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APPLICATIONS OF RADIOTECHNOLOGY AND ELECTRONICS IN BIOLOGY AND MEDICINE

Time–Frequency Analysis of Simultaneous Measurements of Electroencephalograms, Electromyograms, and Mechanical Tremor under Parkinson Disease

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Abstract—A method for the analysis of the time–frequency dynamics of the background brain activity is proposed and used to reveal three main features of the early-stage Parkinson disease (PD): hemispheric asymmetry of the time–frequency characteristics of electroencephalogram in the central lead of the motor zone of the cerebral cortex, generation of the rhythm of electroencephalogram in these leads in a frequency interval of 4–6 Hz and its correlation with electromyograms and mechanical tremor of contralateral limbs upon Parkinsonian tremor, and disorganization of the dominant rhythm corresponding to the general concept of the disorganization of various systems under PD.

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INTRODUCTION

The diagnostics of the preclinical stage of the Parkinson disease (PD) at which the disease is in progress but the clinical features are not manifested is a topical problem of modern medicine and neurophysiology. Such a stage is studied in experiments with animals when the development of the disease is provoked [1]. PD cannot be provoked in clinics, so that the PD clinical features are studied at the earliest stages to extrapolate such features to the preclinical stage and, hence, reveal the high-risk group.

Correct diagnostics of the early clinical manifestations of the PD remains to be a difficult problem. Multiple features of the earliest stages of the disease [2] exhibit relatively low specificity, so that each of them can be related to an alternative brain pathology. The positron-emission tomography is the most informative method for the PD diagnostics. However, such an expensive procedure cannot be widely employed in practice for the diagnostics of preclinical and initial stages. Electroencephalography (EEG) and electromyography (EMG) of muscles and mechanical tremor can be implemented using relatively cheap devices (in comparison with the setups for neurovisualization) and, hence, can be widely used for screening aimed at diagnostics of early stages and identification of the high-risk groups at the PD preclinical stage.

Widely spread available methods for the clinical EEG are used for more than 50 years but the progress in such a study was moderate. It was mentioned in the first works that PD patients exhibit a decrease in the frequency of the EEG dominant rhythm [3, 4]. The progress of the disease is accompanied by a further variation in the EEG power and frequency. A critical attitude to the PD records based on the conventional clinical EEG is due to the fact that EEG primarily characterizes electric processes in the cerebral cortex and is only indirectly related to the pathological processes and functional transformations that take place in complicated cortical and subcortical networks when the PD is in progress.

Recent methods for the analysis of the EEG data are based on variants of wavelet transforms under different brain pathologies [5–7]. Such approaches provide new possibilities, since they allow a detailed analysis of the dynamics of the EEG data. The wavelet transform was used in [8] for the analysis of the EEG data of the PD patients at early stage. The results of the spectral analysis of [9, 10] yield a reliable decrease in the frequency of the dominant interval of the EEG.

However, the most interesting result is related to the disorganization and time-instability of the wavelet spectrograms of EEG data that are clearly manifested in the dominant frequency interval. The corresponding results are in agreement with the well-known data that prove that disintegration syndrome is a characteristic feature of PD manifested at different system levels, primarily, in the motor zones of the cerebral cortex [9, 10].

The methods that make it possible to estimate the time–frequency and space–time dynamics of signals have been developed with allowance for the above features of the electric activity of brain under PD. The application of the wavelet transform of the EEG data for the analysis of the electric activity of brain dates back to the 1990s [6, 11, 14]. However, such a highly informative method is rare in practice, apparently, due to the fact that the wavelet transforms are used only for the visualization of the time–frequency dynamics of the EEG data.

The analysis of tremor of the Parkinsonian-tremor and healthy patients can be found in [12, 13].

The quantitative estimation of the time–frequency EEG spectrograms (in particular, hemispheric asymmetry, presence of theta rhythm, and degree of disorganization and their correlation with the mechanical tremor) can be helpful in the diagnostics of the early-stage PD. Below, we present methods for the quantitative estimation of the wavelet spectrograms (primarily, estimation of the hemispherical asymmetry) and the degree of their disorganization and the results of the simultaneous analysis of the EEG data and mechanical tremor.

1. PATIENTS AND EXPERIMENTAL METHODS

For the simultaneous study of the EEG and EMG data and mechanical tremor, we employ a Neurosoft Neuron-spectr-5 (41-channel measurement system for neurophysiological measurements). The pass band of the EEG signals is 0.3–35 Hz, and the sampling rate is 500 Hz. The pass band of the EMG signals is 0.5–250 Hz and the sampling rate is 500 Hz. The tremor is measured with the aid of piezoelectric accelerometers on the hand back at a sampling rate of 1378 Hz.

We perform clinical and electrophysiological analysis of tremor of patients with essential tremor and Parkinsonian tremor and healthy patients. Variations in the tremor frequency and amplitude are estimated using the accelerometry. The comparison of the time diagrams and spectral components of tremor makes it possible to reveal several characteristic features that are important for interpretation of pathogenesis and differential diagnostics of the diseases.

Fifteen PD patients are involved in the experiments. The diagnostics was based on the PD clinical diagnostic criteria of the UK Brain Bank [15]. The ages of eight women and seven man range from 60 to 74 years. For fourteen patients, the duration of the disease is less than 1 year, and for one patient, the duration is one and a half year. To determine the stage of the disease, we use the Hoehn–Yahr scale [16]. The first and second stages were determined for 14 and 1 patient, respectively. All of patients are right-handers. In accordance with the commonly accepted classification, 15 patients suffer from the mixed (akinetic-origid–tremor) PD and 0 patients suffer from the Parkinsonian tremor. For eight and seven patients, the disease was started from the tremor and bradykinesia of the left and right hand, respectively. To estimate the motor disturbance, we employ a unified PD rating scale (UPDRS) [17]. The UPDRS ratings are 10, 11, and 12 for five, seven, and three patients, respectively. The patients did not receive anti-PD therapy prior to the experiments.

2. ANALYSIS OF THE EEG DATA USING THE MORLET WAVELET TRANSFORM

It is known that the disintegration syndrome that is manifested at different system levels (movement disorders, vegetative and neurohumoral disintegration, and emotional and psychiatric disorders) is a characteristic feature of PD. Variations in the time–frequency structure of the EEG data that are revealed using the wavelet analysis indicate that the disintegration can also be manifested in the dynamics of the electric activity of brain. The results for the second- and third-stage patients (in accordance with the Hoehn–Yahr scale) were analyzed in [9]. Below, we present the results of the wavelet analysis of the EEG data for untreated patients at the first stage in comparison with the results for the control group and the group of the second- and third-stage patients.

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

$$S_x(\tau, f) = |W(\tau, f)|^2, \tag{1}$$

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

$$\psi(\eta) = \frac{1}{\sqrt{\pi F_b}} \exp(2i\pi F_c \eta) \exp\left(-\frac{\eta^2}{F_b}\right), \tag{3}$$

where $S_x(\tau, f)$ is the power spectral density, f is the frequency, T is the compression parameter, $f = 1/T$, $x(t)$ is the original signal, t is the time, τ is the time shift, $W(\tau, T)$ is the wavelet transform of function $x(t)$, $\eta = (t-\tau)/T$ is the dimensionless period, $\psi(\eta)$ is the Morlet wavelet function, $\psi^*(\eta)$ is the complex-conjugated Morlet wavelet function, and F_b and F_c are the parameters. It is commonly accepted that $F_b = F_c = 1$.

The wavelet spectrogram of the EEG data consists of a series of peaks that correspond to variations in the amplitude of spectral coefficients in different frequency intervals. Such a structure is due to the fact that the EEG record consists of trains of oscillations

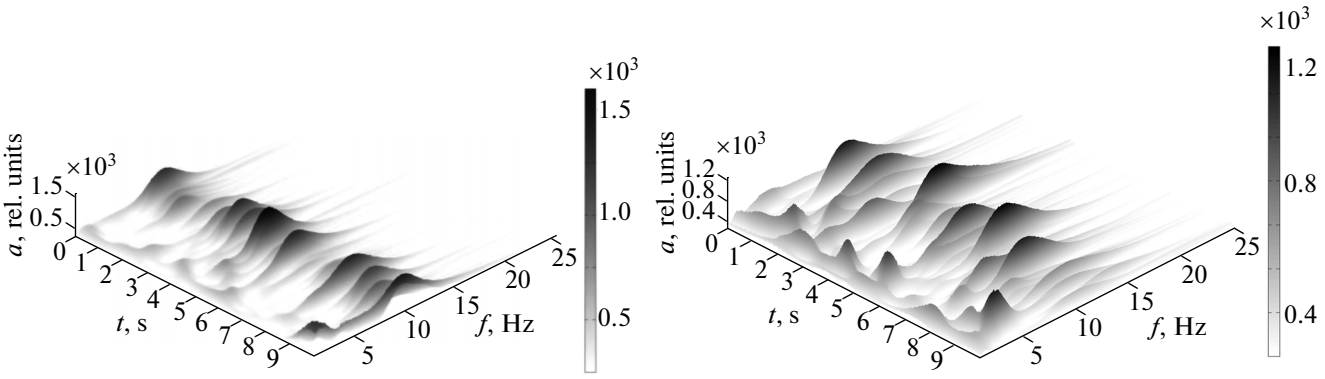

Fig. 1. Wavelet spectrograms of the EEG records of the C3 lead: (left-hand panel) control and (right-hand panel) first-stage PD patient.

with different frequencies and durations. The left- and right-hand panels in Fig. 1 present the wavelet transforms of the EEG records of a healthy patient and the patient with the first-stage PD (in accordance with the Hoehn–Yahr scale), respectively.

It is seen that the wavelet spectrograms of both patients contain series of sloping peaks (one or two peaks per second) of the power spectral density on time–frequency plane. For normal patients, the peaks emerge at approximately the same frequency and form regular ranges, which yield delta, theta, alpha, beta, etc. rhythms upon the Fourier analysis. For the PD patients, the peak positions (coordinates on the time–frequency plane) and the spread of frequencies exhibit substantially stronger variations with time and the corresponding power spectral density is redistributed between the frequency intervals. In particular, note significant growth of the low-frequency (4–6 Hz) peaks. The correlation of the tremor frequency and the EEG oscillations in the theta range has been mentioned in several works (see, for example [18] and references therein).

The dominant EEG rhythm has the amplitude that is higher than the amplitude in the remaining frequency intervals. Multiple frequencies of single local peaks correspond to the interval of the dominant rhythm. For normal patients, the peaks form a developed range that represents the alpha rhythm, which indicates sufficient frequency stability of the dominant rhythm. The 3D pattern is significantly disorganized for the first-stage patients: the range of the wavelet transform consists of peaks that have different (with respect to normal) frequencies.

The PD features can be revealed at early stages using the peak positions on the wavelet spectrograms and the analysis of the statistics of distribution of time–frequency coordinates of the peaks and the corresponding powers [19, 20]. The statistics can be different for patients with different stages of the disease. Histograms of distributions of the number of peaks and/or total power spectral density in a relatively narrow frequency interval can be used as statistical data.

Amplitudes $A_i(f_i, t_i)$ of the spectrogram peaks are determined for the processing and analysis of the wavelet spectrograms of the EEG signals. Then, time–frequency plane $(0–T, f_{min}–f_{max})$ is divided into windows with sizes Δt and Δf. It is expedient to choose time windows of $\Delta t = (0.05–1.00)t$ (s) and frequency windows of $\Delta f = (0.02–0.03)f_{max}$ (Hz). Sums of amplitudes of spectrogram peaks $\sum A_i$ are calculated for each window, and histograms of sums $\sum A_i$ versus frequency are constructed.

Figure 2 shows several distributions of the peak amplitudes in the time–frequency windows. The upper and lower panels correspond to a volunteer from the control group and the first-stage patient, respectively. The left- and right-hand panels correspond to the C3 and symmetric C4 leads, respectively. The distributions show the asymmetry of the brain activity at the initial stage of PD in comparison with the normal activity: the dominant rhythm is disorganized (the frequency spread of the peaks is increased) in the diseased hemisphere.

The inherent nonstationary character of the EEG signals necessitates the quantitative estimation of such instability (disorganization) and the comparison of the results for normal and first-stage patients. The nonstationary behavior is in agreement with the concept of the disorganization of the EEG rhythms under PD. The proposed approach involves the estimation of pairwise correlations for the frequency distributions of the sums of peak amplitudes over the time windows [21].

For the examples of Fig. 2, the number of such windows is 14. Thus, we obtain a symmetric matrix of correlation coefficients with a unity diagonal. Under normal conditions, the correlation matrices contain significant amounts of relatively large correlation coefficients. For a PD patient, the correlation matrix contains a relatively large number of small correlation coefficients. To estimate the degree of disorganization (nonstationary character) of the rhythms, it is expedient to construct histograms of the correlation coefficients in the correlation matrix. Figure 3 shows the

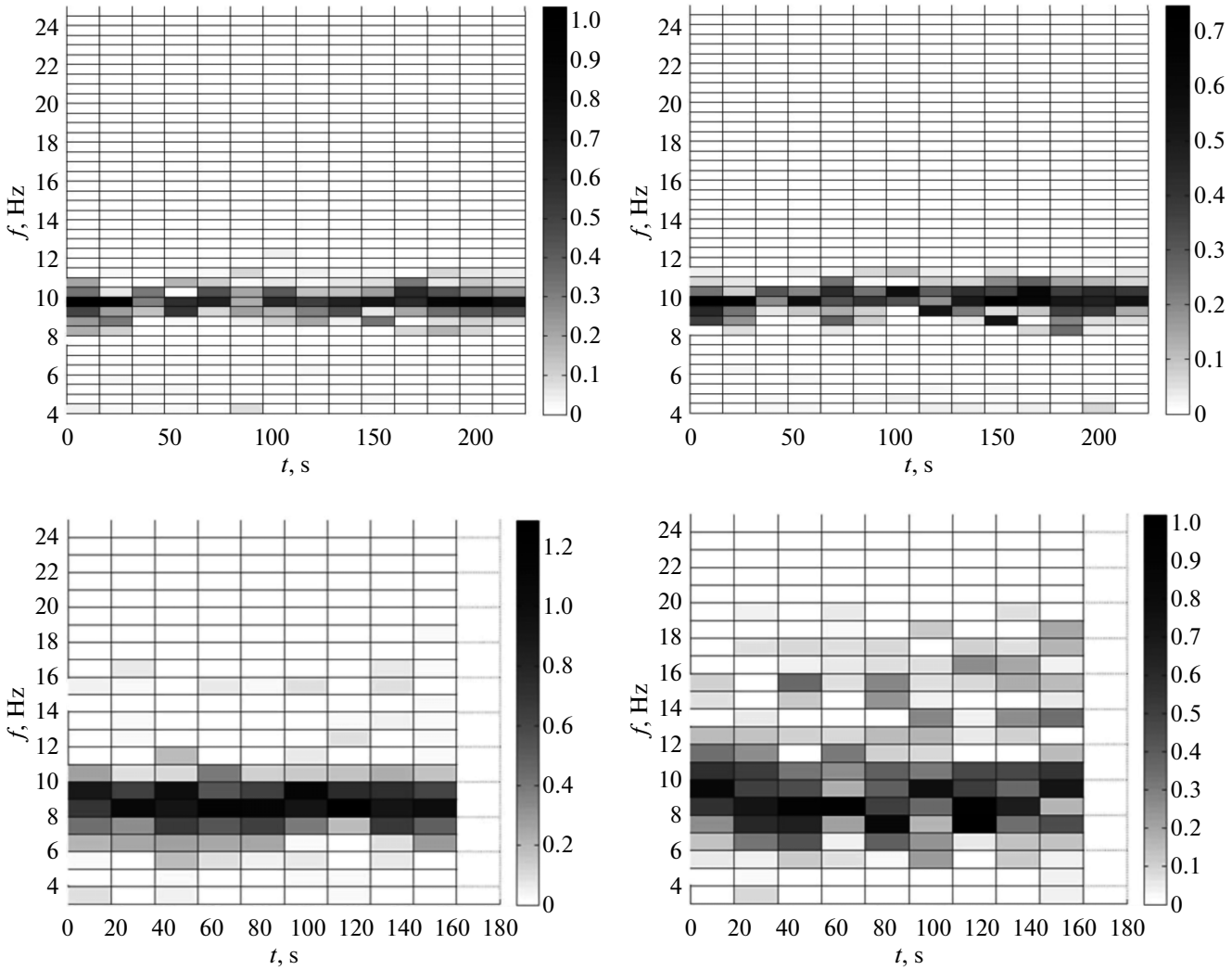

Fig. 2. Distribution of the sum of amplitudes for the extrema of the wavelet spectrograms in time–frequency windows: (upper panels) volunteer from control group, (lower panels) first-stage PD patient with the left-hand manifestations, (left-hand panels) C3 lead, and (right-hand panels) symmetric C4 lead.

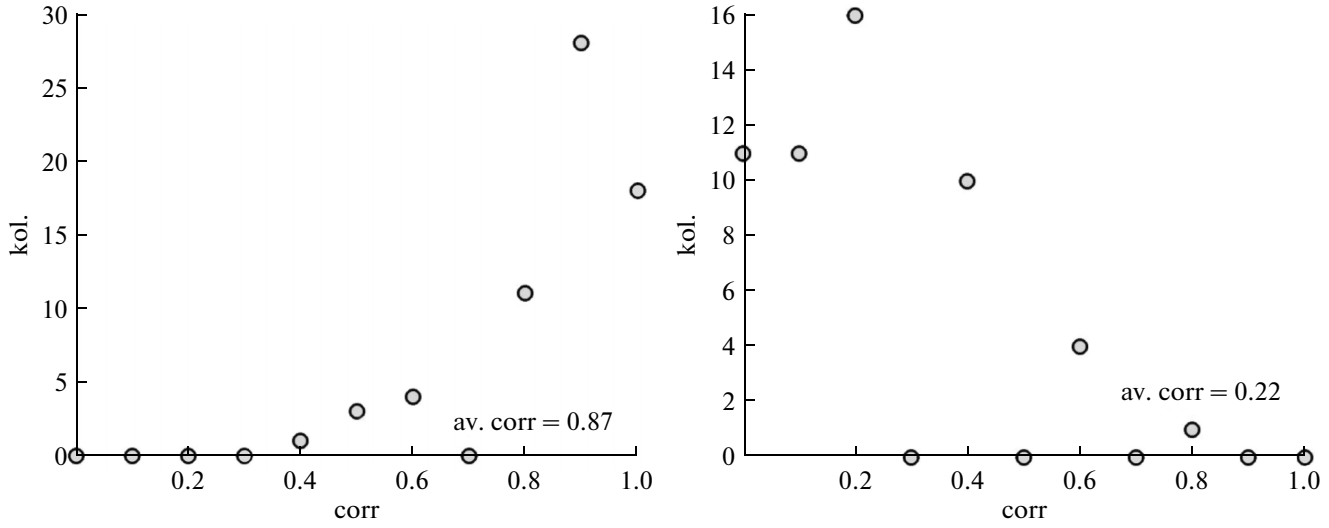

Fig. 3. Histograms of the correlation coefficients of the dominant rhythms for the C3 leads of (left-hand panel) normal patient and (right-hand panel) second-stage PD patient. The arithmetic mean values of the distribution of correlation coefficients are presented, kol is the number of coincidences, corr is the correlation value, and av. corr. is the mean value of correlation.

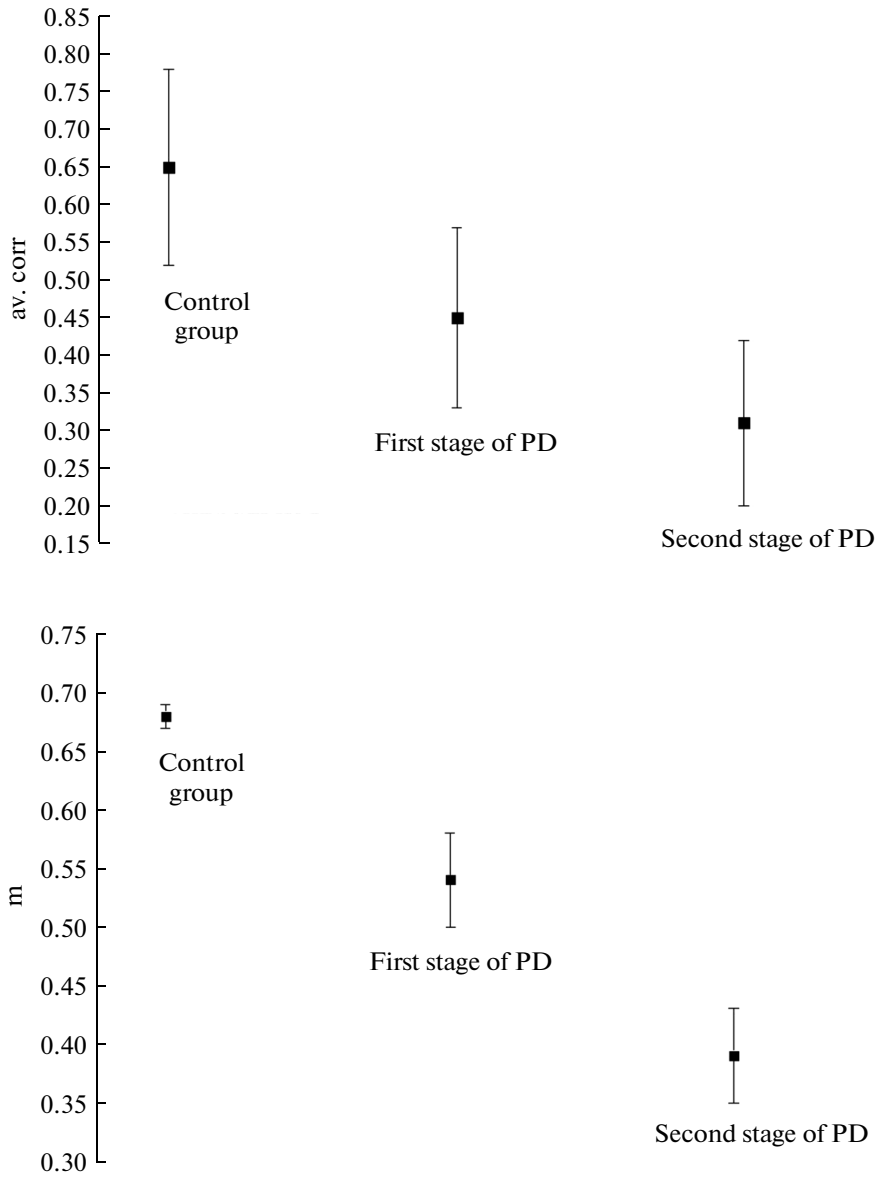

Fig. 4. (Upper panel) Arithmetic mean and (lower panel) median values of the correlation coefficients for the C3 and C4 leads of the control group and the leads in the diseased hemisphere for the first- and second-stage PD patients.

histograms of the correlation coefficients for the C3 leads of the same patients. It is seen that the histograms of the correlation coefficients for normal patients are concentrated at relatively large values, whereas the spread over all correlation coefficients is observed for the PD patient.

Figure 4 shows the mean values and medians of the correlation coefficients for the PD patients and control group. For the first-stage PD patients, we use the C3 and C4 leads of the diseased hemisphere. For the control group and the second-stage patients, we employ the leads of both hemispheres. It is seen that the development of the disease leads to a decrease in the mean values and medians of the correlation coefficients and, hence, an increase in the degree of disorganization of the dominant rhythm.

The comparison of the EEG data for the symmetric fragments of the right- and left-hand-side hemispheres always yields significant differences of the distributions of local maxima of the wavelet spectrograms. The features of the disorganization of the EEG records can be more developed on either side. These results are in agreement with the concept of the asymmetry of the first manifestations of PD [2].

Neurophysiology employs a computer method for the detection and quantitative estimation of tremor that emerges under constant position of the joint

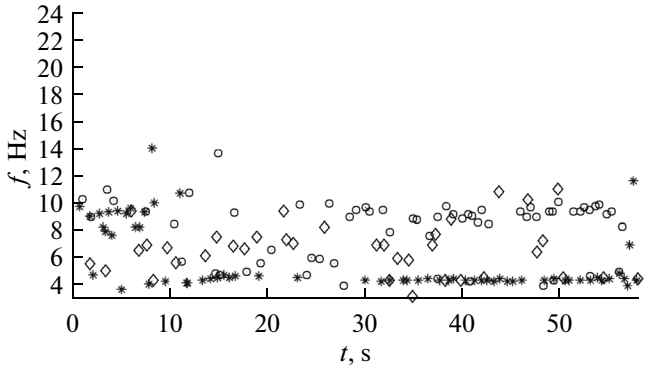

Fig. 5. Local maxima on the time–frequency interval of (circles) EEG C3 leads in the motor zone of cerebral cortex, (asterisks) contralateral MT, and (diamonds) EMG records for the first-stage PD patient in accordance with the qualitative Hoehn–Yahr scale.

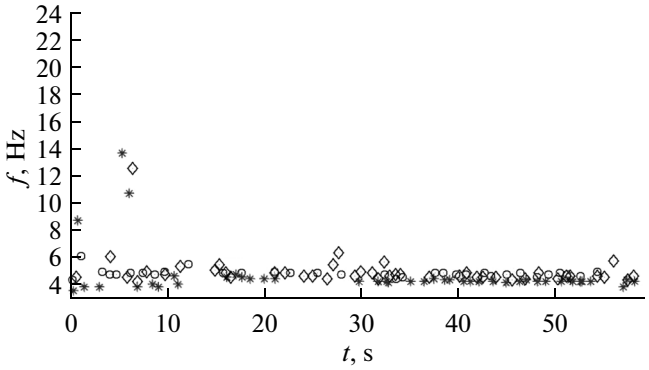

Fig. 6. Local maxima on the time–frequency interval of (circles) hemispheric symmetric lead C4, (asterisks) contralateral MT, and (diamonds) EMG records for the first-stage PD patient in accordance with the qualitative Hoehn–Yahr scale.

angle. Below, we describe the method that makes it possible to select the frequency interval of the broad EMG spectrum that corresponds to the motor action. The method is based on the assumption that the muscle force that is exerted on joint provides the motion the shape of which is close to the EMG envelope [22].

The data on the hand tremor is contained in the EMG envelope rather than the EMG signal, so that the EMG envelope must be selected. The EMG envelope is calculated using the Hilbert transform [23].

To obtain the amplitude and phase of arbitrary signal $u(t)$ (modulated high-frequency signal), we must construct the analytical signal

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

The real part of the analytical signal coincides with desired signal $u(t)$. Imaginary part $w(t)$ is the Hilbert transform of signal $u(t)$. The Hilbert transform is calculated as

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

Substituting formula (5) in expression (4), we obtain the following result:

$$w(t) = u(t) + iv(t) = a(t)\exp(i\pi\omega t), \quad (6)$$

where $a(t)$ is the signal envelope. The EMG envelope is given by

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

The digitized EEG records are processed using the fourth-order Butterworth filter to eliminate the signal at a frequency of 50 Hz and the noise at a frequency of 100 Hz.

Figures 5 and 6 show the time–frequency distributions of the extrema of the wavelet spectrograms for the C3 and C4 leads of the motor zone of the cerebral cortex and the extrema of the EMG envelope and tremor in the contralateral limbs. Figures 7 and 8 present the integral histograms of the frequency distributions of local maxima that correspond to the time–frequency distributions. Figure 8 shows that the extrema in the diseased motor zone of the right-hand hemisphere are partly correlated (i.e., the peaks of the sums of amplitudes almost coincide) with the extrema of the mechanical tremor (MT) and EMG. Note the absence of such correlation for the clinically healthy left-hand hemisphere (the absence of the coincidence of the peaks of amplitude sums) (Fig. 7).

CONCLUSIONS

The developed methods and software make it possible to obtain the main PD features at early stage: hemispheric asymmetry of the time–frequency characteristics of EEG, especially, in the central leads (C3 and C4); rhythm generation in a frequency interval of 4–6 Hz and its frequency synchronization with the EMG activity and MT of limbs; and disorganization of the dominant EEG rhythm that is in agreement with the general concept of the PD-induced disorganization of various systems. We quantitatively estimated the disorganization of the dominant rhythm in the central leads to select the groups of healthy patients, the first-stage PD patients, and the second-stage PD-patients.

The wavelet transform and the further quantitative analysis prove several facts that characterize the EEG features at the second and third stages of PD. Several specific features of the time–frequency organization of the EEG at the first stage of the disease are revealed.

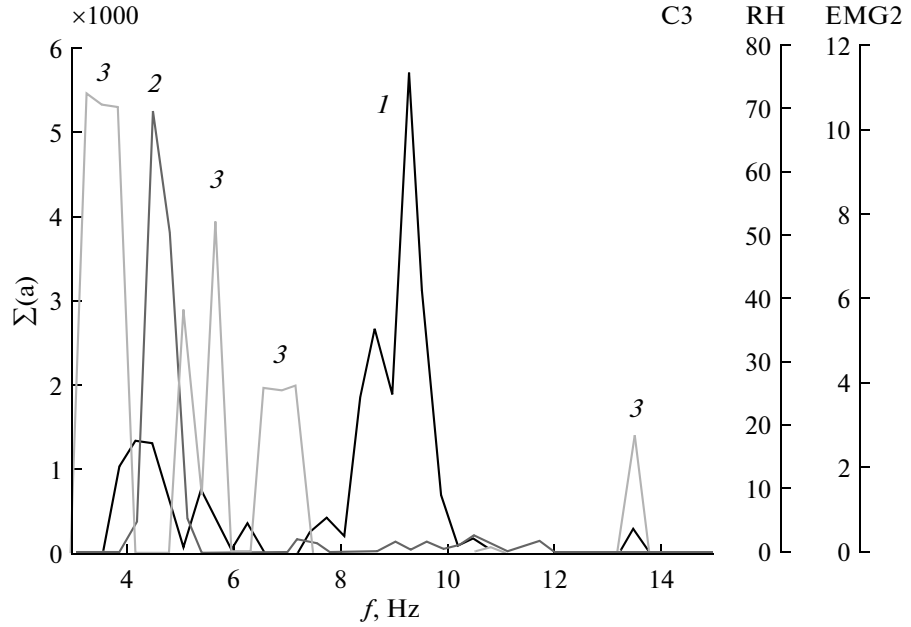

Fig. 7. Integral histograms of the frequency distributions of local maxima (apparently healthy hemisphere) with the frequency mismatching in the theta range: (*1*) C3 lead, (*2*) right-hand (RH) lead, and (*3*) EMG2 lead.

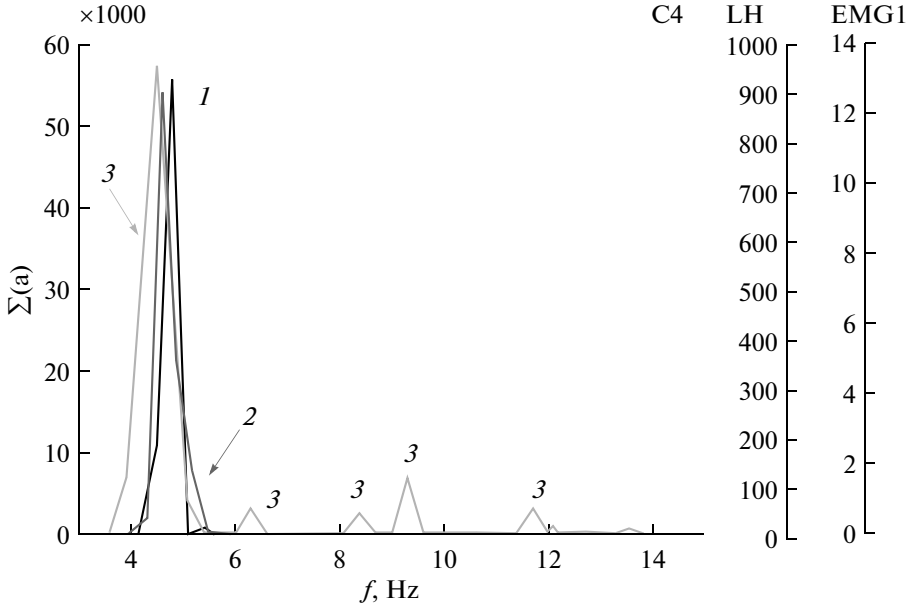

Fig. 8. Integral histograms of the frequency distributions of local maxima (diseased hemisphere) with the frequency matching in the theta range: (*1*) C4 lead, (*2*) left-hand (LH) lead, and (*3*) EMG1 lead.

The proposed approaches and procedures are efficient in the study of PD stages including the earlier stages. In comparison with the Fourier spectra, the histograms of the extrema of the EEG wavelet transforms make it possible to more clearly reveal the PD features and study the corresponding dynamics. The results can be used in a further search for specific EEG markers at the earliest (including preclinical) stages of the disease.

REFERENCES

1. M. V. Ugryumov, *Neurodegenerative Diseases: Fundamental and Applied Aspects*, Ed. by M.V. Ugryumov (Nauka, Moscow, 2010) [in Russian].

2. K. Brockmann and D. Berg, *Diagnosis of Parkinson's Disease. Parkinson Disease and Other Movement Disorders*, Ed. by E. C. Wolters and C. R. Baumann (Int. Ass. of Parkinsonism and Related Disorders, VU Univ. Press, Amsterdam, 2014), p. 229.
3. J. A. Ganglberger, Electroenceph. Clinical Neurophys. **13** (1), 82 (1961).
4. R. Soikkeli, J. Partenen, H. Soininen, et al., Electroencephal. Clinical Neurophys. **79** (3), 159 (1991).
5. L. Pezard, R. Jech, and E. Ruzicka, Clinical Neurophys. **112** (1), 38 (2001).
6. C. E. D' Atellis, S. I. Isaacson, and R. O. Sime, Ann. Biomed. Eng. **25**, 286 (1997).
7. A. V. Gabova, D. Yu. Bosnyakova, M. S. Bosnyakov, et al., Dokl. Biol. Sci. **396**, 194 (2004).
8. D. Yu. Bosnyakova and Yu. V. Obukhov, Pattern Recognit Image Anal. **15** (2), 513 (2005).
9. Yu. V. Obukhov, A. V. Antsiperov, A. B. Gekht, et al., *Neurodegenerative Diseases. Theory and Practice*, Ed. by M. V. Ugryumov (Nauka, Moscow, 2010) [in Russian].
10. A. M. Vein, V. L. Golubev, and N. N. Yakhno, in *Parkinson's Disease: Problems of Clinics, Pathogenesis and Treatment* (Mosk. Nauch. Ob-vo Nevropatol. Psikhiat., Moscow, 1974), p. 57 [in Russian].
11. V. L. Golubev, Ya. I. Levin, and A. M. Vein, *Parkinson's Disease and Parkinsonian Syndrome* (MEDpress, Moscow, 1999) [in Russian].
12. V. L. Golubev and R. K. Magomedova, Zh. Nevrol. Psikhiat. Im. S. S. Korsakova **106** (1), 43 (2006).
13. C. G. Goetz, G. T. Stebbins, D. Wolff, et al., Movement Disorders **24**, 551 (2009).
14. S. J. Schiff, A. Aldroubi, M. Unser, and S. Sato, Electroencephal. Clinical Neurophys. **91**, 442 (1994).
15. W. R. Gibb and A. J. Lees, J. Neurol. Neurosur. Psychiatry **51**, 745 (1988).
16. M. M. Hoehn and M. D. Yahr, Neurology **17** (5), 42 (1967).
17. S. Fahn and R. Elton, *Recent Developments in Parkinson's Disease*, Ed. by S. Fahn et al. (Macmillan Healthcare Inf., Florham Park, 1987), p. 153.
18. A. Oswal, V. Litvak, and P. Brown, *Parkinson Disease and Other Movement Disorders: Motor Behavioural Disorders and Behavioural Motor Disorders*, Ed. by E. C. Wolters and C. R. Baumann, (VU Univ. Press, Amsterdam, 2014), p. 163.
19. Yu. V. Obukhov, M. S. Korolev, A. V. Gabova, et al., RF Patent No. 2484766, Byull. Izobret., No. 17 (20.06.2013).
20. M. S. Korolev and Yu. V. Obukhov, Nelin. Mir, No. 2, 131 (2012).
21. Yu. V. Obukhov, M. S. Korolev, and K. Yu. Obukhov, in *Proc. 16th All-Russ. Conf. "Mathematical Methods of Pattern Recognition (MMPR-16)", Kazan', Oct. 6–12, 2013* (Tezaurus, Moscow, 2013), p. 79.
22. E. A. Andreeva and O. A. Khutorskaya, *Spectral Method for Analysis of Electromyographic Activity of Muscles* (Nauka, Moscow, 1987), p. 192.
23. D. E. Vakman and L. A. Vainshtein, Usp. Fiz. Nauk **123**, 657 (1977).

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