EEG Alpha Band Characteristics in Patients with a Depressive Episode within Recurrent and Bipolar Depression

Характеристики альфа-ритма ЭЭГ у больных с депрессивным эпизодом в рамках рекуррентной и биполярной депрессии

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Original research

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ABSTRACT

BACKGROUND: The search for biological markers for the differential diagnosis of recurrent depression and bipolar depression is an important undertaking in modern psychiatry. Electroencephalography (EEG) is one of the promising tools in addressing this challenge.

AIM: To identify differences in the quantitative characteristics of the electroencephalographic alpha band activity in patients with a depressive episode within the framework of recurrent depression and bipolar depression.

METHODS: Two groups of patients (all women) were formed: one consisting of subjects with recurrent depressive disorder and one with subjects experiencing a current mild/moderate episode (30 patients), and subjects with bipolar affective disorder or a current episode of mild or moderate depression (30 patients). The groups did not receive pharmacotherapy and did not differ in their socio-demographic parameters or total score on the Hamilton depression scale. A baseline electroencephalogram was recorded, and the quantitative characteristics of the alpha band activity were analyzed, including the absolute spectral power, interhemispheric coherence, and EEG activation.

RESULTS: The patients with recurrent depressive disorder demonstrated statistically significantly lower values of the average absolute spectral power of the alpha band (z=2.481; p=0.042), as well as less alpha attenuation from eyes closed to eyes open (z=2.573; p=0.035), as compared with the patients with bipolar affective disorder.

CONCLUSION: The presented quantitative characteristics of alpha activity are confirmation that patients with affective disorders of different origins also display distinctive electrophysiological features which can become promising biomarkers and could help separate bipolar depression from the recurrent type.

АННОТАЦИЯ

ВВЕДЕНИЕ: Поиск биологических маркеров для дифференциальной диагностики рекуррентной и биполярной депрессии является важной задачей современной психиатрии. Электроэнцефалография (ЭЭГ) выступает одним из перспективных инструментов для решения данной задачи.

ЦЕЛЬ: Выявить различия количественных характеристик альфа-ритма электроэнцефалограммы у пациентов с депрессивным эпизодом в рамках рекуррентной и биполярной депрессии.

МЕТОДЫ: Выделены две группы пациентов (женщин): с рекуррентным депрессивным расстройством, текущий эпизод легкой/средней степени тяжести (30 пациентов) и с биполярным аффективным расстройством, текущий эпизод легкой или умеренной депрессии (30 пациентов). Группы пациентов не получали фармакотерапию и не различались по социально-демографическим показателям и суммарной оценке по шкале депрессии Гамильтона. Проводилась запись фоновой электроэнцефалограммы и анализировались количественные характеристики альфа-ритма: абсолютная спектральная мощность, межполушарная когерентность и реакция активации.

РЕЗУЛЬТАТЫ: У пациентов с рекуррентным депрессивным расстройством по сравнению с пациентами с биполярным аффективным расстройством обнаружены статистически значимо меньшие показатели усредненной абсолютной спектральной мощности альфа-ритма (z=2,481; p=0,042), а также меньшая степень депрессии альфа-ритма при открывании глаз (z=2,573; p=0,035).

ЗАКЛЮЧЕНИЕ: Представленные количественные характеристики альфа-активности подтверждают, что больные с аффективными расстройствами различного генеза имеют свои отличительные электрофизиологические особенности, которые могут стать перспективными биомаркерами для различения биполярной и рекуррентной депрессии.

Keywords: *electroencephalogram; alpha rhythm; recurrent depression; bipolar depression; biomarkers*
Ключевые слова: *электроэнцефалограмма; альфа-ритм; рекуррентная депрессия; биполярная депрессия; биомаркеры*

INTRODUCTION

Differential diagnosis of recurrent and bipolar depression, i.e., depressive episodes in recurrent depressive disorder (RDD) and bipolar affective disorder (BAD), presents challenges in practice, despite their obvious clinical features and differences [1, 2]. For example, the clinical guidelines for the diagnosis and treatment of BAD published by the Ministry of Health of the Russian Federation in 2021 [3] state that the diagnostic criteria for a depressive episode in BAD and RDD do not differ; however, certain signs, such as an onset at a younger age (as young as 25 years) or in the postpartum period; acute onset (days or hours) of symptoms and their rapid resolution; features of atypical depression with hyperphagia, hypersomnia, inverted circadian rhythm, etc.; the presence of psychotic symptoms; a prolonged course of the disease; and low susceptibility to antidepressant therapy, are more typical of depression in BAD. However, in clinical practice, the above-mentioned signs of an atypical depressive episode of BAD remain undetected in many cases [4, 5]. At the same time, differentiating between recurrent and bipolar depression is key in the choice of treatment. In the absence of sure-fire clinical criteria, the neurobiological characteristics of depressive conditions may come to play an important role, although their studies have so far been relatively disappointing and in some cases even economically unjustified [6–9].

One of the objectives in clinical neurophysiological studies is to identify reliable markers that could not only detect changes in the functioning of the nervous system in various diseases, but also contribute to an objective diagnosis of the diseases themselves, including differential diagnosis. Electroencephalography (EEG) might be the most promising tool so far in this endeavor. It is a non-invasive, low-cost, and objective method for recording brain neural activity. Unlike neuroimaging methods,

EEG provides a continuous assessment of the neural activity associated with a particular stimulus or reaction with high temporal resolution, even when no external changes in behavior are observed. Consequently, EEG parameters can be useful as biological markers of a mental illness that trace back to specific pathophysiological mechanisms. Data accumulated to date from high-caliber studies [10–12], including the results of our own studies [13, 14], suggest various EEG markers that can be used to differentiate between unipolar and bipolar depression. However, the question of how well they hold up to scrutiny remains open.

A trove of data seems to indicate that the development of depressive conditions is accompanied by a change in the patterns of all EEG frequency ranges [15–17]. These changes mostly affect the main EEG rhythm; the alpha rhythm. According to a number of studies, the generation of the alpha rhythm is associated with impulses that spread in the intercortical and thalamocortical neural networks and its magnitude synchronizes the functional brain activity and determines the interplay between information received from the afferent system and the mechanisms of working memory, thereby regulating adaptive processes in the body [18, 19]. Therefore, the EEG alpha frequency traditionally attracts the attention of researchers due to its high sensitivity to various external influences and the subtle changes that take place in the functional state of the cerebral cortex. Meanwhile, both the neurophysiological mechanisms and the functional significance of the alpha rhythm are still the subjects of debates. According to some studies, the quantitative characteristics of the alpha rhythm can only be fully understood after one takes into account the spectral power and activation intensity (inhibition of the alpha rhythm after one opens their eyes, the Berger effect) [18, 19]. Considerable data now exists on the changes that take place in the alpha power in depressive disorders of various origins [10–17]. However, only a few studies into the activation reaction in patients with depressive disorders can be found in the literature [20].

The objective of this study was to search for differences in the quantitative characteristics of the EEG alpha rhythm in patients with a depressive episode within the framework of recurrent depression and bipolar depression.

METHODS

Setting

The selection of patients for the study was carried out at the 3rd Clinical Psychiatric Department (Department of Affective Conditions) of the Clinic of the Mental Health Research Institute of the Tomsk National Research Medical Center. The EEG study was carried out at the Laboratory of Molecular Genetics and Biochemistry of the Mental Health Research Institute of the Tomsk National Research Medical Center.

Participants

The study sample included a total of 60 female patients (age, years: median 32, interquartile range 27 and 53) admitted for treatment with a diagnosis from the cluster of mood disorders: RDD, current episode mild/moderate (F33.0, F33.1 according to ICD-10, *n*=30) and BAD, and current episode mild or moderate depression (F31.3 according to ICD-10, *n*=30). Diagnostic assessment and clinical qualification of the disorder were carried out by psychiatrists according to the ICD-10 criteria and using the Hamilton Depression Rating Scale (HDRS-17) for the assessment of the severity of symptoms. The medical history was collected, including the age of the patient, the duration of the disease in years, the total number of depressive episodes, and the duration of the current episode in months.

Inclusion criteria: patient consent for the study, established diagnosis of an affective disorder (F31.3 or F33.0-1) according to the ICD–10, age 18–60 years.

Exclusion criteria: refusal to participate in the study, dementia, mental retardation, other severe organic brain diseases with severe cognitive impairment (encephalitis, meningitis, sequelae of traumatic brain injury, etc.), and acute or chronic decompensated somatic diseases requiring intensive treatment.

All patients were examined during hospitalization (before the main course of treatment), usually on days 2–3 after admission to the hospital.

The control group consisted of 30 mentally and somatically healthy women (age, years: median 35, interquartile range 25 and 53) who were examined using the same exclusion criteria (The Kruskal-Wallis test (2, *N*=90)=6.689, *p*=0.158 for comparisons of the RDD, BAD, and control groups).

EEG recording and processing procedure

The EEG was performed in an electrically screened room with dim light. During the study, the patients were in a state of calm, relaxed wakefulness, and in the sitting position. Two functional tests were performed: a baseline study with closed eyes and a test with open eyes. All patients

remained under physician supervision during the EEG recording, and the recording was discontinued if the patient started falling asleep or EEG signs of drowsiness were detected. The EEG was recorded using a 16-channel encephalograph (Neuropolygraph, LLC Neurocor, Moscow) according to the international 10–20 system, in monopolar configuration, with a sampling rate of 1 kHz and Fz as the ground electrode. Reference electrodes (A1 and A2) were positioned on the ear lobes.

The average duration of the EEG recording was 5 minutes. The obtained EEG recordings were band-pass-filtered from 1 to 40 Hz. First, each EEG was cleaned of artifacts (ballistocardiogram, oculographic and electromyographic potentials) based on a visual assessment by a qualified EEG technician. The cleaned EEG recording was subjected to a quantitative analysis using the Neuropolygraph Software package. Topographic maps of the alpha band were constructed to illustrate the gradient changes in the alpha band maxima: dominance region — brain regions with the maximum amplitude (usually in the occipital regions); preserved regional differences — differences in the magnitude of the alpha rhythm in the leads; and assessment of the fronto-occipital gradient — decreasing alpha activity from the occipital to the frontal leads. Average values of the absolute spectral power (μV^2) and interhemispheric coherence (AvCOH) of the alpha rhythm in the standard frequency range (8–13 Hz) with closed and open eyes were calculated for all EEG leads. The magnitude of the activation reaction (the Berger effect) was determined using the following formula:

$$M_a = \frac{P_{ec} - P_{eo}}{P_{ec} \times 100\%},$$

where M_a is the magnitude of the activation reaction, P_{ec} and P_{eo} are the spectral power of the alpha band averaged over all EEG leads with eyes closed and eyes open, respectively (μV^2).

Statistical analysis

Statistical processing of the obtained data was carried out using the Statistica 12 Software package (StatSoft). The distribution was tested for normality using the Shapiro-Wilk test. The obtained data demonstrated a non-normal distribution. Data are presented as medians and interquartile ranges: Me [Q1; Q3]. The Mann-Whitney test was used to compare the demographic and clinical characteristics between the two groups of patients. The Kruskal-Wallis test (ANOVA) and the automatic *a posteriori* pairwise comparison procedure using Dunn's test were used to compare quantitative alpha band characteristics between the control and patient groups. The Spearman rank correlation test was used to assess the presence, level, and direction of the correlations of demographic, clinical, and EEG variables. Differences were considered statistically significant at $p < 0.05$.

Ethical approval

Our study was conducted in full compliance with the Declaration of Helsinki of 1964, as amended in 1975–2013, and was approved by the Local Ethics Committee at the Mental Health Research Institute of the Tomsk National Research Medical Center (Minutes No. 154 dated June 17, 2022, case No. 154/1.20.22). All study subjects provided written informed consent to participate in the study and allow the processing of their personal data.

RESULTS

The socio-demographic and clinical characteristics of patients are given in Table 1.

A comparative analysis of the averaged absolute spectral powers of the EEG alpha band between the control group and patients with BAD and RDD revealed statistically significant differences. Patients with RDD demonstrated a reduced alpha rhythm compared with the control group (z=3.223; p=0.003) and patients with BAD (z=2.399; p=0.042).

Table 1. Socio-demographic and clinical characteristics of patients

Parameter	Patients with BAD *n*=30	Patients with RDD *n*=30	U	*p*
Age, years	36 [23; 53]	37 [26; 52]	1819	0.749
Disease duration, years	7 [4; 13]	7 [3; 11]	1763	0.381
Duration of the current episode, months	6 [3; 10]	3 [2; 8]	1597	0.137
Number of previous episodes	3 [2; 7]	4 [3; 8]	1711	0.501
Total HDRS-17 score	19 [16; 24]	20 [17; 25]	1608	0.277

Note: p is the level of statistical significance for inter-group comparisons using the Mann-Whitney test.

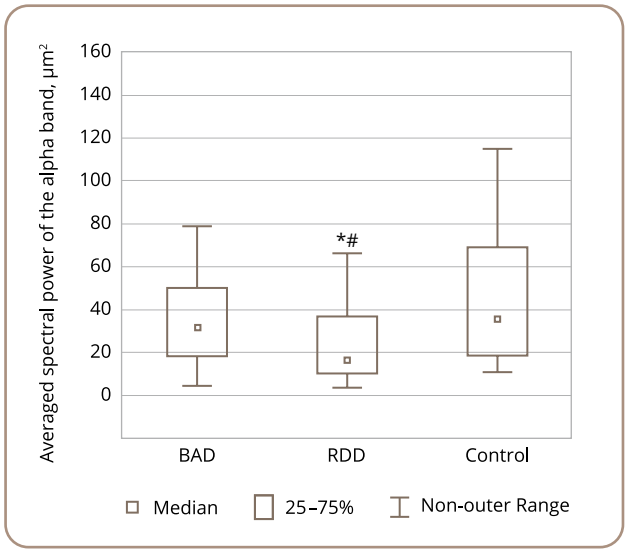

Figure 1. Averaged spectral powers of the alpha band in the study groups of healthy individuals and patients with BAD and RDD.

Note: * statistically significant differences with p <0.05 between the RDD and control groups; # statistically significant differences with p <0.05 between the RDD and BAD groups using the Kruskal-Wallis test (ANOVA).

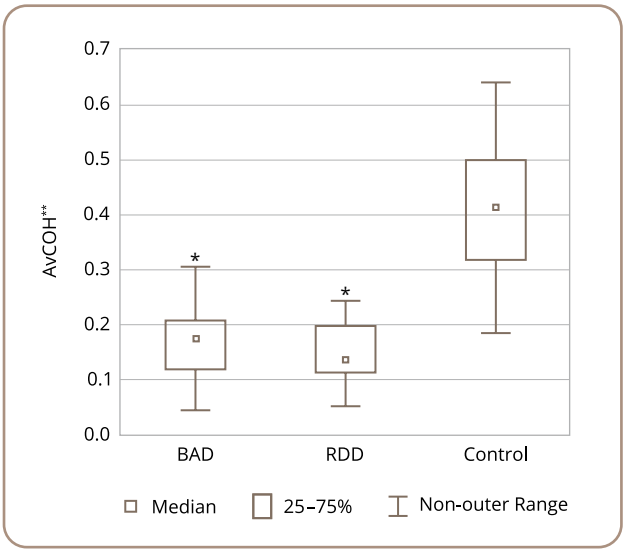

Figure 2. Averaged interhemispheric coherence values of the alpha band in the study groups of healthy individuals and patients with BAD and RDD.

Note: * statistically significant differences with p <0.05 between the control group and patients with BAD and RDD revealed using the Kruskal-Wallis test (ANOVA). ** AvCOH is an average interhemispheric coherence (no dimensionality)

There were no statistically significant differences between patients with BAD and the control group (z=0.976; p=0.986) (Figure 1).

The AvCOH values of the study groups revealed markedly decreased (z >7.121; p <0.001) relationships in all patients compared with the control group (Figure 2). No statistically significant differences were found between patients with BAD and patients with RDD (z=0.951; p=0.961).

According to the visual assessment of EEG recordings (Figure 3), a decrease in the generation of the alpha rhythm in patients with RDD led to a decrease in the fronto-occipital gradient and decreased regional EEG differences, but the highest alpha amplitudes were still observed in the occipital regions in the EEG recordings of patients with RDD. The topographic map of the alpha band distribution in patients with BAD was similar to that in the control group.

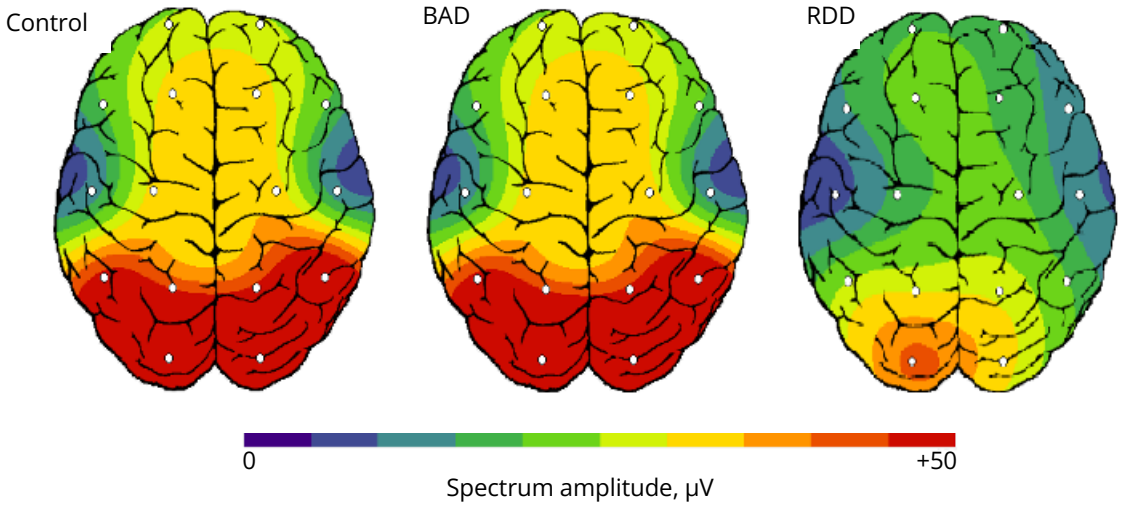

Figure 3. Topographic maps of the alpha band distribution in the control group and in patients with BAD and RDD.

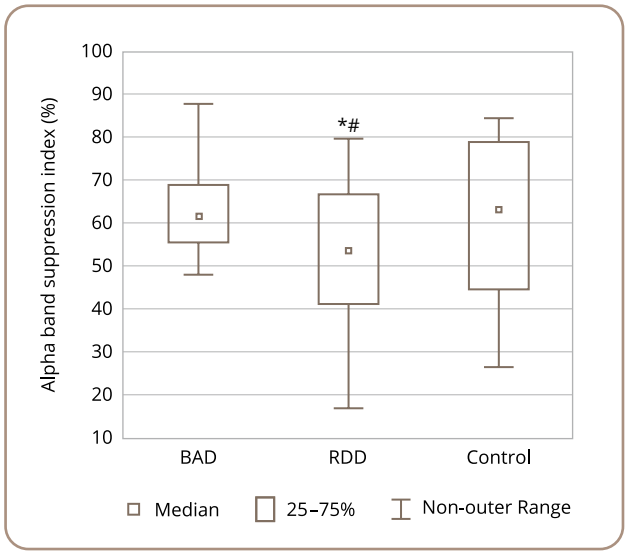

Figure 4. Averaged alpha band suppression indices (%) from eyes closed to eyes open in the study groups of healthy individuals and patients with BAD and RDD.

Note: * statistically significant differences with p <0.05 between the RDD and control groups; # statistically significant differences with p <0.05 between the RDD and BAD groups using the Kruskal-Wallis test (ANOVA).

The degree of alpha rhythm suppression upon opening of the eyes (the Berger effect) was statistically significantly lower in the group of patients with RDD compared with the control group (z=2.481; p=0.042) and patients with BAD (z=2.573; p=0.035) (Figure 4). We found no statistically significant differences between patients with BAD and the control group either (z=0.442; p=0.991).

We could not find statistically significant correlations of the spectral power, AvCOH of the alpha band and the activation reaction with the age and clinical characteristics of the patients in any of the groups (p >0.05) (Tables S1 and S2 in the Supplementary).

DISCUSSION

In this study, we assessed the quantitative characteristics of the EEG alpha rhythm in patients with BAD and RDD who had an ongoing mild/moderate depressive episode. Both the non-specific physical parameters of the waves (power and coherence) and physiological features of the alpha oscillations (response to visual stimulation after opening of the eyes) were evaluated.

The obtained results revealed that each study group of patients possessed their own distinctive electrophysiological features. In particular, patients with RDD typically had a low absolute spectral power of the alpha band, as well as a less pronounced activation reaction compared to patients with BAD. According to current concepts, EEG recordings reflect the neurophysiological mechanisms of excitation and inhibition [22]. On the one hand, low alpha power values indicate increased excitation in the central nervous system of patients with RDD, as compared with BAD. On the other hand, low spectral power values of the alpha band in patients with RDD indicate less synchronization (dysfunction) of the thalamocortical connections [22]. This was additionally confirmed by an AvCOH value that was lower than that in the controls.

A decreased alpha power in response to the opening of the eyes (the Berger effect) is one of the informative signs of stability of the activation reaction and, together with the magnitude of desynchronization (alpha rhythm suppression percentage), is associated with information processing [18, 23], which reflects the transition from a relatively restful state to the state of wakefulness. The magnitude of the alpha power reduction correlates with the intensity of the activation processes. Thus, patients with RDD typically have a decreased intensity of the activation process compared with relatively healthy controls and patients with BAD. In patients with BAD, the magnitude of the activation reaction was the same as that in the control group.

Thus, the study of the EEG alpha rhythm using a spectral and coherent analysis revealed that patients with BAD and RDD have specific bioelectrical brain activity patterns, something that may subsequently allow a differentiated approach to the assessment of the functional activity of the brain during the first depressive episode based on the quantitative characteristics of the alpha rhythm.

In addition to looking for differences in the alpha rhythm characteristics between patient groups, we also assessed the correlations of the alpha rhythm characteristics with clinical data. However, we were unable to find any statistically significant correlations, probably due to the fact that subclinical manifestations of depression in both groups required a more subtle phenomenological analysis than the duration of the disease/episode and the Hamilton score.

The main limitation of this study was the relatively small size of the study sample and the absence of males in the groups. However, it should be noted that we aimed to balance the groups based on their socio-demographic and clinical data. Another limitation of the study was that, although we evaluated both the nonspecific physical parameters of the waves and the physiological features of

alpha oscillations, the selected quantitative characteristics of the alpha rhythm did not cover the full spectrum of possibilities of quantitative EEG assessment. The quantitative characteristics of the alpha rhythm are highly variable and can hardly be fully captured through linear methods of investigation [24]. Unlike other studies [11, 12, 16, 19, 20, 24], our analysis minimized inter-regional differences by averaging the spectral power and EEG alpha rhythm coherence values. Nonetheless, this approach is well justified and is used in many studies [25, 26]. Although our patients were examined during hospitalization (before the main course of treatment), we did not take into account the effect of maintenance therapy, which may well have affected the EEG, another limitation of this study.

CONCLUSION

The data collected in this study provide additional evidence of the specificity of the functional activity of the brain of patients with affective disorders. The differences identified between the patient groups in this study can serve as a starting point for a further search for biomarkers that can help separate recurrent depression from bipolar depression. Using larger groups sizes, as well as including men in the sample, in further studies will help determine whether these differences represented the random occurrence that can often be observed in relatively small groups.

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Supplementary data

Supplementary material related to this article can be found in the online version at doi: 10.17816/CP6140

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