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PHYSIOLOGY

Regularities of Alternate Behavior in Spontaneous Nonconvulsive Seizure Activity in Rats

A. A. Koronovskii[a], G. D. Kuznetsova[b], I. S. Midzyanovskaya [a], E. Yu. Sitnikova[a],
Corresponding Member of the Russian Academy of Sciences D. I. Trubetskov[a], and A. E. Hramov[a]

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The study of the complicated behavior of ensembles of neuronal elements is of great interest. In this connection, the brain, which is a very complicated neuronal ensemble, is an interesting object for investigation. The brain research is of theoretical interest and has a great importance because the study of fundamental laws of brain function helps to find the reasons of origin and development of pathologies in the central nervous system [1].

Processes in the brain are often studied using approaches based on the construction of relatively simple models of single neurons [2], which are subsequently connected together [3]. The next stage in the development of the models in question is the consideration of chains, lattices, and networks consisting of elements that model single brain structures [4]. Evidently, the results obtained using such models should be compared with the results obtained in the experiments.

Another approach is the study of experimental time series and their analysis by methods of nonlinear dynamics [5, 6]. In particular, it is worth mentioning the report [7] in which the authors attempted to determine the direction of the links between different regions of the brain cortex to diagnose their functional interaction.

The purpose of this work was the diagnosis of the dynamic behavior in the case of spontaneous seizure activity of the nonconvulsive type. In our experiments, we used long-term recording of paroxysmal activity of rats genetically predisposed to absentia epilepsy (WAG/Rij rats). Seizure activity was expert assessed using the electrocorticogram (ECoG) recorded from intact freely moving animals with chronically implanted electrodes, as described in [8]. The duration of ECoG recordings varied from 6 h to 4 days. Male ($n = 5$) and female ($n = 6$) rats of the given strain were used in the experiments. Figure 1 represents a fragment of a typical time series (encephalogram). Convulsive peak-wave discharge typical of this type of epilepsy is the outburst of the generalized synchronous activity of brain regions, which is characterized by sudden onset and sudden termination [8]. A typical encephalogram recorded during our observations is an interlace of low amplitude polyrhythmic ECoG segments corresponding to the "normal" brain function (referred to hereinafter as laminar segments) and the segments of high amplitude activity with relatively stable carrier frequency (turbulent phases) corresponding to paroxysms.

We found that the interlace of seizure activity and normal functioning of the brain could be adequately described in terms of on–off alternation [9–11]. This conclusion was based on the analysis of the distributions of the duration of phases of normal brain function (the durations of laminar phases) obtained in the experiment.

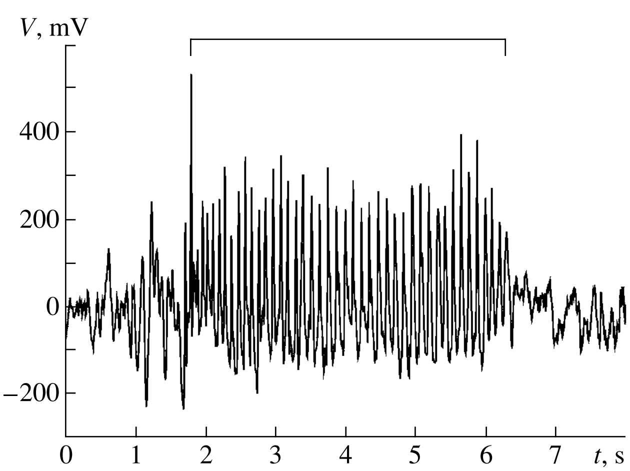

Fig. 1. A fragment of a typical time series (encephalogram) recorded from the frontal region of the rat brain cortex. The time interval corresponding to epileptic seizure is marked by a bracket.

[a] *Institute of Higher Nervous Activity and Neurophysiology, Russian Academy of Sciences, ul. Butlerova 5a, Moscow, Russia*
[b] *Chernyshevsky State University, ul. Astrakhanskaya 83, Saratov, 410012 Russia*

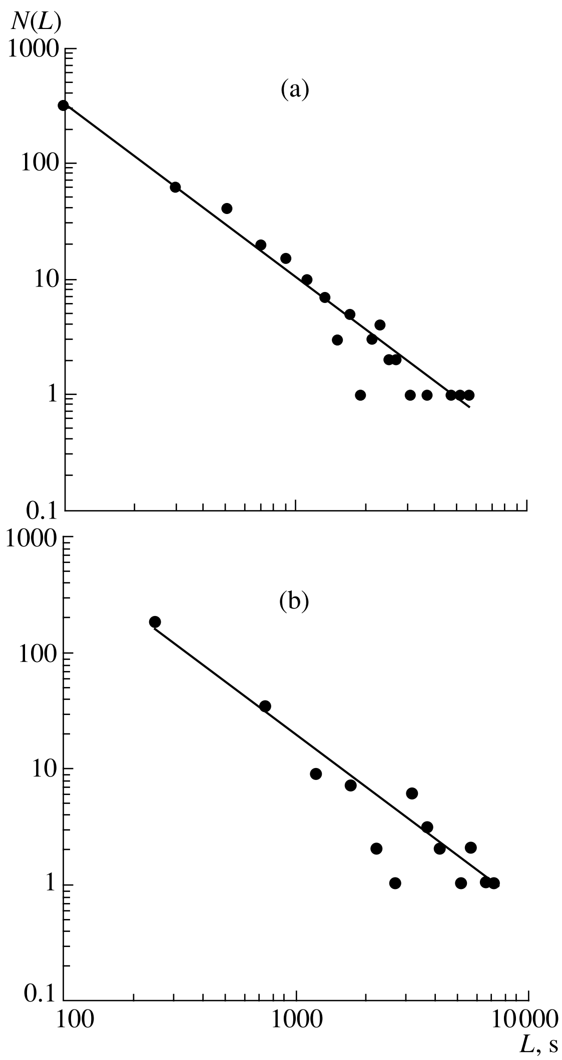

Fig. 2. Distributions $N(L)$ of the durations L of the laminar phases for one of the rats (a double logarithmic scale). Data obtained during the observations are shown by points. Straight lines approximate the distributions obtained experimentally and correspond to the power dependence (1) with a power index of $\alpha = -\frac{3}{2}$: (a) night; (b) day.

The scale of the duration of laminar phases (L) was divided into ranges with a width of ΔL. The number of laminar phases whose durations fall in the time interval $L \in (L_i \text{ in } L_i + \Delta L)$ $(i = 0, 1, 2, \ldots)$ was denoted as $N(L)$. Figure 2 represents the distributions $N(L)$ of laminar phase durations L for one of the rats on the basis of the statistics on 4 days of experiments. The distributions were plotted using a double logarithmic scale. Experimental data obtained on the laminar phase duration were plotted as points. Data analysis was performed for the light and dark phases of day separately, because the seizure activity of this type depends on the time of day (circadian periodicity is present in the frequency of seizures [12]). Figure 2a shows the data obtained at night, when seizure activity is enhanced and more statistical data may be obtained. Figure 2b shows a similar distribution plotted for seizure activity recorded during the day, when the frequency of epileptic seizures is significantly lower.

It is known that the distribution of the laminar phases for the on–off alternation is described by the power law

$$N(L) = \beta L^{\alpha}, \quad (1)$$

where α and β are parameters of the power distribution (the power index and normalization factor, respectively) with a power index $\alpha = -\frac{3}{2}$ (for more detail, see [9, 10]).

It can be seen fin Fig. 2 that the experimental distributions of the durations of laminar phases (points on the figure) on a double logarithmic scale are close to a straight line, which is typical of the power law of distribution with a power index $\alpha = -3/2$. The straight solid lines on Figs. 2a and 2b approximate the distributions obtained during the experiment and correspond to the power dependence (1) with a power index $\alpha = -3/2$. The corresponding parameters of approximation were numerically determined by the minimization of the standard deviation of the theoretical distribution (1) from the experimental data.

Note that alternate behavior was diagnosed for both light and dark day phases, which are very different in the frequency of seizure fits. The given animals are characterized by a larger number of seizures during the night than during the daytime. Accordingly, this results in a decrease in the mean duration (L) of laminar phases. This decrease in the mean duration of laminar phases does not change the type of distribution of laminar phase durations and does not violate the power law with a power index $\alpha = -\frac{3}{2}$.

Similar results were obtained for all analyzed observations of spontaneous seizure activity of the given type in freely moving intact rats (11 rats). Thus, it was concluded that the interlace of seizure and normal brain activities of WAG/Rij rats is an on–off alternation and can be described by the universal relationship typical of the given type of alternate behavior.

The data obtained may give rise to further investigation of different types of epileptogenesis. In particular, it is known that one of the mechanisms underlying the alternate behavior of the on–off type is the coexistence in the system of two different processes, one of which can be considered as some bifurcational parameter of the other (for more detail, see [9, 10]). A stable equilibrium (the laminar phase) is reached in the subsystem responsible for the second process when the first process is characterized by subthreshold values of the corresponding variables. When the first process exceeds a threshold (bifurcational) value, the stationary state loses its stability in the subsystem corresponding to the second process. This loss of stability triggers a fundamentally different type of response (the turbulent phase). This response is observed until the variables corresponding to the first process return to the subthreshold level, which again changes the response type and establishes the laminar phase. Thus, the possibility of seizure activity development in rats with genetic absentia epilepsy may be determined by the some second (relatively slow as compared with the typical duration of turbulent phases) process that regulates the appearance and disappearance of epileptic seizures. Taking into account that the frequency of paroxysms in rats is increased with increasing age [13], it is possible to suppose that the second process regulating the paroxysms is accelerated with time, and its characteristic time scale is decreased. We hope that this hypothetical regulating parameter may be discovered in special experiments. In turn, it allows more effective methods to hold this parameter in the usubthreshold range to be developed and the development of epileptic seizures to be prevented.

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