ISSN 1062-8738, Bulletin of the Russian Academy of Sciences. Physics, 2015, Vol. 79, No. 12, pp. 1484–1487. © Allerton Press, Inc., 2015.
Original Russian Text © V.V. Grubov, E.Yu. Sitnikova, A.A. Koronovskii, A.E. Hramov, 2015, published in Izvestiya Rossiiskoi Akademii Nauk. Seriya Fizicheskaya, 2015, Vol. 79, No. 12, pp. 1695–1699.

Intermittency of Intermittencies in Characteristic Oscillatory Patterns on Epileptic Electroencephalograms

V. V. Grubov[a, b], E. Yu. Sitnikova[c], A. A. Koronovskii[a], and A. E. Hramov[a, b]

[a]Saratov State University, Saratov, 410012 Russia
[b]Saratov State Technical University, Saratov, 410054 Russia
[c]Institute of Higher Nervous Activity and Neurophysiology, Russian Academy of Sciences, Moscow, 117485 Russia
e-mail: vvgrubov@gmail.com

Abstract—The temporal dynamics of characteristic oscillatory patterns in an epileptic EEG are analyzed. A statistical analysis of time gaps between oscillatory events on EEG records is performed following the automatic segmentation of EEG signals. Both sleep spindles and spike-wave discharges exhibit intermittency dynamics, and the collective dynamics of these patterns is characterized by the intermittency of intermittencies.

DOI: 10.3103/S1062873815120187

INTRODUCTION

Interdisciplinary tasks are currently attracting much attention from researchers. Methods developed in radiophysics and nonlinear dynamics for the analysis of complex oscillatory systems can be applied in other areas of scientific research, e.g., biology, medicine, and neurophysiology [1]. These methods are particularly effective in analyzing the electrical activity of the brain. Such activity is a product of the synchronous functioning of highly organized neural networks composed of great numbers of neurons as individual oscillatory elements. Complex oscillatory systems have traditionally been the subject of radiophysics and nonlinear dynamics.

Neurophysiologists obtain information on brain functions mainly through experimental methods. The most promising of these are so-called noninvasive techniques, i.e., those that do not require electrodes or other registering equipment to be introduced directly into brain structures. Electroencephalography (EEG) is one of the most widely used noninvasive techniques; it is relatively easy to employ and at the same time ensures high levels of time–frequency resolution [2]. An EEG signal is produced by the averaged sum of currents generated by the group of neurons in vicinity of the registering electrode placed on the scalp. From the point of view of time–frequency analysis, EEG records complex empirical signals characterized by a set of frequency bands (alpha, beta, gamma, and so on). It is well known that the activity observed on an EEG (particularly the frequency ranges, i.e., oscillatory patterns) correlates with the functional state of an organism [3]. An important aspect in analyzing the electrical activity of the brain is investigating characteristic oscillatory patterns in EEG signals. This is especially important when dealing with various disorders of the nervous system, where certain characteristic oscillatory patterns act as hallmarks of different diseases.

Epilepsy is a rather common disorder that attracts considerable attention. Among the more than 30 types of epilepsy, absence epilepsy is the most difficult to recognize [4]. It is a nonconvulsive form of the disease characterized by spontaneous brief episodes of unconsciousness, of which the patient may be unaware. On the one hand, the properties of absence epilepsy make it difficult to diagnose using conventional clinical methods; on the other hand, absence seizures are accompanied by characteristic oscillatory EEG patterns (spike-wave discharges) [4].

Spike-wave discharges are specific oscillatory patterns characterized by high amplitudes and frequencies of 8–10 Hz. These oscillations are of a generalized character; i.e., a spike-wave discharge involves nearly the whole thalamocortical network of the brain in synchronous activity. However, thalamocortical neural networks can also generate such nonepileptic activity as sleep spindles, which are brief (0.5–1.5 s) episodes of oscillation characterized by frequencies of 10–16 Hz and spindle-like shapes [5]. The potential relationship between the pathological activity of neural ensembles (spike-wave discharges) and normal oscillatory patterns (sleep spindles) is a problem of considerable interest.

The aim of this work was to investigate the complex time–frequency dynamics of characteristic oscillatory patterns (spike-wave discharges and sleep spindles) in order to determine the potential relationship between these patterns. Our study was performed using 24-h EEG records obtained for six rats of the WAG/Rij strain. Rats of this strain have a hereditary predisposition toward absence epilepsy and rep-

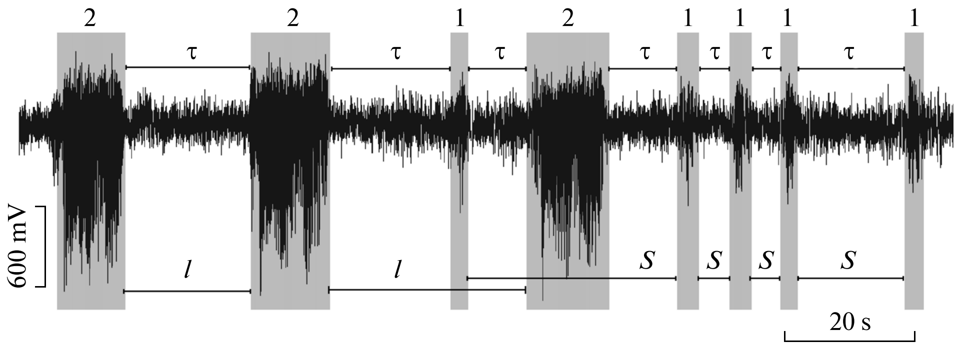

Fig. 1. Segmentation of an EEG record and identification of *s* and *l* time gaps between sequential events of sleep spindles (1) and spike-wave discharges (2), respectively, along with the τ periods used in the collective analysis of sleep spindles and spike-wave discharges.

resent one of the most common animal models of this disease.

EXPERIMENTAL

In this work, we analyzed EEG signals using continuous wavelet transforms [6]. A wavelet transform is a convolution of the $x(t)$ signal (in our case, the EEG signal) and a set of basis functions $\varphi_{s,\tau}$:

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

Each function of the $\varphi_{s,\tau}$ set can be obtained from single function φ_0 termed the mother wavelet:

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

where s is the time scale, τ is the time shift, and $\varphi_0(\eta)$ is the mother wavelet.

In signal analysis using wavelet transform, it is important to select the appropriate mother wavelet. In practice, a wide variety of different mother wavelets are employed in solving different problems. In this work, we used the so-called complex Morlet mother wavelet, since it has proven to be the best tool for the time–frequency analysis of EEG signals [7]:

$$\varphi_0(\eta) = \pi^{-1/4}e^{j\omega_0\eta}e^{-\eta^2/2}. \quad (3)$$

RESULTS AND DISCUSSION

Based on a continuous wavelet transform, we developed a method for the automatic identification of characteristic oscillatory patterns in epileptic EEG signals [8]. A continuous wavelet transform is performed for a given EEG time series, and the energy of the transform is calculated. The average energy is then determined for a particular range of frequencies (which differs for different types of oscillatory patterns), and the average energy is compared to a certain empirically determined threshold value. If the threshold is exceeded, the corresponding oscillatory pattern is identified in the EEG record.

The proposed method was used to perform the automatic segmentation of 24-h EEG records of WAG/Rij rats, and to identify sleep spindles and spike-wave discharges. Data obtained via automatic segmentation were used to analyze the temporal dynamics of sleep spindles and spike-wave discharges, and to investigate the principles behind the emergence of characteristic oscillatory patterns in EEG signals. An example of automatic EEG signal segmentation is presented in Fig. 1, which shows a short fragment of an EEG record with automatically recognized sleep spindles (*1*) and spike-wave discharges (*2*), along with the *s* and *l* time gaps separating sequential oscillatory events.

To investigate the temporal dynamics of characteristic oscillatory EEG patterns, data obtained via automatic segmentation were subjected to statistical analysis. Statistical analysis of the segmentation of characteristic oscillatory patterns can be useful when investigating the modes of neural network functioning that give rise to these oscillatory patterns. It is known that epileptic spike-wave discharges result from the hypersynchronization of thalamocortical neurons [4]; the normal activity of this neural network in the form of sleep spindles is presumably also associated with the establishing of certain synchronized modes. Thus, both of these EEG patterns can be considered short periods of synchronization separated by long periods of asynchronous activity, i.e., background EEG signals and various artifacts. In other words, they exhibit so-called intermittency [9]. Intermittency occurs in a great variety of nonlinear oscillatory systems, biological or otherwise, and involves the nonperiodic switching of the system between so-called laminar and turbulent phases. With EEG signals, the laminar phase corresponds to long periods of asynchronous background activity, while characteristic oscillatory patterns represent a turbulent phase of the synchronized activity of the thalamocortical network.

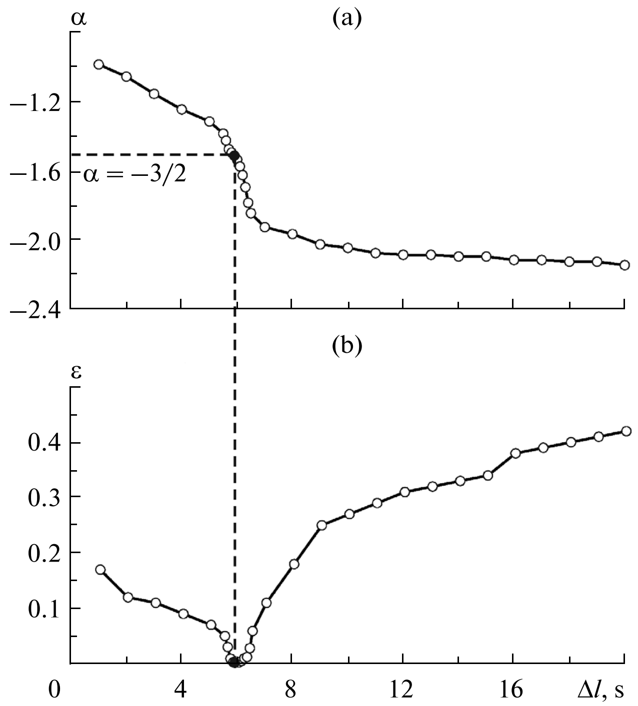

Fig. 2. (a) Dependence of exponent α and (b) the root-mean-square error ε on time step value Δl for sleep spindles registered in one of the test animals. The minimum ε value and the corresponding exponent α are indicated by black dots.

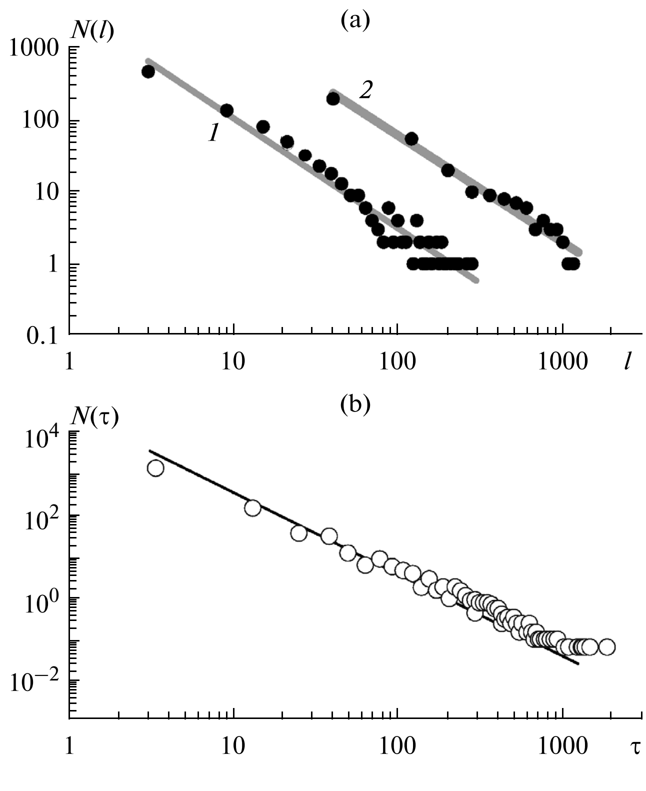

Fig. 3. Experimental and theoretical $N(l)$ distributions for one of the test animals. (a) Sleep spindles (*1*) and spike-wave discharges (*2*) analyzed separately; (b) both patterns analyzed collectively.

To analyze the frequency of characteristic oscillatory patterns in EEG signals, we performed a statistical analysis of laminar phase duration, i.e., of time gaps between sequential sleep spindles and spike-wave discharges in EEG (s and l, respectively), and obtained $N(s)$ and $N(l)$ distributions for these time intervals, respectively.

To identify the dynamic modes generated in the neural network of the brain, the observed $N(s)$ and $N(l)$ distributions were tested for agreement with the theoretically expected power law

$$N(l) = \beta l^{\alpha}. \quad (4)$$

In such analysis, a highly important parameter is the value of the α exponent of the power law, since different α values correspond to different dynamic modes in the system in question, and particularly to different types of intermittency. One such mode is on–off intermittency [10], for which $\alpha = -3/2$. Earlier studies reported that on–off intermittency characterized the behavior of spontaneous oscillatory patterns in human and rat EEG records [11], leading us to assume that the behavior of certain thalamocortical patterns (e.g., sleep spindles and spike-wave discharges) can also be described in terms of the on–off intermittency model.

In our analysis, experimentally obtained $N(s)$ and $N(l)$ distributions were calculated for different time step values, Δs and Δl, and compared to the expected power law $N(l) = \beta l^{\alpha}$; the ε value of the root-mean-square error was calculated to characterize the difference between them. The α value was determined individually for each type of oscillatory pattern studied and for each experimental animal by choosing the Δs and Δl values so as to minimize the root-mean-square error (ε) between the experimental distribution and the theoretical law. This procedure is illustrated in Fig. 2, which shows the dependences of exponent α (a) and the root-mean-square error ε (b) from time step Δl for sleep spindles in the EEG record of one test animal.

Our analysis showed that the optimum exponent in the power law describing the dynamics of sleep spindles and spike-wave discharges in all six experimental animals was $\alpha = -3/2$, which corresponds to the on–off intermittency mode. An example of experimentally obtained distributions $N(l)$ (shown with dots) for sleep spindles (*1*) and spike-wave discharges (*2*) and the corresponding power dependences with the optimized exponent $\alpha = -3/2$ (gray lines) for one of the animals is shown in Fig. 3a.

We found that sleep spindles and spike-wave discharges have similar temporal dynamics that can be described in terms of the on–off intermittency model. In addition, these patterns are produced via synchronization within the same thalamocortical neural network and coexist in the same time series of EEG signals. This led to the hypothesis that the collective dynamics of sleep spindles and spike-wave discharges in EEG signals can be characterized by more complex behavior modes, e.g., the intermittency of intermittencies.

The analysis of intermittency modes is usually restricted to a single type of intermittency occurring in the system; however, it was recently shown that different types of intermittency can actually coexist and alternate in the same system, creating a new level of organization in the temporal dynamics of complex nonlinear systems that is referred to as the intermittency of intermittencies [12].

The intermittency of intermittencies can be observed in systems where two different types of intermittency coexist and alternate. It was shown that systems where two on–off intermittencies coexist are characterized by a power law with $\alpha = -2$ and can be described using a so-called on–off/on–off intermittency of intermittencies model.

In this work, we analyzed the collective temporal dynamics of sleep spindles and spike-wave discharges using the same segmentation of EEG signals as in the first part of the study. In this setting, however, both of these automatically recognized patterns were analyzed collectively (Fig. 1, τ intervals).

As was done earlier, the experimentally obtained $N(\tau)$ distributions were calculated for different $\Delta\tau$ values and compared to the theoretical power law $N(\tau) = \beta\tau^{\alpha}$. Root-mean-square error ε was calculated for the difference between them. Figure 3b presents the experimentally obtained $N(\tau)$ distribution (shown with dots) and the corresponding power law (shown with the gray line) for our collective analysis of sleep spindles and spike-wave discharges in one of the test animals. The exponent's optimum value was $\alpha = -2$ (Fig. 3b). This result was reproduced with satisfactory accuracy for all of the other WAG/Rij rats that were studied, confirming there was an on–off/on–off intermittency of intermittencies mode in the collective temporal dynamics of sleep spindles and spike-wave discharges in the epileptic EEG records of WAG/Rij rats.

CONCLUSIONS

The results obtained in this work suggest that the mechanisms underlying the generation of sleep spindles and spike-wave discharges are deeply connected, since their temporal dynamics are interrelated. Further research in this area would provide information for understanding the processes underlying the development of absence seizures, and should also allow the analysis of sleep spindles in diagnosing absence epilepsy.

ACKNOWLEDGMENTS

This work was supported by the Russian Foundation for Basic Research, project nos. 15-02-00624 and 14-02-31235; and by the Foundation for the Support of Small Enterprises in Research and Development as part of the Research and Innovation Competition for Young Scientists, grant no. 0002038.

REFERENCES

1. Mosekilde, E., Maistrenko, Yu., and Postnov, D.E., *Chaotic Synchronization, Applications to Living Systems*, Singapore: World Sci., 2002.
2. Silva, F.H., Nunez, P.L., and Srinivasan, K., *Electric Fields of the Brain: the Neurophysics of EEG*, Oxford Univ. Press, 2006.
3. Niedermeyer, E. and Fernando, L.S., *Electroencephalography: Basic Principles, Clinical Applications, and Related Fields*, Lippincott Williams and Wilkins, 2004.
4. Kostopoulos, G., *Clin. Neurophysiol.*, 2000, vol. 111, p. 27.
5. Steriade, M. and Deschenes, M., *Brain Res. Rev.*, 1984, vol. 8, p. 1.
6. Daubechies, I., *Ten Lectures on Wavelets*, SIAM, 1992.
7. Sitnikova, E.Yu., Hramov, A.E., Grubov, V.V., and Koronovskii, A.A., *Brain Res.*, 2014, vol. 1543, p. 290.
8. Grubov, V.V., Sitnikova, E.Yu., Koronovskii, A.A., Pavlov, A.N., and Hramov, A.E., *Bull. Russ. Acad. Sci.: Phys.*, 2012, vol. 76, no. 12, p. 1361.
9. Berge, P., Pomeau, Y., and Vidal, C.L., *L'Ordre dans le chaos*, Paris: Hermann, 1988.
10. Platt, N., Spiegel, E.A., and Tresser, C., *Phys. Rev. Lett.*, 1993, vol. 70, no. 3, p. 279.
11. Perez, J.L., *Eur. J. Neurosci.*, 1999, vol. 11, p. 2571.
12. Hramov, A.E., Koronovskii, A.A., Moskalenko, O.I., Zhuravlev, M.O., and Ponomarenko, V.I., *Chaos*, 2013, vol. 23, p. 033129.

Translated by D. Timchenko