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Detection of proepileptic activity patterns in EEG of WAG/Rij rats

Vadim V. Grubov[a], Evgenia Yu. Sitnikova[b]

[a]Innopolis University, 1, Universitetskaya Str., Innopolis, 420500, Russia;
[b]Institute of Higher Nervous Activity and Neurophysiology RAS , 5A, Butlerova Str., Moscow, 117485, Russia;

ABSTRACT

In this paper we study specific oscillatory patterns of proepileptic activity on EEG signals of WAG/Rij rats. These patterns occur during the development of absence-epilepsy before fully-formed epileptic seizures. In the paper we analyze EEG signals of WAG/Rij rats with continuous wavelet transform to find particular features of proepileptic patterns in time-frequency domain. Then we develop new method for automated detection of proepileptic activity on EEG signals. We analyze results of method's performance and its efficiency.

Keywords: Electroencephalogram, absence epilepsy, oscillatory patterns, proepileptic activity, continuous wavelet analysis

1. INTRODUCTION

Modern studies of brain activity attract researchers from various fields of science due to interdisciplinary nature of problem. Considerable progress in spheres of experimental and data processing methods provides opportunities for vast and detailed studies of specific phenomena in brain neural network. Recent works in this field combine approaches of mathematics, physics and nonlinear dynamics with neurophysiological and biological view on the processes in brain neural structures. High interest of researchers to the problem is proved by increasing number of interdisciplinary publications.[1–6]

Source of studied brain activity – neural ensemble – is considered as complex oscillatory network with great number of elements and connections. Activity of individual elements – neurons – along with inter-element interactions result in complex dynamics. Studying of brain activity and its complex dynamics is an essential problem since some features of this activity (like time-frequency properties) can provide information about state of nervous system and whole living organizm.[7]

The most wide-spread method for investigation of brain activity is electroencephalogram (EEG).[8] EEG is commonly used to obtain information about electric activity in different parts of brain in its normal or pathological state. EEG methodics suggests placing special electrodes on scalp (or into brain directly) and recording EEG signals as sum of electric currents generated by group of neurons.[9] EEG signal being a product of complex neuronal network is characterized by complex time-frequency structure with number of specific frequency ranges, oscillatory patterns, noise components (artifacts), etc.[10]

EEG signal is commonly divided into several characteristic frequency ranges such as alpha, beta, gamma, etc.[11] It is well-known, that there is a strong correlation between EEG rhythmic activity in specific frequency range and functional state of organizm.[12] Thus, studying of characteristic oscillatory patterns[1] becomes relevant, especially in case of various central nervous system disorders, when appearance of certain forms of oscillatory activity corresponds to disorder seizures. Such specific patters can be treated as biological markers of the disorder and used for monitoring or even early treatment.

Epilepsy is one of the disorders, which treatment can benefit from research of certain biomarkers on EEG. Epilepsy is a common and dangerous disorder and thus attracts considerable attention. Among the more than 30 types of epilepsy, absence epilepsy is the most difficult to recognize.[13] It is a nonconvulsive form of the disease

Further author information: (Send correspondence to V.V. Grubov)
V.V. Grubov: E-mail: vvgrubov@gmail.com, Telephone: +7 8452 99 88 32

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characterized by spontaneous brief episodes of unconsciousness, of which the patient may be unaware. Lack of visible simptoms during absence epilepsy seizure makes it quite difficult to diagnose with conventional clinical methods. However, manifestation of absence epilepsy is accompanied by characteristic oscillatory EEG patterns – spike-wave discharges (SWD).[14]

SWDs are specific oscillatory patterns on EEG characterized by high amplitude, presence of two main components – spikes and waves – and main frequency of 7-10 Hz with common first harmonic (10-20 Hz) and less common higher harmonics. These oscillations appear in hypersynchronous state of brain network and involve nearly whole thalamocortical brain network. However, thalamocortical network can also produce nonepileptic activity such as sleep spindles – brief (0.5-1.5 s) oscillation with spindle-like form and main frequency of 10-16 Hz.[15] The studying of sleep spindles is also attract considerable interest due to their possible connection with SWDs and absence epilepsy. There is a hypothesis that thalamocortical neural network normally generates sleep spindles, bur also can produce seizure activity under certain epileptic conditions (i.e., SWDs).[14]

Absence epilepsy has reliable animal model – special line of WAG/Rij rats[16] with genetic predisposition to absence epilepsy and ability to demonstrate pronounced SWDs. In WAG/Rij rats epilepsy develops with age of animal. Younger rats demonstrate no absence seizures and thus there are no SWDs on their EEG recordings, in the age of 5-7 month animals can demonstarte first, mostly undeveloped SWDs, and after 9 month almost all WAG/Rij rats have pronounced SWDs. The hypothesis[14] states that sleep spindles can transform to SWDs in epileptic brain, thus, one may expect to observe some kind of transition activity between spindles and SWDs – so-called proepileptic patterns. Investigation of proepileptic activity can provide information about development of absence epilepsy, which can be used for early diagnostics and treatment.

In this work we studied EEG signals of WAG/Rij rats, recorded during development of absence epilepsy. We analyzed proepileptic activity and defined its characteristic time-frequency features. Then we proposed new method for automated detection of proepileptic patterns on EEG signals. We analyzed results of method's performance and its efficiency.

2. METHODS

The current study was performed in WAG/Rij rats with a genetic predisposition to the absence epilepsy[16] at Institute of Higher Nervous Activity and Neurophysiology RAS, Moscow, Russia in accordance with the Guide for the Care and Use of Laboratory Animals. Experimental protocols were approved by the animal ethics committee of this institution.

In current experiments, EEG was recorded in 26 WAG/Rij males (body weight 320-350 g) in age of 5 an 7 month. Each recording lasted for approximately a day (18-25 h).

EEG signals were recorded with epidural screw electrodes placed over the frontal cortex (AP + 2 mm and L 2.5 mm relatively to the bregma) and reference electrode located to the right and above the cerebellum. EEG signals were filtered with band-pass filter between 0.5-200 Hz, digitized with 400 samples/second/per channel and stored in a hard disk.

SWDs in this EEG data represented a sequence of high-voltage repetitive 7-10 Hz spikes and waves with minimal duration of 2 s.[17] Sleep spindles were recognized in EEG as oscillations with spindle-like waveform, main frequency in range of 10-16 Hz and duration >300 ms.[18] Proepileptic activity was registered as spindle-like patterns with occasional spikes, main frequency of 5-9 Hz with first harmonic of 10-20 Hz and duration >1500 ms. Onsets and offsets of patterns were marked on EEG recordings by expert-neurophysiologist.

For detailed time-frequency analysis of EEG signals continuous wavelet transform (CWT) was used.[1,19] The CWT is widely used method for timefrequency analysis of complex nonstationary signals with multiple rhythmic components.[20] During recent interdisciplinary studies this method recommended itself as a powerful instrument for analysis of experimental biological data and obtaining essential information about complex dynamics of physiological systems.[21]

The energy of CWT, $W(s,\tau)$, was obtained by convolution of EEG signal, $x(t)$ with wavelet basis function $\varphi_{s,\tau}$:

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

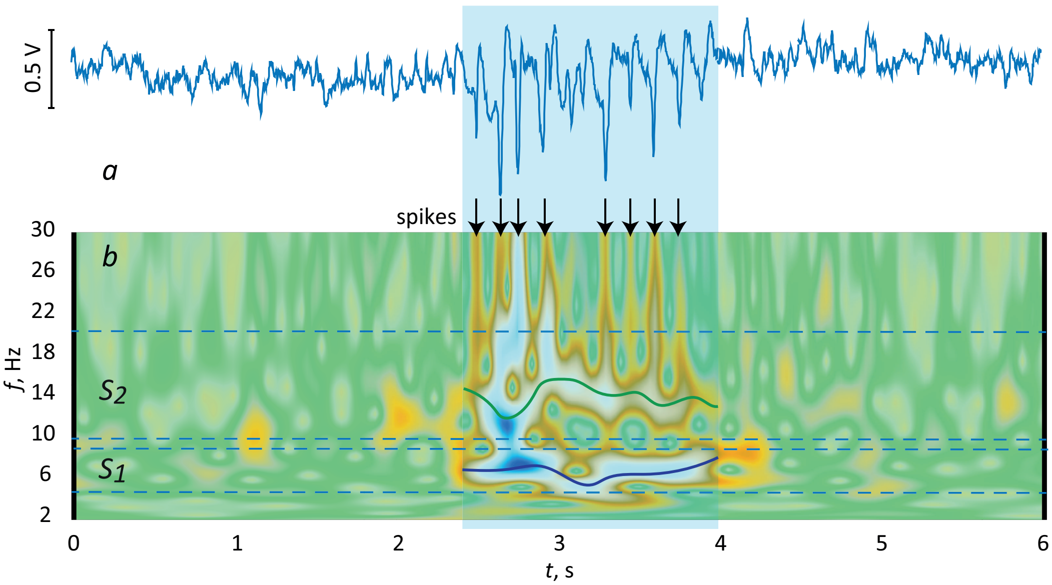

Figure 1. Example of time-frequency EEG analysis for proepileptic pattern: episode of EEG recording with proepileptic pattern (a), wavelet spectrum with marked skeletons (the first skeleton marked with blue solid line, the second – with green solid line) and bounds of frequency ranges S_1 (5-9 Hz) and S_2 (10-20 Hz) (marked with blue dotted lines) (b); transparent blue rectangle localizes proepileptic pattern, black arrows correspond to spikes on both oscillatory pattern and wavelet surface.

Each basis function $\varphi_{s,\tau}$ can be obtained from one function φ_0 called mother wavelet: $\varphi_{s,\tau}$:

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

Complex Morlet-wavelet with parameter $\omega_0 = 2\pi$ was used as mother wavelet:

$$\varphi_0(\eta) = \pi^{-\frac{1}{4}}e^{j\omega_0\eta}e^{-\frac{\eta^2}{2}} \tag{3}$$

Surface of CWT (wavelet spectrum) gives common information about time-frequency structure of the signal, such as length of some pronounced oscillatory patterns and their main frequencies. In order to study temporal dynamics of EEG spectral structure within each pattern we analyzed momentary distribution of wavelet energy and so-called skeletons – lines of local maxima on wavelet surface. Momentary distribution provides detailed information about frequencies in the signal at given time moment, while skeletons show dynamics of dominant frequencies throughout EEG signal.

3. RESULTS

In the first part of our work we analyzed EEG recordings of WAG/Rij rats in order to specify time-frequency features of proepileptic activity. We applied CWT to EEG recordings from frontal cortex of WAG/Rij rats and calculated corresponding wavelet energy distributions for short episodes of EEG with proepileptic patterns. Example of time-frequency analysis on EEG is illustrated on Fig. 1.

It is clear from Fig. 1, that proepileptic pattern is charaterized by number of specific time-frequency features:

1. main frequency of 5-9 Hz
2. presence of the first harmonic of main frequency (10-20 Hz)
3. average duration >1500 ms

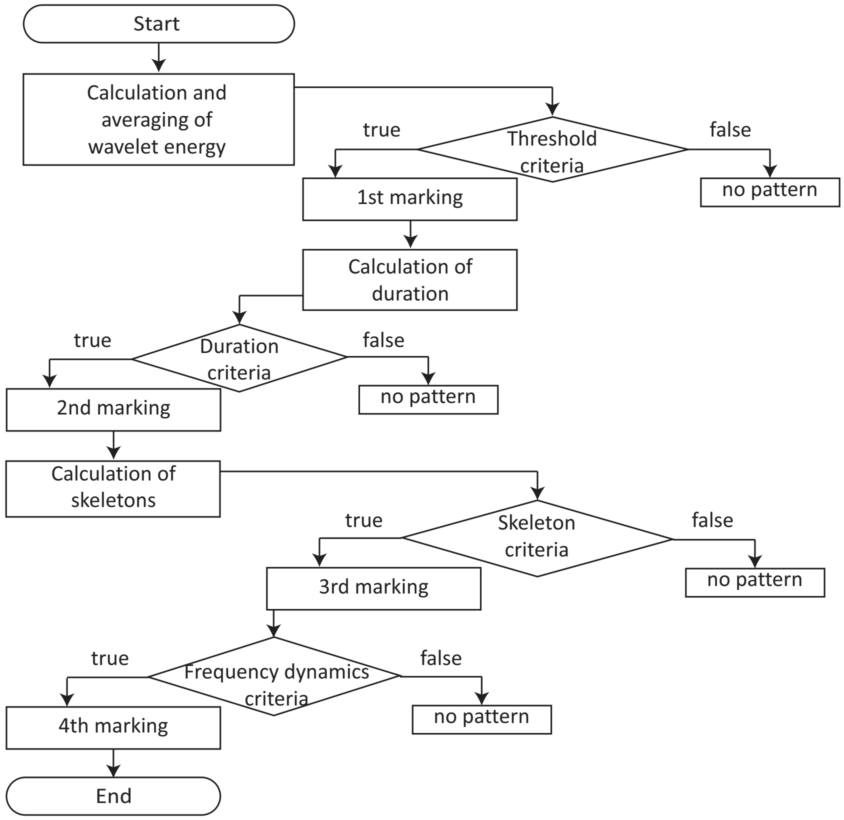

Figure 2. Block diagram of algorithm for automated detection of proepileptic activity on EEG signals.

4. presence of epileptic components – spikes
5. tendency to decrease main frequency from start to end of pattern

These found features were used in development of algorithm for automated detection of proepileptic activity on EEG signals. Algorithm is based on results of our previous work[22,23] and includes three basic steps with one optional step (see Fig. 2).

Step 1. Calculation of wavelet energy and its averaging over frequency range of 5-9 Hz. Searching EEG episodes, where averaged energy exceeds threshold value W_{cr}. Threshold value W_{cr} is chosen as 70% of maximum wavelet energy of EEG signal. During this step the first marking is constructed with patterns, that exceed W_{cr}.

Step 2. Removal of episodes with duration <1500 ms. During this step the second marking is constructed.

Step 3. Testing skeleton-based criteria. Two skeletons are constructed fro each episode from the second marking. If in some time point frequencies lie in ranges: 5-9 Hz for the first skeleton and 10-20 Hz for the second skeleton, then criteria is fullfiled in this point. If skeleton-based criteria is fullfiled in 70% of points of pattern, then this pattern goes to the third marking.

Step 4 (optional). Testing frequency dinamics of pattern. Criteria is fullfiled in some time point if frequency of the first skeleton in this point is higher, than in the next point. If criteria is fullfiled in 70% of points of pattern, then this pattern goes to the fourth marking.

Example of method's implementation is demonstrated on Fig. 3. Fig. 3b shows steps 1 and 2. One can see, averaged wavelet energy on Fig. 3b exceeds threshold value W_{cr} in certain area, which is marked with solid blue frame – according to algorithm this is the first marking. It is obvious from Fig. 3b, that duration of marked pattern is > 1.5 s, so it goes to the second marking. Fig. 3c illustrates steps 3 and 4 of algorithm. Fig. 3c

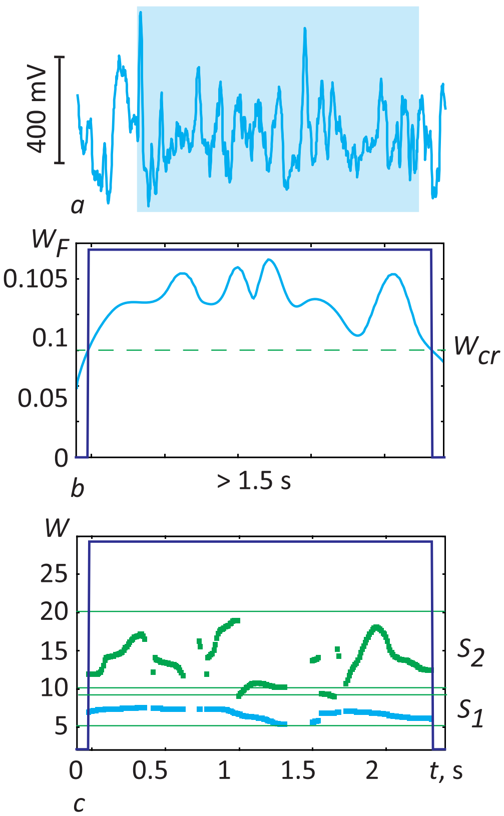

Figure 3. Example of method's implementation: episode of EEG recording with proepileptic pattern (marked with transparent blue rectangle) (a), distribution of wavelet energy averaged over frequency range of 5-9 Hz (marked with blue solid line); green dotted line corresponds to threshold value W_{cr} (b), the first and the second skeletons of wavelet surface (marked with blue and green dots correspondingly); green solid lines mark bounds of frequency ranges S_1 (5-9 Hz) and S_2 (10-20 Hz) (c); solid blue frames correspond to markings made on certain steps of algorithm.

shows two skeletons, constructed for pattern from the second marking. One can see, that the most part of the first skeleton falls to frequency range S_1 (5-9 Hz) and the most part of the second skeleton – to frequency range S_2 (10-20 Hz), so this pattern goes to the third marking. Finally, frequency of the first skeleton on Fig. 3c demonstrates clear tendency to decrease, which allows to include this pattern to the fourth marking.

4. CONCLUSION

In this paper we studied specific oscillatory patterns of proepileptic activity on EEG signals of WAG/Rij rats. We analyzed EEG signals of WAG/Rij rats with continuous wavelet transform to find particular features of proepileptic patterns in time-frequency domain. Then we developed new method for automated detection of proepileptic activity on EEG signals. We described the proposed algorithm of the method and analyzed results of method's performance and its efficiency.

Obtained results can be helpful for further fundamental studies on absence epilepsy. Knowledge on proepileptic activity can prove (or disprove) hypothesis about transformation of some sleep spindles into spike-wave discharges in epileptic brain. Also studies on proepileptic activity can be useful in clinical medicine for monitoring of progress of absence epilepsy or even for early treatment.

5. ACKNOWLEDGMENTS

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