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ANALYSIS OF CHANGES IN ELECTROGENESIS IN SCHIZOPRENIA USING COMPUTER ELECTROENCEPHALOGRAPHY

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Abstract

Rationale. Psychiatrists do not have objective methods for identifying the brain disorders responsible for mental illness, which prevents timely diagnosis. Therefore, the search for markers of this disease, primarily related to CNS activity, is very relevant.

The purpose. A comparative study; by using periodometric analysis of EEG indicators, interhemispheric asymmetry of EEG rhythm amplitudes, and by using multiple regression analysis to identify connections-relations between EEG amplitude and frequency rhythms of different leads in healthy people and schizophrenic patients.

Material and Methods. EEG recording was performed in a state of quiet wake with closed eyes on the Neuron-Spectrum-2 electroencephalograph. The analysis was performed using periodometric analysis.

The differences of the indicators were monitored using the calculation of the coefficients of concordance (CCs). Connections-relations between indicators were investigated using multiple regression analysis.

Own research. In patients with schizophrenia compared with healthy people, there was detected a decrease in the amplitudes of rhythms of EEG, an increase in the duration indices in the delta and theta ranges and a decrease in the duration indices of the alpha and

beta rhythms. In patients with schizophrenia, there was a decrease in negativity and an inversion of functional interhemispheric asymmetry (FIHA) to positivity in the delta, theta, and alpha ranges and an increase of (FIHA) positivity in low-frequency and high-frequency EEG beta rhythms. Multiple regression and correlation analysis of the rhythm amplitudes interactions revealed that in the delta and theta ranges in the main group the number of regression coefficients was less than in the control group and in alpha, beta-LF and beta-HF – more than in control group.

Conclusions. 1. The obtained results indicated the activation of the right hemisphere in comparison with the left in patients with schizophrenia, possibly due to a decrease in the activating effect of the reticular formation of the brain stem.

2. It has been suggested that these changes in the aggregate are the neurophysiological basis of disorders of higher nervous (mental) activity in patients with schizophrenia

Key words: EEG; periodometric analysis; schizophrenia; coherence.

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Rationale. The problem of schizophrenia is one of the most important in psychiatry. Despite a century of schizophrenia research, the nature of the disease remains unrecognized, and the classification and modern diagnostic concept of schizophrenia is conventional [3]. Psychiatrists do not have objective methods of identifying brain disorders responsible for mental illness, which interferes with the timely establishment of the correct diagnosis. In this regard, the search for markers of this disease, primarily associated with the activity of the central nervous system, is highly relevant. Neurophysiological diagnostics, in particular electroencephalography (EEG), most adequately reflects the morpho-functional state of the central nervous system, which is the basis of the mechanisms of mental activity.

It has been shown that EEG studies are promising for brain damage [22], for automatic detection of epileptic seizures [33] and early detection of moderate cognitive impairments in Alzheimer's disease [29] in patients with schizophrenia [8, 10, 16, 20].

Spectral analysis of EEG in schizophrenia revealed increased delta activity, high activity of the fast beta frequency and a decrease in the alpha frequency [14, 17, 19, 24]

However, as noted by A.P. Gelda, T.V.Dokukina (2008), the study of neurodynamic mechanisms in schizophrenia was not carried out in the mode of periodometric analysis of EEG mapping. At the same time, this technique of computed electroencephalography is one of the most informative [13] and promising in terms of identifying pathognomonic electroencephalographic features in schizophrenia [6].

The question of the peculiarities of interhemispheric relations in the clinic of endogenous psychoses is of considerable interest. The conclusions of individual researchers on this issue contradict each other.

It has been shown that in patients with schizophrenia there was a noticeable decrease of interhemispheric asymmetry, especially in slow frequency ranges, compared with a group of mentally healthy men [14]. On the other hand, in the study of S.E. Davtyan, O.V. Ostretsova (1996), the minimum values of motor asymmetry were found in healthy individuals, the maximum - in schizophrenic patients.

It is assumed that many different genes are involved in the pathogenesis of schizophrenia, which take part in the development, functioning of certain brain structures and providing connections between different areas of the cerebral cortex [11]. Neurophysiological methods, in particular electroencephalography, are used to assess the connections between different structures.

One of the basic problems of electroencephalography is the study of the nature and mechanisms of the generation of rhythmic activity. This problem is investigated not only by various neurophysiological methods, but also by methods of mathematical modeling [26].

The distributed nature of the source of the alpha-rhythm of the electroencephalogram (EEG) made it possible to put forward a hypothesis about the existence of multiple discrete sources of alpha-band oscillations - "alphons" [40].

It has been suggested that hypothetical generators of beta 2, beta 1, theta and delta rhythms exist in the same way in the cerebral cortex [25].

It is of interest to compare the architecture of mutually oriented influences of the same indicators - amplitudes and frequencies of EEG rhythms in healthy people and schizophrenic patients.

Purpose. Comparative study, to reveal the connections-relations between the amplitudes and frequencies of EEG rhythms of different leads in healthy and schizophrenic patients by using periodometric analysis of EEG indicators (amplitude, frequency, duration index), interhemispheric asymmetry of EEG rhythm amplitudes and by using multiple regression analysis.

Material and methods

We examined 58 patients with a diagnosis of schizophrenia (according to ICD-10 heading F20.8) aged 20 to 69 years – the main group of patients undergoing inpatient examination and treatment at the Odesa Regional Mental Health Center of the Odessa Regional Council. The control group consisted of 34 people aged 16 to 66 years. EEG recording was carried out in a state of calm wakefulness with closed eyes with an electroencephalograph "Neuron-Spectrum-2" at a sampling frequency of 500 Hz using fitting: bipolar circular 16.

The electrodes were placed according to the "10-20%" system in the l6 zones of the cortex. The EEG was recorded according to the international system "10% -20%" [23] from frontal (F3, F4), central (C3, C4), parietal (P3, P4), occipital (01, 02), anterotemporal (F7, F8), mid-temporal (T3, T4) and posterior temporal (T5, T6) cortical zones (odd numbers indicate the areas of the left hemisphere, even – the right). Bipolar circular fitting 16 was used. Bandwidth 0.5–35 Hz, sampling frequency 500 Hz.

The analysis was performed using periodometric analysis in five standard frequency ranges: σ 0.5–4 Hz. Θ 4-8 Hz,. α 8-13 Hz, β1 13-20 Hz, β2 20-32 Hz.

EEG functional asymmetry coefficients in amplitude were determined by the formula:

$Y_{as} = (L - P) / (L + P) * 100$,

where L is the left hemisphere indicator, P is the right hemisphere indicator.

Thus, positive values meant the predominance of the amplitude of the left hemisphere, negative values – of the right one.

Differences in indicators were monitored using the calculation of ratio coefficients (RC). RC was obtained by dividing the larger value of the compared indicators by the smaller one [26].

Each of the set of indicators selected for the analysis (amplitude and frequency of EEG rhythms) was considered as a target feature (Y-s), and the remaining indicators were considered as influencing variables (set of X-s) and equations of multiple linear regression were constructed as follows:

$Y_1 = a_0 + b_1X_1 + b_2X_2 \dots + b_nX_n$,

where a_0 is a free term, coefficients b_1, $b_2 \dots$, b_n are regression indicators, which reflect the degree of influence on the analyzed indicator of the remaining elements of the set, x_1, $x_2 \dots$, x_n indicators. The probability of manifestation of influence, i.e., the adequacy of the regression coefficients, was estimated using the sigma deviations of the regression coefficients, and the effectiveness of the regression in general was estimated by calculating the multiple correlation coefficient [12].

Own research. Considering the heterogeneity of the diagnosis of schizophrenia itself, before the analysis to identify differences between the main and control groups, each group (main and control) was clustered into two clusters according to the amplitudes of EEG rhythms in order to check the statistical homogeneity. In the control group, clustering did not take place. The main group was divided into two subgroups 42 and 17 people. In a smaller subgroup (17 people), synchronization was more significant, and the amplitude of EEG rhythms was 1.3 times higher on average. The squared Mahalanobis distance between groups was 20.47 (P <0.000001). For further analysis, a subgroup of 42 people from the main group was selected.

Statistical analysis of differences in the amplitudes of EEG rhythms (Table 1) revealed that in patients with schizophrenia the amplitudes of rhythms were determined 1.13-1.28 times less than in healthy subjects. The greatest decrease was observed in the beta-LF rhythm in the parieto-occipital leads in the left and right hemispheres.

Table 1

Statistically significant coefficients of the ratio of the amplitudes of EEG rhythms in patients with schizophrenia compared with the control group

Leads	Delta-rhythm	Tetha-rhythm	Alpha-rhythm	Beta-LH-rhythm	Beta-HF-rhythm
F3-C3	**-1,10***	**-1,16***	**-1,16***	-1,18	
F4-C4			-1,19	**-1,14***	-1,14
F7-T3		-1,12	-1,21	-1,21	-1,24
F8-T4	**-1,11***	-1,16	-1,25	-1,28	-1,19
P3-O1		-1,30	-1,38	-1,41	-1,39
P4-O2		-1,32	-1,43	-1,46	-1,45
T4-T6		-1,22		**-1,13***	-1,25
C3-P3		**-1,17***	-1,20		
C4-P4	**-1,13***	-1,19	-1,24	-1,18	-1,13
T5-O1		-1,33	-1,27	-1,22	-1,18
T6-O2		-1,33	-1,27	-1,22	-1,18
Average	-1,13	-1,28	-1,26	-1,21	-1,16

*- P<0,1>0,05

Duration indices in the delta and theta ranges in schizophrenic patients were determined to be increased in comparison with healthy subjects, and indices of the duration of alpha and beta rhythms – decreased (Table 3).

Table 2

Statistically significant coefficients of the ratio of the frequencies of EEG rhythms in patients with schizophrenia compared with the control group

Leads	Delta-rhythm	Tetha-rhythm	Alpha-rhythm	Beta-LH-rhythm	Beta-HF-rhythm
F8-T4			-1,02		
P3-O1		-1,04			
P4-O2		-1,05			
T3-T5		-1,04			
T5-O1		-1,03	-1,02		-1,04
T6-O2		-1,04			

Table 3

Statistically significant coefficients of the ratio of indices for the duration of EEG rhythms in schizophrenic patients compared with the control group

Leads	Delta-rhythm	Tetha-rhythm	Alpha-rhythm	Beta-LH-rhythm	Beta-HF-rhythm
FP2-F8		1,29			
F3-C3				-1,33	
F4-C4					-1,65
F7-T3					
F8-T4	1,65		-1,25	-1,40	
P3-O1	2,33		-1,17	-1,39	
P4-O2	1,83		-1,25	-1,32	
T4-T6	1,67		-1,22		
C3-P3					
C4-P4		1,20			
T5-O1					
T6-O2	1,73	1,27			

The average FIHA indices for all leads in healthy subjects in the delta, theta and alpha ranges were determined as negative, and in the beta ranges – positive (Table 4, Fig. 1). The average FIHA indices for all leads in patients differed from those in healthy subjects. Negativity of FIHA in the delta rhythm range in schizophrenic patients was determined to be less than in the control group, and in the theta and alpha EEG ranges, FIHA inverted and was determined as positive. In beta ranges, FIHA positivity in patients was determined to be greater than in healthy subjects (Table 4, Fig. 1)

Table 4

FIHA coefficients in the control and main groups

Leads	Delta-rhythm		Tetha-rhythm		Alpha-rhythm		Beta-LH-rhythm		Beta-HF-rhythm	
	Cont-rol	Main	Cont-rol	Main	Cont-rol	Main	Cont-rol	Main	Cont-rol	Main
FP-F	-2,50	-1,21	-0,32	0,12	-2,30	-0,58	-2,92	3,11	3,54	3,81
FP-F	-3,14	0,16	-3,63	-0,21	-4,08	-0,82	-3,80	0,53	1,20	-0,28
F-C	-1,88	-5,53	0,87	-2,37	-0,78	0,79	2,30	0,44	-1,79	3,64
F-T	-0,41	1,97	-1,56	0,32	1,09	2,80	2,08	5,15	7,63	5,71
P-O	6,90	4,35	1,97	2,66	-1,87	0,00	0,14	1,60	-6,15	-4,13
T-T	-10,38	-1,38	-6,84	1,42	-2,44	0,05	1,79	0,47	3,98	6,23
C-P	-3,17	-0,49	-2,40	-0,63	-2,88	-0,05	2,39	1,57	6,61	7,17
T-O	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
Average	-1,82	-0,27	-1,49	0,16	-1,66	0,27	0,25	1,61	1,88	2,77

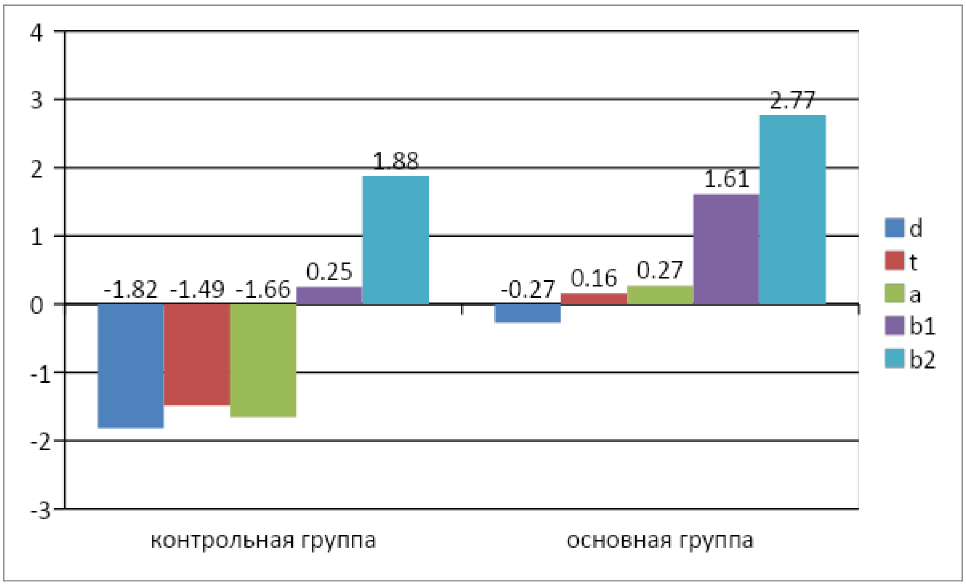

Fig. 1. FIHA indicators in healthy and schizophrenic patients.

Legend: d - delta rhythm, t - theta rhythm, a - alpha rhythm, b1 - beta-LF rhythm, b2 - beta-HF rhythm.

In multiple regression and correlation analysis of the mutual influences of rhythm amplitudes, the total number of statistically significant regression coefficients in the control and main groups differed slightly 254 and 251 (Table 5, Fig. 2). In the delta and theta ranges in the main group, the number of regression coefficients was less than in the control group, and in the alpha, beta-LF and beta-HF – it was more.

The number of two-dimensional correlation coefficients between the amplitudes of the same rhythms in the main group was less than in the control group. It should also be noted that the value of these coefficients in the main group was also lower than in the control group (Table 5, Fig. 2).

Table 5

Statistically significant coefficients of regression and correlation between indicators of amplitudes of EEG rhythms

EEG rhythms	Number of coefficients				Values of correlation coefficients	
	regression		correlation			
	C	M	C	M	C	M
Delta	75,00	38,00	93,00	19,00	0,59	0,44
Theta	61,00	42,00	102,00	47,00	0,64	0,48
Alpha	56,00	79,00	95,00	34,00	0,68	0,47
Beta-LF	31,00	56,00	75,00	48,00	0,57	0,45
Beta-HF	31,00	36,00	58,00	53,00	0,56	0,46
Total	254,00	251,00	423,00	201,00		

C-control group, M-main group

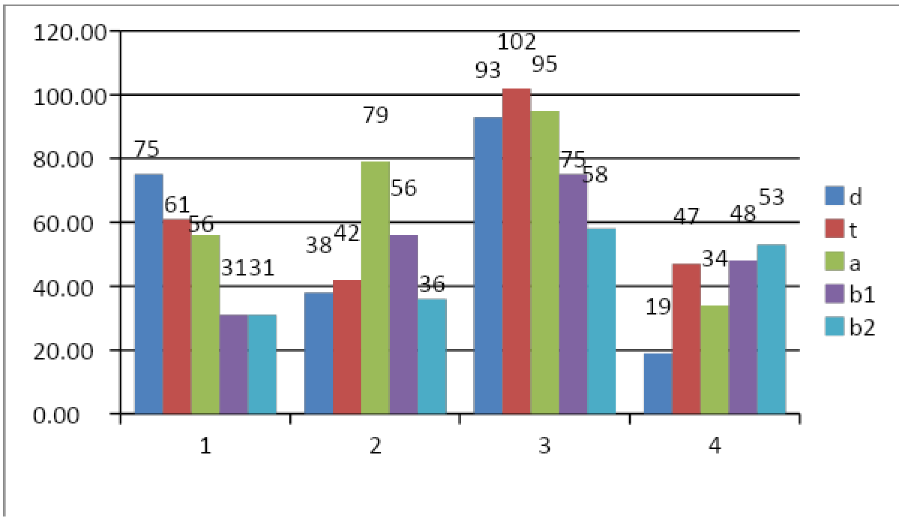

Fig. 2. Statistically significant coefficients of regression and correlation between indicators of amplitudes of EEG rhythms

Legend: D - delta rhythm, t - theta rhythm, a - alpha rhythm, b1 - beta-LF rhythm, b2 - beta-HF rhythm.

In multiple regression and correlation analysis of the mutual influences of the frequencies of EEG rhythms, the total number of statistically significant coefficients of regression and two-dimensional correlation in the control group was greater than in the main group (Table 6).

Table 6

Statistically significant coefficients of regression and correlation between indicators of frequencies of EEG rhythms

EEG rhythms	Number of coefficients				Values of correlation coefficients	
	regression		correlation			
	C	M	C	M	C	M
Delta	32,00	40,00	44,00	28,00	0,50	0,52
Theta	34,00	44,00	84,00	88,00	0,46	0,64
Alpha	29,00	10,00	29,00	71,00	0,54	0,58
Beta-LF	32,00	6,00	22,00	9,00	0,57	0,40
Beta-HF	38,00	48,00	49,00	5,00	0,54	0,59
Total	165,00	148,00	228,00	201,00		

C-control group, M-main group

Discussion. The revealed decrease in the amplitudes of EEG rhythms in patients with schizophrenia, i.e. an increase in desynchronization compared with the control group was accompanied by a decrease in the number of multiple regression coefficients in the delta and theta ranges between the amplitudes of the same rhythms and an increase in the alpha and both beta ranges. The number of two-dimensional correlation coefficients between the amplitudes of EEG rhythms in patients with schizophrenia was determined to be smaller than in the main group. According to the views of the Rusinov school [1], an increase in the number of correlations between various EEG components reflects an increase (in general) in the tone of the cortex, and a decrease – a decrease in this tone.

A seemingly unusual situation has arisen, consisting in the fact that a decrease in the amplitudes of EEG rhythms, indicating an increase in desynchronization, and therefore activation of the central nervous system, is accompanied by a decrease in the two-dimensional correlation coefficients between various EEG components.

The only type of relationship that is measured by the correlation coefficient is a linear (rectilinear) relationship, the multiple regression coefficients operate in addition to linear, also non-linear types of relationship.

The decrease in the number of correlation coefficients between the amplitudes of the EEG rhythms, which we obtained, corresponds to the decrease in schizophrenia in comparison with the norm of coherence, found by a number of researchers [16, 35, 37, 41].

However, only in the delta and theta ranges was there a decrease in the number of bivariate correlation coefficients and regression coefficients in multiple regression analysis. Therefore, it can be argued with a high degree of confidence that in the ranges of delta and theta EEG rhythms in schizophrenic patients, coherence is less than in healthy subjects.

In the alpha and two beta EEG ranges, the number of correlations between the EEG rhythm amplitudes in schizophrenic patients was lower than in the control group, and the multiple regression coefficients were higher. This may indicate that in patients with schizophrenia, the coherence in the alpha and beta ranges is increased compared to the norm, but the connections between the components of the alpha and beta EEG rhythms are realized according to nonlinear functions.

Data on the increase in coherence in schizophrenia compared with the norm are contained in a number of works [28, 30, 34].

The results obtained indicate that the use of the correlation coefficient for identifying and assessing EEG synchronicity, i.e. the determination of the indicators of the EEG correlation synchronicity is apparently insufficient. The combined use of calculations of two-dimensional correlation and multiple regression analysis makes it possible to more correctly assess the mutually oriented connections between neuronal elements of the central nervous system according to EEG data.

FIHA negativity in the delta rhythm range in schizophrenic patients was determined to be less than in the control group, and in the theta and alpha EEG ranges, FIHA inverted and was determined as positive. A noticeable decrease in interhemispheric asymmetry, especially in slow frequency ranges, compared with a group of mentally healthy people, was obtained in [14]. The results obtained indicate the activation of the right hemisphere in comparison with the left in patients with schizophrenia, possibly due to a decrease in the activating effect of the reticular formation of the brain stem [26].

Duration indices in the delta and theta ranges in schizophrenic patients were determined to be increased compared to healthy subjects, and the indices of the duration of alpha and beta rhythms – decreased.

It is suggested that the theta rhythm recorded in the cortex in some cases may be the result of a purely physical (electrotonic) spread of hippocampal activity to the cortex [36], and in others it may be low-frequency oscillations of the alpha range.

Analyzing the literature on the mechanisms of formation and the functional significance of delta activity, I.S. Egorova (1973) comes to the conclusion that the appearance of delta waves in the EEG of an adult means a decrease in cortical tone.

It has been shown experimentally that theta activity is also recorded with a decrease in the activity of the central nervous system (in particular, in a state of drowsiness), as well as under conditions of brain pathology. In this regard, some authors consider the neocortical theta rhythm as a reflection of the inhibitory states of the central nervous system and generalized rhythmic theta activity as evidence of complete dysfunction of the cortex and the subordination of its activity to the ancient limbic systems of the brain [15].

There is every reason to suppose that an increase in duration indices in the delta and theta ranges in schizophrenic patients was determined as a reflection of the inhibitory states of the central nervous system and a decrease in cortical tone.

W.G. Walter (1950) was one of the first to formulate ideas about the existence of the scanning mechanism of the brain and its relationship with rhythmic activity. He believed that the increase in the amplitude of the alpha waves reflects the activation of the scanning mechanism, which carries out "pattern search". Time scanning (“group scan”) is associated with the organization of the processes of perception and memory [18].

Most authors believe that there are sufficiently convincing grounds to associate beta-activity with generalized effects on the cortex from the ascending RF [1, 31, 32].

A decrease in the indices of the duration of the alpha and beta rhythms of the EEG may be evidence of a decrease in patients with schizophrenia of the activating effect of reticular formation on the cerebral cortex and a violation of the processes of perception and memory in this regard.

Earlier, we formed an idea of a unit of mental activity as a psychological, psychiatric, neurophysiological construct formed on the basis of multiple regression analysis of EEG indicators and anxiety indicator of the Luscher test [3]. It has been shown that in mentally healthy individuals between the indicators of psychological tests (Benton's test, pictogram and the Minnesota Multidimensional Personality Questionnaire - MMPI) regression connections-relations are revealed, while in mentally ill people these relationships are detected in very small amounts, or not at all [27]. The result obtained can be considered as evidence that mentally ill patients, both as a result of illness and treatment with psychotropic drugs, break the chains of connections between mental acts and states, and form a disintegration of the psyche.

It can be assumed that the decrease in the amplitudes of EEG rhythms, impaired coherence, an increase in the duration indices in the delta and theta ranges, and a decrease in the duration indices of alpha and beta rhythms, which we have revealed during the periodometric analysis of the EEG of patients with schizophrenia, are the neurophysiological basis of disorders of higher nervous (mental) activity in patients with schizophrenia.

Conclusions. 1. The results obtained indicate the activation of the right hemisphere in comparison with the left in patients with schizophrenia, possibly due to a decrease in the activating effect of the reticular formation of the brain stem.

2. It was suggested that these changes generally are the neurophysiological basis of disorders of higher nervous (mental) activity in patients with schizophrenia.

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