Electroencephalograms Features of the Early Stage Parkinson's Disease[1]

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Abstract—A new method for analyzing the time-frequency dynamics of brain's background electrical activity is described. It is used to detect at least three main features of Parkinson's disease (PD) in its early stages: (1) hemispheric asymmetry in the time-frequency characteristics (EEG) in the central recording areas of the motor cortex, (2) the emergence in these recording areas of EEG rhythms in the frequency range of 4–6 Hz and its relation to electromyograms (EMG) and the mechanical tremor of contralateral limbs in the case of tremor-dominant PD, and (3) the disruption of the dominant rhythm corresponding to views generally held on the disorganization of different systems in PD.

Keywords: Parkinson's disease, mechanical tremor, electroencephalogram, electromyogram, accelerometer, frequency synchronization, wavelet spectrogram, electromyogram envelope

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In many cases, clinical electroencephalography (EEG) is an important part of the differential diagnosis and evaluation of administered treatment. In other cases, its results are less informative because the detectable abnormal EEG changes are not specific enough to make a reliable diagnosis on this basis alone. However, perhaps for different types of brain pathology it is necessary to use the EEG in ways that differ according to each case.

One current problem in clinical electroencephalography is the study of EEG features of patients at different stages of the disease. At the same time, it seems that the search for EEG markers of the earliest signs of brain pathology is the most important for diagnostic purposes. In a number of studies, it has been noted that Parkinson's disease (PD) is characterized by the reduction in the frequency of the dominant EEG rhythms and the change of relative power of the main frequency bands [1–6]. These results were obtained by conventional methods of spectral analysis. In addition, in some studies carried out using nonlinear analysis methods [7] in the study of EEG patients in early stages of PD, an increase in signal entropy value was found. According to the authors, it could be an early indication of a pathological deviation of different structures of the brain.

Proper diagnosis of early clinical manifestations of Parkinson's disease is still quite difficult. There are numerous signs of the earliest stages of the disease, but in most cases they are only relatively specific, as each of them can indicate some other brain pathology. Modern neuroimaging techniques are considered to be informative for the diagnosis of Parkinson's disease, but they are very expensive and cannot be widely used in medical practice. Affordable and fairly common methods of clinical electroencephalography (EEG) have been used for the examination of patients with PD for the past five decades, but until recently progress in this area was quite modest. Even in the earliest studies, it was noted that patients with PD are characterized by a reduction in the frequency of the dominant EEG rhythm [1, 2].

A sufficiently critical attitude to data on PD obtained from conventional clinical EEG recording is associated with the fact that the EEG reflects primarily the electrical processes in the cerebral cortex and can only indirectly indicate the pathological processes and functional changes that occur in complex cortico-subcortical networks during the development of the disease.

Clinical research studies of patients implanted with electrodes in various basal ganglia for therapeutic purposes contributed to a more successful understanding of the relationship between pathological changes of

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rhythmic electrical activity and specific disorders in brain structures associated with the motor functions. In addition to the stimulation of the striatum, subthalamus, and some other structures, these electrodes are also used to record of the electrical activity. EEG recording and evaluation of the type and degree of motor disorders have also been conducted. In the latest detailed review of these studies [22] electrical activity in a very wide frequency range was considered from theta-oscillations to oscillations of 200–350 Hz. The greatest attention was paid to the high-frequency range. The relationship between the intensities of beta and gamma EEG bands and the deficit of dopamine in the brain was proven. The correlation between the strength of the beta range in the subthalamus and the depth of pathological changes of the motor area were shown. The pathological increase of the EEG beta range depends on the type of motor disorder; it is observed in the case of dyskinesia and rigidity but is not correlated with tremor. It should be specially noted that those patients implanted with electrodes in the brain whose EEGs of subthalamus, thalamus, and striatum were analyzed, and correlations of the activity of cortical and basal structures of whom were considered, were in late stages of PD.

As for the alpha and theta frequency bands, data on the relationship of theta activity of different brain structures with tremor are given with sufficient detail in the literature. The clear peaks of theta activity that correlate with the tremor frequency (or with harmonics of this frequency) have been found in the subthalamus, globus pallidus, and thalamus [31]. The theta rhythm that reflects the tremor rhythm has been detected in the contralateral motor cortex, premotor area, somatosensory area, and in the cerebellum using magnetical encephalography (MEG) [32, 33]. The presence of tremor oscillators in the nervous network "basal ganglia–thalamus–cortex" can be assumed based on electrophysiological and morphological data.

Almost all the work related to the analysis of EEG features in the case of PD has traditionally been used to analyze the Fourier transform, which considers the EEG as a stationary process and gives average data about the frequency composition of the EEG during the analyzed period of time. The only exceptions are some studies [7] in which nonlinear methods of analysis were used and an increase of the signal entropy was found in the course of the development of the pathology.

Currently, there are new approaches to the EEG analysis. In particular, there are studies of various wavelet transforms for all kinds of brain pathologies [8–10]. This approach opens new possibilities because it makes it possible to investigate in detail the EEG in its dynamics. In [11], the wavelet transform was used for the analysis of EEG patients with Parkinson's disease at an early stage. Similarly to studies carried out using the spectral analysis, a significant frequency drop of the dominant EEG range was observed. However, the most interesting result of this work was the disruption and instability detected in the time of wavelet spectrograms of the EEG, which was especially pronounced in the dominant frequency range. These data are consistent with the well-known data in the literature stating that a characteristic feature of PD is the syndrome of disintegration, which manifests itself at different system levels, especially in the motor area [12, 13].

In connection with these views on features of brain electrical activity in PD, it has been attempted to develop new methods of analysis that would make it possible to estimate the spectral-temporal and spatial-temporal dynamics of signals. The use of wavelet EEG transformation for the analysis of the electrical activity of the brain back started as early as the 1990s [8, 14, 15]. However, this highly informative analytical method has not yet achieved a sufficiently wide practical application. The reason is that wavelet transformations in this method are used only to visualize the time-frequency dynamics of the EEG. However, there are a number of developments that demonstrate the adequacy of this method for the diagnosis and prediction of pathological disorders of cerebral activity, such as various types of epilepsy [16–21].

In this regard, the quantitative evaluation of EGG time-frequency spectrograms, such as hemispheric asymmetry, the presence of theta rhythm, degree of disorganization, etc., can be a useful tool for studies of the features of the electrical activity of the brain in the early stages of PD. Below we will introduce methods of the quantitative evaluation of wavelet spectrograms, and first of all of the evaluation of their degree of disorganization, and the results of the application of these methods to the analysis of EEG time-frequency features of PD patients in the early and later stages of this disease.

PATIENTS AND DIAGNOSTIC TECHNIQUES

Nineteen-channel background EEGs were analyzed, including joint measurements of EEG and EMG. For EEG studies, 19-channel electroencephalographs made by ATES, MEDICA, and Neurosoft were used. The signal passband was from 0.3 to 35 Hz. For the simultaneous recording of EEG and EMG, a 41-channel multifunction complex for neurophysiological studies Neuron-Spectrum-5 made by Neurosoft was used with a signal passband greater than 0.3 Hz. The sampling frequency in the signal measurement of EEG and EMG was 500 Hz, and when the tremor was measured using accelerometers it was 1378 Hz.

Figure 1 shows the location of EEG electrodes on the patient's head according to the 10×20 system, EMG electrodes on the hands, and accelerometers on the back of hands and feet. EEG background recordings and recordings in the case of tensed patient hands with eyes closed were measured. The EEG amplifier passband was 0.3–35 Hz, and for EMG it was 60–120 Hz.

EEG examination was carried out on 82 people, including 34 patients with the tremor form of Parkin-

son's disease, 18 patients with the rigid form, and a control group of 30 people.

Among the patients with the rigid form there was an equal number of men and women, the average age was (M + σ) 59.75 ± 8.5, the average age of onset of the disease was 57.4 ± 12.3, and the average score on the UPDRS scale was 18.4 ± 8.6. Only one patient had early onset PD (45 years old).

Among patients with the tremor form there were 26 women and 8 men. The average age of patients with the tremor form was 64.1 ± 8.6, the average age of the onset of the disease was 62.4 ± 8.7, the average score on the UPDRS scale was 23.1 ± 11.1. Those patients with the tremor form are comparable with those patients with the rigid form according to their age and the age of disease onset, but among patients with the tremor form women dominate, and these patients have a higher score on the UPDRS scale ($p > 0.05$), which probably can be explained by the presence of an expressed tremor among the symptoms of the disease.

For the joint examination of EEG, EMG, and mechanical tremor 15 patients with Parkinson's disease were selected. The diagnosis was made using diagnostic and treatment criteria for Parkinson's disease of the UK Brain Bank (Gibb, Lees, 1988) [34]. The group consisted of eight women and six men. The age range was from 60 to 74 years. Fourteen patients had the disease for less than a year, and one person was ill for 1.5 years. In order to determine the stages of the disease the Hoehn and Yahr scale was used (Hoehn, Yahr, 1967). For 14 patients the disease was diagnosed at stage 1, and for 1 patient, at stage 2. All patients were right-handed. According to the accepted classification of forms of the disease all 15 patients had mixed (akinetic-rigid-trembling) form of PD. There were no patients with the akinetic-rigid or trembling forms. Disease onset with tremor and bradykinesia from the left and right hands was registered for eight and seven patients, respectively. In order to assess motor impairment, a unified Parkinson's disease rating scale (UPDRS) was used (C. Fahn et al., 1987). Five people scored 10 points, seven people scored 11 points, and three people scored 12 points on the UPDRS. At the time of the study they were not receiving anti-parkinsonian therapy.

EEG ANALYSIS USING MORLET WAVELET TRANSFORMATION

It is known that a characteristic feature of Parkinson's disease is the syndrome of disintegration, which manifests itself at different levels of the system (movement disorders, autonomic and neurohormonal disintegration, and emotional and mental disorders). Changes in the time-frequency structure of EEG detected by wavelet analysis showed that disintegration can also manifest itself in the dynamics of brain electrical activity. In [11], data mainly on patients in the second and third stages of the disease (on the Hoehn and Yahr scale) were analyzed. Below the results of the wavelet analysis of EEG of untreated patients in the first stage of PD will be compared with the ones of the control group and the group of patients in the second and third stages.

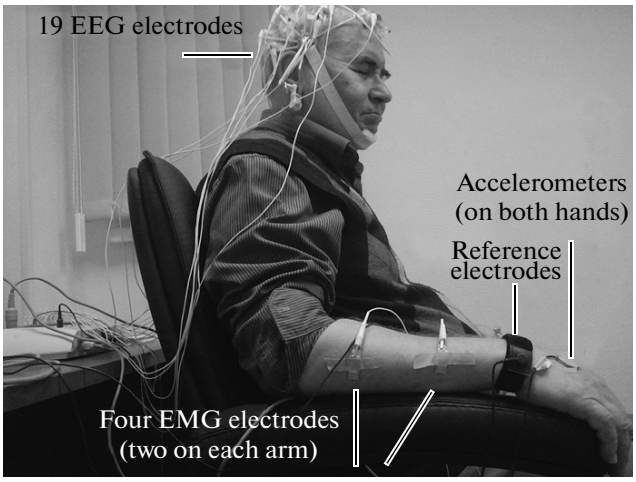

Fig. 1. Electrode placement.

The time-frequency spectrogram of the continuous Morlet wavelet transform is given by the formula

$$S_x(\tau, f) = |W(\tau, f)|^2, \quad (1)$$

$$W(\tau, T) = \frac{1}{\sqrt{T}}\int x(t)\psi^*\left(\frac{t-\tau}{T}\right)dt, \quad (2)$$

$$\psi(\eta) = \frac{1}{\sqrt{\pi F_b}} e^{2i\pi F_c \eta} e^{-\frac{\eta^2}{F_b}}, \quad (3)$$

where $S(\tau, f)$ is the power spectral density, $f = 1/T$, F_b, F_c are parameters, usually they are taken as $F_b = F_c = 1$.

The EEG wavelet spectrogram consists of a series of peaks that reflect the changes in the amplitude of spectral coefficients on different frequency ranges. This is not surprising given that the EEG consists of trains of oscillations of different frequencies and durations. Figure 2 shows EEG wavelet transforms of a healthy subject (left) and a patient with Parkinson's disease in Hoehn and Yahr stage 1 (right).

Figure 2 shows that wavelet spectrograms of healthy subjects and patients with PD consist of a series of shallow peaks (about 1–3 peaks per second) of the spectral power density on the time-frequency plane. For normal subjects, these peaks occur at approximately the same frequency and form regular ridges, which in the case of the Fourier analysis yield conventional rhythms, i.e., delta, theta, alpha, beta, etc. For patients with PD the position (coordinates on the time-frequency plane) and the spread of frequency peaks changes significantly over time, and their spectral power is redistributed between frequency bands. In particular, the number of peaks in the low frequency

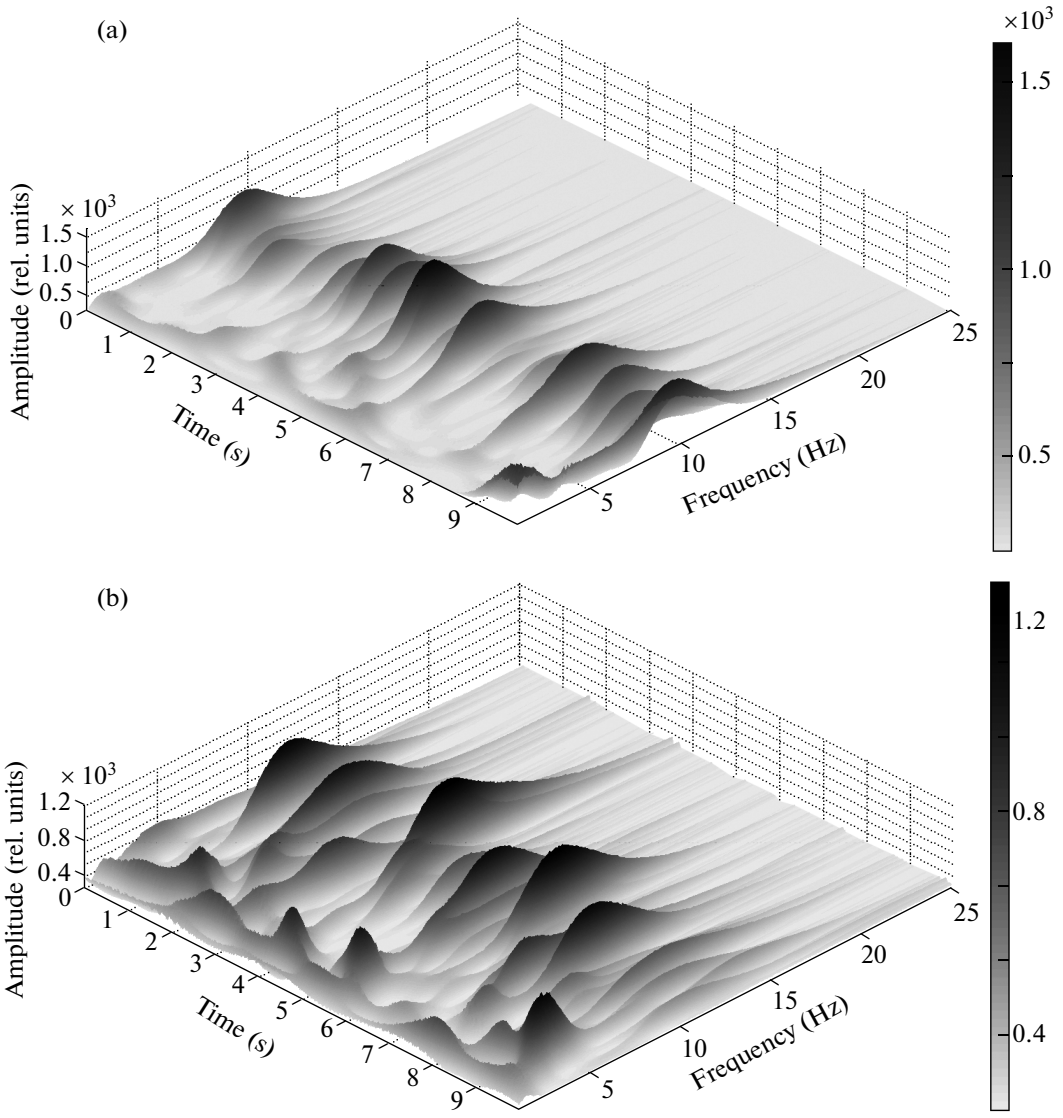

Fig. 2. EEG wavelet spectrogram of the C3 area. Control (a) and the patient in the first stage of PD (b).

range (4–6 Hz) significantly increases. The correlation between tremor frequency and EEG oscillations in the theta band was noted in a number of papers (an overview of these papers is given, for example, in [22]).

The dominant EEG rhythm has an amplitude that exceeds the amplitude of rhythms in other frequency bands. The set of frequencies of individual local maxima represents the range of the dominant EEG rhythm. Normally, all the vertices of the peaks constitute a distinct ridge, the alpha rhythm, which implies a sufficient frequency stability of the dominant EEG rhythm, which is found in a healthy person. Patients in the first stage of PD usually have a significant disruption of this three-dimensional picture: the wavelet transformation ridge consists of peaks with a frequency different from a normal one.

The idea of [23, 24] is that by pointing out the extrema of wavelet spectrogram peaks and analyzing statistics on the distribution of time-frequency coordinate extrema and their power it is possible to detect signs of PD in the early stages. In addition, statistics can be different for patients in different stages of the disease. Histograms of distribution of extrema in frequency and/or total spectral power density in a narrow frequency range are used as statistics.

The processing and analysis of the wavelet spectrograms of EEG signals consists in the determination of the amplitudes $A_i(F_i, t_i)$ of spectrogram peaks. Next, the time-frequency plane from $(0-T, F_{\min}-F_{\max})$ is broken down into windows with sizes $(\Delta T, \Delta F)$. It is advisable to select the window size according to time $\Delta T = (0.05-1.00)T$, s and frequency $\Delta F = (0.02-0.03)F_{\max}$, Hz. Then, in each window the sums of peak

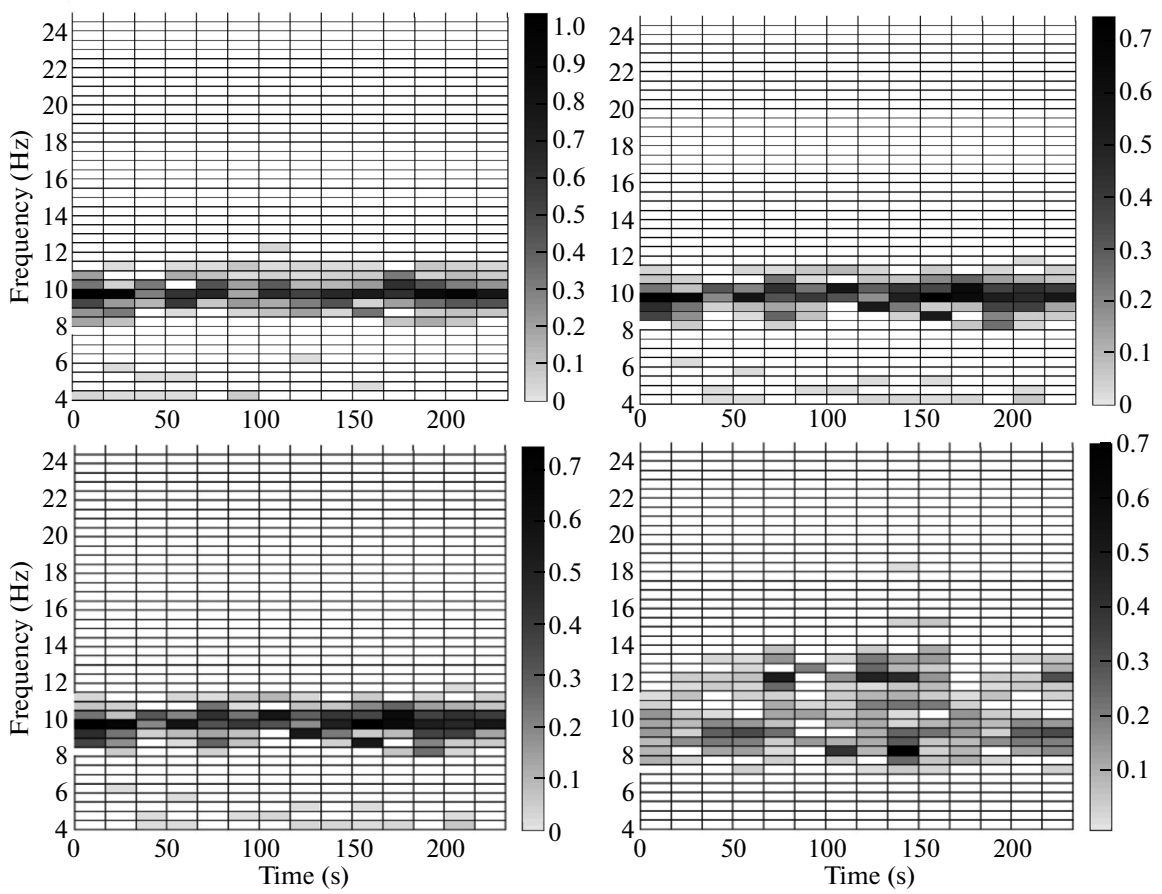

Fig. 3. Distribution of sums of amplitudes of extrema of the wavelet spectrograms in time-frequency windows. Volunteer from control group (top) and patient in the 1st stage of PD with left manifestations (bottom). Area C3 (left) and the symmetrical area C4 (right).

amplitudes from the spectrograms ΣA_i are calculated and histograms of the distribution of sums ΣA_i depending on the frequency.

Figure 3 shows examples of distributions of sums of extrema amplitudes in time-frequency windows. At the top it is given for a volunteer from the control group, at the bottom, for a patient in stage 1 of PD. On the left and right the area C3 and the symmetrical area C4 are given. These distributions show the asymmetry of the brain electrical activity in the initial stages of PD compared with control consisting in the disorganization of the dominant rhythm, namely, in the increase of the frequency spread of its peak in the diseased hemisphere.

EEG signals are inherently nonstationary. Therefore, it seems advisable to introduce a quantitative evaluation of this nonstationarity (disorganization) and compare it in the normal state with the early stages of PD. This nonstationarity corresponds to ideas of EEG rhythm disorganization in Parkinsonism. The essence of the proposed assessment is to assess pairwise correlations of frequency distributions of sums of extrema amplitudes according to time windows [25–27].

For the examples shown in Fig. 3, the number of windows is 14. Accordingly, a symmetric matrix of correlation coefficients with a unit-diagonal size of 14×14 is obtained. Normally correlation matrices contain a significant number of large correlation coefficients, and conversely, in a patient with PD correlation matrices contain a significant number of small correlation coefficients. It is therefore advisable to build histograms of correlation coefficients in a correlation matrix in order to assess the degree of disorganization (unsteadiness) of the rhythms. Figure 4 shows histograms of correlation coefficients for areas C3 and C4 of the same subjects. It is evident that for normal values of histograms of correlation, the coefficients are concentrated in the area of large values, and conversely, in a PD patient these values are scattered over all the values of correlation coefficients.

Figure 5 shows mean and median correlation coefficients according to groups of patients and control groups. For a group of patients in stage 1 of PD recording electrodes C3 or C4 of the "sick" hemisphere were taken, while for the control group and patients in

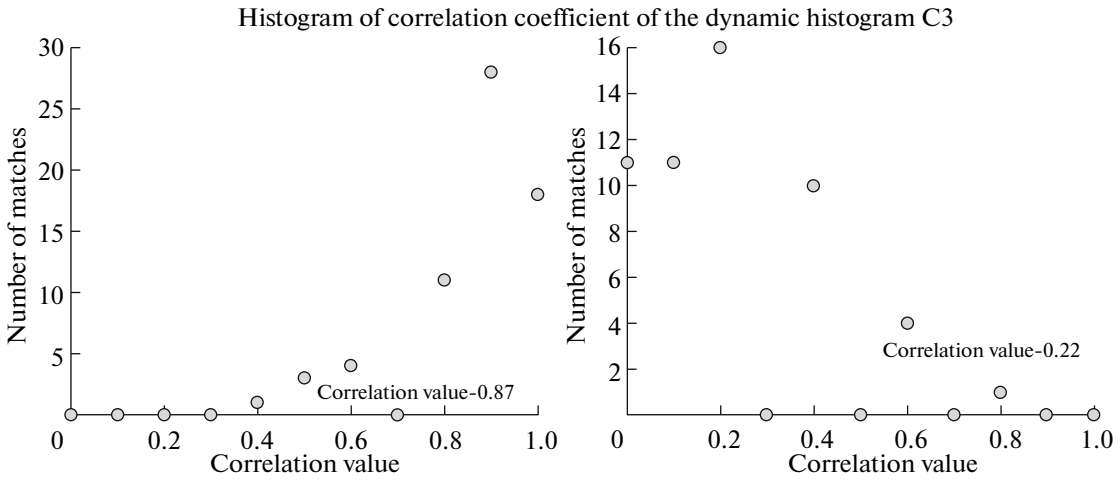

Fig. 4. Histograms of correlation coefficients of dominant rhythms: normal (left) and patient in 1st stage of PD (right). The panels show the arithmetic mean of the distribution of correlation coefficients.

stage 2 areas from both hemispheres were used. It can be seen that the averages and medians of correlation coefficients decrease with the stage of progress of the disease. Thus, the degree of disorganization of the dominant rhythm increases.

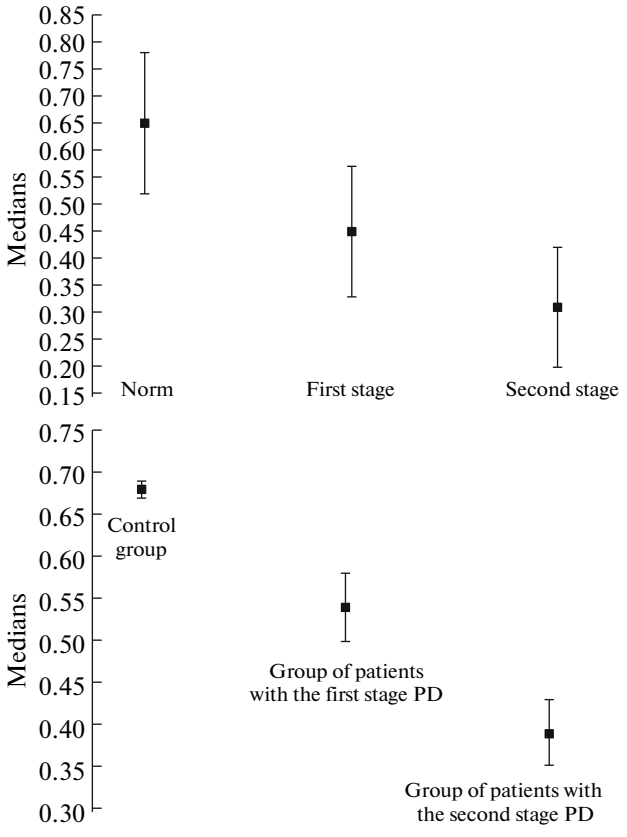

Fig. 5. Arithmetic mean (left) and medians of correlation coefficients for areas C3 and C4 from control group and areas in the diseased hemisphere of groups of patients in first and second stages of PD.

When comparing the symmetrical EEG intervals of the right and left hemispheres of examined patients, significant differences in the distribution of local maxima of wavelet spectrograms were consistently detected. Signs of EEG disorganization could be more pronounced either on the right or on the left. These data are consistent with the concept of the asymmetry of the first manifestations of Parkinson's disease [28].

Table 1 shows evaluations of disease stages according to EEG analysis results and their comparison with the clinical diagnosis. Evaluations of stages were carried out using the presence of the theta rhythm, frequency of the alpha rhythm, hemispheric asymmetry, and disorganization of the dominant rhythm in areas C3, C4, O1, and O2.

JOINT ANALYSIS OF TIME-FREQUENCY CHARACTERISTICS OF EEG, EMG, AND MECHANICAL TREMOR

One of the methods for detecting signs of Parkinson's disease (PD) is a joint analysis of signals of different modalities, i.e., electroencephalograms (EEG), electromyograms (EMG), and mechanical tremor (MT) measured using accelerometers. This analysis can lead to an understanding of the EEG frequency structure characteristics and more reliable detection of the early stages of PD. The synchronization of EEG, EMG, and MT can be estimated by the time-and-frequency distribution of extrema of wavelet spectrograms of EEG, MT, and the envelope of amplitude-modulated high-frequency EMG.

In neurophysiology, a method for computer recording and quantification of the tremor occurring at a constant angle of joint posture has been developed. This method will be described in more detail in the next section. The method makes it possible to select

the frequency range of a signal that creates a motor act from a wide electromyogram spectrum. The method is based on the concept that the force of muscles acting on a joint creates a movement, the form of which is close to the curve of the EMG envelope [29].

Data on hand tremor is not contained in the EMG signal itself but in its envelope, which can be computed using the Hilbert transform [30]. In order to select an amplitude and phase of an arbitrary amplitude-modulated signal $u(t)$, it is necessary to create an analytical signal (4) on its basis

$$w(t) = u(t) + iv(t). \quad (4)$$

The real part of the analytical signal coincides with the source signal $u(t)$. The imaginary part of $w(t)$ is called the Hilbert transform of the signal $u(t)$. It is calculated using the Hilbert transform

$$v(t) = \int_{-\infty}^{+\infty} \frac{u(\tau)}{\pi(t-\tau)} d(\tau). \quad (5)$$

By substituting (5) into (4) and converting (4) into the given form (6) it is possible to identify the EMG envelope (4).

$$w(t) = u(t) + iv(t) = a(t)e^{i\pi(\omega t)}, \quad (6)$$

where $a(t)$ is the signal envelope

$$a(t) = \sqrt{(u(t))^2 + (v(t))^2}. \quad (7)$$

Digitized EEG recordings were processed using a Butterworth filter of the fourth order in order to remove frequencies of 50 and 100 Hz.

Figures 6 and 7 show the time-frequency distributions of extrema of EEG wavelet spectrograms in areas C3 and C4 of the motor cortex, as well as the extrema of the envelope of the EMG and mechanical tremor (MT) in the contralateral limbs.

Table 1. Evaluation of the stages of PD based on EEG analysis and comparison with clinical diagnosis

	Number of people with clinical diagnoses	Number of matches of diagnoses based on EEG with clinical diagnoses	% of matches
Control	30	27	90
First stage	34	29	85
Second stage	18	12	66
Total number of test subjects	82	68	83

Corresponding integral frequency histograms of local maxima are given in Figs. 8 and 9.

Figure 9 shows that the extrema in the affected motor area of the right hemisphere are correlated in frequency with extrema of MT and EMG. In contrast, in the clinically healthy left cerebral hemisphere there is no such correlation (Fig. 8).

Table 2 shows evaluations of the PD stage by quantitative EEG and tremor characteristics and their comparison with clinical diagnoses. The ratio of peak amplitudes of frequency histograms of wavelet spectrogram extrema in the theta range and the dominant rhythm A_θ/A_α in areas C3 and C4, the ratio of the similar peaks of the tremor LH/RH, and the ratio of average r(C3)/r(C4) and standard deviations σ(C3)/σ(C4) of the distribution of correlation coefficients of dynamic histograms of the dominant rhythm in areas C3 and C4 were used as quantitative EEG characteristics. From these values it is possible to formulate an estimate of the proximity of the R of the test subject to an abstract ideal

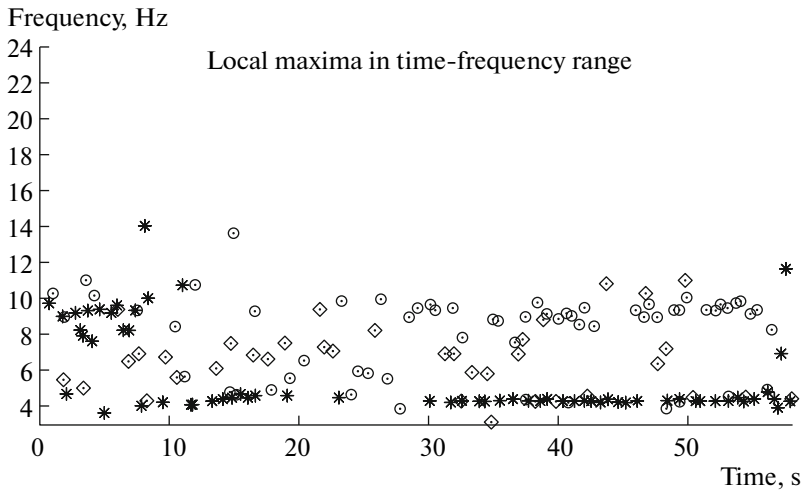

Fig. 6. Local maxima in time-frequency range of EEG areas in the motor cortex C3 (circles), contralateral MT (asterisk), and EMG (diamonds) of the patient in the first stage PD on the Hoehn and Yahr scale.

$$R = \sqrt{(A_\theta/A_\alpha(\mathrm{C3}))^2 + (A_\theta/A_\alpha(\mathrm{C4}))^2 + (1 - LH/RH)^2 + (1 - r(\mathrm{C3})/r(\mathrm{C4}))^2 + (1 - \sigma(\mathrm{C3})/\sigma(\mathrm{C4}))^2}, \quad (8)$$

which lacks a rhythm in the theta range. Hence, $A_\theta/A_\alpha = 0$ in both areas C3 and C4, while the amplitudes of limb tremor, the average correlation coefficients of dynamic histograms of the dominant rhythm, and their standard deviations are equal. The proximity estimate R is the Euclidean distance in the space of these characteristics of an abstract ideal test subject.

Table 2 shows that for the representatives of a control group the distance $R < 1$, while for patients it significantly exceeds $R = 1$. It should be noted that the evaluation of R emphasizes primarily the interhemispheric asymmetry. Therefore, it focuses on the initial diagnosis of the first stage of PD.

CONCLUSIONS

Basic signs of PD in the early stages are obtained using the developed methods and programs: (1) the hemispheric asymmetry of time-frequency characteristics of EEG especially in the central areas (C3, C4), (2) the occurrence of the rhythm in the frequency range of 4–6 Hz and its frequency synchronization with the electromyographic activity and mechanical

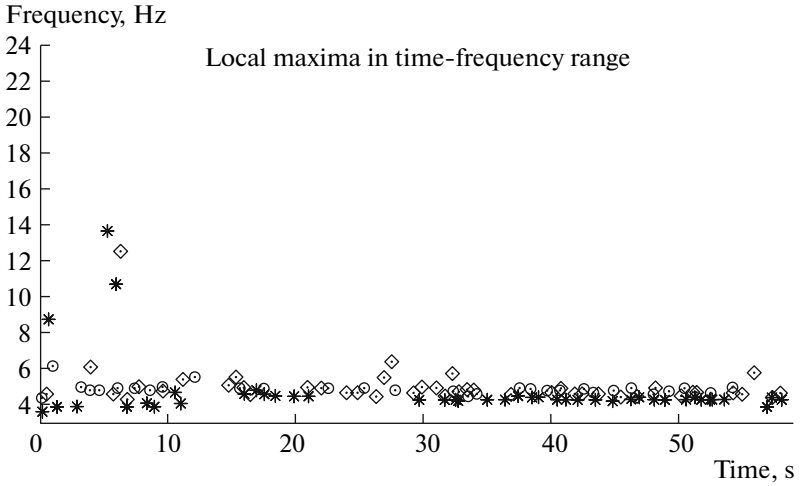

Fig. 7. Local maxima in time-frequency range of the interhemispheric symmetric area C4 and contralateral MT and EMG of the patient in the first stage of PD on the Hoehn and Yahr qualitative scale.

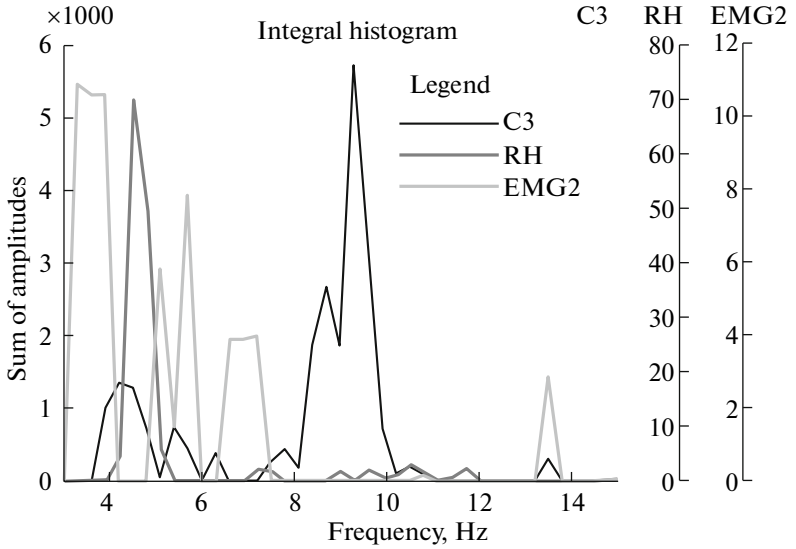

Fig. 8. Integrated frequency histograms of local maxima ("healthy" hemisphere) with frequency asynchronization in theta range.

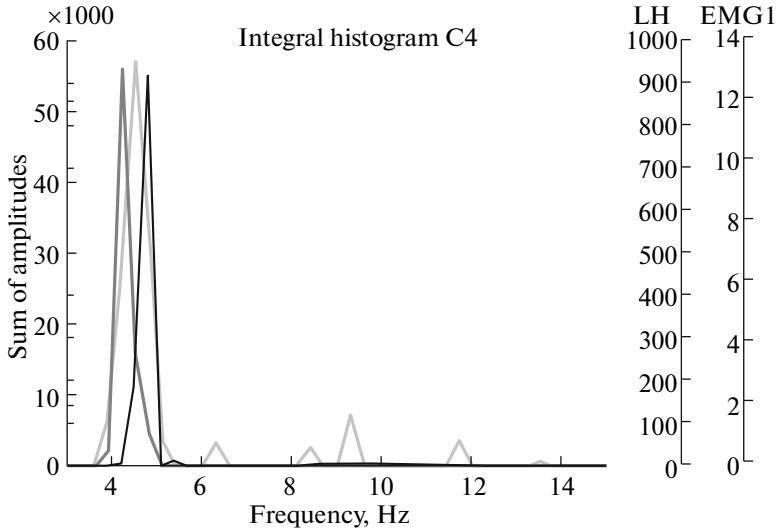

Fig. 9. Integrated frequency histograms of local maxima ("affected" hemisphere) with frequency synchronization in the theta range.

limb tremor, (3) the disorganization of the dominant EEG rhythm corresponding to the general views on the disorganization of various systems in PD. Quantitative evaluations of the disruption of the dominant rhythm in central areas have been obtained that make it possible to distinguish between groups of nearly healthy people and patients with PD in the first stage, on the one hand, and between patients in the first stage

Table 2. Evaluation of PD stages based on the quantitative analysis of characteristics of EEG and tremor and their comparison with a clinical diagnosis

No.	Clinical diagnosis	EEG analysis result	A_θ/A_α		LH/RH	r(C3)/r(C4)	σ(C3)/σ(C4)	R
			C3	C4				
Patients								
1	2	1	0	0.6	5	0.58	0.23	4.2
2	1	1	0.6	0	0.04	0.97	1.25	1.2
3	1	1	0.8	0.6	0.15	0.77	1.23	1.3
4	1	1	0.5	0.95	0.14	0.88	0.89	1.4
5	1	1	0	0	14.3	0.81	1.4	13.3
6	2	1	0.15	0	117	1.01	1.04	116.0
7	1	?	0	0.3	0.1	0.98	1.03	0.95
8	1	1	0.7	1.7	0.06	1.8	0.76	2.2
9	1	1	0.47	0	0.01	1.38	1.13	1.2
10	1	1	0	0	87.5	0.96	0.95	86.5
11	1	1	0.4	0	20	0.71	1.43	19.0
12	1	1	0	33	2.5	1.16	0.81	33.0
13	1	1	125	1.3	0.002	1.45	1.09	125.0
14	1	1	3	0	80	0.82	1.06	79.1
15	1	1	2.17	70	112	2.4	1.44	131.3
Control								
1	0	?	0	0	0.33	0.85	1.76	1.0
2	0	0	0	0	1.7	0.86	1.32	0.8
3	0	0	0	0	1.43	0.97	0.93	0.4
4	0	0	0	0	0.91	1.28	0.83	0.3
Abstract ideal								
			0	0	1	1	1	0

of the patients and the ones in the second stage, on the other. The comparison of PD recognition using quantitative EEG characteristics with clinical diagnoses showed a more than 80% match for the control group and patients in the first stage of PD. The less-than-perfect match with a group of patients in the second stage of PD can be explained by the small sample size and the fact that PD recognition techniques are focused on the diagnosis of the first stage. The reliability of the quantitative diagnosis of the early stage of PD can be significantly enhanced, if the results of simultaneous measurements of EEG and tremor are used for recognition.

Thus, using the wavelet transform and a further quantitative analysis, a number of facts were confirmed that characterize EEG characteristics in the second and third stages of Parkinson's disease and a number of specific characteristics of the EEG time-frequency organization of the first stage of the disease were found. Developments and approaches proposed in this paper proved to be adequate for the study of various stages of the PD development including the early stages. Histograms of the EEG wavelet transform extrema of stress PD signs more clearly compared with Fourier spectra and make it possible to study their dynamics. These data indicate directions of further research on the specific EEG markers of the earliest stages of the disease, including preclinical stages.

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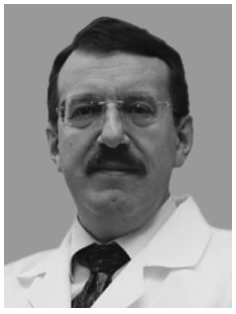

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