



# Behavioral measurement of interhemispheric interactions during multiple episodes of falling asleep

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**Abstract** Studies of hemispheric asymmetry in humans during sleep and falling asleep give contradictory results—there is evidence of the dominance of both the right and left hemispheres when falling asleep. Such a discrepancy in the results may be due to both the high heterogeneity of asymmetry patterns and the difficulty of ensuring homogeneous experimental conditions in neurophysiological testing. 102 healthy participants repeatedly performed a monotonous bimanual psychomotor test at home. 227 trials were selected for analysis. We extracted sequences of microsleep episodes, indicating which hand executed motor activity last before falling asleep, and calculated various complexity measures (Shannon entropy, ordinary/normalized Lempel–Ziv complexity, ordinary/conditional permutation entropy, Petrosyan dimension). After clustering the data, the extracted clusters were pairwise compared according to the indicators of the psychomotor test (total tap number, number of sleep episodes, total sleep duration, inter-tap interval). We obtained four clusters based on the complexity measures estimates. They are characterized by similar psychomotor characteristics of the research participants. The third cluster is of the greatest interest, characterized by the absence of “global” asymmetry (i.e., without a clearly expressed dominance of one of the hands), high drowsiness level and the existence of temporary hand dominances for relatively short time intervals. The results indicate against the existence of a pronounced hemispheric asymmetry when falling asleep, while at the same time testifying to the existence of short-term hand dominance episodes, possibly due to the local dynamics of functional connectivity during the wake–sleep transition.

## 1 Introduction

In the last 2 decades, new evidence has emerged indicating that both sleep and wake are regulated locally and that sleep and wake-like activities can often co-occur across distinct brain areas [1]. The most dramatic examples of such local states are “mixed states” occurring as unihemispheric and asymmetric sleep, when one cerebral hemisphere exhibits low-amplitude high-frequency EEG activity, whereas the other simultaneously shows high-amplitude slow waves. Unihemispheric sleep [2] is prevalent in migrating birds [3] and marine mammals [4] and provides important insights into the function and evolution of local brain states. Regional NREM sleep often occurs with one eye open, enabling birds to visually monitor their environment for predators and continuously control their flight and supports residual swimming in dolphins for intermittent breathing.

Mixed states have also been observed in humans [5] for example during the first night of sleep in an unfamiliar environment, when sleepers exhibit inter-hemispheric asymmetry in their NREM slow-wave activity (SWA) [6, 7].

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Behavioral lapses (delayed responses or errors of omission), a hallmark of sleep deprivation, are often brief ( $< 1$  s), and their detection requires special tests such as the psychomotor vigilance task [8]. Similarly, the gamut of electrophysiological changes associated with high sleep pressure, including microsleeps [9], local "neuronal lapses" [10] and local sleep-like oscillations with OFF periods [11]. In such cases, different regions exhibit state switches at different times [12] as is often the case in the hippocampus and neocortex [13]. These oscillations may be analogous to the human somatosensory mu rhythm that disappears with movement, reflecting intermittent "idle" states in wakefulness [14].

Another approach to the study of hemispheric lateralization during sleep is presented in the works of Casagrande et al. [15–17]. Based on behavioral indicators and EEG, a change in lateralization patterns was shown during the wake–sleep transition; the left hemisphere "falls asleep" faster, leaving control to the right hemisphere which falls asleep last and wakes up first. These works are devoted to the study of motor and partially cognitive functions of volunteers before falling asleep. Casagrande concludes that the nature of lateralization changes during the transition to sleep: a task of maintaining alertness and awareness of the environment moves from the left to the right hemisphere, which supports the hypothesis of two vigilance systems [18]. However, the results described in these papers, despite their statistical significance, have a relatively high variance (especially for latency— $385.26 \pm 376.12$  s for the left hemisphere and  $399.90 \pm 386.36$  s for the right hemisphere) and are found in a relatively small sample (27 participants).

Such contradictions may indicate the presence of pronounced heterogeneity of interhemispheric interactions during the transition to sleep. To assess this heterogeneity, we used a bimanual monotonous psychomotor test, previously proposed in the works of Dorokhov et al. [19–22], which allows us to observe multiple episodes of falling asleep and spontaneous awakening during 1 h of the trial. We used a version of this test adapted as the Android mobile application [23], which made it possible to conduct research in familiar home conditions. In addition, it allowed us to perform a significant number of trials and, accordingly, to conduct an adequate statistical analysis of the results.

During this psychomotor a volunteer taps on Bluetooth-connected buttons alternately with their left and right hands. The motor activity of the left/right hands corresponds to the cross-activation of the right/left hemispheres of the human brain, as is well known and shown today, for example, in [24].

The performance of this psychomotor test makes it possible to behaviorally quantify the episodes of falling asleep/waking up for each trial and observe the possible dynamics of the change of lateralization. To analyze complex dynamical sequences of button taps, we used methods of complexity science, a theoretical and methodological approach based on the ideas and methods of nonlinear physics, dynamical systems theory, fractal geometry, information theory and a number of other areas related to the analysis of complex multicomponent systems with nontrivial patterns of interactions [25]. Today, the notion that the brain can be described as a complex multicomponent self-organizing system is the mainstream of interdisciplinary neuroscience. The use of complexity science approaches allows us to assess the complexity of the measured patterns of behavior and physiological indicators, and, accordingly, to quantify the global characteristics of the state of the studied organism. There are many indicators that emphasize different aspects of "complexity"—in terms of (non)regularity of the signal, temporal (non)predictability, characteristics of the reconstructed state space of the system, variability of dynamics depending on the scale of measurement, and much more [26, 27]. These indicators are also used in sleep studies to assess a person's condition during the transition to sleep and staying in various stages of sleep [28].

These methods are very useful and can be adapted for analyzing the information obtained as a result of our psychomotor test. In addition to assessing the degree of lateralization (i.e., the predominance of falling asleep when a specific hemisphere is activated) in a particular subject, we can also assess the possible variability of lateralization change patterns during the study.

## 2 Methods

All procedures performed in this nap study of human participants were in accordance with the ethical standards of the 1964 Helsinki Declaration and its later amendments, and in accordance with the ethical standards of the institutional research committee. The study was approved by the Ethics Committee of the Institute of Higher Nervous Activity and Neurophysiology of the Russian Academy of Sciences (Protocol No. 2 of June 3, 2019). The study participants were informed in detail about all procedures, and informed written consent was obtained from each participant.

### 2.1 Participants

73 medical students (58 female and 15 male, mean age = 19.5 years, SD = 1.5) participated in the study. The participants reported no history of psychiatric/neurological conditions and no diagnosed sleep disorders at the study period.

Each participant filled in a modified version of Annett Hand Preference Questionnaire [29], adapted in Russian by Chuprikov [30]. It consists of 12 items, describing situations of hand usage (“Which hand do you hold a toothbrush with?”), which are scored on a 5-point Likert scale ranging from  $-2$  (“Always left”) to  $2$  (“Always right”). The scores are summed resulting in a scale ranging from  $-24$  to  $24$ , where values ranging from  $-8$  to  $8$  indicate no clear hand preference (ambidexterity), lower negative values indicate a left-hand preference, higher positive values indicate a right-hand preference. For this study we picked only participants with a right-hand preference to eliminate a possible confound (test score  $> = 9$ ).

## 2.2 Study protocol

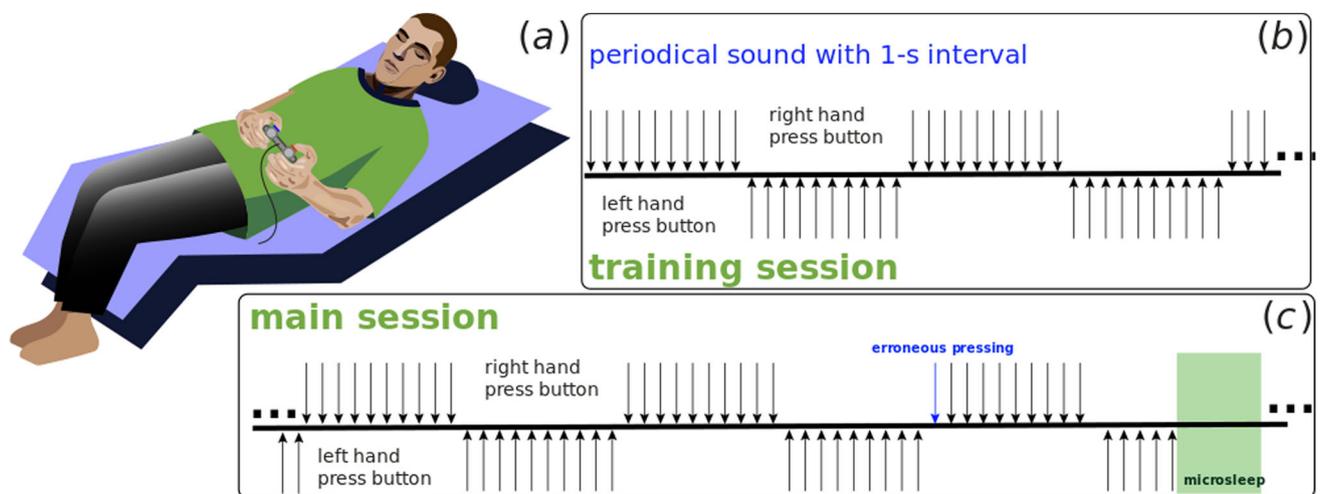
Each participant installed a mobile application on their smartphone and received two Bluetooth buttons. In the application, the participant entered basic information about themselves (name, gender, birthdate, city and university) and completed the Epworth Sleepiness Scale [31] to assess the level of daytime sleepiness (mean = 10.2, SD = 4.89). In addition, before each trial, the participant completed the Karolinska Sleepiness Scale [32] to assess the current sleepiness level (mean = 4.84, SD = 1.83).

The basic setup and design of a study trial is schematically presented in Fig. 1 and further elaborated upon later in the text.

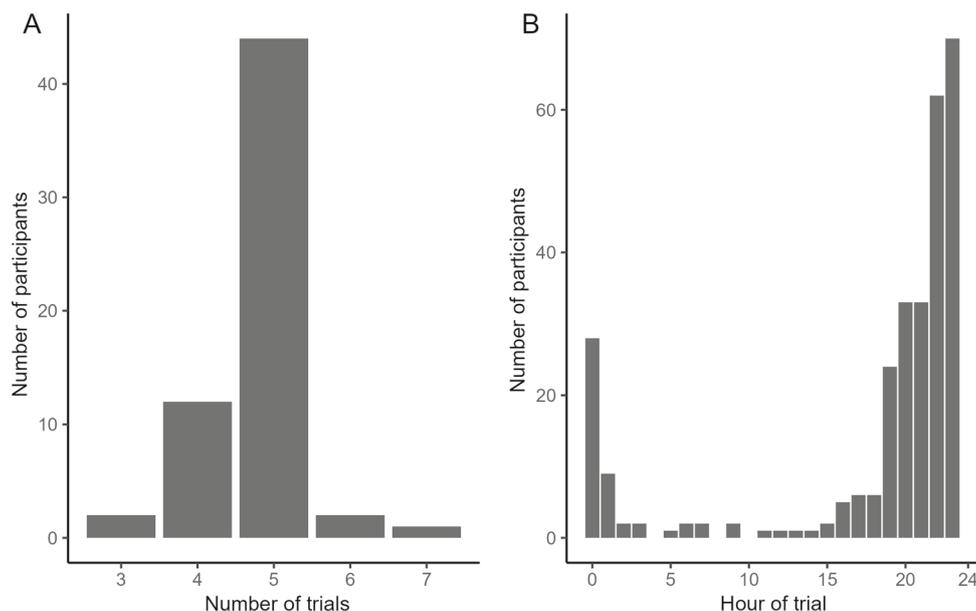
The participants were instructed to conduct the study in a quiet isolated room, take a comfortable horizontal position, put on headphones or turn on the phone at maximum volume for better audibility of the wake-up signal. Each participant attempted 3–7 trials of the study; the distribution of successfully completed trials across participants and the hours during which these trials were attempted are shown in Fig. 2.

Each trial lasted 60 min, during which the participant had to keep their eyes closed and to silently count from 1 to 10 with a frequency of approximately 1 time per second, simultaneously tapping the button 10 times with his right and left hand alternately. If the participant did not tap the buttons for 2 min, the software application on the smartphone generated a sound signal for the subject to wake up and continue the test. If the participant did not resume pressing after the signal, it was repeated every 10 s. An example of several trials for one participant is shown in Fig. 3. After an hour, the study was automatically finished, and a report with the results was sent to a remote server.

The exclusion criteria at this part of the study were: no ID in the reports; the total length of one trial attempt is less than 50 min; there was no message about the termination of the trial; the duration of a separate no-taps episode exceeded half an hour (since we conducted trials remotely, it was impossible to determine whether the participant fell asleep or just put the phone away); the participant violated the instructions throughout the time of the trial.



**Fig. 1** **A** A schematic illustration of a participant position during the study trials, **B** an illustration of a training session before each trial. All participants were instructed to tap buttons in accordance with periodical sound appearing at 1-s intervals—10 times with each hand alternately. Each arrow signifies a single tap; the direction and position of arrows signifies the hand which tapped the button (left or right). **C** An illustration of a main trial session. There were no periodical sounds during this sessions—each participant had to tap buttons approximately 1 tap per second without external hints. The colored arrow signifies an erroneous button tap—during the trial the fatigued participant can miscount the number of needed taps which could also represent the microsleep onset. The green rectangle signifies the microsleep episode—a time period without any buttons pressed



**Fig. 2** **A** A distribution of number of trials attempted by a single participant. **B** A distribution of day times during which the participants undertook the study trials. This figure was created using ggplot2 v3.4.2 R package [33]

For each subject, the onsets of microsleep ( $T_s$ ) and the duration  $\Delta T_s$  of microsleep episodes were determined. It was also determined which hand made the last tap before the onset of the microsleep episode (“fell asleep last”). The criterion of “microsleep” was the absence of taps for more than 10 s. An example of such sequences is shown in Fig. 4.

For the final analysis, we considered only sequences of 10 or more microsleep episodes. Consequently, only 191 trial was used in subsequent computations.

### 2.3 Complexity estimation

Each sequence of microsleeps during this psychomotor test was represented as a binary set of numbers (0, 1, 0, 0 ...), where 0 is the left hand and 1 is the right hand. These sequences can be characteristic of the test subject’s state during a psychomotor test and be the measure of their drowsiness. To quantitatively evaluate the features of these sequences, we calculated several information complexity measures.

First of all, we estimated “classical” Shannon entropy [35] according to

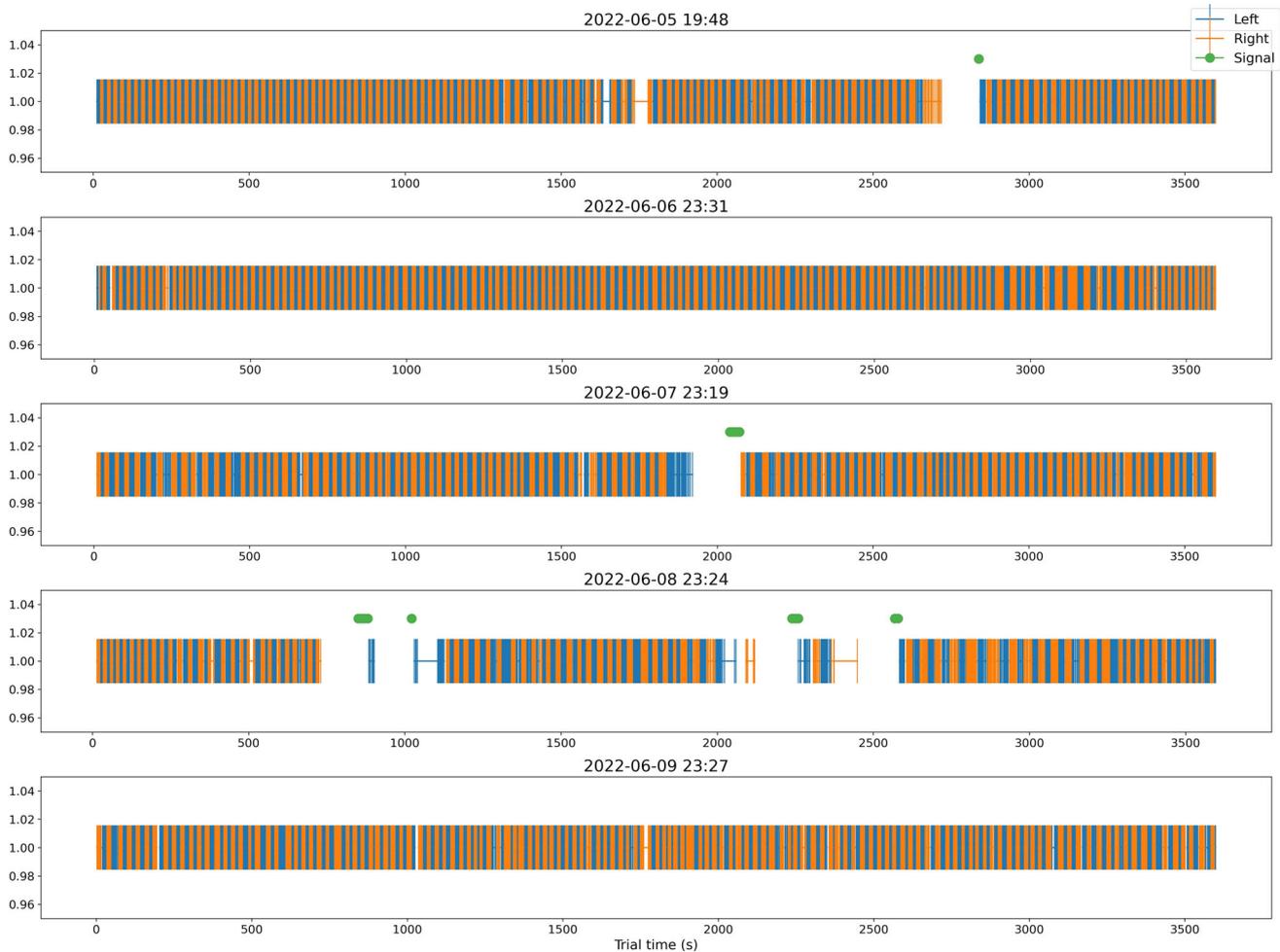
$$H(X) = - \sum_x P(x) \log_2(P(x)),$$

where  $x$  is the event,  $P(x)$  is the probability of that event,  $X$  is the set of all considered events. For a binary sequence, this measure tends to 0 if one value appears more often than another, and tends to 1 if both values are equally probable. For example, the sequences 00000000 and 11111111, corresponding to left-hand or right-hand taps only, have zero entropy—and the sequence 01000111 has entropy equal to one (since both the left and right hand occur equally often). Thus, the Shannon entropy in the context of this psychomotor test was considered as an indicator of hand symmetry.

After that we calculated the Lempel–Ziv complexity [36], which provides information about the number of unique patterns within the entire duration of the sequence viewed from left to right. For example, the sequence 01000111 contains 5 patterns—0, 1, 00, 01, 11. Since the Lempel–Ziv complexity is extremely dependent on the length of the analyzed sequence, we also calculated normalized Lempel–Ziv complexity [37] using the following formula:

$$LZn = \frac{LZ}{n \div \log_2(n)},$$

where LZ is the ordinary Lempel–Ziv complexity,  $n$  is the total length of analyzed sequence. Thus, both indicators reflect the degree of diversity of hand patterns in falling asleep.



**Fig. 3** A graph of taps from one subject during five trials (row wise). The time is represented along the  $x$ -axis. Orange vertical lines are right hand taps, blue are left hand taps, empty spaces represent absence of taps (microsleep, less than 2 min) green dots represent wake-up sounds (if there were no taps for more than 2 min). This figure was created using matplotlib v3.7.1 Python library [34]

Permutation entropy [38] was estimated according to

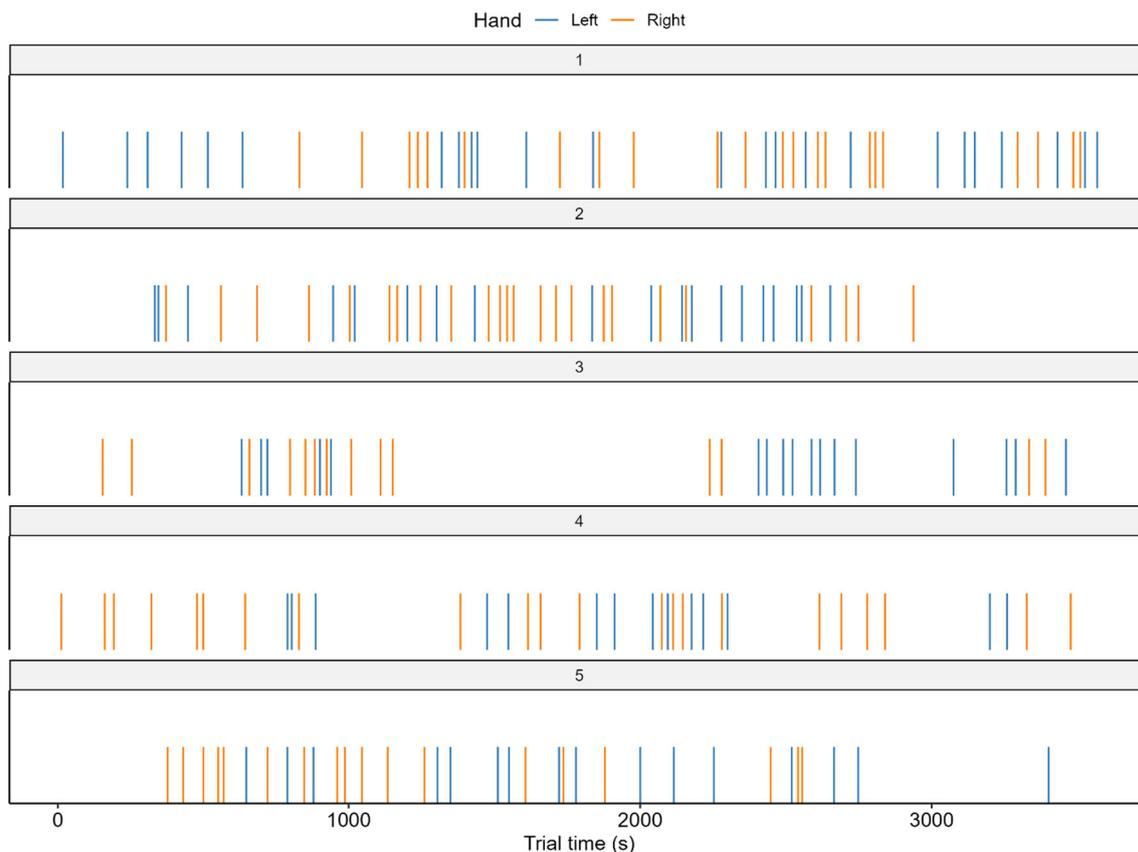
$$H(X) = - \sum_{\pi} P(\pi) \log_2(P(\pi)),$$

where  $\pi$  is an ordinal pattern consisting of three symbols. Evaluation of the sequence complexity using permutation entropy is performed as follows: every three consecutive values are sorted in ascending order, after which their order in the original sequence is determined. For example, the sequence 01000111 contains patterns 010, 100, 000, 001, 011, 111, which, when sorted, turn into patterns 021, 201, 012, 012, 012, 012. Accordingly, the higher the diversity of these ordinal patterns, the higher the entropy value.

Additionally, we estimated conditional permutation entropy [39], which represents a diversity of ordinal patterns following other ordinal patterns. Thus, the permutation entropies reflect the variability of hand switching in repeated microsleeps.

Finally, we estimated Petrosian fractal dimension [40] using the following formula:

$$P = \frac{\log_{10}(N)}{\log_{10}(N) + \log_{10}(\frac{N}{N+0.4N_{\delta}})},$$



**Fig. 4** Sequences of falling asleep with each hand from one subject during five trials (row wise). The time is represented along the  $x$ -axis. Each vertical line indicates a microsleep episode. The blue vertical lines represent the left hand, the orange vertical lines represent the right hand. This figure was created using ggplot2 v3.4.2 R package [33]

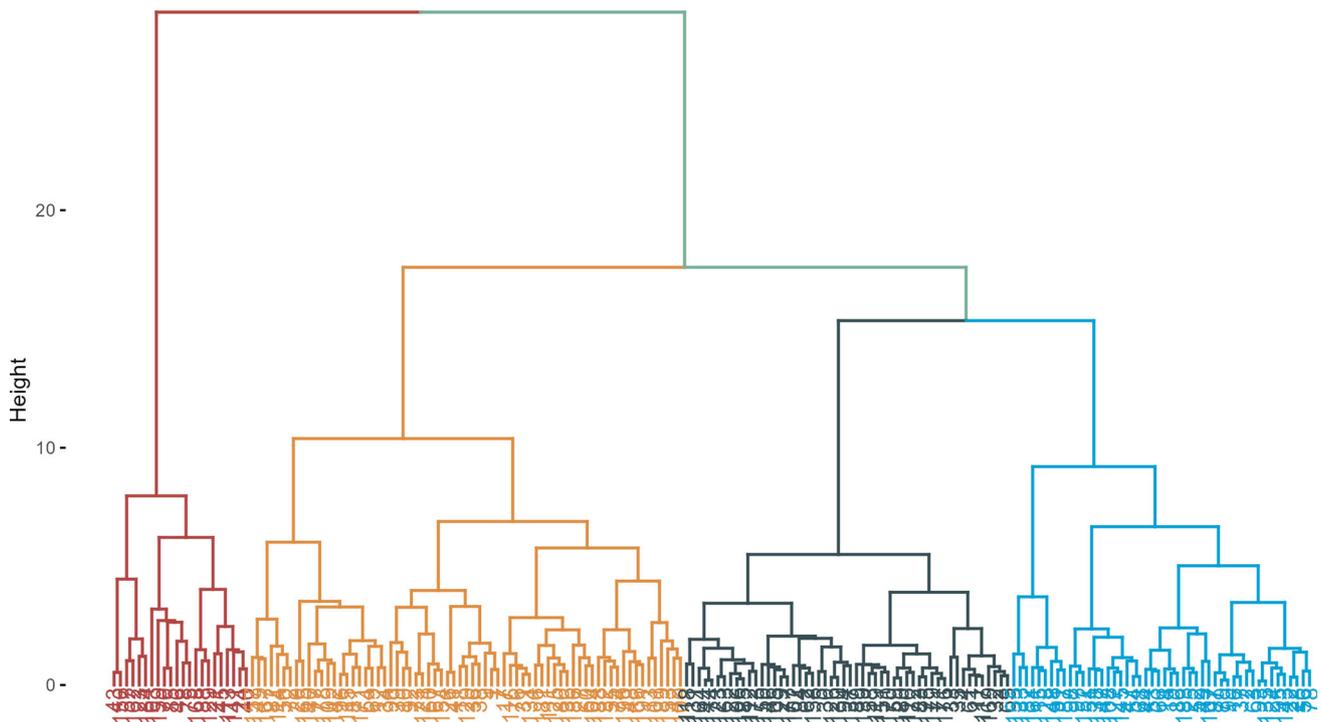
where  $N$  is the sequence length,  $N_\delta$  is the number of zero crossings (when 0 switches to 1 and vice versa). Basically this measures the frequency of hand switching relative to the length of the entire sequence, growing with increasing frequency.

The calculations were performed using the Python v3.8.16 programming language, specifically Antropy v0.1.5 [41] and NeuroKit2 v0.2.4 [42] libraries.

## 2.4 Statistical analysis

Statistical data analysis was carried out using the R v4.3.0 programming language. We used several packages and meta-packages—specifically tidyverse v2.0.0 (data reading and preparation), ggplot2 v3.4.2 (data visualization) and easystats v0.6.0 (analysis and result evaluation) [43, 44]. We also used lme4 v1.1–33 [45] for model estimation. Measures of information complexity (Shannon entropy, ordinary and normalized Lempel–Ziv complexity, ordinary and conditional permutation entropy, Petrosian fractal dimension) were  $z$ -standardized across the sample and subjected to hierarchical cluster analysis using the *cluster\_analysis* function—Ward’s algorithm was used [46], differences between observations were estimated using Euclidean norm. We selected minimum number of clusters in which the intercluster variance exceeded the intracluster variance; the estimation of these variances was carried out using the *cluster\_performance* function. The resulting dendrogram is shown in Fig. 5.

We additionally compared the obtained clusters according to the psychomotor test indicators reflecting the sleepiness of the test subject (total tap number, total number of microsleep episodes, total sleep duration, mean inter-tap interval). Differences between clusters and their statistical significance were estimated using a mixed-effects general linear model [48] using  $\alpha = 0.05$ ; the subject’s ID was used as a random effect to account for intra-individual variability. All the resulting  $p$  values were adjusted for multiple comparisons using the Holm correction [49].



**Fig. 5** A dendrogram of clustered data. The selected clusters are marked with different colors. This figure was created using ggplot2 v3.4.2 R package [33] and factoextra 1.0.7 R package [47]

### 3 Results

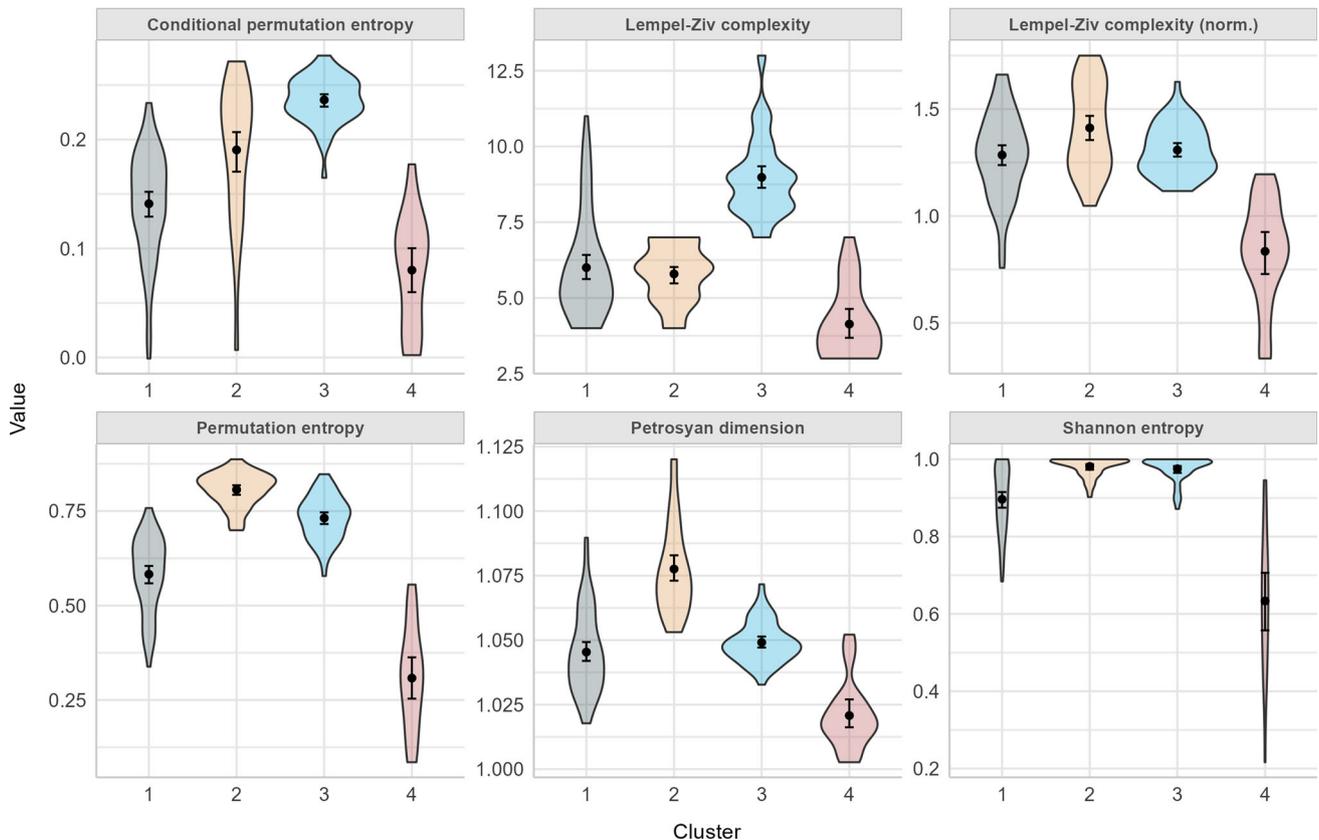
Analysis of all trials allowed us to obtain 4 clusters with the following characteristics:

- Cluster 1—69 observations. The asymmetry is slightly pronounced—some Shannon entropy values are considerably lower than 1. Relative to the other groups, the complexity measures are relatively low, but not the lowest of the whole set. The asymmetry is not pronounced—Shannon entropy is close to 1.
- Cluster 2—48 observations. The asymmetry is not pronounced—Shannon entropy is close to 1. In addition, the highest values of all complexity measures are observed, except for the “ordinary” Lempel–Ziv complexity and conditional permutation entropy.
- Cluster 3—52 observations. The asymmetry is not pronounced. It has the highest “ordinary” Lempel–Ziv complexity and conditional permutation entropy.
- Cluster 4—22 observations. The most pronounced asymmetry and the lowest complexity measures.

These results are presented visually in Fig. 6.

Based on psychomotor test indicators, we observed these differences between clusters:

- Cluster 1—the “average” values of the psychomotor indicators: 2586 total taps, 22 microsleep episodes, 19 min of sleep, the inter-tap interval is 1151 ms.
- Cluster 2—the number of microsleep episodes is slightly lower than in first cluster (18 microsleep episodes,  $p = 0.049$ ), the other measures do not differ significantly: 2623 total taps, 19 min of sleep, the inter-tap interval is 1141 ms.
- Cluster 3—on average, the lowest total tap number is observed relative to other clusters (2019 taps, the largest  $p = 0.039$ ), the largest number of microsleep episodes (35 episodes, the largest  $p < 0.001$ ), the largest total sleep duration relative to clusters 1 and 4 (24 min,  $p = 0.022$  against cluster 1,  $p = 0.005$  against cluster 4). The cluster also has the largest inter-tap interval, but the difference is not statistically significant (1194 ms,  $p = 1.0$ ).
- Cluster 4—on average, there are more microsleep episodes than in cluster 2 (24 episodes,  $p < 0.039$  relative to both clusters). At the same time, the total sleep duration and the inter-tap interval do not statistically significantly differ from clusters 1 and 2, and the total tap number is the highest and statistically significantly differs from cluster 1 (3211 clicks,  $p = 0.039$ ).



**Fig. 6** The distributions of complexity measures in each of the four clusters (represented as truncated violin plots), as well as their average values with 95% confidence intervals (represented as dots with whiskers). Cluster numbers are represented along the  $x$ -axes, and values of a specific measure are represented along the  $y$ -axes. Confidence intervals were constructed using the bias-corrected and accelerated bootstrap [50]. This figure was created using ggplot2 v3.4.2 R package [33]

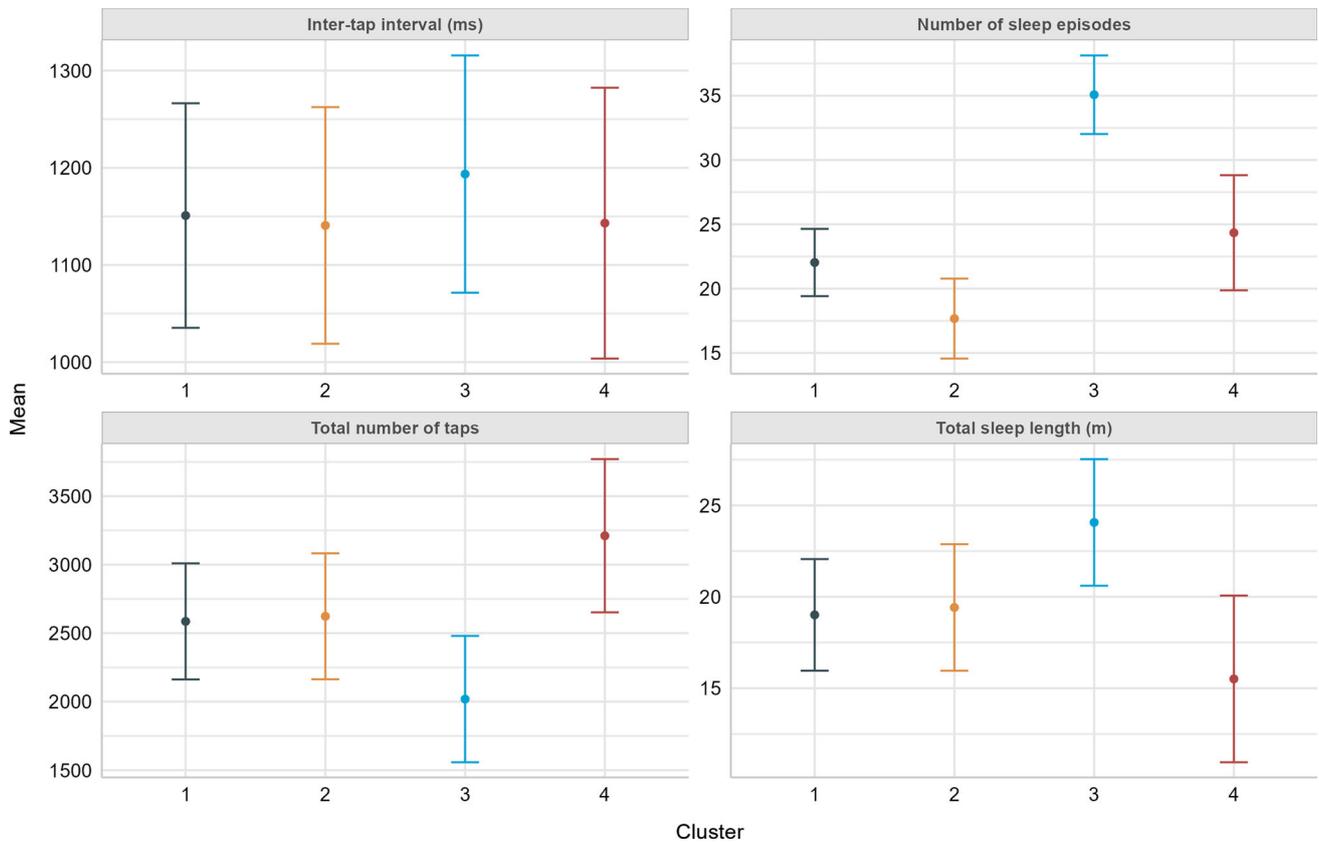
These differences are presented visually in Fig. 7. Also, the full results of pairwise comparisons for each indicator are presented in Table 1.

The Param column contains the names of indicators: the total tap number (Taps), the total number of microsleep episodes (Sleeps), the total sleep length (Sl. len) and the mean interval between taps (ITT). The remaining columns are as follows: Groups—the clusters being compared, Diff—the difference in means between clusters, CI (95%)—the lower and upper bounds of the 95% confidence interval of the difference in means, SE—standard error,  $df$ —degrees of freedom,  $t$ — $t$  statistic,  $p$ — $p$  value. The pairs of comparisons for which the  $p$ -value turned out to be  $< 0.05$  are highlighted in red. The comparisons were carried out using the `estimate_contrasts()` function from the `modelbased` v0.8.6 R package [51] belonging to the `easystats` ecosystem. This table was created using `flextable` v0.9.1 R package [52].

The performed analysis is based on the use of two independent approaches—clustering according to the information complexity measures of lateralization processes during falling asleep and the indicators of psychomotor test. Such multidimensional modeling allowed us to observe that the initial clusters demonstrate significantly different characteristics both in lateralization of psychomotor processes and, accordingly, in hemispheric activity, and in behavioral parameters. For brevity, the resulting clusters can be named as “average” (cluster 1), “alternating” (cluster 2), “sleepy” (cluster 3) and “predictable” (cluster 4).

## 4 Discussion

During the analysis of microsleep data, we obtained 4 clusters with different complexity profiles and mean psychomotor indicators. Based on these measures, we were able to assess the asymmetry in two different ways: as a global phenomenon (the general tendency to the dominance of a particular hemisphere before falling asleep) and as a local phenomenon (the dominance of a particular hemisphere at a particular time).



**Fig. 7** Estimated marginal means for each psychomotor test indicator in each group with 95% confidence intervals. The *estimate\_means()* function from the modelbased v0.8.6 R package [51] belonging to the easystats ecosystem was used for the estimation. This figure was created using ggplot2 v3.4.2 R package [33]

To explain the difference between “global” and “local” asymmetry, it is useful to consider the following sequences of falling asleep: “left–left–left–left–left–left”, “left–left–left–right–right–right”, “left–right–left–right–left–right”. In the first case, we see a situation where the left hand is the last to fall asleep six times in a row—this is a “global” asymmetry, showing the dominance of a particular hand/hemisphere throughout the recording. In the second case, the number of both left and right hands is the same—there is no “global” asymmetry—however, the hands are grouped in sequences, showing the dominance of the left hand at the beginning and the right hand at the end. This is what we call “local” asymmetry. Finally, in the third case there is neither “global” nor “local” asymmetry, since there are no patterns of consistent dominance of one hand over the other.

Using these measures, it is also possible to assess the degree of stability of this asymmetry (how long the dominance of a particular hemisphere lasts before the pattern changes to the opposite). For example, in the sequence “left–left–left–right–right–right” hands dominate the same number of iterations (3 left, 3 right); in turn, the sequence “left–right–right–left–left–left” has a greater variation in the duration of dominance by each hand (1 left, 2 right, 3 left), which may indicate a less stable state of the subject or even transitions between several microstates.

#### 4.1 Global asymmetry

From the point of view of “global” asymmetry, we found that the cluster with the most pronounced indicators of drowsiness according to the psychomotor test (cluster 3, “sleepy”) also has the highest values of Shannon entropy, close to 1—which indicates the absence of pronounced dominance of one hemisphere over the other. Moreover, the cluster with the lowest values of Shannon entropy, indicating the dominance of one of the two hemispheres (cluster 4, “predictable”) is the smallest group in the sample, and also shows signs of low levels of drowsiness and shallow sleep when microsleep episodes occur. Thus, the obtained results indicate against the dominance of either of the two hemispheres when falling asleep—the presence of behavioral asymmetry in microsleep episodes seems unrelated to the processes of falling asleep themselves.

**Table 1** Pairwise comparisons of psychomotor test indicators between groups

Param	Groups	Diff	CI (95%)	SE	df	t	p
Taps	Cluster1—cluster2	− 37.178	[− 564.993; 490.638]	197.325	145.332	− 0.188	0.851
	Cluster1—cluster3	567.195	[60.734; 1073.655]	189.251	140.487	2.997	0.016
	Cluster1—cluster4	− 625.070	[− 1290.381; 40.241]	248.622	140.978	− 2.514	0.039
	Cluster2—cluster3	604.373	[23.534; 1185.211]	217.162	146.033	2.783	0.024
	Cluster2—cluster4	− 587.892	[− 1313.398; 137.615]	271.211	144.503	− 2.168	0.064
	Cluster3—cluster4	− 1192.264	[− 1915.825; − 468.704]	270.462	143.691	− 4.408	0.000
Sleeps	Cluster1—cluster2	4.358	[− 0.76; 9.477]	1.919	182.731	2.271	0.049
	Cluster1—cluster3	− 13.042	[− 18.034; − 8.05]	1.872	181.733	− 6.968	0.000
	Cluster1—cluster4	− 2.312	[− 8.949; 4.324]	2.487	175.019	− 0.930	0.354
	Cluster2—cluster3	− 17.400	[− 22.949; − 11.852]	2.081	184.999	− 8.363	0.000
	Cluster2—cluster4	− 6.671	[− 13.754; 0.412]	2.655	181.478	− 2.512	0.039
	Cluster3—cluster4	10.730	[3.682; 17.777]	2.642	183.039	4.061	0.000
Sl.len	Cluster1—cluster2	− 0.406	[− 5.252; 4.439]	1.814	160.834	− 0.224	0.823
	Cluster1—cluster3	− 5.056	[− 9.743; − 0.37]	1.754	155.519	− 2.883	0.022
	Cluster1—cluster4	3.501	[− 2.658; 9.66]	2.304	153.197	1.520	0.359
	Cluster2—cluster3	− 4.650	[− 9.97; 0.671]	1.992	164.076	− 2.334	0.083
	Cluster2—cluster4	3.907	[− 2.765; 10.58]	2.497	159.116	1.565	0.359
	Cluster3—cluster4	8.557	[1.897; 15.217]	2.493	159.291	3.433	0.005
ITT	Cluster1—cluster2	10.193	[− 102.711; 123.096]	42.545	341.584	0.240	1.000
	Cluster1—cluster3	− 42.707	[− 150.515; 65.102]	40.620	334.356	− 1.051	1.000
	Cluster1—cluster4	7.822	[− 133.951; 149.596]	53.420	336.261	0.146	1.000
	Cluster2—cluster3	− 52.899	[− 177.167; 71.368]	46.828	341.591	− 1.130	1.000
	Cluster2—cluster4	− 2.371	[− 157.46; 152.719]	58.442	340.733	− 0.041	1.000
	Cluster3—cluster4	50.529	[− 103.983; 205.041]	58.222	339.105	0.868	1.000

It is important to note that unlike Casagrande [15–17], who studied such dynamics on a full night’s sleep, our results are based on episodes of microsleep—therefore, the differences in conclusions can be justified by different research schemes and differences in the studied state. However, taking into account the small sample size and the relatively small size of the differences between the arms/hemispheres in the Casagrande studies, as well as the possibility of a rapid transition to a deeper sleep state from a microsleep state [21], our conclusions can still serve as reasonable evidence against pronounced hemispheric asymmetry in falling asleep.

## 4.2 Local asymmetry

From the point of view of “local” asymmetry and its stability, it is important to discuss the following two clusters—the already mentioned “sleepy”, as well as cluster 2 (“alternating”). The common property between them is high values of Shannon entropy, indicating the absence of “global” asymmetry, and high values of other complexity measures compared to the other two groups. However, the groups have different interpretations in terms of the level of drowsiness and patterns of complexity measures:

- The “alternating” cluster has the fewest episodes of falling asleep, which indicates a low level of drowsiness—especially compared to the “sleepy” cluster.
- The “alternating” cluster has the highest values of permutation entropy, Petrosian dimension and normalized Lempel–Ziv complexity.
- The “sleepy” group has the highest values of the “ordinary” Lempel–Ziv complexity and conditional permutation entropy.

What can these differences mean? First, these results could indicate the presence of a tipping point, where the system under study can rapidly change its characteristics in a qualitative way. This is indicated by pronounced

differences in the level of wakefulness between clusters while having comparable complexity measures; most likely, the transition point between wakefulness and drowsiness is associated with a specific combination of complexity measures of a certain value.

Secondly, the high values of complexity measures in the “alternating” cluster are consistent with observations of a higher dynamic diversity of physiological signals in wakefulness compared to the sleep state [28]. However, their higher values compared to the “sleepy” cluster may also indicate the absence of pronounced “local” asymmetry in these groups—most importantly, this is reflected in the high Petrosian dimension values, sensitive to the frequency of changes from one symbol to another. All other things being equal, the Petrosian dimension will be maximal in the sequence like “left–right–left–right–left–right”, which, as we have already mentioned, reflects the absence of “local” asymmetry. Lower values of the Petrosian dimension in the “sleepy” cluster may indicate a greater tendency to form sequences of falling asleep with the same hand (“getting stuck” on one hand)—which reflects the processes of “local” asymmetry. Moreover, such patterns might mean that hemispheres are constantly changing vigilance in this state—while one of them is “resting”, the other is more active, and after a while the order changes; basically, hemispheres are “working in shifts”. This is less of a hemispheric asymmetry and more of an interhemispheric interaction; physiologically we could observe a decrease in intrahemispheric and increase in interhemispheric connections, a pattern shown in [53].

Finally, high values of Lempel–Ziv complexity (the number of unique subsequences in the sequence) and conditional permutation entropy (the measure of how hard it is to predict the next “sleeping” hand from the current subsequence) in the “sleepy” cluster may indicate instability of episodes of asymmetry—with a large variety of consecutive lengths and unpredictable switching between dominance patterns. This together with observations from the previous paragraph may reflect a phenomenon known as “critical slowing down”—in the theory of dynamic systems, this represents a set of patterns denoting the “borderline” nature of the current state of the system and the high possibility of a system transition to another state [54]. For example, a similar phenomenon was described in the context of climate change [55], desertification [56], financial crises [57], epileptic seizures [58] and onset of depression [59]. Among the signals of a critical slowing down is a simultaneous increase in variance and autocorrelations in the signal associated with a slowed restoration of equilibrium in the system after its perturbation and a longer memory for this perturbation. The “getting stuck” described earlier—the tendency to fall asleep again on the same hand during a sequence of microsleep episodes—may indicate high autocorrelations in the continuous process behind the dynamics of falling asleep, and the instability of the durations of these sequences may be correlated with variance in the same process.

### 4.3 Probable physiological basis

What physiological changes can underlie the observed phenomena? Building on the idea of interhemispheric interactions we mentioned earlier [53], local changes in functional connectivity associated with the phenomenon of local sleep seem to be the most natural explanation [60]; in particular, the results obtained may reflect the disintegration of global functional connectivity in the alpha range and interactions between time-unstable brain networks [61]. Kalauzi et al. [62] describe the dynamics of alpha rhythm phase synchronization between the EEG electrodes during the wake–sleep transition—among other things, they found four types of changes in the synchronization of the alpha rhythm, which echoes the four clusters we identified. Their later work [63] describes the more complex and disorganized nature of the alpha activity synchronization patterns in a drowsy state compared to waking. Considering the pronounced alpha activity during microsleep episodes which we described earlier [64, 65], the features of the spatio-temporal dynamics of alpha rhythm may be related to the nature of the patterns of falling asleep and, consequently, the patterns of interhemispheric interactions. The verification of this hypothesis will be the material of our subsequent research.

Note that when testing this hypothesis, it is very important to separate the alpha dynamics from the broadband characteristics of the spectrum. Donoghue et al. [66, 67] show that the so-called 1/f-component of EEG power spectrum—aperiodic or «fractal» [68] component—can change independently of the actual periodic activity, which can lead to masking of the real changes or “mimicry” of aperiodic activity as periodic. The last point is clearly demonstrated in the article by Ouyang et al. [69], where the paradoxical correlation of the alpha rhythm with the cognitive task performance is fully explained by changes in the aperiodic component.

At the same time, aperiodic activity is not something epiphenomenal: theoretical models suggest the connection of this component with the excitation/inhibition balance in populations of neurons, which in itself may reflect the characteristics of brain activity as a self-organizing system. [70–72]. Changes in aperiodic component correlate well with changes in consciousness as a result of anesthesia, impaired consciousness and falling asleep [73–76], while alpha rhythm dynamics may interact with it [77]—which makes it a good second candidate process for testing.

## 4.4 Conclusions

To wrap up, our results indicate against the existence of a “global” hemispheric asymmetry when falling asleep; however, they are consistent with the existence of a “local” asymmetry—episodes of unihemispheric dominance for a certain period of time, after which lateralization pattern is reversed. Interestingly, a participant cluster with the most pronounced drowsiness (“sleepy”) may show signs of a critical slowing down, expressed in a lower frequency of changing hands when falling asleep and a higher instability of episodes of dominance compared to the awake “alternating” cluster. The exact neural mechanisms of these observed patterns are yet to be determined; however, dynamics of functional connectivity in the range of alpha rhythm and aperiodic activity could be a probable explanation for the emergence of various subgroups and patterns of interhemispheric interactions during the transition to sleep.

## Author contributions

Conceptualization: AEM and VBD. Data curation: AEM. Formal analysis: AEM. Funding acquisition: VBD. Investigation: NOP. Methodology: AEM. Project administration: VBD. Resources: DSS, EBY, ZVB, and TVI. Supervision: VBD. Visualization: AEM. Writing—original draft: AEM. Writing—review and editing: VBD, AER, and MOZ.

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**Data availability** The datasets generated during the current study are available from the corresponding author on reasonable request.

## Declarations

**Conflict of interest** The authors declare no competing interests. The funders had no role in the design of the study, the collection, analyses, or interpretation of data, the writing of the manuscript, and the decision to publish the results.

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