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Extraction of Diagnostic Information on Brain Diseases by Analyzing Wavelet Spectra of Biomedical Signals

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New approaches to the analysis of Morlet wavelet spectra of electroencephalograms, electromyograms, and accelerometer signals are proposed. The proposed approaches are based on the analysis of time–frequency distributions of local extrema and ridges of wavelet spectrograms. The paper describes the results of application of the proposed techniques for the diagnosis of the early stage of Parkinson's disease and essential tremor, monitoring of postoperative patients with epilepsy, and assessment of inter-channel phase coupling of EEG during cognitive tests of patients after traumatic brain injury.

Electroencephalography (EEG) allows both screening examination and continuous long-term monitoring of postoperative patients. EEG signals are non-stationary, which necessitates development of various methods for their time–frequency analysis. Among these, wavelet analysis is the most widely used. The goal of this work was to describe new approaches to the identification of signs of some brain pathologies. The suggested approaches are based on the analysis of the time–frequency distributions of local extrema of the electromyogram (EMG) envelope and accelerometer signals (AM) as well as the ridges of EEG wavelet spectrograms.

Methods and algorithms for the analysis of wavelet spectra of EEG, EMG envelope, and AM signals have been developed to provide early diagnosis of Parkinson's disease (PD) and essential tremor (ET), as well as for monitoring postoperative patients with epilepsy or traumatic brain injury (TBI).

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Early Diagnosis of Parkinson's Disease and Essential Tremor

A method for analyzing the distribution of spectral power density (SPD) peaks of wavelet spectrograms was developed [1, 2]. The method was applied to 0.5-4 Hz wavelet spectra of the surface EMG envelope and AM signals in patients with PD and ET.

The group of patients with PD included 20 patients at the first stage of the disease according to the Hoehn and Yahr scale. The number of patients with ET was 13; healthy volunteers, 8. The records in each subject were taken for 2 min, while the subject was sitting in a chair, arms straightened in front of the body. The obtained EMG signals were preprocessed using a Butterworth filter with a bandwidth from 60 to 240 Hz. After filtering, the Hilbert transform was applied to the EMG signals to isolate the envelope.

The number of SPD peaks was calculated for the entire EMG envelope and AM records made in each subject. Then, it was normalized to the duration of the signal (in seconds). The dependence of the area under the ROC curve (*AUC*) on the frequency range boundaries in the space of the number of SPD peaks was investigated for different frequency ranges. The numbers of SPD peaks per unit time were compared for the groups of patients with PD and ET and control subjects using the non-parametric Mann–Whitney test. Statistically significant dif-

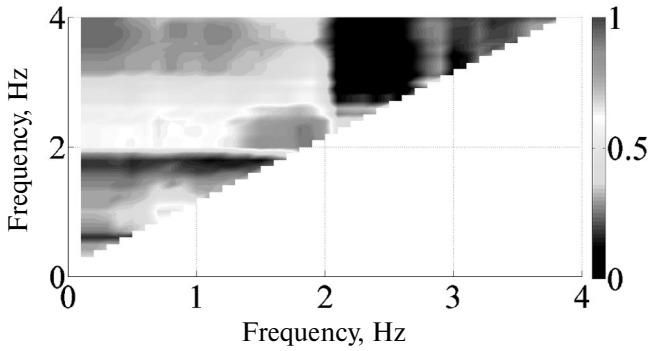

Fig. 1. *AUC* diagram for extensor muscles; EMG envelope for the left arm with hyperkinetic tremor in patients with PD. The abscissa is the lower boundary of the frequency ranges; the ordinate, the upper boundary. The frequency range is 0.5 to 4 Hz (step, 0.1 Hz).

ferences were observed between the numbers of SPD peaks per unit time for the EMG envelope and AM signals in the range of 0.5-4 Hz measured in patients with PD and ET and in the control group. The differences were statistically significant both for hands with hyperkinetic tremor and for "healthy" hands of patients with PD, as well as for patients with ET of both hands. An example of the frequency *AUC* diagram for the extensor muscles of the left hand with hyperkinetic tremor for PD patients is shown in Fig. 1. There are pronounced patterns in the frequency ranges 0.5-1.8, 1.8-2.3, and 2.1-3.9 Hz in the diagram.

If for different frequency ranges $AUC > 0.5$, the number of SPD peaks in patients is greater than in healthy subjects. If $AUC < 0.5$, the number of peaks in patients is less than in healthy subjects.

Parkinsonian and essential tremors cannot in some cases be detected with the naked eye. Thus, a need arises for a method of computer diagnostics of PD and ET. Tremor often disappears during the examination, which can lead to incorrect diagnosis by the doctor. Patients with both hands shaking simultaneously can be misdiagnosed with ET if the doctor fails to recognize PD at the second stage according to the Hoehn and Yahr scale (when the patient also has both hands shaking at the same time). The developed method of computer diagnostics differentiates patients with PD and ET from control subjects even in the absence of a pronounced tremor in the patients. In addition, the developed signal analysis method revealed statistically significant differences between PD patients and ET patients in the low-frequency range of 0.5-4 Hz.

It was shown that the analysis of patients with PD and ET using EMG envelope and AM data gives similar results. Experiments showed that the suggested method of analysis holds much promise for revealing EMG envelope and AM patterns in patients at the early stages of PD and ET, providing thereby new knowledge about these diseases [3].

Automated Segmentation of Long EEG Signals into Regions of Interest

A method for analysis of wavelet spectrum ridges was developed to solve the problem of automated segmentation of long (recorded for several days) EEG signals into regions of interest for the diagnosis of post-traumatic and postoperative epilepsy. EEG wavelet spectrograms were obtained using the complex Morlet wavelet as the basis function.

It was shown in the Appendix to [4] that for the signal $S(t) = A_S(t)\exp[i\Phi_S(t)]$ (where $A_S(t)$ changes slower that the phase) satisfying the following asymptotic properties [5]:

$$\left|\frac{d\Phi_S(t)}{dt}\right| >> \left|\frac{1}{A_S(t)}\frac{dA_S(t)}{dt}\right|, \quad \left|\frac{1}{A_S(t)}\frac{dA_S(t)}{dt}\right| << \left|\frac{1}{\psi(t)}\frac{d|\psi(t)|}{dt}\right|, \quad (1)$$

the following is true:

$$A(t) \approx |W[t, f_r(t)]|,$$
$$\Phi(t) \approx \arctan\left(\frac{\mathrm{Im}\{W[t, f_r(t)]\}}{\mathrm{Re}\{W[t, f_r(t)]\}}\right), \quad \Phi_S'' << 2f^2, \quad (2)$$

In Eqs. (1) and (2), $\psi(t)$ is the mother (analyzing) Morlet wavelet, $W(t, f_r) = \max|W[t, f_r(t)]|$ is the ridge of the Morlet wavelet transform of the signal $S(t)$, and $f_r(t)$ is the frequency of the ridge.

The ridges of the wavelet spectrograms, i.e. the points of global maxima of the wavelet spectrogram at the sampling time points, were determined. The SPD histogram was analyzed at the ridge points to find the threshold SPD value for identifying the ridge points as background activity or as regions of interest. For the regions of interest, the amplitude–frequency characteristics (features) of ridge fragments were calculated and used to classify signal fragments by the type of activity: epileptic seizure or chewing artifact. These characteristics can also be used to eliminate other artifacts [6]. This method allows the workload on the medical personnel to be reduced by reducing the time spent on marking the daily EEG monitoring signals, which is currently done manually. The periodicity of peaks at time points of the wavelet spectrogram ridge corresponding to peak-wave epilepti-

form activities during an epileptic attack and activities during chewing was studied to solve the problem of identifying the features of epileptiform activity during an epileptic attack that distinguish it from chewing artifacts [7]. Wavelet spectra cutoffs (SPD vector) at frequencies above the maximum frequency of the wavelet spectrogram ridge were considered. The Fourier spectra were calculated for the cutoffs at frequencies above 4 Hz. At frequencies above 4 Hz, the half-width for the peaks of the Fourier spectra of the chewing artifact is almost twice as large as in the case of an epileptic seizure, while the peak frequencies differ by a factor of 2.5 or more (Fig. 2). These features made it possible to distinguish signal fragments with epileptiform activity from those with chewing artifacts [8].

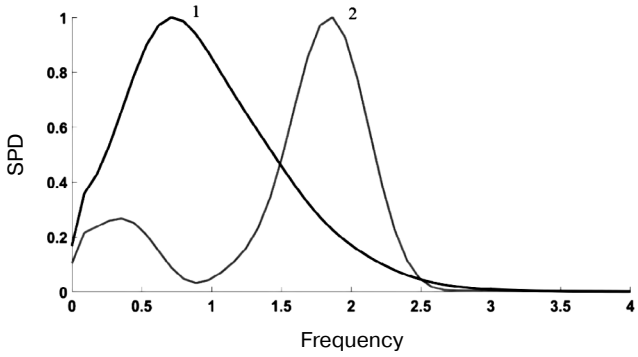

Fig. 2. Fourier spectra at the 4 Hz cutoff frequency of the EEG wavelet spectrogram: 1) chewing artifact spectrum; 2) epileptic seizure.

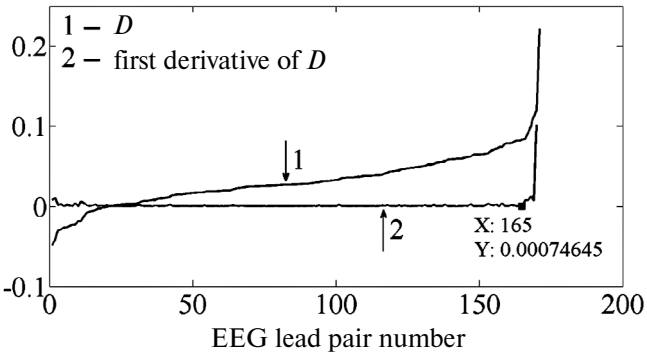

Fig. 3. 1) Curve of D vs. EEG lead pair number in the ascending order of D; 2) first-derivative curve. The EEG was measured in a healthy subject.

Assessment of EEG Phase Coupling in Cognitive Tests

Various methods of EEG analysis are traditionally used in cognitive tests to assess the coupling of brain regions in healthy subjects and patients with TBI. We analyzed the EEG of patients with moderate TBI during cognitive tests (for counting and logical reasoning and for spatial intelligence and visual thinking). During counting and logical reasoning test (T1), the subject was presented with a random list of items belonging to the categories of "clothing" or "food". The task was to count mentally the number of objects belonging to one of the two categories. During the test for spatial intelligence and visual thinking (T2), the doctor told randomly the time of day. The task of the subject was to imagine the dial of a clock and the location of the clock hands corresponding to this time of day and to say "yes" if both hands were in the same half of the dial; if in different halves, the subject was to remain silent. The duration of each test was 60 s. EEG was recorded both during the tests and when no tests were performed. The criteria for inclusion in the studies were the ability to stand without help and follow the doctor's instructions and the absence of hemipareses or other neurological disorders.

The inter-channel coherence of two EEG signals is usually assessed by determining their normalized complex cross-coupling. As argued in [9], phase synchronization is preferable to coherence. We have developed a new method for assessing the inter-channel phase synchronization of the EEG during cognitive tests in healthy subjects and patients with moderate TBI. The method is based on the analysis of the ridges of the complex Morlet wavelet transform of EEG signals (see Eq. (2)).

Phases of EEG signals are calculated and compared at the ridge points of their wavelet spectrograms. EEG recordings made during cognitive tests and without tests are used. Then, the phase differences between two signals in two EEG leads are calculated and histograms of $\rho_{x,y} = n_{x,y}/N$ are constructed for different pairs of EEG leads, where $n_{x,y}$ is the number of points of the ridge readouts at $\Delta\Phi_{x,y}(t) < 0{,}01\pi$ and N is the total number of EEG readouts during the test [10]. A and B are, respectively, the histogram maxima $\max\rho_{x,y}$ for the T1 test and for the EEG recording made when no tests were performed. It is convenient to consider the difference $D = A - B$ sorted by pairs of EEG leads in the ascending order of D. Figure 3 shows the curve of D vs. EEG lead pair number in the ascending order of D, as well as the first-derivative curve. The EEG was measured in a healthy subject.

Analysis of the first-derivative curve shows that pairs of leads can be considered as phase-coupled if they have numbers greater than that corresponding to the sharp increase in the derivative. This rule was used to identify

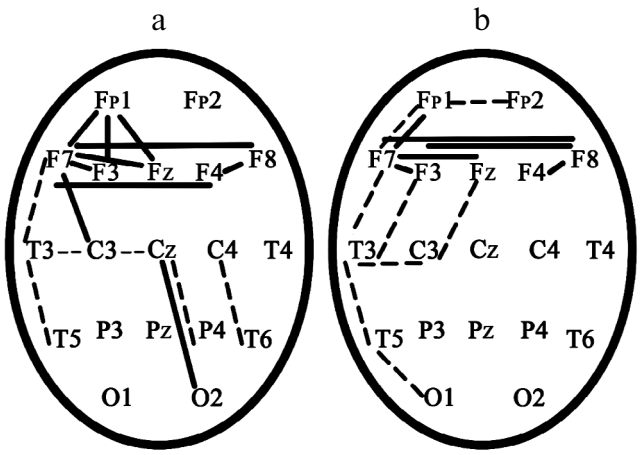

Fig. 4. Phase-coupled pairs of EEG leads for a patient with TBI before and after rehabilitation: a) an example for the T1 test; b) an example for the T2 test. Dotted lines show phase-coupled pairs of EEG leads before rehabilitation; solid lines, after rehabilitation.

phase-coupled pairs of EEG channels before and after rehabilitation of patients with moderate TBI. Figure 4 shows the phase-coupled pairs of EEG leads for a patient with TBI (the lead pairs are phase-coupled only during a certain test before and after rehabilitation). In accordance with the literature data, cognitive tests in healthy subjects activate interhemispheric connections in the frontal regions of the brain [11].

Figure 4 shows a positive rehabilitation dynamics in a patient with TBI. The cognitive test after rehabilitation revealed that interhemispheric connections appeared and the frontal areas became involved, as in control subjects, which is indicative of a positive rehabilitation dynamics [12].

Conclusions

A method for early diagnosis of PD and ET based on processing and analysis of wavelet spectra of biomedical signals was developed. The method involves construction of *AUC* diagrams and nonparametric testing of statistical hypotheses used to identify statistically significant differences in the number of SPD peaks per unit time. A detailed analysis of the data of patients with PD and ET was carried out in the frequency range of 0.5-4 Hz. Statistically significant differences from the control group were found both for the hands with hyperkinetic tremor and for the "healthy" hands of the patients. The obtained patterns in the EMG envelope and AM data can be useful for early diagnosis of PD and ET.

A method for automated segmentation of daily EEG monitoring signals was developed. It is based on the analysis of the ridges of wavelet spectrograms with the purpose of classifying them into regions of interest. The developed method makes it possible to reduce the workload on doctors involved in analyzing long-term EEG monitoring data from patients with post-traumatic and postoperative epilepsy. The amplitude–frequency characteristics of fragments of the wavelet spectrogram ridge were calculated to provide further classification of the areas of interest into those reflecting epileptic seizure and artifacts. The features of the EEG wavelet spectra were identified that allow distinguishing the peak-wave epileptiform activity from chewing artifacts.

A new method based on the analysis of the Morlet wavelet ridges in EEG signals was developed. The method can be used to assess the inter-channel phase synchronization of EEG during cognitive tests in patients with moderate TBI. For this purpose, the phases of the EEG signals recorded during cognitive tests are calculated and compared at the ridge points of their wavelet spectrograms. The pairs of EEG leads that become phase-coupled during cognitive tests are identified. The phase-coupled pairs of EEG leads in patients with moderate TBI before and after rehabilitation are compared with those in control. This makes it possible to determine whether the rehabilitation dynamics is positive or negative.

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