Nonlinear Relationships in the Patterns of Neuronal Spiking in Cortical Neurons *

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Abstract. The pattern of neuronal spiking of cortical neurons was investigated in an awake non-immobilized rabbit. The characteristics of the interspike intervals (total number of intervals, mean interval, mean-square deviation) and of the burst (group) activity (burst number, mean spike frequency in a burst, mean spike number for a burst, mean burst duration) were considered. Nonlinear relationship between the values of mean interspike intervals and the number of spike bursts was found. A number of functions were applied to describe the observed phenomena. On the basis of regression analysis two populations of cortical neurons with distinct neuronal spiking patterns were identified. Bursts occur at a higher rate in one population than the other, although both populations exhibit bursts and are otherwise indistinguishable.

Key words: Cortex, interspike intervals, neuron, neuronal spiking, spike bursts, spontaneous activity

1. Introduction

The modern interpretation of cognitive functions at the level of neuronal networks and the consideration of cellular mechanisms underlying higher neural function make us pay close attention to the patterns of neuronal activity of neurons, in particular of neurons of the cortex [14, 16].

Among cortical structures the motor cortex has special significance [2, 3]. The motor cortex is one of those brain structures with distinct plastic changes in neuronal activity. Neurons of the motor cortex are known to exhibit altered activity which reflects the integration of information. The organization of the motor cortex makes it possible to consider it as a self-regulated system with direct and feedforward connections creating neuronal circuits [2, 3].

At present it has been established that the relations between the frequency of neuronal discharges and functional features of neurons on the one hand and the kind of the distribution of interspike intervals on the other hand are not pronounced [2]. Mathematical analysis has shown that, on the basis of discharge frequencies it is difficult to form a true notion of interspike interval characteristics [8].

* The project was supported by the Russian Foundation of Fundamental Investigation, grant no. 00-04-48139

The pattern of spike firing in cortical neurons is a rather complicated phenomenon in which burst (group) activity can play an important part [15]. Actions of a system of neuronal circuits are undoubtedly reflected in the pattern of firing of neurons [2, 3].

In connection with the above, questions arise with respect to the relation between the values of interspike intervals and the likelihood of neurons generating bursts of discharges and with respect to the relations between different parameters of the bursts themselves. The present investigation addresses these questions.

2. Methods

The experiments were carried out in 8 awake nonimmobilized rabbits (males) of the New Zealand breed (weight 2.5–3 kg). Preliminary under anesthesia animals were scalped, and electrodes for stimulation of the pyramidal tract (PT) and electrodes for recording of EEG and firing of neuronal populations of the cortex were implanted as previously described [4, 6]. Mathematical analysis of spike firing of neuronal populations and relationship between EEG characteristics and the behaviour of neuronal populations will be considered in other work.

In the motor cortex spike activity of single neurons was picked up by glass micropipettes with a tip of 2–5 μm and with a resistance of 1–3 $\text{M}\Omega$. The micropipettes were filled with a 2.7 M solution of sodium chloride. These microelectrodes were leaded into the cortex before an experiment through a trepanized hole [3].

The localization of the neurons in particular layers of the cortex was judged on the basis of the depth of advancement of the microelectrodes in accordance with published data [1]. The occurrence of the neurons with axons in PT was evaluated on the basis of their activity during stimulation of the PT. The small and stable latency of the reaction, the capacity of the neurons to respond to stimuli delivered at a frequency not less than 110 Hz, as well as the presence of competitive relationships between the baseline and test action potentials, served as the criteria of the antidromic response [3].

The spike activity of single neurons was recorded on a magnetic tape and then was subjected to computer analysis. Each neuron was recorded for 1 minute. The characteristics of the interspike intervals and the activity events in the form of bursts or groups of spikes were evaluated. Data taken on the interspike intervals were total number of intervals, mean intervals and mean-square deviation. As for the burst activity, the indices were burst number, mean spike frequency in a burst, mean spike number for a burst, and mean burst duration. To analyse the burst activity, threshold levels 5, 10 and 20 ms, were used. In the first case, associations of spikes were considered to be part of burst provided intervals between the spikes were less than 5 ms, in the second case, if they were less than 10 ms, and in the third case, if they were less than 20 ms.

Table I. The characteristics of burst (group) activity

(a)	(b)	(c)	(d)	(e)
5	329.27 ± 22.08	401.25 ± 9.27	2.51 ± 0.04	3.66 ± 0.10
10	338.40 ± 22.68	303.55 ± 9.98	2.85 ± 0.09	5.68 ± 0.35
20	273.59 ± 16.79	150.77 ± 7.56	4.90 ± 0.22	20.01 ± 1.66

(a) Threshold of spike bursts (group) identification (ms);

(b) burst (group) number per min;

(c) mean spike frequency in a burst (Hz);

(d) mean spike number in a burst;

(e) mean burst duration (ms).

Comparison of parameters of the spike bursts identified by the three thresholds was carried out using Student's t-test and Fisher's test. The curves of the dependence of the number of different spike bursts upon the values of mean spike intervals were compared by White's and Van der Varden's tests [18].

The uniform approach to the analysis of spike firing in all recorded neurons was essential to consider different associations of spikes and to summarize results obtained in different units. Factor analysis [18] permitted summation of experimental material obtained from different animals.

3. Results

PARAMETERS OF PATTERN OF NEURONAL SPIKING

The overall results from 47 recorded neurons showed the following.

The mean interspike interval in neuronal activity was 56.65 ± 10.88 ms (range 13.4–462.2 ms). The spike firing patterns were complex. Neuronal discharges were not rhythmical. Groupings of neuronal spiking occurred. These groupings differed as revealed by sorting on the three time intervals used to discriminate bursts. The characteristics of burst activity are presented in Table I.

The bursts of spikes at 5 ms interspike intervals or less possessed the highest spike frequency, the least number of spikes, and the least duration. The spike bursts revealed by the 20 ms cutoff had opposite characteristics. The bursts at 10 ms or less interspike intervals had intermediate features.

The spike bursts identified by the 5 ms threshold may be considered as components of ones identified by the 10 and 20 ms thresholds. The spike bursts identified by the 20 ms threshold included ones by lower thresholds. The compound composition of bursts revealed by higher thresholds, particularly at 20 ms, affected the pattern structure of the bursts themselves. This problem will be analysed in other work.

As for the trend of the present investigations, dependences of mean spike frequency in a burst, mean spike number in a burst, and mean burst duration upon burst number themselves per min were rather indistinct though linear correlations

Figure 1. Dependence of the number of spike bursts identified by the 5 ms threshold on the values of mean interspike intervals. The ordinate is the number of spike bursts, the abscissa is the values of mean interspike intervals in ms. The data are presented as the geometrical locus on the basis of 47 events.

took place in some cases if the 20 ms threshold was used. Moreover, the burst activity was observed both in neurons sending axons to the PT as well as in those not sending axons to the PT approximately to a similar extent in upper and lower layers of the cortex.

RELATIONSHIPS BETWEEN INDICES OF MEAN INTERSPIKE INTERVALS AND BURST ACTIVITY IN FIRING OF NEURONS

The summarized data on the dependence of the number of spike bursts upon the values of mean spike intervals are presented in Figures 1, 2 and 3. These Figures demonstrate results on the burst activity for the three thresholds used for spike bursts identification. Figure 1 corresponds to data by the 5 ms threshold, Figure 2 shows them by the 10 ms threshold, and Figure 3 gives them by the 20 ms threshold. The native geometrical locus is more suitable than constructed curves for revealing the essentials of these events.

Figure 2. Dependence of the number of spike bursts identified by the 10 ms threshold on the values of mean interspike intervals. Designations as in Figure 1.

A similarity exists across Figures 1, 2 and 3. The distinct nonlinear dependence of the number of spike bursts on the values of mean spike intervals in neuronal spiking can be seen from these Figures. The effect was found in experimental data by all the 3 thresholds of spike burst identification. A number of different elementary functions were applied to describe the revealed dependences by means of a computer construction of theoretical curves. On the basis of the sum of difference squares it was established that the exponential function ($y = Ae^{Bx}$) and in particular the geometrical function ($y = Ax^B$) were appropriate.

It can be seen from the Figures that the registered population of neurons is heterogeneous. At any rate two of sub-populations of neurons exist. In that case according to special features of the geometrical locus the total aggregate of 47 events can be divided into two parts including approximately 29 and 15 events. In the Figures the larger of them locates under the smaller one. Moreover, 3 events did not belong to these parts and maybe are components of some another aggregate.

It is very interesting that the kind of the dependence of the number of spike bursts on the values of mean spike intervals was similar in all aggregates. The divi-

Figure 3. Dependence of the number of spike bursts identified by the 20 ms threshold on the values of mean interspike intervals. Designations as in Figure 1.

sion of the total aggregate into constituent parts emphasized some advantage of the geometrical function for the description of the analysed dependence particularly in the aggregate of 29 events.

The total aggregate of 47 events and its constituent parts of 29 and 15 events had no statistically significant differences in the values of mean spike intervals ($t = 1.04$, $p > 0.05$). Perhaps, these aggregates were distinguished more by the level of the connection between burst activity and mean spike intervals than characteristics of the latter.

It should be noted that the division of the total aggregate was carried out conditionally according to the peculiarity of the geometrical locus. The features of the drawing are considered as principal indicator of kinds of dependences, characteristics of distributions and so on. Statistical analysis plays a subsidiary part [18]. Nevertheless, the aggregates carried out by the division of the total geometrical locus had statistically significant distinctions according to a number of non-parametric criteria (in particular, White's test: $w = 1.18-1.50$, $p < 0.05 - 0.01$).

4. Discussion

The results of these investigations throw light on some features of the structure of spike firing of cortical neurons.

On the whole in an intact rabbit values of mean interspike intervals as well as other parameters of neuronal firing show little differences between the upper and lower cortical layers though the role of neurons of these layers is dissimilar in trace phenomena and learning [2, 3]. In particular, neurons of upper layers develop the most considerable rearrangements of activity under conditioning, and neurons of lower layers are more sensitive to repetition of stimuli.

The pattern of neuronal firing is, to a considerable extent, conditioned by the occurrence of spike bursts [4, 6]. In the cortex the similarity of spike bursts in background activity and in evoked responses has been described [15]. The origin of burst activity is likely related to both intrinsic events in the recorded neurons and to the actions of feedback connections in the cortical circuits. This kind of neuronal activity is supposed to connect with the encoding of information and to play an important part in detection of signal parameters [15, 17, 19].

The application of the 5 ms threshold of the spike burst identification made it possible to find that in all 47 records of neuronal activity, bursts consisting of 2–3 spikes exist. The increase of the threshold of spike burst identification to 20 ms showed that these small bursts can be consolidated into bigger bursts of 4–6 spikes.

The modular construction of the cortex is considered in another works [2, 3, 7, 10, 13]. The unit modules are the result of the morphological-functional organization of the cortex under the influence of afferentation. There are external (with respect to the cortex) and internal modulations of cortical unit circuits [9]. For the action of these circuits the decisive feature is functioning of cortical GABA-ergic interneurons which possess different characteristics in upper and lower layers of the cortex [2, 3, 11, 20].

The complexity of the modulation of neuronal activity contributes to the creation of the pattern of firing of neurons and leads to nonlinear relationships between parameters of neuronal spiking. The existence of adaptation and control in biological objects causes nonlinearity in the behaviour of numerous systems and processes [12]. In particular, nonlinear events in neuronal populations of the cortex were discovered following pharmacological manipulations [5].

The division of neurons into two populations according to special features of neuronal spiking did not relate to the value of mean interspike interval or to their localization in either layer of the cortex. But the latter can be seen in other animals and perhaps in rabbit under another experimental circumstances [2]. The observed 2 populations of neurons were distinguished primarily by features of the relationship between the number of spike bursts and the values of interspike intervals. In both cases the dependences of the number of spike bursts on the values of mean interspike intervals were described best by geometrical functions which only differed a little in coefficient values.

This effect can be the result of the fact that each circuit includes different neurons possessing activity with different values of mean interspike intervals. But these circuits have some specific features of construction, which influence the duration of the processes of excitation and of inhibition. Most likely in the present investigations we are dealing with the manifestation of some action of individual kinds of cortical circuits. However, it is necessary to consider the origin of the discovered phenomenon in more detail, which is the purpose of our next study.

5. Conclusion

The pattern of neuronal firing of cortical neurons was investigated in an awake nonimmobilized rabbit. Characteristics of mean interspike intervals and activity events in the form of bursts or groups were analysed.

It was established that a nonlinear relationship exists between the values of the mean interspike intervals and the number of spike bursts. On the basis of special features of dependences of the number of spike bursts on the values of the mean interspike intervals it was concluded that two distinct neuronal populations occur in the cortex even when overall firing patterns are similar.

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