

Levels of consciousness in psychopathology according to monitoring of neural network centers alpha rhythm rs-EEG

Sergey Lytaev, Ksenia Belskaya

Department of Normal Physiology, Saint Petersburg State Pediatric Medical University, Saint Petersburg, Russia

Article Info

Article history:

Received Nov 12, 2024

Revised Jun 20, 2025

Accepted Jul 5, 2025

Keywords:

Brain functional blocks
Level of consciousness activity
Neurocognitive deficit
Paranoid schizophrenia
Resting state
electroencephalography
Resting state networks

ABSTRACT

Consciousness is the highest mental function that integrates attention, memory, individual experience, emotions, and all modalities of perception, information processing and other manifestations of higher nervous activity of a person. This research was aimed to theoretically substantiate the functional connection of the brain alpha regulatory system with the modulation of conscious activity and to identify pathological electroencephalography (EEG) patterns of the alpha rhythm characterizing a decrease in the level of consciousness. 40 patients (main group) with current symptomatic schizophrenia associated with neurocognitive and depressive symptoms, and 38 healthy subjects (control group) were examined. Both nonspecific physical parameters of the alpha wave process—index, frequency and amplitude, and physiological features of alpha oscillations—regularity, auto rhythmicity (modulation) and stability of the EEG alpha rhythm were analyzed with using WinEEG, EEG Studio, and Loreta-Key viewer programs. A line of indicators for the alpha rhythm in schizophrenia have been calculated—based on coherence in different brain areas, the latent period (LP) of desynchronization, the average number of bursts and the tone of the cerebral cortex.

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Corresponding Author:

Sergey Lytaev

Department of Normal Physiology, Saint Petersburg State Pediatric Medical University

Litovskaya St., 2, Saint Petersburg, 194100, Russia

Email: physiology@gpmu.org

1. INTRODUCTION

Brain imaging studies show unique possibilities for studying the processes of consciousness in the brain. Even the application of well-known methods often opens up new possibilities. The results obtained by recording the cognitive component of P₃₀₀ event-related potentials (ERPs) are well known. The results of functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) show the peculiarities of the functioning of brain structures in the implementation of executive functions [1]-[3].

Electroencephalography (EEG), ERPs, fMRI, and PET have become unique technical means in the study of consciousness. The advantage of high temporal resolution of EEG is the ability to record neural electrical signals at the millisecond level and record changes in the neural discharge of the brain at the stages of recognition, encoding and cognition of information. fMRI and PET have the advantage of spatial resolution and provide localization of the brain during information processing. The spatial advantages of high resolution of fMRI and PET provide localization of brain functional areas during cognitive processing and record the brain's response through changes in blood oxygen saturation and material metabolism. Studies have identified important functional brain regions such as the frontal lobe, cortical midline structure, and temporal lobe of self-processing, and have discussed in detail the self-processing brain bias. There is a point

of view that ERPs play an intermediate role between the temporal capabilities of EEG and the spatial capabilities of PET and fMRI, that is, ERPs are able to reflect both brain processes [4], [5].

EEG/fMRI and EEG/PET studies have shown an inverse relationship between alpha power and regional metabolism, which has been observed in the occipital, parietal and sensorimotor cortices. Therefore, in a resting state with eyes closed, alpha activity is associated with regional deactivation and decreased metabolism. Given these relationships, it is expected that the decrease in prefrontal metabolism in schizophrenia should be associated with an increase in power in the alpha frequency band in the anterior regions of the brain. However, this is rarely observed. Much of the existing EEG literature suggests that, if any difference exists, it is due to decreased alpha power in schizophrenia compared with healthy subjects. There is also evidence of diffuse reductions in alpha power, both compared with controls and in association with negative symptoms and type of schizophrenia [1], [6].

Studies show the importance of specific early responses and non-specific late components of EPs. Thus, self-information was unique in early and late stages of cognition. The N_{170} and N_{250} components in early cognition reflect the specificity of encoding of the self-face, while the amplitude and latency of the P_{300} potential in late cognition were the most significant components of the difference between self and non-self information [7].

There are many approaches and definitions in understanding the nature of consciousness [7]-[9]. However, new challenges and scientific discoveries introduce a line of uncertainty that requires proof. In practice, an important topic is the dynamic network relationships that arise in psychoneurological pathology with impaired consciousness [10], [11]. Long-term research in neuroscience has led to a certain consensus that consciousness, like numerous forms of complex behavior, are network-level phenomena, i.e., a functional product of a neural network [12], [13]. Such behavior requires high-level integration of various sensory channels, synchronization of motor patterns, and coordination of their activity within generalized neural networks. Consequently, the accumulation of data on the functioning of neural networks contributes to the formation of a number of testable hypotheses regarding the neural bases of cognitive functions, memory, and motivated behavior. Currently, the study of consciousness consists of three main areas of levels: the search for neural correlates of consciousness (NCC), the mechanisms of functioning of these correlates, and the reproducibility of the hypotheses put forward [14]. Neurophysiological research in psychopathology plays a dual role. On the one side, it is a solution to clinical-diagnostic and clinical-expert tasks. From the other side the brain in psychopathological conditions is a model for studying neural networks in these conditions [15].

In general, power disturbances in the alpha-band EEG in schizophrenia are believed to have several sources. The most likely causes are widespread disruption of local cortical circuits and damage to thalamo-cortical circuits. Such disturbances affect the EEG of the anterior parts of the brain in opposite directions. In particular, thalamo-cortical deafferentation of the prefrontal cortex promotes innate cortical autorhythmicity, that is, an increase in the power of the alpha signal in (pre)frontal areas, while a deficit of cortico-cortical circuits favors a global reduction in the expression of alpha waves in the EEG. These mechanisms can be affected to varying degrees in different forms of schizophrenia and, depending on the composition of patients, manifest themselves differently in changes in EEG power [16]. Interestingly, patients with schizophrenia show significantly lower resting-state alpha power compared to healthy subjects, specifically in the prefrontal and parietal regions. Alpha oscillations are important for top-down information processing in various cortical regions. This is due to the activation of the ascending reticular activating system of the brain [10], [15]. Significantly lower alpha band power has also been reported in schizophrenia compared to healthy controls during the self-referential state [16].

Most studies of resting state networks (RSNs) have been performed using static methods, i.e., networks were determined across the entire recording ("stationary" processing) [7], [17]. The suppose, that connections between brain areas are static throughout resting-state recordings has often been criticized. In particular, it has been reported [13] that the state of functional connectivity of networks obtained as a result of dynamic analysis differs greatly from the static activity. On this basis [18], the term "chronnectome" was proposed to describe dynamic patterns of interaction in a temporal sequence between brain regions. The transition of activity between centers in terms of graph data allows us to study how brain centers alternate with each other over time. Thus, the center is considered either a peripheral hub or a connecting hub. However, the same brain area can play the role of both a peripheral node and a connective node at two levels at different times for the same subject at rest [19], [20].

The alpha regulatory system of the brain, as a dynamic network neural structure, is involved in the regulation of multimodal perception, semantic processing of information and the formation of memory engrams, as well as in the regulation of attention and level of wakefulness [9], [21]. The individual frequency of the EEG α -rhythm is an important integral indicator of the state of the brain, reflecting high-speed neurodynamic characteristics. At a high α -frequency, a faster alternation of excitation and inhibition phases

occurs and, accordingly, the speed of information processing and motor reactions increases. The variability of the individual α -rhythm frequency in the frequency range of 10.2-13.0 Hz reflects the dynamics of cortico-thalamic interaction [21].

An increase in the α -rhythm EEG frequency reflects the readiness of neural networks for cognitive activity and is accompanied by a subjective feeling of increased level of wakefulness, consciousness activity, and a surge of energy. In case of brain pathology that limits individual cognitive resources, a decrease in the frequency of the α -rhythm correlates with a decrease in the speed of cognitive operations [22].

Recently, deep learning (DL) algorithms such as convolutional neural networks (CNNs), recurrent neural networks (RNNs), and transformers have been used to evaluate neural networks in psychopathology, demonstrating their effectiveness in processing EEG signals [1]. In addition, these methods enable new approaches to process EEG signals and classify different disorders of consciousness (DOC) states. However, one of the limitations of these approaches is the general rule for training an effective DL model with excellent generalization. A larger training dataset usually leads to better model performance, and datasets obtained from natural scenarios in clinical practice are usually characterized by small samples, which poses significant challenges for DL models. How to obtain a robust and effective DL model based on limited data size to support accurate classification of DOC states and improve neurorehabilitation treatment is a topic worthy of further research [23], [24].

So, consciousness characterizes the state of cognitive and other functional systems of the brain that ensure adaptive human behavior. In this regard, there is a need to develop methods for assessing the level of consciousness activity as an integral indicator of the functional state of the brain. On this basis, the present research was aimed at theoretically substantiating the connection between cognition's modulation and the brain alpha regulatory system for determining resting state EEG (rs-EEG) criteria and assessing the level of consciousness based on abnormal alpha rhythm patterns from patients suffering from schizophrenia associated with neurocognitive deficits.

2. METHOD

78 persons were examined, including 40 outpatients (main group, 37.7 ± 3.3 years, 26 women and 14 men) with a diagnosis of current symptomatic schizophrenia, and 38 healthy subjects (control group, 38.6 ± 3.7 years, 23 women and 15 men). Outpatients underwent a routine expert examination for social support according to a single protocol at the St. Petersburg Psycho Neurological Dispensary No. 1. They were characterized mainly by depressive and cognitive symptoms and did not have active productive symptoms. Also, during the study period, antipsychotic medications were discontinued according to indications. rs-EEG was recorded using a 21-channel hardware-software complex with a bandwidth from 0 to 40 Hz and a time constant of 0.3 sec, according to the international 10–20 system (Figure 1) with a monopolar reference electrode of combined ear clips. EEG from 16 monopolar electrodes was recorded. Then the data from which were analyzed in pairs: Fp1-Fp2, F3-F4, F7-F8, C3-C4, P3-P4, O1-O2, T3-T4, and T5-T6. An 8-second EEG segment with a well-defined alpha rhythm in the recording channels under study is shown in Figure 2.

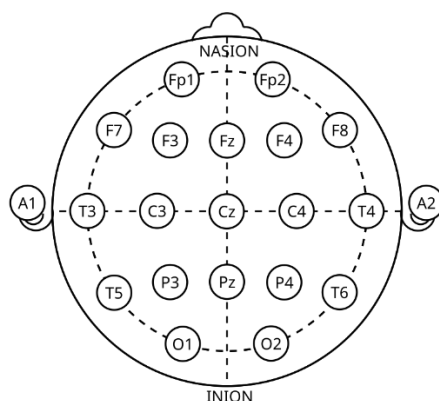


Figure 1. Electrode arrangement diagram according to the international 10–20 system explanation in the text

The study according to the guidelines of the declaration of Helsinki and was approved by the local ethics committee of the St. Petersburg State Pediatric Medical University (protocol no. 12/1, 4 December 2017) was performed. Informed consent was obtained from all subjects involved in the study.

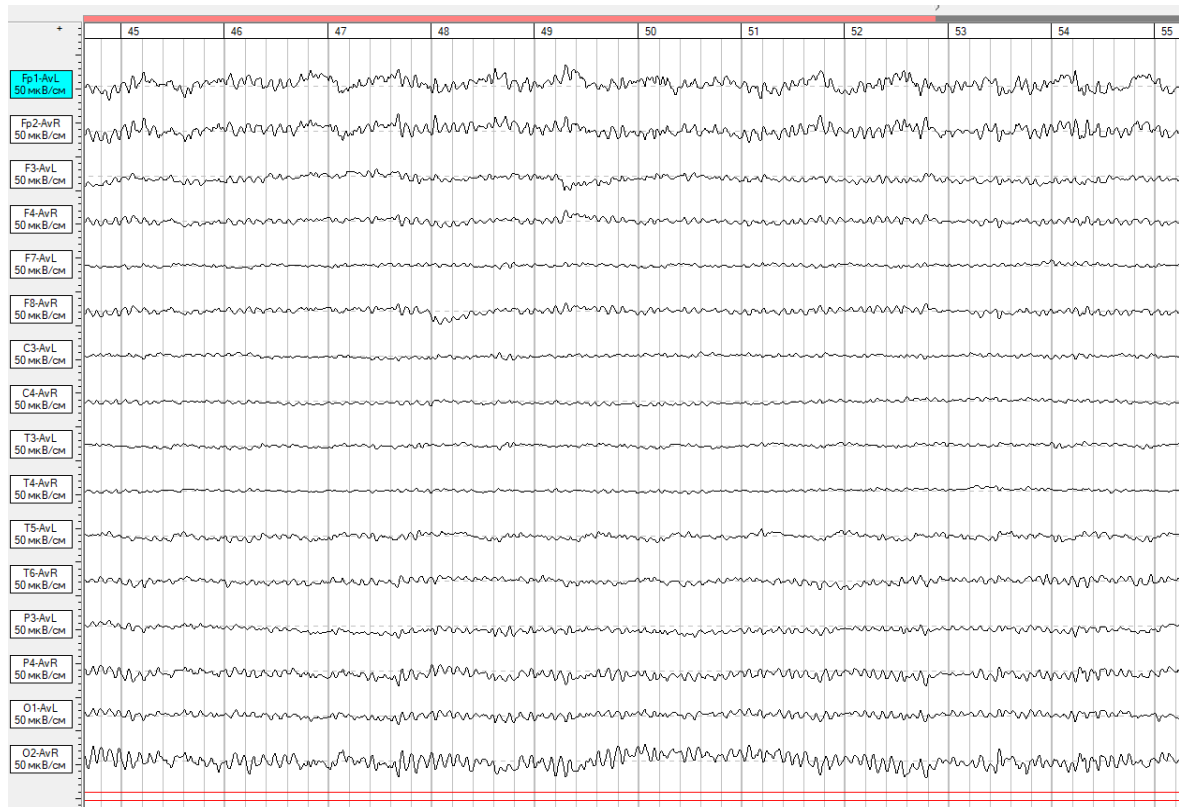


Figure 2. Fragment of EEG of a healthy subject (male, 42 years old) and location of the recording channels under study epoch-8 sec

2.1. The criteria for selecting subjects for investigation

The research criteria for selecting all subjects (healthy and patients) were; i) no history of severe somatic and neurological diseases; traumatic brain injury (TBI) with loss of consciousness for more than 5 min; ii) no history of alcohol or drug addiction; iii) right-handedness; and iv) subjective perception of the subjects to the study—person with a negative attitude towards the tasks were not included in the survey. There were no significant differences in age or education between subjects in both groups.

The control group consisted of university employees without a hereditary history of psychosis. None of the subjects in the control group sought help from psychiatrists or neuropsychiatrists; they did not exhibit psychopathological symptoms. The group of patients with psychopathology included patients with varying clinical presentations according to ICD-11 (06 mental and behavioral disorders, schizophrenia or other primary psychotic disorders) from the psychiatric institution (hospitals) where the patient was observed. The average medical history was 9.8 ± 3.1 years.

2.2. Resting state electroencephalography data coherence analysis

The parameters of oscillatory brain activity were assessed using spectral analysis data based on the Fourier transform. First, a coherence analysis of the total EEG was performed, as well as by rhythms, for this study, in particular, the alpha-1 and alpha-2 EEG ranges. The calculation was carried out for 8 pairs of electrodes (Table 1 and Figure 2) for 3-5 min with preliminary removal of artifacts using software and manually [9], [20].

In relation to EEG, coherence is a quantitative indicator reflecting the interconnectedness of electrical processes in the brain and allowing one to assess the degree of synchronization of EEG frequency parameters between different parts of the cerebral cortex. In other words, coherence is the correlation of the EEG spectral power for different electrodes in the same frequency range and is the Fourier transform of the cross-correlation. If the main goal of the study is the stability of the relationship between two processes, then the best method is coherence analysis. It is also believed that coherence analysis is more informative in case of brain pathology, and under normal physiological conditions the influence of the spectral power level on coherence can be neglected, since the differences will be statistically insignificant.

Table 1. Coherence analysis indices for alpha-1, alpha-2 frequency ranges and total EEG for symmetrical pairs of electrodes according to the 10-20 system

Channels 10-20 system	Control		Research group		Control		Research group	
	Alfa-1		Alfa-2		Alfa-2		Total EEG	
Fp1-Fp2	0.60±0.03	0.35±0.06 **	0.61±0.05	0.33±0.07 ***	0.61±0.05	0.35±0.07 **		
F3-F4	0.56±0.06	0.36±0.06 **	0.53±0.04	0.38±0.05 **	0.56±0.05	0.41±0.05 *		
F7-F8	0.57±0.04	0.41±0.07 **	0.54±0.04	0.42±0.06 *	0.53±0.05	0.43±0.08 *		
C3-C4	0.47±0.06	0.40±0.08 *	0.45±0.05	0.39±0.07	0.47±0.04	0.37±0.09 *		
P3-P4	0.61±0.07	0.43±0.08 ***	0.57±0.05	0.45±0.07 *	0.55±0.05	0.41±0.09 *		
O1-O2	0.62±0.05	0.49±0.05 **	0.55±0.06	0.47±0.04	0.54±0.06	0.41±0.07 *		
T3-T4	0.52±0.06	0.45±0.09 *	0.46±0.04	0.31±0.09 *	0.49±0.04	0.39±0.09 *		
T5-T6	0.28±0.05	0.15±0.07 *	0.26±0.07	0.20±0.07	0.39±0.07	0.29±0.07 *		

Note. * – $p < 0.05$, ** – $p < 0.01$, *** – $p < 0.001$.

Thus, coherence analysis is a derivative method from the spectral analysis of the EEG. The neurophysiological substantiation of the coherence method is based on the model of similarity of the spectral composition in different leads and reflects the degree of synchronization of the activity recorded in the selected leads. Synchronization of activity reflects, in turn, the level of consolidation of various neural networks and centers, the activity of which is reflected in the EEG parameters in the selected sites.

The calculation of coherence is based on the principle of repeatability of wave events in time, therefore the analyzed sections of the electroencephalogram (analysis epochs) should be sufficiently long. 3-5 min of resting EEG in this study. Coherence is calculated for two channels–8 pairs in this study. Thus, from a functional point of view, coherence is a measure of correlation between EEG powers calculated in the same frequency range but in different leads. Mathematically, EEG coherence is calculated as:

$$Coh = |S_{xy}(f)|^2 / (S_{xx}(f) * S_{yy}(f))$$

where *Coh* is the coherence, $S_{xy}(f)$ is the value of the cross-spectrum at a given frequency, $S_{xx}(f)$ and $S_{yy}(f)$ are the values of the autospectra *x* and *y* at the same frequency.

2.3. Nonspecific electroencephalography parameters, Loreta-key

Next we analyzed both nonspecific physical parameters of the alpha wave process–index, frequency and amplitude, and physiological features of alpha oscillations–regularity, autorhythmicity (modulation) and stability of the alpha rhythm. Analysis of bioelectric signals was carried out using WinEEG, EEG Studio and Loreta-Key Viewer programs in accordance with the requirements of the International Federation of Clinical Neurophysiology. At the first stage, EEG patterns were assessed visually by amplitude-time characteristics, as well as by the distribution of EEG rhythms over the surface of the scalp and the degree of recording desynchronization in a test with opening/closing eyes and/or presentation of single flashes of light. The total duration of EEG recording was 10–15 min with most of the time with eyes closed. Artifacts were removed using software, and manually.

The functional state of the reticular formation was assessed by the parameters of latent period (LP) of synchronization (normally 0.4-1.0 s), desynchronization (normally 0.01-0.03) and the depth of desynchronization (normally 5-6-fold) in the test opening/closing eyes. The tone of the cerebral cortex was assessed by the ratio of frequency indices of alpha and delta rhythms. The paroxysmal index was calculated by the number of flashes per minute segment of the EEG recording. The functional stability of cortical rhythms was assessed by the stability of the background frequency of the alpha rhythm: alpha frequency fluctuations exceeding 0.5 Hz are regarded as a sign of instability of the oscillatory activity of the brain [9], [25].

EEG data were assessed using the WIN-EEG software product, version 1.3, developed at the Institute of Human Brain of the Russian Academy of Sciences. Statistical analysis of the obtained data was carried out using the STATISTICA package. The reliability of the results was assessed using p-value of the one-way ANOVA.

At the second stage of EEG analysis, spectral power in the main frequency ranges was assessed. In this research only EEG alpha waves were analyzed. In addition, correlation coefficients were calculated using the alpha range to compare intrahemispheric and interhemispheric interactions. The following spectral power parameters were chosen: the EEG window was 10 sec with an analysis epoch of 5 sec. The overlap of analysis epochs was 50%. The Hann time window and the low-frequency range of the signal were selected at 0.25–1.25. Also, the average spectrum was calculated for all recording points free from artifacts of EEG segments. All secondary results were transformed into percentages so that the total sum across all frequency ranges for each recording point was 100%. The reliability of the obtained data was assessed using p-value of the one-way ANOVA. Statistical differences were considered significant at $p < 0.05$.

In addition, neuroimaging of local changes in the spectral power of the alpha rhythm was carried out using a specialized low-resolution electromagnetic tomography application (LORETA, soft Loreta-Key Viewer 04) with the construction of 2- and 3-dimensional graphs of activity on brain structures. LORETA Method–low resolution brain electromagnetic tomography. The main objective of this method is to estimate the density of brain sources distribution, which best explains the distribution of potentials recorded on the scalp. In other words, the electric current power indicator in a specific range or in all presented ranges (the area of data processed by LORETA) can be corrected by presenting it as topographic anatomical maps in both 2D and 3D projection. By analogy with topographic maps, this viewer is mainly used to improve the presentability of data.

3. RESULTS AND DISCUSSION

In this study, coherence analysis was calculated for the total EEG, as well as for the frequency characteristics of the alpha range of EEG 1 and 2 (Table 1). First, let us consider the comparative characteristics for the total EEG, where, in general, there are significant differences in all pairs of electrodes ($p < 0.05$) with some increase in the frontal channels Fp1-Fp2 ($p < 0.01$).

More pronounced differences in coherence are recorded for the frequency ranges of the alpha rhythm. For alpha-1 (8-10.5 Hz), the maximum differences are noticeable in all pairs of frontal and occipital electrodes ($p < 0.01$), and in the parietal recording points the difference increases ($p < 0.001$). Against this background, the difference in the coherence analysis values for alpha-2 (10.5-13 Hz) looks less significant. The maximum is characteristic only in the frontal Fp1-Fp2 ($p < 0.001$) and F3-F4 ($p < 0.01$) recording channels, in the rest the differences are minimal F7-F8, P3-P4, T3-T4 ($p < 0.05$) or no differences were found – C3-C4, O1-O2 and T5-T6 ($p > 0.05$).

In Figure 3 shows a typical diagram of coherent connections. For healthy subjects in the control group, a fairly symmetrical pattern of coherence is observed in all pairs of electrodes Figure 3(a), with a virtually complete absence of coherence in psychopathology Figure 3(b). Figure 4 shows a typical pattern (topo map) of activity in a state of waking rest. In subjects of the control group Figure 4(a), at rest in the range of the high-frequency dominant alpha2 rhythm, interhemispheric coherent connections between the frontal, central, parietal, temporal and occipital brain areas were preserved. The symmetrical activation of the occipital areas is well expressed. Figure 4(b) patients experience destruction of coherent connections with activation in the right temporo-parietal region. These findings are confirmed by low-resolution electromagnetic tomography data from Loreta in 2D and 3D projections (Figure 5).

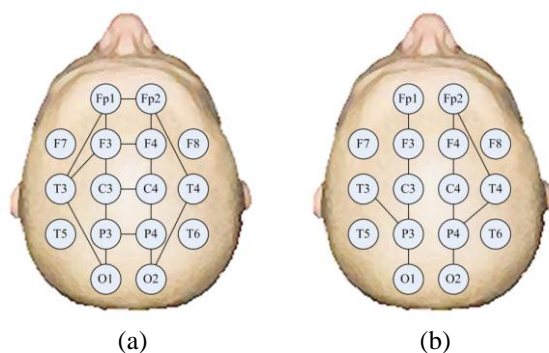


Figure 3. Dynamics of the spatial distribution of alpha rhythm coherence according to the alpha rhythm in; (a) a control group and (b) a main group

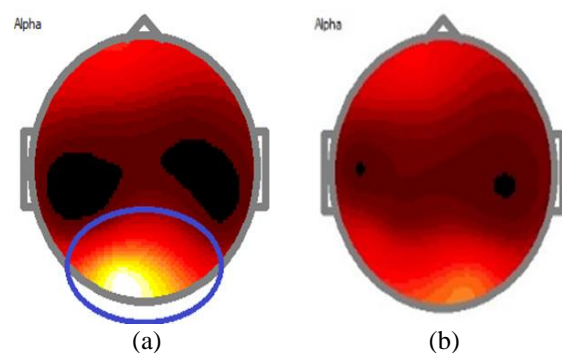


Figure 4. EEG topomaps according to the alpha rhythm in; (a) a control group and (b) a main group

As digital data show, the level of integrative processes in the alpha range reliably prevails in the frontal regions of the brain and decreases towards the occipital regions of the brain. The minimum physiological level of coherence was recorded between the temporal regions. In the control group, coherent interactions characteristic of a state of functional rest were preserved, predominantly in short intrahemispheric pairs, without the formation of a lateralized focus of coherence.

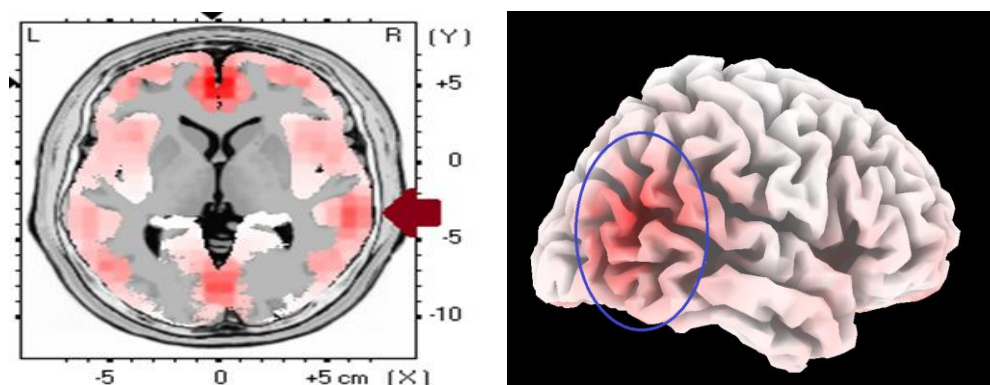


Figure 5. Same patient (see Figure 2) left-2D projection of the Loreta electromagnetic neurovisualization of local changes in the right temporo-parietal area (red arrow), right-3D projection of the Loreta neurovisualization of local changes in the right temporo-parietal area (highlighted with a marker)

The preservation of the functional mechanisms of nonspecific brain systems of the subjects was determined by the values of the LPs of synchronization, desynchronization, and the depth of desynchronization of the alpha rhythm in the “opening-closing eyes” test, as the basic neurodynamic processes of the formation of integral EEG patterns. The specificity of dysfunctional states of the thalamo-cortical system was determined by the degree of deviation of the spectral characteristics of the alpha rhythm from normative values and the characteristics of its zonal distribution. The functional state of subthalamic and thalamo-cortical neural networks was assessed by the number of flashes recorded per 1 min of background EEG recording and characterizing the degree of brain paroxysmalness. The energy- tonic status of the brain was determined by the ratio of indices of the alpha/delta frequency ranges, and the level of wakefulness and activity of consciousness was assessed by the presence on the EEG of the ratio of fast-wave and slow-wave activity–beta/delta frequency ranges (Table 2).

Table 2. Comparative analysis of key neurodynamic parameters in subjects main and control groups

Neurodynamics indicators	Normal values	Main group	Control group
LP desynchronization, sec	0.01–0.03	0.07±0.002	0.02±0.012*
LP synchronization, sec	0.4–1.0	1.61±0.009	0.75±0.03*
Desynchronization depth coefficient	5-6-times decline	3-4-times decline	5-6-times*decline
Coefficient of tone and activation of the cortex	12.2	4.50±2.58	12.50±2.15*
Flashes	No more 2/sec	5.1±0.85	1.8±0.25*

Note. See Table 1

Analysis of the research results shows that in the subjects of the main group, the LP of alpha rhythm desynchronization with open eyes exceeded the normative values by 2.3 times ($p<0.05$), and the LP of the main rhythm synchronization turned out to be 1.6 times higher than the normative values ($p<0.05$). At the same time, the depth of synchronization in patients with schizophrenia was 1.22 times lower than normal. The totality of the data obtained indicates a violation of the functional state of the ascending activating and ascending inhibitory systems of the brainstem.

The values of the coefficient of cerebral cortex tone in schizophrenia turned out to be significantly lower than the normative values by 2.3 times ($p<0.001$), which indicates a deficiency of energy- tonic influences that ensure the maintenance of the level of consciousness activity.

In patients the average number of outbursts exceeded the normative values by 2.5 times ($p<0.04$), which indicates an increase in the degree of paroxysmality of the brain and is an objective sign of a dysfunctional state of the ponto-hypothalamic and thalamic structures of the 1st functional block of the brain.

Taking into account the close morpho-functional connection of the alpha rhythm with the fronto-thalamic system, which provides modulation of the semantic aspects of consciousness, an analysis of nonspecific (index, frequency, amplitude) and physiological features of alpha oscillations was carried out – regularity, authoritativeness (modulation) and stability of alpha-rhythm (Table 3).

From the presented data (Table 3) it is clear that in persons with psychopathology all parameters of alpha activity are significantly changed. A zonal decrease in the frequency of the alpha rhythm below 9.15 indirectly indicates the disintegration of the thalamo-cortical system, which plays a key role in providing energy-informational influences on the cerebral cortex, modulating the level of wakefulness and

consciousness. Fluctuations in the frequency of the basic alpha rhythm exceeding 0.5 Hz indicate instability of the oscillatory activity of the alpha frequency range, which provides basic brain regulatory processes. The totality presented in Table 3 structural-spatial disturbances of the alpha rhythm can be interpreted as a manifestation of thalamic-cortical dysrhythmia.

Table 3. Comparative analysis of background parameters of alpha rhythm in individuals main and control groups

Parameters of alpha rhythm	Main group	Control group
Index, %	38.6±6.6	65.7 **
Frequency, Hz	8.8	10.1 *
Alpha band width, Hz	7.2–12.1	8–13 *
Amplitude, uV	49.8	62.2 **
Regularity, Hz	1.9	0.47 **
Modulations	—	+++
Stability	—	+++
Zonal distribution	Violated	Saved

Note. See Table 1

Network data on the state of basic interhemispheric integration based on the results of coherent analysis of the EEG in main and control groups are presented on network coherentograms for alpha-1 Figure 6(a) and alpha-2 EEG Figure 6(b). Analysis of coherence indicators indicates a significant decrease in the temporal coherence of the operational activity of neural networks in patients (blue line) compared to healthy (green line) subjects Figures 6(a) and (b). For alpha-1 EEG segment Figure 6(a) a decrease in the average synchrony index was noted in a line interhemispheric pair of EEG points of registration. Especially in the frontal sites (Fp₁-Fp₂, $p<0.001$), (F₃-F₄, F₇-T₈, $p<0.01$), parietal (O₁-O₂, $p<0.05$), (mostly on the left) and right parietal-central region (P₃-P₄, $p<0.01$).

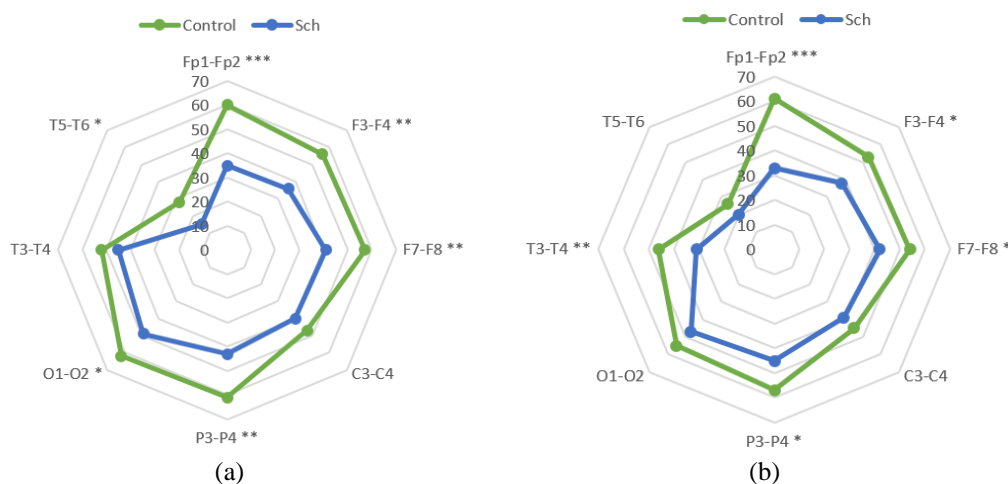


Figure 6. Network coherentograms; (a) –alpha-1 rhythm and (b) –alpha-2 rhythm of the EEG, the green line – control group, the blue line – main group, note (see Table 1)

For alpha-2 EEG segment a decrease in the average synchrony index was noted in all interhemispheric pairs of EEG sites, and especially in pairs of channels related to the frontal (Fp₁-Fp₂, $p<0.001$), temporal (T₃-T₄, $p<0.01$), (mostly on the left) and right parietal-central region (P₃-P₄, $p<0.05$). The data obtained show that the most pronounced changes in the integrative processes of the brain are observed mainly at the level of interhemispheric connections in the fronto-temporal areas Figure 6(b).

In general, when comparing the results of EEG coherence analysis between groups, significant differences between the level of integration in the main and control groups are noteworthy. The disruption of coherent processes in patients with schizophrenia is generalized. In 8 interhemispheric pairs, there is either a significant decrease in the level of spatial synchronization ($p<0.05$, $p<0.01$, $p<0.001$) or the indicated direction of brain disintegration manifests itself at the level of a trend.

In the study of consciousness, one of the main issues is the morpho-functional characteristics of the neural substrate of consciousness. There are views that even local biological neural networks demonstrate some form of phenomenal consciousness [25]-[27]. In this regard, theories of NCC have been formed, which can predict the emergence of biological neural networks capable of learning in a virtual environment, somehow reproducing the behavior of their embodied counterparts.

Existing NCC theories consider the problem of consciousness against the background of the whole brain, without defining the minimal neural networks (systems) capable of supporting consciousness. This is a limitation of how an in vitro cluster of neurons can be considered as a neural correlate of consciousness. NCC theories suggest that the entire brain is necessary and sufficient for the formation of consciousness. Based on this, the question arises, which of the subcomponents of consciousness are necessary for the creation of conscious experience. In general, all NCCs provide a set of requirements and thresholds for consciousness based on the central idea that consciousness is, after all, bound up with specific areas of the brain and associated neural tissue. These theories thrive on their ability to point to brain mechanisms that might support varying degrees or forms of consciousness. Progress in addressing the problem of mind can be made by focusing on questions that are relatively simple and relevant. On this basis, assessing levels of consciousness in known psychopathology provides a useful model for both studying levels of consciousness and the neural networks that support consciousness in psychopathology [26].

According to our hypothesis, the main function of the brain alpha oscillatory system is not only the optimization of the cognitive sphere, aimed at processing information, maintaining attention, brain tone, and wakefulness, but also modulating the level of consciousness as a complex metacognitive function. In the real cognitive process, optimal psychophysiological conditions for the implementation of cognitive-mental functions are formed with the necessary and sufficient tone and activation of the brain, ensuring the activity of consciousness. In our study, in psychopathology, this parameter was reduced by 2.3 times, which is a reliable sign of a decrease in the activity of consciousness. In the practice of EEG studies, calculation and analysis of parameters of brain tone, as the most important psychophysiological indicator of the general state of the brain and the level of consciousness activity, is rarely carried out [7], [28].

When comparing the results of EEG coherence analysis between research groups, significant differences between the level of integration in the main and control groups are noteworthy. The disruption of coherent processes in patients with schizophrenia is generalized. In 8 interhemispheric pairs, there is either a significant decrease in the level of spatial synchronization or the indicated direction of brain disintegration manifests itself at the level of a trend.

The loss of amplitude modulations of the α -rhythm in psychopathology indicates dysfunction of the desynchronizing and synchronizing systems of the brain, disorganization of afferent and efferent control and disruption of the mechanisms of activity of neural networks, which also contributes to a decrease in the activity of consciousness.

Episodes of a spontaneous decrease in the frequency and/or amplitude (power) of the alpha rhythm, spontaneous irradiation of the main rhythm to the anterior parts of the brain indicate a decrease in the level of wakefulness and consciousness. In almost half of the subjects in the main group (42.5%), short-term 0.5–1–2 sec episodes of spontaneous decrease in the α rhythm to 7.5–9.2 Hz were recorded on the EEG. At the same time, the alpha rhythm was characterized by uneven amplitude with signs of disorganization and periods of sharp spontaneous decrease in amplitude.

Episodes of spontaneous total 1–2-sec reduction of bioelectrical activity were recorded sporadically in all parts of the hemispheres in 50% of patients. The noted EEG phenomena are also legitimately interpreted as reliable signs of a decrease in the level of consciousness, since they reflect disorganization of the thalamo-cortical system of the brain. Short-term 1–2 sec episodes of spontaneous synchronization of the alpha rhythm, local or diffuse in nature, a local increase in delta-theta activity in the anterior parts of the brain is also associated with a reflection of a decrease in the brain functional state and the level of activity of consciousness.

There is evidence that in schizophrenia, abnormal characteristics of alpha oscillations are recorded during a poststimulus of 100–300 ms. These characteristics include decreased time-frequency distributions in prefrontal, parietal, and occipital regions; lower functional capabilities of the phase delay index strength in the parietal and occipital regions; the nodal effectiveness of local centers is increased in the temporal regions and decreased in the occipital region for the properties of the dynamic topology of the network. The authors support the hypothesis that abnormal alpha rhythm may be a major contributor to dysfunctional self-referential processing in patients with schizophrenia [29].

In another research, a slower individual alpha peak frequency (IAPF) was observed in a group of patients with schizophrenia. This was associated with cognitive task solving with attentional activation, as well as impairment of global awareness as measured by neuropsychological tests. Notably, visual attention deficits fully mediated the relationship between IAPF and global awareness. The slower alpha oscillation cycle explains global cognitive deficits in schizophrenia through impairments in perceptual discrimination

measured during a visual attention task. The study results provide evidence that slower IAPF may reflect a neural mechanism responsible for generalized cognitive impairment in schizophrenia. Analysis suggests that such perceptual sensitivity ultimately plays a role in higher order cognitive functions, particularly consciousness. It is emphasized that the relative timing of diffuse neural activity is a likely neural mechanism of generalized cognitive deficits in schizophrenia [21].

It is known that psychopathological conditions, as well as stress or long-term depression can lead to atrophy and death of neurons in the limbic structures of the brain, which play a decisive role in the formation of emotions and disorders associated with the emotional sphere [30], [31]. Over the past 20 years, it has been established that long-term stress promotes generalized neuronal atrophy and synaptic inhibition in the prefrontal cortex and hippocampus [26]. In contrast, the amygdala and NAc exhibit neuronal hypertrophy and synaptic facilitation [26], [30]. The hippocampus provides inputs to other brain regions, including the prefrontal cortex, cingulate cortex, and amygdala, which contribute significantly to mood and emotional changes in depression [26]. Many studies have reported a decrease in the size of the hippocampus and prefrontal cortex in patients with depression [11], [32]. In addition, it has been found that 20–40% of patients with depression show abnormal EEG characteristics [25], with asymmetry of EEG activity in the frontal regions [22]. The prefrontal cortex is affected by depression, anxiety and stress. At the same time, alpha waves in the prefrontal cortex are usually less active in patients with depression than in normal people [33].

Various studies have described an average reduction of alpha and theta waves with an increase in the beta rhythm component of the EEG of patients with depression [21]. Neurotransmitters such as serotonin and dopamine play a role in regulating mood and cognitive function. Stress also affects the beta rhythm, which is associated with selective attention and persistence of EEG parameters [25], [34]. Reducing the release of norepinephrine into target areas such as the prefrontal cortex and amygdala inhibits the development of anxious behavior [35]–[37].

Thus, in schizophrenia, EEG abnormalities are as follows [33], [38]. The first effect is a global decrease in the absolute power of the EEG, manifested in the alpha and beta frequency ranges, as well as in the broadband EEG. The second effect is a relative increase in the power of alpha radiation in the prefrontal areas of the brain against the background of its decrease in the posterior areas. Both effects are not only consistent in the alpha range, but are also associated with schizophrenia symptoms and disease duration. In general, the concept of hypofrontality is confirmed, the alpha rhythm is a marker. From a neurobiological point of view, a distortion of the anterior-posterior gradient of the alpha rhythm in schizophrenia seems plausible. In particular, this phenomenon is consistent with abnormalities of thalamic metabolism and thalamo-cortical circuitry in schizophrenia [13], [15]. Patients have higher relative glucose metabolism in the pulvinar, which is connected to many posterior regions, and lower metabolism in the mediodorsal and centromedial nuclei of the thalamus, which project broadly to the frontotemporal cortex.

In our work we considered only one indicator of brain and consciousness functioning—EEG alpha rhythm. Speaking about promising research, we see the application of machine learning methods to EEG processing, comparison with indicators of other functional studies (fMRI, MRI, ERPs, and PET), intelligent video stream. Evaluation of alpha rhythm activity dynamics can be considered as a prognostic criterion in the dynamics of schizophrenia.

Limitations; all studies of participants in the main and control groups were carried out in an outpatient clinical Psycho-Neurological dispensary. The diagnosis of paranoid schizophrenia was established in psychiatric inpatient hospitals in accordance with ICD-11 (06. Mental and behavioral disorders, Schizophrenia or other primary psychotic disorders). The average anamnesis was 9.8 ± 3.1 years. The main task of the examined patients was to confirm the diagnosis for subsequent receipt of social support. In this regard, a complex of functional and psychological research methods was performed. Confirmation of the diagnosis was based on the clinical picture, documentary data and the results of related studies. If necessary, some patients were sent to inpatient hospitals. Neurophysiological research (rs-EEG) was carried out in a darkened, shielded room with the patient reclining in a special chair, lasting 10–15 min.

4. CONCLUSION

The present study shows that based on the specifics of changes in the rs-alpha rhythm of the EEG, it is possible to assess the individual level of consciousness, as well as the possible role of disorganization of consciousness in the mechanisms of formation of schizophrenia symptoms. Our proposed hypothesis about the possibility of EEG assessment of the level of consciousness based on an analysis of the main parameters of the rs-alpha rhythm is confirmed. In general, when comparing the results of EEG coherence analysis between groups, significant differences between the level of integration in the main and control groups are noteworthy. The disruption of coherent processes in patients with schizophrenia is generalized. In 8 interhemispheric pairs, there is either a significant decrease in the level of spatial synchronization ($p < 0.05$,

$p < 0.01$, $p < 0.001$) or the indicated direction of brain disintegration manifests itself at the level of a trend. Taking into account the close morpho-functional connection of the alpha rhythm with the fronto-thalamic system, which provides modulation of the semantic aspects of consciousness, an analysis of nonspecific (index, frequency, and amplitude) and physiological features of alpha oscillations was carried out—regularity, authoritativeness (modulation) and stability of alpha-rhythm. The LP of alpha rhythm desynchronization with open eyes exceeds the normative values by 2.3 times ($p < 0.05$), and the LP of the main rhythm synchronization turned out to be 1.6 times higher than the normative values ($p < 0.05$). The depth of synchronization in patients with schizophrenia was 1.22 times lower than normal. The totality of the data obtained is associated with changes in the functional state of the ascending reticular activating system of the brain. In patients the average number of outbursts exceeded the normative values by 2.5 times ($p < 0.04$), which indicates an increase in the degree of paroxysmality of the brain and is an objective sign of a dysfunctional state of the ponto-hypothalamic and thalamic structures.

FUNDING INFORMATION

This research by Saint Petersburg State Pediatric Medical University was supported. Project No. AAAA-A19-119112290090-9.

AUTHOR CONTRIBUTIONS STATEMENT

This journal uses the Contributor Roles Taxonomy (CRediT) to recognize individual author contributions, reduce authorship disputes, and facilitate collaboration.

Name of Author	C	M	So	Va	Fo	I	R	D	O	E	Vi	Su	P	Fu
Sergey Lytaev	✓	✓		✓			✓			✓	✓	✓	✓	✓
Ksenia Belskaya		✓	✓	✓	✓	✓	✓	✓	✓		✓			

C : **C**onceptualization

M : **M**ethodology

So : **S**oftware

Va : **V**alidation

Fo : **F**ormal analysis

I : **I**nterpretation

R : **R**esources

D : **D**ata Curation

O : **O**rganizational

E : **E**ditorial

Vi : **V**isualization

Su : **S**upervision

P : **P**roject administration

Fu : **F**unding acquisition

CONFLICT OF INTEREST STATEMENT

Authors state no conflict of interest.

INFORMED CONSENT

We have obtained informed consent from all individuals included in this study.

ETHICAL APPROVAL

The research related to human use has been complied with all the relevant national regulations and institutional policies in accordance with the tenets of the Helsinki Declaration and has been approved by the local ethical committee of the Saint Petersburg State Pediatric Medical University.

DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author, [SL], upon reasonable request.

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BIOGRAPHIES OF AUTHORS



Sergey Lytaev    Professor 1978-1984 MD student, S.M. Kirov Military Medical Academy, Saint Petersburg, Russia. 1988-1991 Ph.D. student, Normal Physiology, Ibid. 1991-2004 Lecturer, Assistant Professor, Chief of Department, Ibid. 2000-2006 Professor Medical Psychology & Psychophysiology, Saint Petersburg State University. 2004 until present head of scientific departments and labs in Russian Academy of Sciences and Ministry of Health. Head of Russian and International scientific awards on issues of psychology, neurophysiology and psychophysiology. The author/co-author more than 350 scientific papers on neurophysiology, psychophysiology, neuropsychology, and artificial intelligence. Since 2018-national delegate at the International Federation on Clinical Neurophysiology (IFCN, Chicago, IL, and USA). Member of the Russian Committee of Physiologists, Russian Academy of Science, Moscow. He can be contacted at email: physiology@gpmu.org.



Ksenia Belskaya    is an Associate Professor at the Department of Normal Physiology, Saint Petersburg State Pediatric Medical University, Russia. She has been a faculty member since 2002 and graduated at 2008. From 2008-2011, she was also the Ph.D. student of the department of Normal Physiology. In 2013, she received Ph.D. degree after submitting a dissertation at the S.M. Kirov Military Medical Academy in St. Petersburg on the topic "Psychophysiological mechanisms of perception of simple and complex auditory images in psychopathological conditions". In 2013-2019 Assistant of the Department of Normal Physiology, St. Petersburg State Pediatric Medical University. 2019-2022 Senior Lecturer, ibid. 2022 until present Associate Professor, ibid. Research interests-neurophysiology, artificial intelligence, consciousness, and psychopathology. She can be contacted at email: belskaya.k.a@gmail.com.