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THEORETICAL AND MATHEMATICAL PHYSICS

Method for Diagnostics of Characteristic Patterns of Observable Time Series and Its Real-Time Experimental Implementation for Neurophysiological Signals

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Abstract—A method is proposed for analysis and automatic diagnostics of characteristic oscillatory patterns of the electric activity of the brain in real time on the basis of a continuous wavelet transformation. The results of experimental investigation of automatic recognition of epileptic activity episodes on experimental animals based on the proposed approach are considered.

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INTRODUCTION

Modern mathematical methods of analysis and diagnostics of complex oscillatory processes (including the dynamic chaos regimes), which are being rapidly developed in the modern theory of oscillations and waves in radio physics, have found application in various fields of natural science. The application of the nonlinear dynamics methods to problems arising in the study of complex behavior of living systems including the analysis of temporal and space–time signals of physiological origin is of considerable interest.

Examples of successful application of the methods developed in the dynamic chaos theory to analysis of oscillatory processes in physiological and medical systems can be found in [1–4]. Among most striking examples of such investigations into living systems using the methods of nonlinear dynamics and radio physics, we can mention the effect of an external factor on the encephalograms of the brain [5, 6], the interrelation of rhythms of respiratory and cardiovascular systems [7–10], synchronization of the dynamics of neuron ensembles of various parts of the brain of an epileptic patient [11, 12], analysis of intermittent behavior in neuron ensembles [13–15], and so on. Such methods of investigation become especially important in analysis of the dynamics of neural networks of the brain, which are extremely complicated objects consisting of a large number of oscillatory elements (neurons). Recording of electroencephalograms (EEG), which are averaged sums of electric currents generated by a large group of neurons in the vicinity of a recording electrode, is a traditional and rather effective method of study of the electrical activity of the brain. For testing a human being, such an electrode is placed on the surface of the head; in the case of animals, more accurate measurements can be taken by implanting electrodes directly into the cerebral cortex. Using such approaches, prolonged EEG recording can be carried out.

In such experiments, data processing using contemporary methods and approaches, simulation, and analysis of the general dynamics of emergence of certain rhythms and oscillatory patterns on the EEG is of key importance along with experimental studies. The application of a powerful mathematical apparatus developed and used in radio physics and nonlinear dynamics (in particular, the methods based on spectral and wavelet analysis) paves the way for developing new effective methods for analysis of experimental data, determining new regularities, and automation of experimental data processing. It is important to note that considerable attention of researchers was concentrated on analysis of processes in the formation of special modes of rhythmic activity characterizing various functional states (episodes of epileptic activity, sleep, and wakeful state). It is well known that the emergence of rhythmic components on the EEG is the reflection of synchronous operation of a huge number of nerve cells combined into ensembles [16–18]; for this reason, analysis of rhythmic activity in the EEG dynamics of brain is closely related to an important problem of radio physics such as analysis of synchronous behavior in networks with a complex topology of links [19–22].

It should be noted that signals of biological origin are often characterized by substantial instability (their spectral composition and amplitude vary with time); for this reason, it is expedient to study these signals with the help of wavelet analysis [23–25], which suits well for investigating such nonstationary processes. We are aware of a number of successful applications of the

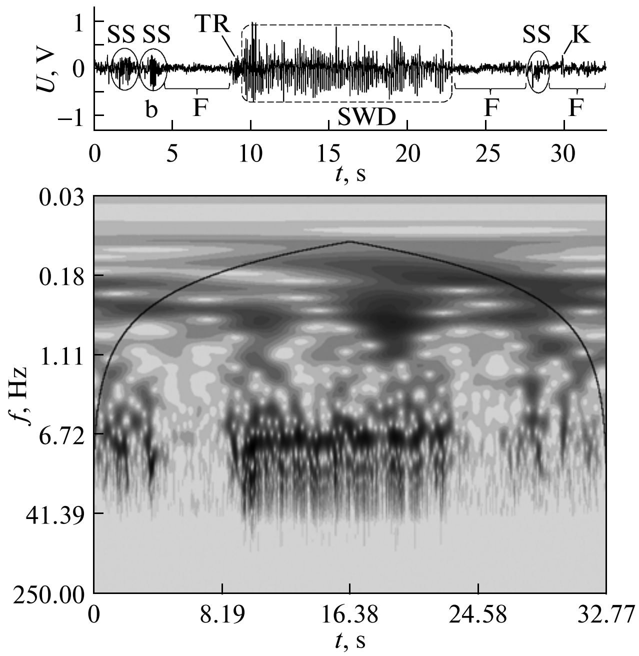

Fig. 1. Fragment of epileptic EEG and the corresponding wavelet spectrum. Selected regions are a spike wave discharge (SWD), sleep spindle (SS), theta rhythm (TR), K complex (K), and normal background brain activity (F).

wavelet transformation for studying nonstationary signals of physiological origin (in particular, for studying the coordination of rhythms in the human cardiovascular system [9]; for revealing typical features in electrocardiograms, which make it possible to diagnose ventricular tachycardia and fibrillation [26], and for determining informative points of a pulse signal [27]). The apparatus of wavelet analysis (both discrete and continuous) and the methods for analyzing synchronous dynamics of the brain based on the wavelet were also successfully used for studying normal and pathological EEGs of animals and human beings [15, 25, 28–33]. Among these publications, we distinguish the work [28] in which the wavelet transform was used in a quantitative description of transient processes in EEG upon photostimulation [29, 30]; the signal was cleaned from artifacts with the help of a wavelet transform, and typical features permitting the classification of EEGs were singled out.

The above arguments support the statement that the contemporary apparatus (including wavelet analysis) developed in the theory of nonlinear oscillations as applied to random processes makes it possible to considerably advance in understanding specific features in the dynamics and synchronization in the neural ensemble of the cerebrum. In this direction, important results were obtained; in particular, frequency–time patterns in the cerebral activity, which could be diagnosed from EEG signals and are specific for each patient, were revealed [32]; alternation was observed in the synchronous/asynchronous brain activity [34]; and phase locking modes between different EEG taps for a human being were revealed [35]. From the standpoint of applications, this is very important for monitoring the pathologic activity of the cerebrum [36, 37].

This study aims at the development of a new method for diagnosing oscillatory patterns in real time on scalar temporal series being recorded as applied to neurophysiological signals on EEG for animals, which demonstrate epileptic activity. It will be shown below that the main advantage of the proposed method is the possibility of its application in analysis of EEGs in real time and in the diagnostics of the corresponding oscillatory activity at its very beginning. The merits of the method also include minor computer time expenditures required for such processing, which makes it possible to effectively carry out multichannel data analysis in real time. This method is based on the application of continuous wavelet transformation [25, 29–32, 38]. The use of the wavelet transform is justified because the method of data processing described here is effective in analysis of nonstationary data with a short time of oscillatory activity, which is typical of EEG signals recorded from the cerebral cortex of epileptic patients [16, 39]. We also report on experimental results of testing the real-time algorithm developed here for monitoring epileptic events from recorded EEGs.

1. METHOD OF AUTOMATIC ANALYSIS OF A NONSTATIONARY SIGNAL IN REAL TIME

Let us consider a temporal signal shown in Fig. 1 in the form of a fragment of an electroencephalogram; this signal is a typical example of electrical activity of the cerebrum of a WAG/R*ij*-line rat having absence epilepsy (WAG/R*ij* rats are a specially bred line of rats genetically liable to congenital absence epilepsy [41]). It can easily be seen that certain segments (corresponding to desynchronized behavior of the neural ensemble of cerebral cortex, or F region) that can be singled out in the EEG signal differ from the background dynamics in amplitude and form of oscillations. Such EEG fragments will be henceforth referred to as oscillatory patterns. Oscillatory patterns can be classified in accordance with their form or frequency content. The former approach is traditionally used by neurophysiologists [42, 43], while the latter approach is a more precise instrument for analyzing the dynamic series and can be used for solving problems of automatic recognition of structures in the time domain. In the signal depicted in Fig. 1, we can single out such oscillatory patterns as sleep spindles (SSs), theta rhythms (TRs), K complexes (Ks), and spike wave discharges (SWDs) using the first approach.

It should be noted that a number of original methods have been employed for analyzing the features of the neural ensemble dynamics from EEGs using the wavelet transform. For example, a method for classification of EEGs by estimating the values of waveletpacket coefficients in certain frequency ranges was described in [30], while in [29], the wavelet transform was applied for preliminary processing of the signal (namely, its cleaning from artifacts by discrimination of insignificant wavelet coefficients obtained from the expansion in orthogonal wavelet packets); a method for analyzing transient processes observed on EEGs upon photostimulation, which is based on the observation of the dynamics of spectral components on the wavelet surface, was proposed in [28]. All these methods demonstrate high accuracy and sensitivity; however, the range of their application is limited to processing of preliminarily recorded signals; at the same time, in many cases, it is necessary to detect, even at the instant of its emergence. In the method proposed here, we use analysis of the energy distribution of a continuous wavelet transform over frequencies. It will be shown below that this method makes it possible to detect oscillatory patterns in the *real* time mode.

Let us consider the main features of this method. For separating oscillatory patterns, we used the continuous wavelet transform in the form of a convolution of the signal $x(t)$ under investigation and a certain basis function [38],

$$W(s, \tau) = \int_{-\infty}^{+\infty} x(t)\varphi^*_{s,\tau}(t)dt, \tag{1}$$

where the asterisk indicates complex conjugation.

Basis function $\varphi_{s,\tau}(t)$ can be obtained from the mother wavelet with the help of the following transformation:

$$\varphi_{s,\tau}(t) = \frac{1}{\sqrt{s}}\varphi_0\left(\frac{t-\tau}{s}\right), \tag{2}$$

where s is the time scale determining the expansion or contraction of the mother function, τ is the time shift of the wavelet transform, and φ_0 is the prototype of the wavelet function known as the mother wavelet. It was shown in [39] that the mother wavelet most suitable for the problem of recognition of SWDs is the complex Morle wavelet

$$\phi(\eta) = \frac{1}{\sqrt[4]{\pi}}e^{j\omega_0\eta}e^{-\eta^2/2}, \tag{3}$$

where parameter ω_0 determines the shape and width of the wavelet function. It can be stated that parameter ω_0 defines the ratio of the time scale s of the transform and frequency f of the initial signal: if we choose $\omega_0 = 2\pi$, the wavelet transform scale and the frequencies of the Fourier spectrum obey the simple relation $s = 1/f$.

Parameter $w(s, \tau) = |W_{s,\tau}|$ is the instantaneous value of the transform energy, viz., the energy corresponding to time instant τ over scale s.

The wavelet surface corresponding to the EEG segment in Fig. 1a is shown in Fig. 1b; it can be seen that different EEG patterns correspond to different energy distributions of the wavelet spectrum $w(s, \tau) = |W_{s,\tau}|$.

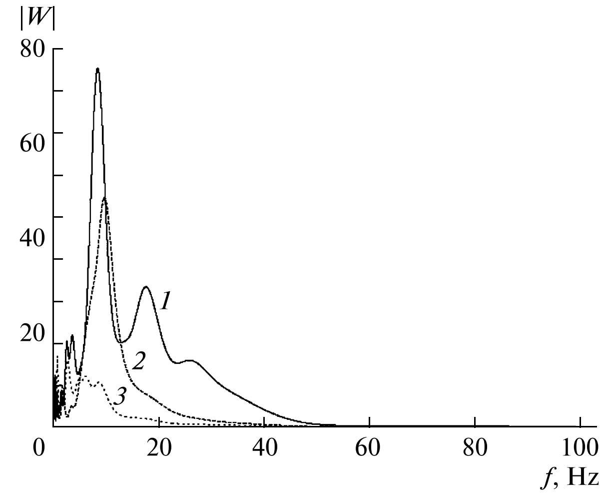

Fig. 2. Instantaneous wavelet spectra of oscillations: *1*—spike-wave discharge; *2*—sleep spindle; *3*—background activity.

Figure 2 shows the frequency distributions of the wavelet transform energy for different high-amplitude distributions on the EEG as well as the background EEG. It can easily be seen that spike wave discharges and sleep spindles have different frequency compositions. For example, it was shown in [39] that sleep spindles demonstrate an increase in the amplitude of the wavelet coefficients in the frequency range 5–14 Hz, while the SWD is characterized by high values of the wavelet transform coefficients in a wider frequency range (10–80 Hz), indicating the clearly manifested second and third spectral harmonics of the basic rhythm.

It is noteworthy that the SWD and SS spectra in the low-frequency range are similar, and the increase in energy in the range of high frequency is observed only in the spike wave discharge. In [39], this fact formed the basis for diagnostics of various types of oscillatory activity on EEGs. The main idea of the method was that the wavelet transformation was carried out for the dynamic series under investigation, and instantaneous energy $w(t)$ of the transform was calculated in the characteristic frequency range F_s. Various quantities can be used as a characteristic proportional to the instantaneous energy of the wavelet spectrum [38–40]. In this work, the instantaneous energy was calculated as follows:

$$w(\tau) = \int_{F_s} |W_{s,\tau}| ds. \tag{4}$$

When the value of $w(t)$ exceeded a certain critical level, it was concluded that a certain pattern is present. It should be noted that this method was used in [39] for processing preliminarily recorded signals, while our study is devoted to the development of a method for real time diagnostics of oscillatory patterns. This task involves considerable difficulties because structures belonging to different classes may have close spectral compositions. For this reason, the method used for recognition of structures must clearly distinguish patterns with close frequency compositions and energies on the one hand and must be effective in numerical implementation for constructing an actually operating system on the other hand. Another difficulty is separating oscillatory patterns in the real time mode is the lack of the complete time implementation required for performing transformation (1) at a given instant; for this reason, the researcher has to use available data from the beginning of observation to the present instant. Thus, the construction of a universal method for diagnostics of oscillatory patterns is an interesting but extremely complicated problem; for this reason, we will confine ourselves only to the description of the method for diagnostics of spike-wave discharges.

Since a SWD is characterized by an elevated energy corresponding to a certain range of scales, we consider the integrated value of instantaneous energy (4). If a spike-wave discharge takes place at instant t, the following relation holds:

$$w_{F_s}(t) \geq w_{\text{thr}}, \tag{5}$$

where w_{thr} is the threshold value of energy determined experimentally. This property is used in the method proposed here for automatic diagnostics of an epileptic event.

It should be noted that the application of the wavelet transform of type (1) for diagnostics of SWDs in real time involves certain difficulties. Convolution (1) presumes that a signal operating on an infinitely long time interval is available to the researcher. Obviously, it is impossible to obtain such a dynamic series, and the researcher usually deals with discrete values of signal amplitudes obtained from the beginning of measurements to the present instant. This problem can be solved if we take into account the fact that wavelet function (2) is always bounded in time; i.e., the main part of the power is concentrated in a certain interval $[\tau_s, \tau_e]$ and, hence expression (1) can be replaced by the following expression almost without loss of accuracy:

$$W_{s,\tau} = \int_{\tau-\tau_s}^{\tau+\tau_s} x(t)\psi^*(s,t)dt, \tag{6}$$

in other words, to calculate the transform energy corresponding to a certain scale at a certain instant, we must have a fragment of temporal implementation of duration $[\tau_s\tau_e]$. It is important to note that we can find out whether or not a SWD took place at instant t only at instant $t + \tau_e$; therefore, quantity τ_e is the basically irremovable delay in automatic diagnostics. The value of τ_e is determined by the type of the mother wavelet and by the time scale on which the transformation is performed. We can easily show that for a Morle mother wavelet, $\tau_e = 4s$, where s is the time scale under investigation.

For the problem considered here and for the time scale range $F_s \in (0.01, 0.03)$ [s] being analyzed, the value of τ_e was less than 150 ms, while the average duration of a SWD is 6 s; this allows us to speak of applicability of the proposed method in the real time diagnostics of SWDs.

Let us now consider important features of implementation of the given algorithm in the diagnostics of patterns. The instantaneous energy of wavelet transform (4) was calculated by numerical integration using the method of rectangles. We considered 15 time scales proportional to 15 frequencies distributed uniformly over the indicated range. Analysis shows that 15 scales in the case under investigation is a reasonable compromise between the accuracy of calculation of the wavelet spectrum and the computation speed (an increase in the number of scales would only reduce the error in calculation of $w(t)$) owing to a more accurate calculation of wavelet spectrum (6); however, computer time expenditures would then also increase.

It should be noted that EEG is a complex signal in which individual spikes in high-frequency activity (in particular, K complexes [44]) can appear against the background of the normal (i.e., nonepileptic) EEG dynamics due to functioning features of the neural ensemble of the cerebral cortex. Such events may sharply increase the instantaneous energy of the transform and cause false detection of the epileptic pattern. Such energy spikes are quite frequent events; for this reason, the above algorithm was modified to improve the accuracy of analysis. For example, for diagnostics of the type of oscillations, threshold value w_{thr} in formula (5) was compared not with instantaneous energy (4) of the transform, but with the value averaged over a certain time interval:

$$\langle w(t)\rangle = \frac{1}{T}\int_T w(t)dt. \tag{7}$$

The larger the size T of the window over which averaging is performed, the smaller the error of the diagnostic method; however, the time required for the detection of a SWD increases in the same proportion.

Thus, the algorithm worked out for automatic diagnostics of oscillatory activity of a certain type in an EEG signal can be described as follows: at each instant of discrete time determined by the sampling frequency of the data collection system, a wavelet transformation is performed for all scales from the indicated range; instantaneous (4) and averaged (7) value of the wavelet energy is calculated in the range of scales F_s, after which condition (5) is verified.

High reliability of the method is attained when threshold energy w_{thr} is selected individually from an EEG fragment with a 1-h duration for each object being analyzed. The value of this quantity is usually 2.5–3 times larger than the mean value of energy in the same frequency range without a SWD. The characteristic time dependences of the signal and of the wavelet energy are shown in Fig. 3.

The method proposed here formed the basis of real-time diagnostics of discharges, which is used together with the WinDAQ data collection system [45]; for this reason, the possibility of bidirectional data exchange with ADC/DAC was materialized. The element of calculation of the characteristic of wavelet transform (4) was implemented as a part of the program of ADC/DAC data exchange. When a SWD was detected, the diagnostic system sent a rectangular pulse to one of the DAC terminals (see Fig. 3c), which could be used for recording of the SWD as well as for controlling a certain external device (e.g., electronic oscillator acting on the cerebrum of a laboratory animal), thus producing a feedback required for a number of experiments for studying the action of current pulses on the evolution of hypersynchronous activity (epileptic seizure) in the neural ensemble of the cerebrum cortex.

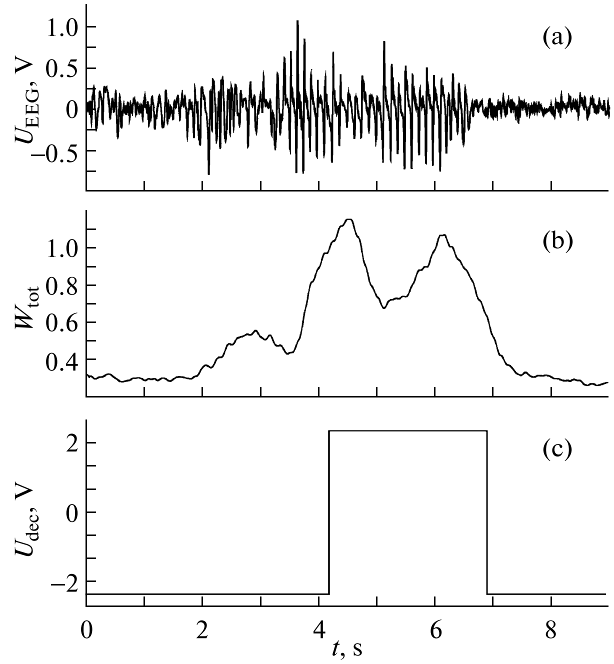

Fig. 3. Results of operation of the real-time SWD detection system: (a) typical SWD; (b) variation of averaged energy (7) of wavelet transform during a SWD; (c) rectangular pulse indicating the detection of an SWD. Threshold value w_{thr} was chosen as 0.85 for a given animal. In experiments, WinDAQ data collection system was used. Sampling frequency f_d = 500 Hz. EEG signal was additionally filtered prior to processing in the range 0.5–100.0 Hz.

2. VERIFICATION OF THE METHOD AND RESULTS OF REAL TIME DIAGNOSTICS

To verify the effectiveness of the system of real-time detection of oscillatory patterns worked out at the Institute for Brain, Cognition and Behavior, Nijmegen University (The Netherlands), special experiments were performed. In the first experiment, the system was tested on eight animals having absence epilepsy. Electroencephalograms were recorded with the help of electrodes implanted in the region of the frontal and occipital cerebral cortex. For each animal, optimal values of parameters of the method (threshold value of energy and duration of the averaging window) were selected from the results of preliminary 1-h recording. After the determination of optimal values of parameters, the experiment on real-time diagnostics of oscillatory patterns was performed; the duration of recording was 5 h. Each EEG recording was then processed by an experienced electrophysiologist; the results of processing were compared with the results of operation of the program for determining the number of correctly recognized SWDs, missed SWDs, and the number of false actuations.

Collected statistics on the quality of recognition of epileptic seizures on EEGs forms the basis for analysis of important statistical characteristics of "binary" decision making (presence or absence of epileptic seizure) using a certain criterion that can lead (with a certain probability) to a false result, such as confidence level β and power of test δ [46, 47]:

$$\delta = \frac{N_{TP}}{(N_{TP} + N_{FN})}, \quad \beta = \frac{N_{TP}}{(N_{TP} + N_{FP})}, \tag{8}$$

where N_{TP} is the number of true positive events and N_{FP} is the number of false positive events (i.e., the number of events which were identified by the program as a SWD, but were identified by the expert as a certain other type of activity), and N_{FN} is the number of false negative SWDs. The former characteristic (δ) makes it possible to estimate the sensitivity of the method (i.e., the fraction of recognized SWDs from the total number of SWDs on the EEG), while the second characteristic (β) is the fraction of events correctly identified as SWDs from the total number of events diagnosed as SWDs (in percent).

The results of experimental verification of the method are compiled in the table. The main results can be formulated as follows: the confidence level δ of the method was maximal (100%), the mean value of the power of test β = 96.9%, and the mean time required for recognition of a SWD was 1.00 ± 0.55 s from the beginning of the event.

The latter parameter is primarily determined by the size of the window over which averaging was performed and can be reduced or increased to a considerable extent because, for the sampling frequency used here (500 Hz), the time required for a transformation is considerably shorter than the time between collection of two successive counts. It should be noted, however, that for the problem formulated here, the reduction of the SWD diagnostics time is undesirable because, according to [41], one of the characteristic properties of an SWD is its duration; for this reason, events with a duration less than 1.5 s are not classified

Results of operation of the program for real-time detecting epileptic patterns

Animal number	Number of events determined by expert	Number of events recognized by program			δ, %	β, %
		N_{TP}	N_{FP}	N_{FN}		
1	101	101	3	0	100	97.1
2	29	29	0	0	100	100
3	43	43	2	0	100	95.6
4	66	66	1	0	100	98.5
5	44	44	2	0	100	95.7
6	66	66	4	0	100	94.3
7	115	115	3	0	100	97.5
8	56	58	2	0	100	96.6
Average value	65 ± 29	65 ± 29	2.1 ± 1.3	0.0 ± 0.0	100 ± 0	96.9 ± 1.8

by the expert as SWDs; accordingly, classification of such short oscillatory patterns as SWDs by the program will be treated as erroneous. This is one of the main sources of an N_{FP}-type error in the diagnostics, especially for a small size of the averaging window. On the other hand, a strong increase in the duration of the interval over which averaging is performed may considerably increase the time required for diagnostics of an epileptic seizure, and operation in the real time mode can hardly be performed in this case.

It was noted above that the proposed implementation of the method makes it possible to process a large body of data at a speed much higher than the speed with which new EEG counts arrive. This property of the proposed implementation can be used for simultaneous processing of several EEGs. Since neurophysiological experiments often take a long time, the latter property will make it possible to reduce the duration of such tests due to parallel operation on several objects. In view of technical limitations inherent in the WinDAQ data collection system, this possibility has not been put in practice so far; however, according to estimates, the implementation of the algorithm for recognition of SWDs in experiments would help to process the EEGs of 10–20 objects of investigation simultaneously without any loss in the performance efficiency and precision of the diagnostics.

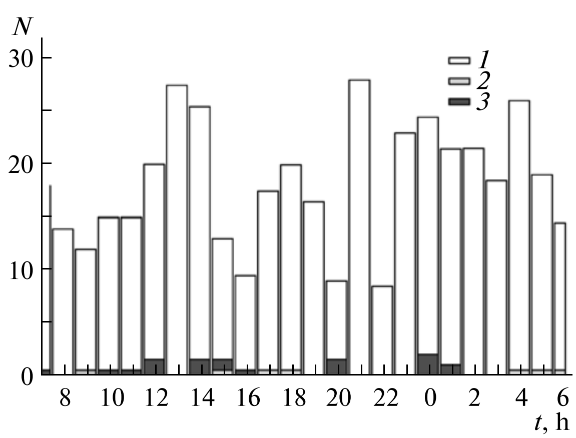

Fig. 4. Time distribution of the number of correctly recognized events (*1*), events erroneously identified as an SWD (*2*), and missed SDWs in the 24-h experiment (*3*).

To estimate the efficiency of the method under the conditions of a prolonged autonomous experiment, the experiment on EEG analysis lasting 24 h was performed. The experiment was carried out on two animals, and the method of preparation for experiment and estimates of the results are completely analogous to those described earlier. The experimental results are shown in Fig. 4. It can easily be seen that the number of erroneously detected and unrecognized events remains small during the entire experiment. The lower value of the power of the test as compared to the 5-h experiment can be due to peculiarities of brain dynamics: during 24 h, the distribution of energy over frequency ranges occupied by different oscillatory patterns experiences small variations leading to the periodic emergence of some structures on EEGs, which are erroneously recognized as SWDs. However, the precision of the method still remains quite high over this time interval.

CONCLUSIONS

In this study, we have proposed a method for diagnostics of oscillatory patterns in nonstationary dynamic series on the basis of the results obtained in [15, 39]. The method is based on the continuous wavelet transform of signals being analyzed in real time and on the calculation of instantaneous wavelet energies in the frequency ranges typical of oscillatory patterns being singled out.

The method was implemented and tested using the available system of collection and processing of EEGs for operative diagnostics and separation of the beginning and end of epileptic discharges in cerebral cortex of animals having absence epilepsy. The results have proved the high sensitivity and efficiency of the method, as well as a high rate of data processing; this renders this method applicable for diagnosing the epileptic activity in real time in several animals simultaneously. Experiments have shown that the approach developed here makes it possible to attain a confidence level of 100% and the power of the test at a level of 97%, which are very high indices for a laboratory system.

It should be noted in conclusion that this method can be used in various automated systems of data collection and monitoring of the state of a wide class of technical, biophysical, chemical, and other systems.

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