal, Montreal, CA, [2]University of Oxford, Oxford, UK, [3]INSERM, Paris, FR, [4]University of Haifa, Haifa, IL, [5]University of Liège, Liège, BE

Objectives: Older persons exhibit normal MSL but not gains in performance (i.e. consolidation) following sleep. Sleep spindles are associated with activation of the striatum and the hippocampus (HPC); regions required for motor sequence learning (MSL) consolidation. Evidence from our laboratory indicates that age-related changes in spindles may be responsible for impaired MSL consolidation, but the morphological basis for this deficit is unknown. Thus, we hypothesized that grey matter (GM) intensity in structures that support MSL consolidation (e.g. striatum, HPC), would be correlated with gains in MSL and spindles in young (Y) but not older (O) subjects.

Methods: Groups of 13 years (20–35 years) and 13 O subjects (55–70 years) were trained on a MSL task (five-items, 12 sequences/block, 14 blocks/session) before and after a 90-min daytime nap. Structural T1-weighted images were acquired using magnetic resonance imaging with a 3D-MPRAGE sequence at a resolution of 1.3 mm. Voxel-based morphometry was performed on GM segmented images that were non-linearly registered to a study-specific template. Permutation-based tests were run on a threshold-free cluster enhancement-based procedure using a region of interest approach for areas involved in MSL consolidation: the HPC, striatal-cortical and cerebellar-cortical networks. Peak cluster values for t-tests (Y>O, O>Y) were thresholded using uncorrected *P*-values ($P < 0.002$, cluster > 5 voxels).

Results: Greater GM intensity in the Y>O contrast was correlated with MSL gains following a daytime nap in the supramarginal gyrus (BA 40; $P = 0.001$), SMA ($P < 0.005$), HPC ($P = 0.001$) and somatosensory cortices ($P = 0.003$). Greater GM intensity in the O>Y contrast was correlated with MSL gains in the precuneus ($P < 0.005$). Greater GM intensity in the Y>O contrast was correlated with spindle density (#/min) in the HPC ($P < 0.006$), caudate nucleus ($P = 0.008$), SMA ($P = 0.002$), BA 40 ($P < 0.003$) and the precuneus ($P < 0.002$). Greater GM intensity was correlated with spindles in the O>Y contrast in the SMA ($P < 0.007$).

Conclusions: The preliminary results of present study suggest that spindles are associated with age-related differences in GM intensity in the striatal-cortical (SC) network and HPC in Y but not O individuals. This is in line with previous work showing that sleep-dependent gains in MSL are related to increased functional activation of the SC network and HPC. Thus, morphological differences in GM correlated with sleep spindles may underlie age-related MSL consolidation deficits.

P1037

Sleep in frontotemporal dementia

A. BONAKIS[1], N. T. ECONOMOU[2], T. PAPARRIGOPOULOS[2], E. VAGIAKIS[1], P. KTONAS[2] and S. G. PAPAGEORGIOU[2]

[1]Evangelismos Hospital, Athens, GR, [2]University of Athens, Athens, GR

Objective: In contrast to other neurodegenerative diseases, such as Alzheimer's disease (AD), sleep in frontotemporal dementia (FTD) has been poorly studied. Although some evidence exists that sleep-wake disturbances occur, little is known regarding sleep macrostructure and data on the presence of primary sleep disorders are lacking. The objective of the present study was to thoroughly investigate these issues in this population.

Methods: Twelve drug-naive behavioral-variant FTD (bvFTD) patients (7M/5F) of mean age 61.0 ± 7 years were compared with twelve drug-naive AD patients (7M/5F) of mean age 64.5 ± 8 years ($P = 0.304$). Both groups were fully clinically assessed through a sleep interview and sleep inventories; also, one-night video-polysomnography recordings were performed in all patients.

Results: The two groups were comparable in terms of cognitive impairment and AD patients had a significantly longer duration of disease compared with FTD patients ($P = 0.053$). Sleep complaints did not differ between groups, although FTD patients reported more often daytime sleepiness. Primary sleep disorders (obstructive sleep apnea syndrome, periodic leg movements) equally occurred in the two groups. Sleep parameters and sleep macrostructure were better preserved in AD versus FTD patients (e.g., delayed sleep onset in 50% of FTD versus 16.5% of AD patients, reduced sleep efficiency in 66.5% of FTD versus 33% of AD patients, increased sleep latencies in FTD patients). This more disturbed sleep pattern in FTD than AD patients was apparent even after controlling for primary sleep disorders.

Conclusions: In a relatively small sample of FTD patients several sleep parameters were found to be similarly and sometimes even more affected by degeneration than in AD patients, in a much shorter time span. These findings, unrelated to primary sleep disorders, probably indicate a centrally originating dysregulation. Since in FTD patients sleep disturbances are obvious from an early stage of their disease, and considerably earlier than in AD patients, physicians and caregivers should be alert for the early detection and treatment of these symptoms.

P1038

Medication use and its relation to measures on sleep, pain, depression and anxiety in older chronic pain patients

T. BLÅGESTAD[1], S. PALLESEN[1], L. LUNDE[1], B. SIVERTSEN[2], I. H. NORDHUS[1] and J. GRØNLI[1]

[1]University of Bergen, Bergen, NO, [2]Norwegian Institute of Public Health, Bergen, NO

Objective: Sleep problems are common in older chronic pain patients, but little is known about the effects of medication use on the sleep-pain interaction. Studies on chronic pain patients do rarely have discontinuation of medication use as an inclusion criteria, hence data are influenced both by pain and medications. The present study explores whether the use of hypnotics, analgesics, antidepressants and anxiolytics are related to measures on sleep problems, pain, depression and anxiety, respectively, in older chronic pain patients.

Methods: The present study includes 24 older subjects with chronic pain (mean age 67.7 years). Subjective measures include sleep problems (Pittsburgh Sleep Quality Index), pain problems (McGill Pain Questionnaire), and the presence of depression (Beck Depression Inventory) and anxiety (State-Trait Anxiety Inventory) in addition to reported medication use. ANOVA and T-test for independent groups were applied to investigate relations between medication use and subjective parameters. For variables not meeting approximate normal distribution, Mann–Whitney U test and Kruskall-Wallis tests were used. The level of statistical significance was set to 0.05.

Results: The prevalence of the use of hypnotics was 50%, a use related to increasing age (U = 28.500, $P = 0.011$) and more sleep problems (F = 5.397, $P = 0.0.31$). A trend was found for lower scores on pain, however not significant. The prevalence of the use of at least one form of analgesics was 83.3%, while 46.8% used two analgesics or more. The use of pain medication was related to higher scores on depression (F = 5.043, $P = 0.009$), anxiety (H = 10.21, $P = 0.017$), and showed a trend towards relating to decreasing age and duration of the pain condition. Only 8.3% of the older chronic pain patients used anti-depressants, but the use was related to higher scores on depression (F = 4.367, $P = 0.048$). Anxiolytics was used by 12.5%, but the use was unrelated to any of the outcome variables.

Conclusions: The use of hypnotics and anti-depressants was related to their respective targeted problems. The use of hypnotics showed an almost inverse relationship with pain, which might suggest a positive effect of better sleep on pain. The use of pain medications was unrelated to subjective pain scores, which might suggest adequate pain managing. Further studies are needed to elucidate the sleep-pain interaction in relation to its subsequent medication use.

P1039

Zolpidem modifies EEG power spectra in aged subjects

M.-L. BOCCA[1], P. CLOCHON[1], F. BERTRAN[2], C. COUQUE[2], T. DESFEMMES[2], F. DOIDY[1], J.-N. AMATO[1], S. MARIE[1], B. LEGLINEL[1] and P. DENISE[1]

[1]INSERM, Caen, FR, [2]CHU de Caen, Caen, FR

Zolpidem (Zp) is actually in most countries the most prescribed hypnotic. The purpose of this work was to study the effects of Zp on sleep stages and spectral analysis in the context of an evaluation of the residual effects on driving performance in aged subjects.

Thirty two healthy older middle-aged subjects (55–65 years) were included in this balanced, double-blind study. The medication, Zp 10 mg or a placebo was administered at 11.00 pm at each subject's home under the supervision of an experimenter. The subjects went to bed within the next 15 min, and sleep was recorded using polysomnography (PSG) ambulatory monitoring (Medatec Dream). Sleep stages were visually scored according to standard criteria by experienced clinicians. The analyses were performed for the whole, the first and second part of the night for both the architecture and spectrum analysis by FFT. The EEG power density in the range of 1–30 Hz was calculated for all electrodes (FP1, FP2, C3, C4, T3, T4, O1, O2). The parameters used were the relative power (PSD) and the centroid frequency (CF) for delta, theta, alpha and beta band. Only significant results ($P < 0.05$) were presented below.

For the whole and the first half-night, compared to placebo, Zp increased the sleep efficiency and the SWS and decreased the number of awakenings and the REM. Although no significant modifications on sleep stages durations were observed in the second half-night of the sleep, spectral analysis revealed sleep EEG modifications on all electrodes. During SWS, a decrease of the PSD in the theta range was found. During REM sleep, in the alpha range, the PSD was decreased and the CF was increased.

These results indicated that the spectral analysis was able to reveal modifications of the sleep after Zp intake which was not the case with sleep stages analysis. These modifications may explain the impaired driving performance observed in the morning and described in Bocca et al. (2011).

P1040

Effects of light supplementation on mood, alertness and rest-activity rhythms in older people living in care homes

P. L. MORGAN[1], S. HOPKINS[1], L. J. M. SCHLANGEN[2], D. J. SKENE[1] and B. MIDDLETON[1]

[1]University of Surrey, Guildford, UK, [2]Philips Research, Eindhoven, NL

Objectives: The aim of the study was to increase the light exposure in older people living in care homes and to investigate the effect of increasing lighting levels (blue-enriched white light) on their mood, alertness and rest-activity rhythms.

Methods: Supplementary overhead fluorescent (blue-enriched 17 000 K–1000 lux or control 4000 K–200 lux) white lighting was

administered (08:00–22:00 h) in selected communal rooms of 7 care homes in south-east England. The 12-week study consisted of 1 week baseline, 4 weeks each light condition separated by 3 weeks washout (original care home lights) in a randomised cross-over design. Non-demented residents (n = 80), aged 86 ± 8 years, completed a variety of questionnaires (Karolinska Sleepiness Scale, 9 point mood/alertness scales, Hospital Anxiety and Depression scale, Mini Mental State Exam, Geriatric Depression Scale, Pittsburgh Sleep Quality Index), Psychomotor Vigilance task and/or wore activity and light monitors (AWL) continuously. Rest-activity rhythms were assessed by cosinor and NPCRA analysis. The time spent in light above 100, 500, 1000 and 2000 lux was assessed in all light conditions. Comparison of light conditions (17 000 versus 4000 K) was conducted with a subject n ranging from 63 to 17 (repeated measures model, covariates: age, mobility, medication and light exposure (% time in lights (observational data) for Model 1 or time spent in light above 100 lux (AWL data) for Model 2).

Results: The time that participants spent in light levels >100, >500 and >1000 lux was significantly higher ($P < 0.001$) during the 17 000 K light condition (170 ± 19, 57 ± 10, 23 ± 5 min/day, mean ± SEM) compared to washout (87 ± 14, 16 ± 4, 6 ± 2) and the 4000 K light condition [107 ± 15 (not significant), 15 ± 4, 6 ± 2]. Compared to control 4000 K lighting, blue-enriched 17 000 K lighting significantly advanced the rest-activity rhythm (cosinor, $P = 0.04$), increased daytime activity (NPCRA M10 Model 2, $P = 0.03$), increased nighttime activity (NPCRA L5, $P = 0.04$), reduced subjective anxiety (HAD, $P = 0.004$) and reduced sleep quality (PSQI, $P = 0.004$) of the participants.

Conclusions: Increasing the light levels in selected communal rooms significantly increased the time that residents spent in moderate to bright light conditions. The results show both positive and negative effects of blue-enriched white light supplementation.

Supported by the Cross-Council New Dynamics of Ageing (NDA) initiative (Grant number RES-339-25-0009) and Philips Lighting (The Netherlands)