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IDENTIFICATION OF VARIATIONS IN TIME FREQUENCY CHARACTERISTICS OF SLEEP STAGES FOR HUMANS WITH DIFFERENT CHRONOTYPES

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Abstract

The paper reports the results of a partial-time analysis of EEG signals from healthy volunteers obtained during the recording of polysomnography with an expanded arrangement of electrodes (19 leads). An analysis of the characteristics of frequency patterns (their number, duration, and energy power) was carried out in theta – band (4 – 6 Hz) in five brain areas (central, occipital, frontal zones, and left and right hemispheres). A comparison of the obtained characteristics was carried out according to the chronotypes of the respondents. Based on the results of the study, it was possible to demonstrate chronobiological patterns of nocturnal EEG activity in healthy volunteers. REM sleep stage in groups of participants with morning and evening chronotypes demonstrates statistically significant differences in the number and duration of EEG oscillatory patterns for different areas of brain activity. The report was presented at PhysCon 2024 "Local nocturnal EEG activity of healthy people depending on chronotype".

Key words

EEG-activity, oscillatory wavelet-patterns, chronotype, polysomnography analysis

1 Introduction

Research in the field of sleep neurophysiology has attracted the attention of the scientific community and clinicians for a long time. Interest in this issue is also explained by the fact that disturbances in the processes of initiation, prolongation, and suppression of sleep are closely related to the general physical and mental state of the human health [Kostenko et al., 2013].

Currently, sleep disturbance is a stable scenario of everyday life for many thousands of people. Today, sleep timing shifts, sleep deficits and their irregular characteristics are often caused by an unstable schedule, a break with a continuous production/control cycle. At the same time, a number of studies have shown that regular sleep disturbance correlates with an increased risk of metabolic disorders, obesity, high blood pressure [Huang et al., 2019], etc., as well as, for example, with changes in intestinal microbiota [Maki et al., 2020] or an increased risk of early cognitive dysfunction, as well as manifestations of Alzheimer's disease [D'Rozario et al., 2020]. Moreover, there are studies demonstrating a long-term decline in memory, attention, and other cognitive functions that accompany sleep deprivation and/or insomniacite [Shokri-Kojori et al., 2018].

Research into human chronotype and circadian rhythms of various conditions has intensified in recent years in a variety of areas, for example, from studies of immunity [Collins et al., 2021] to neuropsychological assessments of sleep problems, mood, etc. [Holler et al., 2021]. In addition to the fundamental interest in human self-knowledge, such studies of sleep disorders

have significant practical importance, directly related to the social burden of increasing the risk of developing a spectrum of extremely severe disabling diseases and the search for ways to reduce such threats.

According to the literature, EEG activity of the brain has its own characteristics depending on the daily type of initiation of sleep and wakefulness processes (in other words, chronotypes). It is already known that morning types have a greater spectral power of EEG signals in the low band (12 – 14 Hz) compared to evening types, while the rate of decay of slow-wave activity (1 – 5 Hz) tends to be greater in morning types compared with evening types ($P = 0.06$) [Mongrain et al., 2005]. Studies of EEG activity today attract a lot of attention from researchers, both from the standpoint of experimental study [Gromov, et al., 2024; Maksimenko, et al., 2019] and mathematical modeling [Dolinina, et al., 2022]. Among the methods of mathematical tools, it is necessary to highlight the methods of frequency-time analysis, which have a significant history, but do not lose their leading position due to the clear interpretation of the results obtained and well-developed approaches [Dolinina, et al., 2022; Grishchenko, et al., 2020].

The aim of this study is to clarify the characteristics of local EEG activity in 5 brain zones in healthy volunteers, depending on the chronotype, in theta – band (4 – 6 Hz). Today, theta activity is directly linked to memory reconsolidation during sleep during emotional recovery processes [Hutchison, Rathore, 2015]. This type of theta activity is studied in various neural network models and is associated with modulation of the generation of high-frequency activity that correlates with cognitive activity [Sevasteeva, et al., 2021].

2 Materials and methods

2.1 Materials

A total of 103 volunteers were included in the study at the Pain Treatment Clinic's sleep laboratory. Each respondent signed an informed consent to participate in the study.

Study inclusion criteria:

- age over 18 years;
- body mass index (BMI) within 18.5 – 25 kg/m2;
- volunteer must observe sleep hygiene (no jet lag or sleep deprivation the night before);
- no sleep disorders: respiratory (snoring, obstructive/central sleep apnea syndrome, chronic alveolar hypoventilation);
- motor (restless legs syndrome, periodic limb movements); parasomnia, insomnia, hypersomnia, etc.;
- no acute and chronic somatic, neurological, or psychiatric diseases;
- no heart rhythm or conduction disturbances, no ischemic changes on the ECG or in the anamnesis;
- absence of infectious diseases (including acute and chronic in the acute stage);
- absence of dyshormonal, dyselectrolyte conditions;
- not taking psychotropic drugs and drugs that can affect the quality of sleep and cognitive functions (hypnotics, anxiolytics, neuroleptics, antidepressants, normothymic drugs, etc.).

Exclusion criteria

- the presence of acute and chronic somatic diseases, including sleep-related breathing disorders, sleep-related movement disorders, and parasomnias,
- the presence of neurological diseases in the acute phase,
- the presence of hormonal disorders, electrolyte imbalance, and circadian rhythm disorders,
- regular intake of psychotropic and other medicines that can affect sleep.

Each volunteer underwent two sleep studies with psychophysiological testing before and after each polysomnographic recording. The polysomnography recording included extended EEG registration (19 channels instead of the standard 4 – 6 in PSG); 2 EOG channels; EMG of the chin, 2 channels of chest excursion and abdominal respiratory excursion; 2 channels of EMG of the calf muscles; registration of respiratory flow from the nose and snoring; registration of the level of blood saturation from a finger photoplethysmographic sensor; registration of body position. The clinical characteristics of the volunteers are presented in Table 1.

Table 1. Clinical characteristics of volunteers (M $\pm$ SD – mean $\pm$ standard deviation; Me [25%; 75%] – median [lower quartile; upper quartile]; AHI – apnea/hypopnea index per hour; BMI – body mass index, kg/m2; SBP – systolic blood pressure, mmHg; DBP – diastolic blood pressure, mmHg; HR – heart rate, beats per minute.)

Total, n	103
Male gender, n (%)	40 (38.83 %)
Age, years (M $\pm$ SD)	27.6 $\pm$ 8.2
BMI, kg/m2 (Me [25 %; 75 %])	21.4 [19.5; 23]
Rhythms, n (%)	49 (47.57 %)
AHI, no./h, (Me [25 %; 75 %])	1.65 [1; 2.5]
SBP, mmHg (Me [25 %; 75 %])	110 [110; 120]
DBP, mmHg (Me [25 %; 75 %])	70 [70; 80]
HR, bpm (Me [25 %; 75 %])	76 [73.5; 79]

According to the data in Table 1, 40 men and 63 women participated in the study, the average age of the study participants was 27.6 $\pm$ 8.2 years. It was shown that, on average, the BMI of the volunteers corresponded to normal values, and the blood pressure values were in

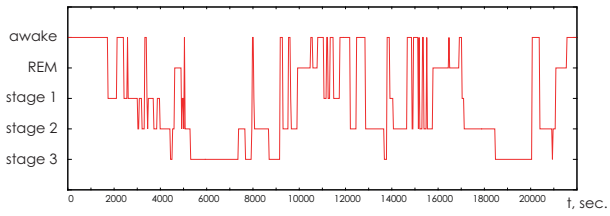

Figure 1. Example of a hypnogram of a healthy 22-year-old study participant

the normotensive range. The heart rate of the participants was within normal values. More than a third of the respondents (35 %) were classified as "rhythmics".

According to the design of the study, all participants underwent a polysomnogram recording with subsequent clinical and numerical analysis of the signals obtained. Each polysomnographic study was processed in accordance with accepted standards of clinical sleep studies, namely, a hypnogram was constructed with a window duration of 30 seconds and the identification of five main states for the patient – light sleep N1, N2, deep sleep N3, rapid sleep REM and wakefulness AWAKE. The standart clinical analysis of PSG was supplemented by automatic construction of a hypnogram based on standart spectral algorithms. An example of a hypnogram of a healthy volunteer is shown in Figure 1. The differences between the clinical assessment of the somnologist and the automatic processing of hypnograms amounted to no more than 10 % (on average – 7.84 % for the detection time of each stage and 8.23 % for the assessment of their durations), which was considered a satisfactory result.

In addition, all study participants were sorted by their chronotypes: evening, morning, daily. The definition of chronotypes was based on the Horn-Ostberg Chronotype Questionnaire.

2.2 Evaluation of oscillatory patterns in EEG activity

The analysis of EEG activity of the brain was performed using the method of oscillatory patterns based on the calculation of the continuous wavelet transform [Runnova et al., 2021]. Below we briefly described the main steps of the performed mathematical processing of the recorded EEG signals. We denoted the array of EEG signals of each patient as $EEG_1(t_j);...;EEG_e(t_j);...;EEG_{19}(t_j)$, where $EEG_e(t_j)$ is the the value of the signal registered in current EEG channel e-number at the moment of discrete time t_j. For each EEG signal $EEG_e(t_j)$ a continuous wavelet transform (CWT) with the basic morlet function of the following form was calculated:

$$W_e(f_i,t_j)=\sqrt{\frac{1}{f}}\sum_{j=1}^{N}\exp\left(\frac{-\left[f_i\cdot(t_j-\frac{1}{f_i})\right]^2}{2}\right)\bullet$$
$$\bullet E_e(t_j)\left[-\exp\left(\imath 2\pi f_i(t_j-\frac{1}{f_i})\right)-e^{-\pi}\right]\Delta t \quad (1)$$

In equation (1), the following notation was introduced: f_i is the signal frequency, similar to that for the usual Fourier transform, t_j is the discrete recording time, N is the number of time samples in the signal analyzed, $\imath$ is the imaginary unit, $\Delta t = (t_{j+1} - t_j) = 0.004$ s is the time step of the signal sampling. We chosen sampling along the frequency axis equal to 0.01, i. e. $\Delta f = (f_{i+1} - f_i) = 0.001$ Hz.

Next, on the surface line $W_e(f_i,t_0)$, all points of maxima, $extr\left[W_e(f_i,t_0)\right]_{t_0}$, were extracted. At the next time point, $t_1 = t_0 + \Delta t$, all maxima $extr\left[W_e(f_i,t_1)\right]_{t_1}$ for a given surface line $W_e(f_i,t_1)$ were detected again. For the two generated arrays of maximum points, the operation of controlling their location on the plane $(f;t)$ was performed, viz:

$$\|(f_{i^0},t_0)-(f_{i^1},t_1)\|\le\varsigma, \quad (2)$$

where $\varsigma = 0.01$.

Thus, of the two arrays of extreme maximum values $extr\left[W_e(f_i,t_0)\right]_{t_0}$ and $extr\left[W_e(f_i,t_1)\right]_{t_1}$, only those that formed continuous lines on the plane $(f;t)$, referred to as patterns, P, were retained. This procedure was repeated at each time step, $t_{i+1} = t_i + \Delta t$. This step-by-step processing resulted in a set of patterns that included only extreme CWT values:

$$P=\left\{extr\left[W_e\left(f_{P1}^1,t_{P1}^1\right),\ldots,W_e\left(f_{P1}^{L_{P1}},t_{P1}^{L_{P1}}\right)\right];\right.$$
$$extr\left[W_e\left(f_{P2}^1,t_{P2}^1\right),\ldots,W_e\left(f_{P2}^{L_{P2}},t_{P2}^{L_{P2}}\right)\right];\ldots;$$
$$\left.extr\left[W_e\left(f_{PN}^1,t_{P1}^1\right),\ldots,W_e\left(f_{P1}^{L_{P1}},t_{P1}^{L_{P1}}\right)\right]\right\} \quad (3)$$

After the processing of the entire duration of the EEG time series was completed, all detected patterns were checked for duration in order to exclude random noise interference. For each pattern, P, we calculated average frequency, $\langle f_P\rangle$

$$\langle f_P\rangle=\frac{\sum_{i=1}^{L_P}f^i}{L_P} \quad (4)$$

and average duration, $\langle T_P\rangle$

$$\langle T_P\rangle=\sum_{i=1}^{L_P}t^i. \quad (5)$$

Next, in each time t_j we form an array of all energy values $\{E_{1,j},\ldots,E_{k,j},\ldots\}$, where $k = 1,\ldots,r$, and r is the number of frequencies observed for time t_j on the computed pattern surface P. In the array

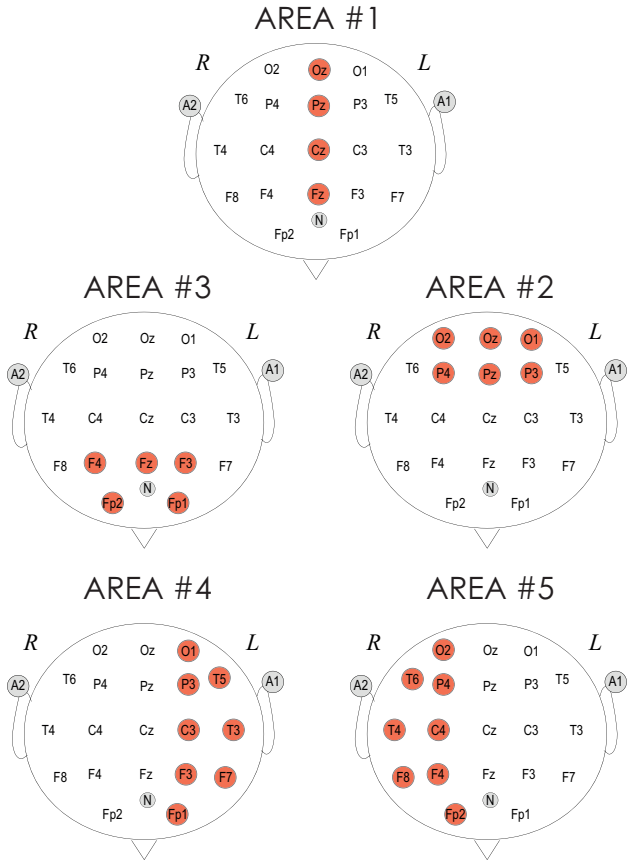

Figure 2. Schematic diagram of the electrode placement during polysomnography recording and the locations of the brain regions for which averaging of oscillatory pattern characteristics was performed.

$\{E_{1,j}, \ldots, E_{k,j}, \ldots, E_{r,j}\}$ we estimate the maximum energy value $E_{max,j}$, $E_{max,j} > E_{k,j}$, for $\forall k$. And we normalize energy values as:

$$\{\langle E_{1,j}\rangle, \ldots, \langle E_{k,j}\rangle, \ldots, \langle E_{r,j}\rangle\} = \\ = \{\frac{E_{1,j}}{E_{max,j}}, \ldots, \frac{E_{k,j}}{E_{max,j}}, \ldots, \frac{E_{r,j}}{E_{max,j}}\}. \quad (6)$$

Normalization is performed separately for each moment j of time, which allows use standard parallel mode for program realization of this algorithm [Simonyan et al., 2022].

Next, we again return to the sorting of patterns P, and for all points $(f,t)_p$, constituting one pattern P with duration m, we calculate the average energy characteristic E of the pattern as

$$E = \frac{\sum\limits_{p=1}^{m} \langle E(f,t)_p\rangle}{m}. \quad (7)$$

Therefore, each pattern is described by three characteristics: mean frequency f_{md}, duration or lifetime T, mean energy E.

The entire EEG recording was divided into Δ_{30s} intervals of 30 seconds duration. Then all patterns detected during this Δ_{30s} interval were sorted according to the frequency of oscillatory activity. Each pattern according to its mean frequency $\langle f_P\rangle$ (4) was assigned to the theta – band: Δf_θ [4, 6] Hz. To study the oscillatory activity of the brain, the following local areas of the brain were examined: area #1 – the central sulcus (Fz, Cz, Pz, Oz), area #2 – the occipital region (P3, P4, O1, O2, Pz, Oz), area #3 – the frontal region (Fp1, Fp2, F3, F4, Fz), area #4 – the left hemisphere region (Fp1, F3, F7, C3, T3, P3, T5, O1), area #5 – the right hemisphere region (Fp2, F4, F8, C4, T4, P4, T6, O2) (see Figure 2).

2.3 Statistical data processing

Mean, median, and standard deviation were used in descriptive statistics of collected data. The Mann-Whitney U test for independent samples was performed for the comparison of quantitative data. Calculation and graphing of distributions of Tr coefficients made in OriginLab version 6.1. The results with a p-value ≤ 0.001 were assumed statistically significant. Statistical analyses were conducted by SPSS version 22.0 software for Windows (IBM, Armonk, NY, USA).

3 Results

3.1 Assessment of sleep structure based on hypnogram characteristics

When dividing the entire array of information into three groups – morning, daily and evening chronotypes, it is possible to identify the following features. Firstly, the average and median number of moments of wakefulness, as well as stages N1, N2, N3, is higher in the group of morning chronotype (see Fig. 3, *a*).

Secondly, the number of REM stages of paradoxical sleep is the same for all three chronotypes. It is not possible to distinguish the chronotypes of daily and evening chronotypes by the number of sleep stages. Thirdly, the analysis of the duration of various stages of sleep in various chronotypes demonstrates an increase in the relative duration of awakening periods in group of morning chronotype (Fig. 3, *b*). However, at the same time, the analysis of the absolute values of the duration of the stages of wakefulness does not show such changes in group of morning chronotype (Fig. 3, *c*).

The early morning chronotype has a reduced duration of sleep stages N2, N3 and, to a lesser extent, REM. However, the average duration of stage N1 is somewhat increased. Note that the relative durations of stages N3 and REM are also somewhat reduced, as can be seen in Fig. 3, *b*.

Finally, no such differences in the duration of various sleep stages can be observed in participants groups with daily and evening chronotypes. At the same time, note that, according to Tables 2 and 3, it can be observed that

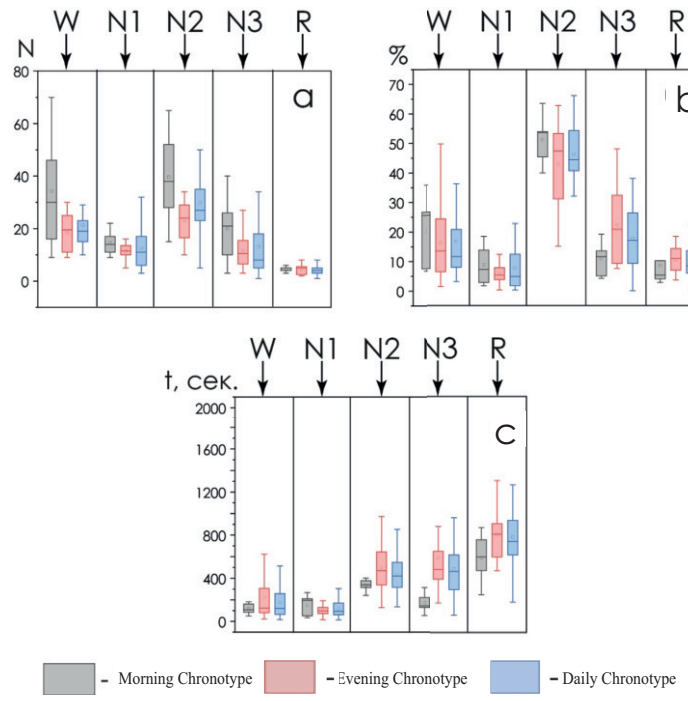

Figure 3. Statistical diagrams of the number of sleep stages (*a*), the percentage of duration of each sleep stage (*b*), and the average duration of each sleep stage (*c*) for nocturnal PSG recordings in subjects with different chronotypes.

Table 2. Average statistical features of hypnograms: % of PSG – total percentage of time during PSG spent in a given sleep stage; NS – total number of sleep stages during PSG; AD – average duration of a sleep stage during PSG

Sleep stage	% of PSG	NS	AD, s
Evening Chronotype			
W	16.22	18.50	220.54
N1	5.93	11.44	106.69
N2	42.85	23.00	498.03
N3	22.30	11.56	594.76
REM	10.50	4.44	811.09
Morning Chronotype			
W	20.49	34.2	288.18
N1	8.82	14.20	151.16
N2	51.29	48.20	434.42
N3	10.72	23.00	232.66
REM	8.63	4.60	675.03
Daily Chronotype			
W	16.78	21.35	176.03
N1	7.61	12.56	118.54
N2	46.37	29.97	429.15
N3	17.72	13.06	493.69
REM	10.19	4.41	789.95

the average number of sleep stages in evening chronotype group is less than that in groups of morning and daily chronotypes. This is especially evident for stage N2, as well as periods of awakening. However, the duration of these states in evening chronotype group prevails over that in groups of morning and daily chronotypes. For example, for stage N2, test subjects with evening chronotype demonstrate an average duration of about 498 seconds, while study participants with morning and daily chronotypes demonstrate 434 and 429 seconds, respectively. Thus, the difference is about 13 – 15%.

Note that the characteristics of transitions between different stages of sleep also differ significantly (see Table 3). For example, in evening chronotype group, the probability of transition from the state of wakefulness to the state of deep sleep (N3) is three times higher than in larks. The probability of the onset of stage N2 after stage N1 in pigeons exceeds that of larks by 20 %. Note that in general, the organization of sleep in larks demonstrates the following tendency – the minimum probability of awakening at stage N3. Usually, the stage of the deepest sleep N3 ends with the transition to stage N2 and never to REM sleep. At the same time, considera-

Table 3. Average percentages of the probability of transition from one stage of sleep to another during PSG recording in subjects with different chronotypes

	W	N1	N2	N3	REM
Evening Chronotype					
W	0.00	51.65	38.49	1.61	4.28
N1	34.15	0.00	64.24	0.00	0.42
N2	39.42	7.68	0.00	40.57	11.19
N3	32.95	1.55	57.49	0.00	0.48
REM	52.65	7.29	40.06	0.00	0.00
Morning Chronotype					
W	0	49.57	45.58	0.58	2.65
N1	41.98	0	54.27	0	3.75
N2	40.85	6.35	0	44.25	8.55
N3	16.79	10	73.21	0	0
REM	55.33	10	29.67	5	0
Daily Chronotype					
W	0	46.84	49.33	1.26	1.2
N1	27.09	0	70.24	1.61	0
N2	44.96	7.91	0	34.83	10.73
N3	27.26	0.68	65.79	0	0.94
REM	51	2.45	42.14	0	0

tion of the transition to wakefulness from all other stages of sleep indicates an increased probability compared to other chronotypes.

3.2 Assessment of oscillatory sleep structure based on CWT patterns

The results of statistical evaluation of the oscillatory structure of sleep are presented in the Figure 4. First of all, we note that all the statistically significant differences identified are concentrated between the groups of study participants with evening and morning chronotypes. Volunteers with an arrhythmic type (daily chronotype), as such, show a wide range of oscillatory activity, which does not allow them to be distinguished from participants with evening or morning chronotypes.

Let us discuss the changes in oscillatory EEG activity observed in study participants with evening and morning chronotypes. First of all, such changes do not affect the deep stages of sleep, focusing mainly on the stages of REM sleep and, less often, light sleep N1, N2. Then, we note that the stage of REM sleep experiences significant changes when considering any of the brain activity zones for analyzing the number N and duration T of oscillatory CWT patterns. Finally, the energetic characteristics of the E patterns do not show any differences for participants with different chronotypes.

4 Discussion

The study was able to show that clinical analysis of sleep structure does not reliably differentiate people depending on chronotype, which is consistent with literature data [Mongrain et al., 2005; Mongrain et al., 2007]. However, mathematical analysis of EEG activity allows us to identify a number of patterns associated with the circadian rhythms of volunteers. It was previously shown that EEG activity in leads Fz, Cz, Pz, Oz during slow-wave sleep in morning types demonstrated a sharper decrease in slow-wave activity (1 – 5 Hz) per sleep cycle in the fronto-central leads and a sharper increase in activity 13 – 14 Hz in the parieto-occipital leads than in the evening types. Nonlinear regression analysis showed that the rate of exponential decline in the relative values of slow-wave activity during slow-wave sleep was faster in the morning than in the evening types in the frontal abduction. In the REM sleep phase, morning types showed a sharper decrease in the activity of high sigma (14 – 16 Hz) and beta (16 – 24 Hz) during the night in the central-parietal leads than evening types [Mongrain et al., 2006].

The observed differences in the oscillatory EEG activity of the brain of the study participants are concentrated in the REM sleep phase. In addition, these differences can be identified only by using a special mathematical apparatus – an assessment of oscillatory patterns based on continuous wavelet analysis. Moreover, the absence of differences in the area of energy characteristics for all three groups with different chronotypes suggests that the construction of simpler spectral characteristics does not provide sufficient information about the nature of the sleep microstructure of patients with different chronotypes to separate them.

The results of this study complement the literature data and also allow us to confirm the connection between the quantitative and qualitative characteristics of EEG activity in various areas of the brain during all stages of sleep and the types of daily regulation of the sleep-wake cycle in healthy young people. In addition, the identified features of the organization of the microstructure of the oscillatory activity of the EEG of the brain during the REM stage of sleep may indicate different mechanisms of reconsolidation of emotional memory in healthy people with early morning and late evening chronotypes. This pilot study requires continuation of experimental work on the formulation of appropriate psychophysiological experiments.

5 Conclusion

Thus, the sleep structure in healthy volunteer groups changes weakly for different chronotypes determined

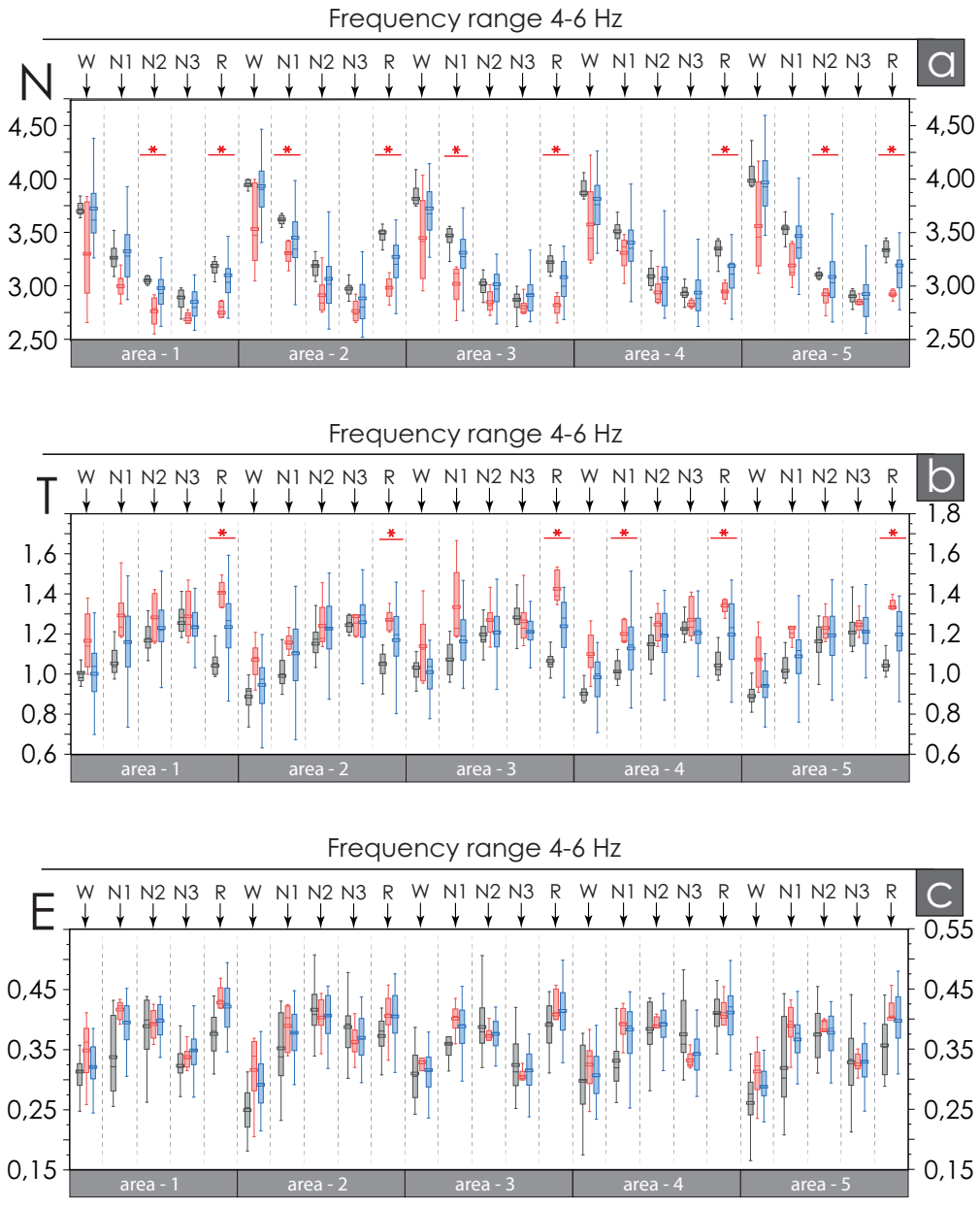

Figure 4. Statistical diagrams of the number N (*a*), the duration or lifetime T (*b*) and mean energy E (*c*) of oscillatory CWT patterns, calculated for EEG, recorded in different brain areas. The different colors of the diagrams correspond to different groups of study participants according to their chronotypes, namely: gray color – evening, red color – morning, blue – daily chronotypes. The red line with an asterisk above the diagrams corresponds to statistically significant differences between the data in the groups with morning and evening chronotypes ($p \leq 0.001$)

according to the Horn-Ostberg Chronotype Questionnaire. At the same time, the oscillatory structure changes quite significantly, at a high level of statistical reliability ($p \leq 0.001$). In addition, the maximum differences occur in the REM sleep phase, which correlates with memory consolidation processes and, possibly, dreaming processes. This issue requires further, more in-depth study.

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