

Original Research

Neural Network of Alpha Rhythm rs-EEG Activity for the Assessment of Consciousness in Psychopathology

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Abstract

Consciousness is an integrative process that combines several executive functions, as well as the analytical and synthetic activity of the brain. In some psychopathological conditions, in particular, in schizophrenia, low-information "borderline" disorders of the executive functions and consciousness are often formed at the onset. The present study was aimed at assessing the integration of the brain alpha regulatory system and the modulation of consciousness based on the data of recording the alpha rhythm of resting state EEG associated with a decrease in the level of consciousness. The study involved 40 outpatients with actual symptomatic schizophrenia associated with neurocognitive and depressive symptoms, and 38 healthy subjects. Using the WinEEG, EEG Studio and Loreta-Key Viewer programs, we analyzed both non-specific physical parameters of alpha rhythm generation - index, frequency, amplitude, and physiological characteristics associated with executive functions - regularity, autorhythmicity (modulation) and stability of the EEG alpha rhythm. A line of indicators for the alpha rhythm in schizophrenia has been calculated based on coherence in different areas



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of the brain, the latent period of desynchronization, the average number of bursts, and the tone of the cerebral cortex.

Keywords

rsEEG; brain functional blocks; resting state networks; neurocognitive deficit; level of consciousness activity; schizophrenia

1. Introduction

The healthy and diseased brain at rest generates cycles of bioelectrical activity that differ significantly in psychopathological conditions and, in particular, in schizophrenia. It is known that individual peak alpha frequency is integrally related to sensory processes at the level of recognition and can have a further impact on executive cognitive functions such as attention, working memory, decision-making, and consciousness [1, 2]. Assessing functional brain networks is a new area of research that will help us to explain better the nature of a range of pathological conditions, among which schizophrenia is undoubtedly one of them. In addition, it should be understood that functional networks determine emotional functioning, cognitive-executive functions, and stress responses of the brain [3-5]. The range of research methods that allow online assessment of the network dynamics of the activity of nerve centers is relatively narrow [6-8]. These are EEG, functional magnetic resonance imaging (fMRI), and event-related potentials. Suppose EEG is considered the primary method for assessing temporal events. In that case, fMRI measures better identify the spatial dynamics of changes, and event-related potentials (ERPs) are an intermediate option that combines the advantages of EEG and fMRI [9, 10]. A lot of valuable and interesting information about brain function can be obtained using PET scans. However, when studying dynamic networks, this method has a significant time constraint due to the use of radioactive isotopes [11]. Current neuroimaging methods were thought to assess stable spatiotemporal functional connectivity by scanning and then constructing brain networks for a specific epoch of analysis. However, recent findings have suggested that the human brain is more dynamic and generates scale-free oscillations in space and time [11]. Thus, dynamic network analysis methods are increasingly being used better to detect oscillations in brain functional connectivity [12].

Most studies of resting state networks (RSNs) have been performed using static methods, i.e. networks were determined across the entire recording (“stationary” processing) [11, 13]. The assumption that connections between brain areas are static throughout resting-state recordings has often been criticized [14]. In particular, it has been reported [15] that the state of functional connectivity of networks obtained as a result of dynamic analysis differs significantly from the static activity. On this basis [16], 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 [17, 18].

Many sciences, even those not related to the study of the brain, have their concepts of the nature and mechanisms of consciousness [6, 19, 20]. Today, a practically important topic has formed the direction of research into spatio-temporal dynamic network integration associated with several executive functions with impaired consciousness [21-24].

In neuroscience, consciousness is associated with two groups of research areas of fundamental and applied significance. On the one hand, this is the diagnostics of the level of consciousness (wakefulness), based on which adequate behavior is formed when interacting with other subjects and the environment. On the other hand, this is the assessment of the internal content of consciousness with complex analytical and thought processes, the basis of which is subjective experience and awareness of the "inner self" [20].

There is no doubt that different levels of consciousness activation provide different perceptions of new information, changing the volumes of information flows at the stages of processing. This mechanism allows us to control different amounts of executive cognitive operations. It is information processing that becomes the most essential function of consciousness, which in humans is supplemented by the functions of speech and thinking [25].

From the standpoint of neuropsychology, consciousness is not generated by any brain structure. Still, it is a model of a network neural process that can change in a split second, which has given rise to new areas of research - insight, augmented consciousness, etc. Evaluation of network neural mechanisms shows that activation of consciousness is not primarily accompanied by increased activity of the neocortex, but rather by activation of vertically oriented parts of the brain, functional blocks. Consciousness in this case is based on emotional perception, which is primarily activated in the brainstem, and higher parts of the brain are connected at the next stage as a result of coordinated interaction of many parts of the brain [10, 26].

Psychotic changes are widespread, ranging from subclinical borderline disorders to various forms of neurodegenerative and psychiatric diseases. Deciphering the functional connectivity and neural networks of the brain in psychopathology is key to interpreting the neural mechanisms of psychosis [27]. In particular, functional neural network activity in 487 resting-state fMRI recordings in subjects with schizophrenia spectrum disorder (SCZ), bipolar disorder with psychotic experiences (BD), subclinical psychosis (SCP), and healthy controls (HC) was investigated [28]. Patients with BD had less pronounced integration of neural networks, but no abnormalities in connectivity were found. There were also no differences in parameters between SCP and SCZ or between BD patients who took antipsychotics or lithium compared with those who did not. It was concluded that neural networks in psychosis-prone patients have different characteristics in patients with SCZ and SCP compared to patients with drug-limited BD [28].

In general, it is believed that the shifts in the EEG alpha power in schizophrenia have different causes. Among them, the most probable mechanisms are considered to be generalized disintegration of local neural networks and thalamo-cortical interactions. Such disturbances affect the EEG of the anterior parts of the brain in opposite directions. In particular, thalamo-cortical deafferentation of the prefrontal cortex contributes to innate cortical autorhythmicity, i.e., an increase in the alpha signal power in the (pre)frontal areas. In contrast, the deficit of cortico-cortical circuits contributes to a global decrease 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 [29-31]. Interestingly, patients with schizophrenia show significantly lower alpha-band power at rest

compared to healthy subjects, especially in the prefrontal and parietal regions. Alpha oscillations are essential for top-down information processing in various cortical areas. This is associated with activation of the reticular formation of the brainstem [1, 22]. Significantly lower alpha-band power has also been reported in patients with schizophrenia compared to healthy individuals in a self-referential state [32, 33].

Recent decades of research have contributed to a certain consensus based on the fact that consciousness, as well as individual forms of complex mental functions, are network-level phenomena, that is, a phenomenological product of a neural network [34, 35]. High-level behavior requires high-level integration of various sensory inputs, synchronization of motor patterns, and their coordination with the assistance of large-scale neural networks. In turn, the accumulation and integration of data on the functioning of neural networks contributes to the formation of several testable hypotheses regarding the neural bases of cognitive functions, memory and behavior. In such conditions, today three main directions can be distinguished in the study of consciousness: the search for neural correlates of consciousness, the mechanisms of functioning of these correlates, and the reproducibility of the hypotheses put forward [36, 37].

The brain structures involved in the generation of 8-13 Hz bioelectric activity are often combined in scientific research into the alpha regulatory system of the brain. This system is represented as a dynamic neural network that ensures the processes of sensory perception, information processing, and short-term memory while simultaneously regulating attention and the level of wakefulness [7, 38]. Specific parameters of the EEG α -rhythm directly indicate the state of the brain and executive functions. An increased frequency of the α -range is accompanied by an acceleration of the change in excitation and inhibition periods, which, accordingly, increases the speed of information processing and motor reactions. The variability of the α -range parameters from 10 to 13 Hz is associated with increased activity of interaction between the cortical structures and the thalamus [7]. In addition, the upper limit of the EEG α -range is related to the preparation of neural networks to ensure executive functions, which is assessed by the subjective feeling of the level of wakefulness, activity of consciousness, and a surge of energy. Psychopathology, on the contrary, limits executive cognitive functions with a reduction in the α -range and speed of mental processes [39].

EEG/fMRI and EEG/PET studies have shown an inverse relationship between alpha power and regional metabolism, which has been observed in the occipital [40], parietal [41] and sensorimotor [42] 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 related to 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 [43] and in association with negative symptoms and type of schizophrenia [44].

Thus, the analysis of the literature shows that changes in the level of consciousness with impaired cognitive executive functions in psychopathology have a significant impact on the dynamics of neurocognitive dysfunctions, which is not always possible to take into account in treatment tactics [5, 33]. Thus, consciousness is interconnected with both cognitive executive functions and neural networks that ensure adaptive human behavior. This is the basis for research into methods for assessing the level of consciousness activity as an integral indicator of brain state. Based on this, the

present study was aimed at determining the level of consciousness based on resting EEG alpha activity (rs-EEG) with an emphasis on abnormal alpha rhythm patterns in patients with schizophrenia.

2. Materials and Methods

78 persons were selected, including 40 outpatients (leading 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 with a monopolar reference electrode of combined ear clips. All EEGs of the study of healthy subjects and patients were carried out in a licensed laboratory for functional research.

2.1 The Criteria for Selecting Subjects for Investigation

The research criteria for selecting all subjects (healthy and patients) were: a. no history of severe somatic and neurological diseases; TBI with loss of consciousness for more than 5 min; b. no history of alcohol or drug addiction; c. right-handedness; d. The study excluded persons with a negative attitude towards the tasks. 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. Among them, 40% had higher education, 40% had incomplete higher education, 20% had specialized secondary education, 50% of the subjects were married, 20% were divorced and 30% were never married.

The final diagnosis during a psychiatric examination by ICD-11 (06. Mental and behavioral disorders) were established—Schizophrenia or other primary psychotic disorders in a psychiatric institution (hospital) where the patient was observed. The average observation period was 9.8 ± 3.1 years. Among the examined patients, 30% had higher education, 30% had incomplete higher education, 30% had specialized secondary education, and 10% had secondary education. Additionally, 30% were married, 15% were divorced, and 55% were never married.

The main risk factors for schizophrenia, according to medical history, were distributed as follows: stress (70%), traumatic brain injury (63.3%), hereditary predisposition to mental disorders (36.7%), thyroid pathology (16.6%). Concomitant pathology was noted - osteochondrosis of the cervical spine, including aging vertebral artery syndrome, alcohol dependence, drug poisoning, and chronic adrenal insufficiency, which accounted for 6.7% of cases. An increased level of stress before the manifestation of schizophrenia was detected in 58.3% of cases. In addition, 20% of patients noted a severe stressful situation immediately preceding the manifestation of schizophrenia. In an in-depth analysis, the prevalence of occurrence was dominated by “change in sleep habits, sleep disturbance, change in daily routine” (45.5%), “change of job” (36.4%) and “death of a close family

member” (36.4%), “increased conflict in relationships with a spouse,” “sexual problems,” and “serious injury or illness” (31.9% each).

2.2 rs-EEG Data Analysis

The frequency of bioelectrical activity of the brain was measured based on the data of the Fourier transform spectral analysis. Both non-specific physical parameters of the alpha-range waves - index, frequency and amplitude, and some physiological features - regularity, autorhythm (modulation) and stability of the alpha rhythm were assessed. The analysis of bioelectric signals using the WinEEG, EEG Studio, and Loreta-Key Viewer programs was performed. Initially, the EEG patterns were visually evaluated by the amplitude-temporal characteristics, as well as by the distribution of EEG rhythms over the scalp surface and the degree of recording desynchronization in the test with opening/closing the eyes and/or presenting single flashes of light. The total duration of the EEG recording was 10-15 min; most of the time, the eyes were closed. Artifacts were removed using software and manually. 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, T₅-T₆. An 8-sec EEG segment with a well-defined alpha rhythm in the recording channels under study is shown in Figure 1. The most clear spindle of the alpha rhythm with frequency characteristics (8-13 Hz) is expressed at the frontal points of registration (upper waves on Figure 1) and the occipital-parietal (lower waves on Figure 1).

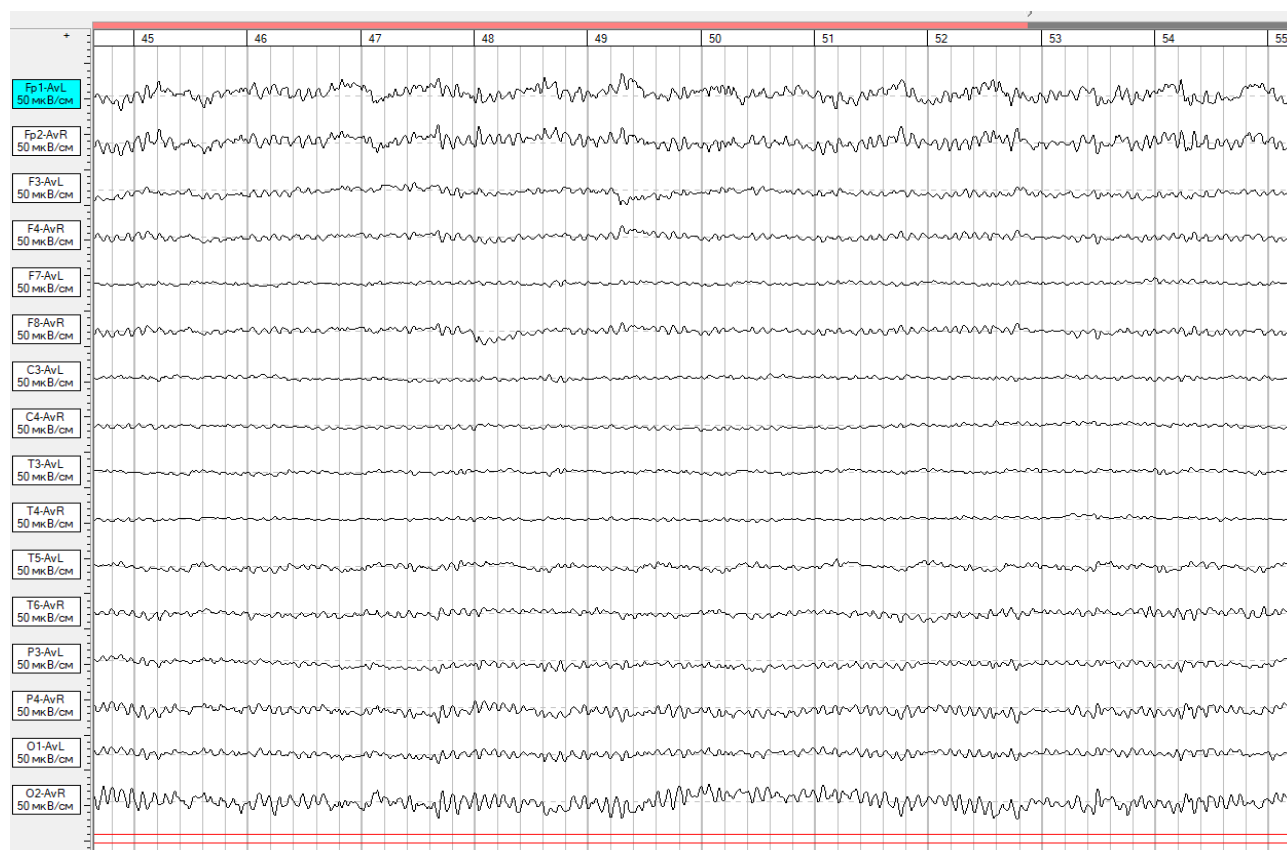


Figure 1 Fragment of EEG of a healthy subject (male, 42 years old) and location of the recording channels (left) under study epoch-8 sec.

The activity of the ascending activating system of the brain was analyzed by the time characteristics of the latent period (LP) of synchronization (usually 0.4-1.0 s), desynchronization (normally 0.01-0.03 s), and the depth of desynchronization (normally 5-6-fold) using the eye opening/closing test. The general tone of the cerebral cortex by the ratio of the time characteristics of the alpha and delta rhythms was analyzed. The index of paroxysmal activity was determined by the number of bursts in the epoch of EEG analysis in 1 min. The stability of background waves in the alpha range was analyzed to determine the general stability of the formation of rhythms of the cerebral cortex. In this case, frequency fluctuations exceeding 0.5 Hz are regarded as a sign of instability of the frequency brain activity [4, 34]. The EEG data using the WIN-EEG version 1.3 software product were evaluated. Statistical analysis of the obtained data was performed using the STATISTICA package, and reliability was assessed using the p-value of 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 the EEG segments. All secondary results were transformed into percentages so that the total sum across all frequency ranges for each recording point was 100%.

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. The reliability of the obtained data was assessed using the p-value of the one-way ANOVA. Statistical differences were considered significant at $p < 0.05$.

2.3 Ethics Statement

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.

3. Results

Data on the state of basic interhemispheric integration based on the results of coherent analysis of the EEG in the main and control groups are presented on network coherentograms for alpha-1 (Figure 2A) and alpha-2 EEG (Figure 2B).

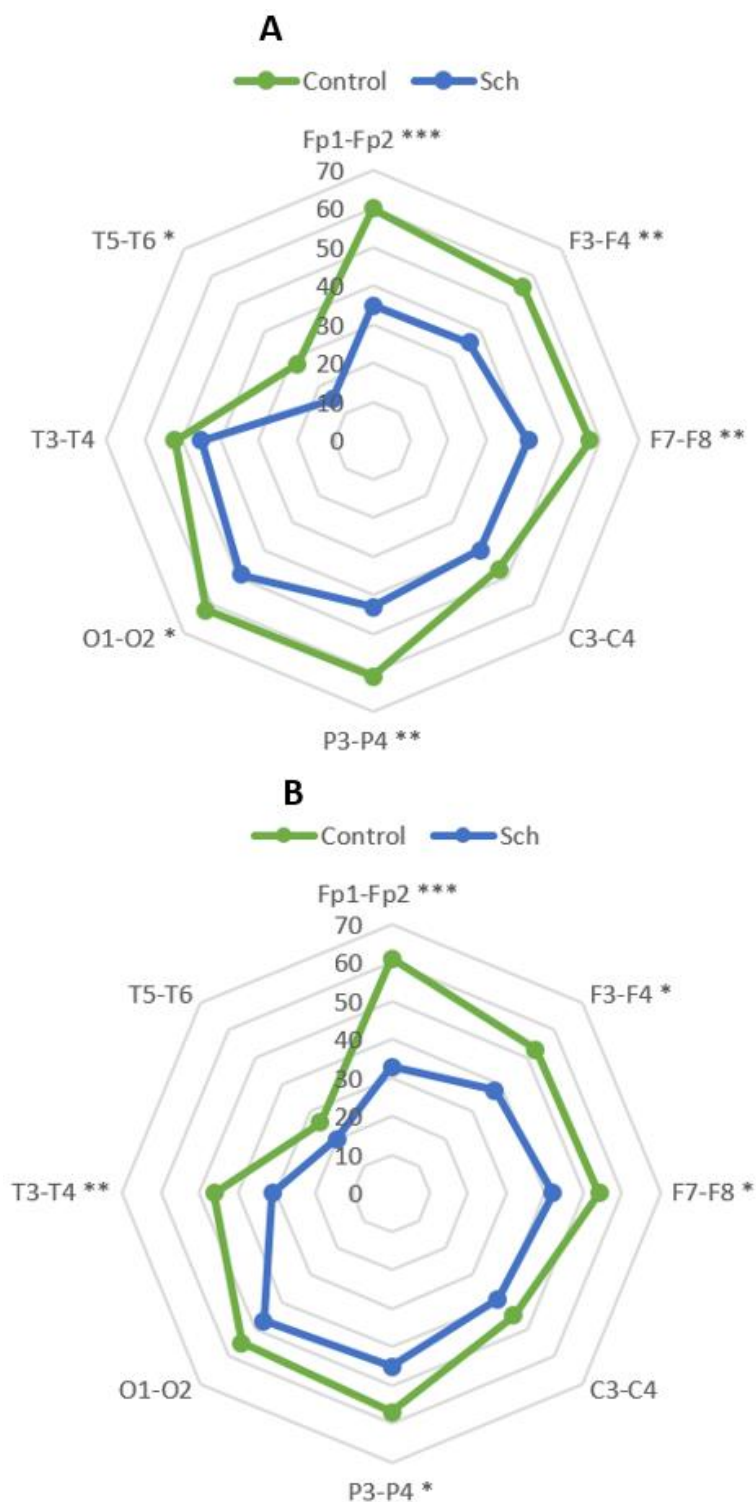


Figure 2 Network coherentograms. A - alpha-1 rhythm, B - alpha-2 rhythm of the EEG. The green line - control group, the blue line - main group. **Note.** * - $p < 0.05$, ** - $p < 0.01$, *** - $p < 0.001$.

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 (Figure 2A, B).

For the alpha-1 EEG segment (Figure 2A), a decrease in the average synchrony index was noted in the line interhemispheric pairs 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, $p < 0.05$), (mainly on the left) and right parietal-central region (P₃-P₄, $p < 0.01$).

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, $p < 0.01$), (mainly 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 2B).

In general, when comparing the results of EEG coherence analysis between groups, significant differences in integration levels between the primary 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.

Figure 3 shows a typical diagram of coherent connections and a typical pattern (topomap) of activity in a state of waking rest. In subjects of the control group, at rest in the range of the high-frequency dominant alpha-2 rhythm, interhemispheric coherent connections between the frontal, central, parietal, temporal, and occipital brain areas were preserved. The symmetrical activation of the occipital regions is well expressed. Patients experience destruction of coherent connections with activation in the right temporo-parietal region. Low-resolution electromagnetic tomography data from Loreta confirm these findings in 2D and 3D projections (Figure 4). As digital data show, the level of integrative processes in the alpha range reliably prevails in the frontal brain areas and decreases towards the occipital brain regions. The minimum physiological level of coherence was recorded between the temporal areas. 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.

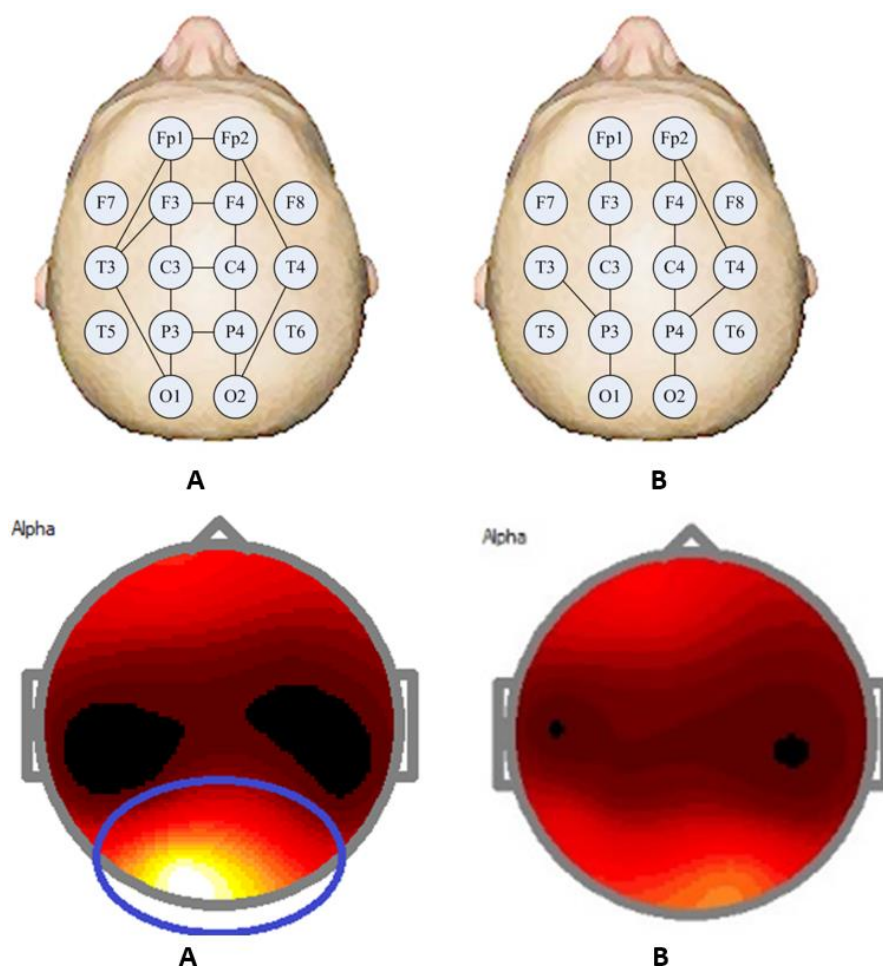


Figure 3 Dynamics of the spatial distribution of alpha rhythm coherence (top) and the EEG topomaps according to the alpha rhythm (bottom) in a control group (A) and a leading group (B).

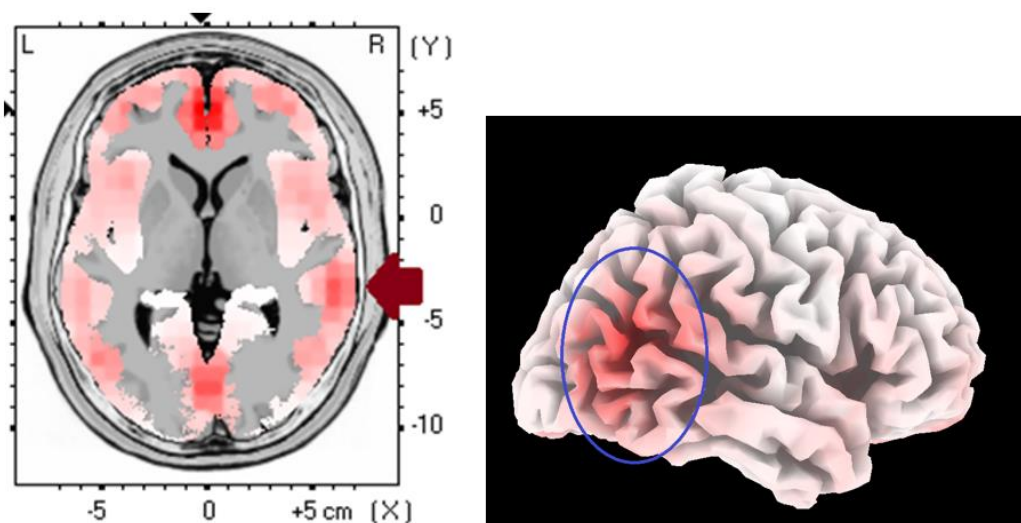


Figure 4 Same patient, see Figure 3. Left - 2D projection of the Loreta electromagnetic neurovisualization of local changes in the right temporo-parietal area (red arrow), ordinate - μV . Right - 3D projection of the Loreta - neurovisualization of local changes in the right temporo-parietal area (highlighted with a marker).

The analysis of the activity of non-specific brain systems, thalamo-cortical and related alpha-regulatory brain systems, depending on the physiological role in maintaining the general tone of the brain, the level of wakefulness, and the activity of consciousness, according to the spectral analysis of the EEG, was performed.

The time epochs of synchronization, desynchronization, and the degree of desynchronization of the alpha rhythm were analyzed to determine the functional stability of non-specific brain systems. The activity of thalamo-cortical interaction based on the dispersion of deviations in the spectral characteristics of alpha waves compared to the norm and the features of the cortical distribution was recorded. The activity of subthalamic and thalamo-cortical neural networks was assessed by the number of bursts in 1 min of the background EEG, characterizing the degree of paroxysmal brain activity. Brain tone by the ratio of alpha/delta waves, and the level of wakefulness and the degree of activation of consciousness were analyzed by the ratio of fast-wave and slow-wave activity - beta/delta waves was determined (Table 1).

Table 1 Comparative analysis of the EEG nonspecific parameters in outpatients and healthy subjects.

Parameters	Norm	Outpatients	Healthy
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 brain cortex tone	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 Figure 2.

Table 1 demonstrates several changes in outpatients with psychopathology compared to healthy subjects. Thus, the alpha activity desynchronization epoch with open eyes exceeds the normal values by 2.3 times ($p < 0.05$), while the synchronization epoch, on the contrary, is higher than the normal values by 1.6 times ($p < 0.05$). Against this background, the degree of synchronization in psychopathology is 1.22 times lower than the norm. In addition, pronounced differences are noted in the cortex tone coefficient - 3 times less in patients and, on the contrary, the number of activity bursts exceeds almost 3 times per unit of time.

Since the generation of EEG alpha activity is interconnected with fronto-thalamic projections that provide executive functions controlled by consciousness, several non-specific (index, amplitude-temporal characteristics) and physiological parameters expressed in regularity, authority (modulation), and stability were analyzed (Table 2).

Table 2 Analysis of amplitude-temporal characteristics of alpha rhythm in outpatients and healthy subjects.

Amplitude-temporal data	Outpatients	Healthy subjects
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 Figure 2.

In particular, the expression of the alpha rhythm index in patients is almost 2 times lower than the norm ($p < 0.01$), the average frequency is 1.3 Hz higher ($p < 0.05$), the frequency band is reduced ($p < 0.05$), the amplitude is reduced by about 20% ($p < 0.01$), the regularity, on the contrary, is almost 4 times higher ($p < 0.01$). Modulation and strengthening of the alpha wave formation are practically absent in psychopathology, and the distribution zone is damaged (Table 2).

4. Discussion

Consciousness, being the highest integrative process, exercises direct control over several executive functions, in particular, sensory perception, selective attention, short-term and long-term memory, emotions and motivations, and behavior in the environment [5, 10, 20]. The optimal level of consciousness, depending on the level of wakefulness, is ensured by the stable activity of neural networks, which is expressed in the ability to concentrate, short-term and long-term memorization with subsequent reproduction of information, as well as in the temporal and semantic characteristics of speech and thought-analytical activity, intellectual and psycho-emotional stability [7, 45].

According to the existing modern concepts, which were taken as the basis for the hypothesis of this study, the brain alpha oscillatory system is not only associated with the optimization of executive functions for the perception and processing of information with the activation of selective attention and generalized tone of the brain, but also provides modulation of the level of consciousness as a whole. Optimal conditions for the implementation of executive functions controlled by consciousness are formed with the appropriate tone and activation of the brain, which in turn support the activity of consciousness. It is noted that in the present study, in schizophrenia, this indicator is reduced by 2.3 times, which is regarded as a reliable sign of narrowing of consciousness [2, 6].

When comparing the results of EEG coherence analysis between research groups, significant differences in the level of integration in the primary 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 as a trend.

Reduction of the α -wave range of the EEG in schizophrenia is considered an indicator of dysfunction of the brain synchronization system, as well as processes of disorganization of afferent and efferent synthesis, which is reflected in the narrowing of the level of consciousness. These processes are directly related to the epochs of spontaneous reduction of the amplitude-temporal characteristics of the alpha rhythm, as well as spontaneous irradiation to the frontal areas, which indicate a decrease in the level of wakefulness and consciousness. Thus, in almost half of the outpatients with schizophrenia (42.5%), short-term 0.5-1-2-sec epochs of spontaneous reduction of α -waves to 7.5-9.2 Hz were noted on the EEG. At the same time, alpha waves were characterized by pronounced unevenness of amplitude with signs of disorganization and periods of significant spontaneous reduction of amplitude.

In 50% of outpatients, epochs of generalized reduction of bioelectrical activity lasting 1-2 seconds were spontaneously recorded. Such EEG phenomena are also assessed as reliable indicators of narrowing of consciousness, since they are associated with thalamo-cortical projections by their origin. Thus, short 1-2-sec epochs of spontaneous local or generalized synchronization of the alpha rhythm, against the background of a local increase in slow-wave activity in the frontal parts of the brain, also reflect both the tone of the brain as a whole 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 frequency distributions in prefrontal, parietal, and occipital areas; lower functional capabilities of the phase delay index strength in the parietal and occipital areas; 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 view that desynchronized alpha activity may be the underlying mechanism supporting information processing impairments in the executive functions system under the regulation of consciousness in patients with schizophrenia [1].

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 [31].

Neural measurements, especially EEG, are widely used to study and understand the underlying mechanisms of major depressive disorder (MDD), as a model syndrome for more severe mental illness. However, most of these studies examined either rs-EEG data or EEG data with the presentation of cognitive tasks. A comparative study of rs-EEG and cognitive EEG found in subjects more vulnerable to depression an increased EEG amplitude in the left frontal recording point and, on the contrary, a reduced amplitude in the frontal and occipital regions on the right for rs-EEG. Cognitive EEG data from a selective attention task to measure spontaneous thinking showed increased EEG amplitude at central recording sites in subjects with low vulnerability to depression and increased EEG amplitude in right temporal, occipital, and parietal regions in subjects prone to

depression. It has been established that in predicting the tendency to depression, the long-short-term memory model gives a maximum accuracy of up to 91.42% based on delta waves in cognitive tests, and a convolutional neural network shows a maximum accuracy of 98.06% based on EEG rs-waves. Thus, rs-EEG is considered more informative for predicting the onset of depression compared to cognitive EEG data. However, it is undeniable that cognitive EEG data will be more effective in understanding the mechanisms of depression. It is proposed to take into account several critical rs-EEG biomarkers, among which Higuchi fractal dimension, phase delay index, correlation and coherence functions are considered the most essential indicators for predicting vulnerability to depression [46].

To date, it has been established that some brain diseases, as well as psychoemotional stress or prolonged depression, contribute to the conditions for the formation of atrophy and death of neurons, primarily in the structures of the limbic system of the brain associated with the formation of emotions and disorders of the emotional sphere [19, 47, 48]. In addition, in the last 20 years it has been shown that prolonged psycho-emotional stress contributes to generalized neuronal atrophy and synaptic inhibition not only in the structures of the limbic system, but also in the frontal regions and hippocampus [49]. At the same time, the amygdala and NAc increase activity due to neuronal hypertrophy and acceleration of synaptic transmissions [49, 50]. The hippocampus provides an input into the structures of the limbic system of the brain, including the prefrontal cortex, cingulate cortex and amygdala, which make a significant contribution to changes in mood and emotions in depression [19]. Many studies have reported a decrease in the size of the hippocampus and prefrontal cortex in patients with depression [29, 45]. In addition, it has been found that 20-40% of patients with depression have abnormal EEG characteristics [51], with asymmetry in EEG activity in the frontal areas [46]. 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 individuals [52].

Studies conducted in different laboratories have shown data on a decrease in the average amplitude-temporal characteristics of alpha and theta waves with a simultaneous increase in the beta-frequency component of the EEG in depression [35]. It is known that among the CNS mediators, serotonin and dopamine, first of all, participate in the regulation of mood and the effectiveness of executive functions. Stress also affects the beta rhythm, which is associated with selective attention and the maintenance of EEG parameters [51, 53]. The task of minimizing the parameters of the EEG waves directly, so the number of electrodes used, is relevant in the clinic of the pathology of the brain [54, 55].

In addition to the above, it should be noted that recent data on the dynamics of synaptic elimination have been summarized. There is an opinion that synaptic elimination is the primary mechanism explaining neurophysiological changes in schizophrenia and correlates with clinical symptoms. Comparison of the results of studying the mechanisms of postnatal "synaptic pruning" with the clinical symptoms of schizophrenia allowed us to formulate a new theory of etiopathology, suggesting that the disease is formed as a result of pathological synaptic pruning. This hypothesis was subsequently expanded and suggests that excessive reduction of collateral axons in the prefrontal cortex directly leads to the clinical manifestations of schizophrenia [56].

Most studies of impairments in synaptic elimination in schizophrenia involve several structural and morphological parameters. Among these indicators, changes in bark thickness stand out; reduction in the size of neurons in the limbic, temporal and frontal regions, abnormal density of

dendritic spines in the cortex, changes in cytoarchitecture (which may be associated with abnormal migration, differentiation of neurons or a decrease in the number of cells) [23, 57-59]. Molecular genetic studies have linked structural brain changes to structural gene abnormalities that promote expression abnormalities associated with synaptic function, energy metabolism, immune system activation, and oligodendrocyte transcripts [8, 60]. In turn, all these disorders may be related to a pathological reduction in existing synaptic transmissions, resulting from genetic predisposition, as well as under the influence of environmental factors. The methodological problem here is the fact that the above studies were carried out mainly a considerable time after the onset of the disease. However, there is no data on the neurophysiological mechanisms of the occurrence of the first psychotic episode in the form of hallucinatory-paranoid syndrome.

Thus, in schizophrenia, EEG abnormalities are as follows [30]. 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 regions. 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 [1, 22, 31, 61]. 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.

4.1 Limitations

All studies of participants in the primary and control groups were carried out in an outpatient clinical Psycho-Neurological dispensary. The diagnosis of paranoid schizophrenia was established in psychiatric inpatient hospitals by 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.

5. Conclusions

The results of this study, when compared with the data of scientific research, indicate that the features of the dynamics of the rs-alpha rhythm of the EEG are an indicator of the level of consciousness activity, as well as an essential criterion in the disorganization of consciousness in schizophrenia. In general, when comparing the results of the analysis of EEG coherence between the groups, significant differences in integration levels between the primary and control groups are noteworthy. Violation of coherent processes in patients with schizophrenia is generalized. In 8 interhemispheric pairs, either a reliable decrease in the level of spatial synchronization is noted (p

< 0.05 , $p < 0.01$, $p < 0.001$), or the specified direction of brain disintegration is manifested at the level of tendency. Based on the interaction of the alpha-frequency system of the brain with the thalamo-frontal projections, non-specific (index, amplitude-temporal characteristics) and physiological features - regularity, ability to modulate, and stability of the alpha rhythm - are analyzed. The alpha wave desynchronization epochs with open eyes exceed the norm by 2.3 times ($p < 0.05$), and the rhythm synchronization epochs are 1.6 times higher than the norm ($p < 0.05$). The degree of synchronization in schizophrenia is 1.2 times lower than the norm. The obtained results show shifts in the functional state of the ascending reticular activating system of the brain. In schizophrenia, the average number of flashes exceeded the norm by 2.5 times ($p < 0.04$), which indicates an increase in the degree of paroxysmal activity in brain function and is an objective sign of the dysfunctional state of the stem and subcortical structures of the brain.

Author Contributions

Conceptualization, SL and KB; methodology, SL; software, KB; validation, SL, KB; formal analysis, KB; investigation, KB; resources, KB; data curation, KB; writing—original draft preparation, KB; writing—review and editing, SL; visualization, KB; supervision, SL; project administration, SL All authors have read and agreed to the published version of the manuscript.

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Competing Interests

The authors have declared that no competing interests exist.

Data Availability Statement

The data for this project are confidential, but may be obtained with Data Use Agreements with the Saint Petersburg State Pediatric Medical University, Department of Normal Physiology. Researchers interested in access to the data may contact [Sergey Lytaev] at [physiology@gpmu.org]. It can take some weeks (months) to negotiate data use agreements and gain access to the data. The author will assist with any reasonable replication attempts for two years following publication.

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