NEW VIEW ON CEREBELLAR CORTICAL BACKGROUND ACTIVITY IN RAT:
SIMULATION

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SUMMARY

The aim of this study was to reveal the nature and meaning of interspike background activity (RBA) recorded in Purkinje cell layer of rat cerebellum. We compared Fourier amplitude spectra of recorded, extracted and averaged simple spike(s) - SS and complex spike(s) - CS with the mean amplitude spectrum of the remaining interspike RBA. A much greater similarity of spectral characteristics was noticed between SS and RBA, than between CS and RBA. Then, we simulated background activity (SBA), by superimposing averaged SS with randomized amplitudes and time delays. There was a significant correlation (p<0.005) between linearly transformed simulated and recorded amplitude spectra. Mean amplitude spectra of SBA were positively correlated with the number of superimposed SS. We propose to use this fact as a qualitative indication about the direction of change in the mean activity of surrounding neuronal population.

KEYWORDS background activity; Purkinje cell; Fourier amplitude spectrum; simulation

INTRODUCTION

There are unanswered questions about Purkinje neuron physiology. The effect of temporal spike patterns of parallel fiber activity on Purkinje neuronal simple spikes has recently (2) modified the previous findings (6, 7). There are new data on occurrence of Purkinje complex spikes as well as spiking of other cerebellar cortical neurons, which suggest their role as gain controllers (13). Moreover, interspike cerebellar background activity, during extracellular recording of Purkinje (or
other cerebellar cortical) neurons, was described recently in different experimental conditions (12). Our preliminary results (9) implied high contribution of simple spikes of Purkinje cells to the background activity and its modeling.

The aims of the present study were to explore the nature of interspike background activity in greater detail, by comparing Fourier amplitude spectra of RBA, simple and complex spikes. Further, to simulate RBA by superimposing an appropriate number of averaged simple spikes at which simulated (SBA) signals start to resemble the original recorded background activity (RBA). Finally, to explore how spectra of RBA could be related to the mean firing frequency of the surrounding neurons, in order to model the changes in the neuronal population of cerebellar cortex.

MATERIALS AND METHODS

Operative procedure

The acute experiments were performed on 4 adult Wistar male rats with all precautions for animals not to suffer. More details, particularly, on the anesthesia, electrical stimulation of inferior olive (IO) or locus coeruleus (LC) procedure was described elsewhere (3, 4). The activity of individual neurons of the right cerebellar vermis was recorded extracellularly with glass microelectrodes filled with 0.9% NaCl (resistance ~ 5 MΩ). Purkinje cells were electrophysiologically identified by the presence of complex and simple spikes in the cerebellar neuronal activity (5). After classic amplification and filtering the unitary signal was further processed.

Signal acquisition and template construction

The 12 neuronal recordings, 120 s duration each, were acquired using A/D conversion with a sampling rate of 30 kHz. Software for spike detection and extraction was previously described (8). The A/D converted RBA file - the segments between SS or CS spikes of the Purkinje cell, were transferred and concatenated to a new file up to 115 seconds.

Also, all simple and complex spikes that occurred in each of the Purkinje cell recordings were detected, extracted and separately averaged so that a simple (SST) and a complex (CST) spike templates were formed. Prior to the averaging procedure, the spikes had been aligned in such a way that previously selected waveform extremum (the first maximum or minimum) from all individual spikes were positioned one over another.

RBA simulation

After SST formation, sampling frequency was reduced to 6 kHz both for SBA formation and RBA processing, Fourier epochs FFT analysis were 600 samples (0.1 sec) long, setting the frequency resolution to 10 Hz.

For each RBA, the corresponding SBA was formed by superimposing SST waveforms. These SST waveforms had both random intensities and positions within the SBA signal. We used the uniform probability distribution for the two random variables: spike intensity and spike position.

A series of background activity simulations was generated in order to investigate their spectral characteristics. In this SBA series, their mean amplitude spectra, $\text{Amp}_{\text{SBA}}(f)$, were calculated (frequency range 10 - 3000 Hz). Twelve SBA were formed by superimposing SST waveforms.
obtained from each of the 12 cell recordings. Since RBA and SBA were derived from the same initial signal, for each recording, in case of SST and CST waveform presentation, as well as RBA and SBA spectra comparison before/after stimulation, Fourier amplitudes were presented in arbitrary units.

Fourier amplitude spectra of the simulated (SBA) and recorded (RBA) background activities were compared and significance of their linear dependence tested using Student’s t-test.

RESULTS

Typical simple and complex spike templates of a particular Purkinje neuron, as well as their amplitude spectra, are shown on Fig. 1. This neuron was recorded in controlled anesthesia with a mean discharge rate of about 30 simple spikes/s and 0.14 complex spikes/s.

![Simple and complex spike templates and their corresponding Fourier amplitude spectra.](image)

Fig. 1 Example of a simple and a complex Purkinje spike template and their corresponding Fourier amplitude spectra.

Spectrum of SST had one peak, positioned around 500 Hz, while CST spectrum was characterized by three peaks (around 200; 800 and 1500 Hz). Very similar spectral template characteristics were obtained for the other 11 recordings of 6 cortical neurons (before or after brain stimulation).

In time domain, the more superimposed simple spike templates, the better resemblance of SBA to RBA. A portion of the SBA signal series and original RBA, where number of superimposed simple spike templates \( f_{sup} \) was varied is presented on Fig. 2.
Fig. 2  Simulated background activity signals (SBA), where simple spike superposition frequency ($f_{sup}$) was varied (2 upper panels). Resemblance of SBA with the corresponding recorded background activity (RBA - lowest panel) was achieved for $f_{sup} > 4 \times 10^3$ spikes/s.

An example of two RBA spectra, before and after the LC stimulation, is presented in Fig. 3., upper panel. This change was accompanied by a corresponding change, in the same direction, of the firing frequency of the neuron nearest to the electrode. Analogous accordance of change directions (simultaneous increase or decrease) was detected in five of the six recorded cells. The manner in which the change of $\overline{\text{Amp}}_{\text{RBA}}$ could be simulated by two SBA signals, formed by superimposing different number of template spikes, is shown on the lower panel of Fig. 3. Direction of changes of $\overline{\text{Amp}}_{\text{RBA}}$ and $\overline{\text{Amp}}_{\text{SBA}}$ corresponded to the direction of change of $f_{sup}$ in SBA.

A much greater similarity of profiles could be observed between the amplitude spectrum of simple spike template (Fig.1) and the RBA mean spectrum (Fig. 3), than between the complex spike spectrum and the RBA mean spectrum. Fourier amplitudes of the SST spectra are vanishing for low and high frequencies, while in case of the RBA mean spectrum, these limits were not zero indicating that a wide band noise was present. As well, scaling of the two spectra was different. An approximative linear dependence could describe this relationship: $\overline{\text{Amp}}_{\text{RBA}} (f) = Sc \times \overline{\text{Amp}}_{\text{SBA}} (f) + W_n$, where $Sc$ stands for the scaling factor, $W_n$ for the wide band noise level. T-test values for 12 RBA/SBA spectra pairs showed that a statistically significant (at the level of 0.995) linear correlation existed between the mean RBA and their corresponding mean SBA Fourier amplitudes.
Fig. 3  The mean amplitude spectra of the recorded (RBA) and simulated (SBA) background activity. On the upper panel RBA1 spectrum before LC stimulation and RBA2 spectrum after stimulation are presented. It should be mentioned that the recorded target cell decreased its discharge frequency from 49.96 (before LC stimulation) to 24.2 spikes/s (after LC stimulation). On the lower panel two SBA signals are presented: SBA1 was formed by superimposing $f_{sup} = 10000$ spikes/s, SBA2 with $f_{sup} = 5000$ spikes/s. Thus the inhibitory effect was qualitatively simulated.

Fig. 4  Dependence of the mean amplitude spectra of simulated background activity (SBA) on the number of simple spike templates superimposed, i.e. superposition frequency ($f_{sup} > 4 \times 10^4$).

Mean value of the SBA Fourier amplitudes, presented on Fig. 4, reflected the activity level of the simulation neurons, forming the SBA, since the empirically obtained dependence of $\overline{\text{Amp}_{SBA}}$ on $f_{sup}$ shown for $f_{sup} \geq 5 \times 10^3$ spikes/s, pointed to an ascending function.
DISCUSSION

The first result obtained in this work was the elucidation of RBA origin. The 500 Hz peak in the RBA spectra may have originated from simple spikes of Purkinje neurons surrounding the recording site. However, it is possible that simple spikes of neuronal cell types, other than Purkinje, are as well contributing to the RBA. It was recently shown that RBA was related to the types of Purkinje cell action potentials: spectral changes of rat cerebellar background activity (12), during relatively short periods of time (several tens of milliseconds) could foresee the expression of a complex spike. In this work we tried to explore whether a link could be established between mean RBA amplitude spectra and average firing activity of the surrounding neurons on a longer time scale (~ 100 s).

Therefore, our second result referred to establishing a dependence between the mean RBA spectra and the average neuronal population activity. By superimposing averaged simple spikes, with random time delays and random amplitudes, we tried to simulate the actual situation around the recording site. According to our first result, RBA consisted mainly of spikes, of different intensities, generated by the surrounding cerebellar neurons. We had to establish a link between $\overline{\text{Amp}_{\text{RBA}}}$ and $f_{\text{imp}}$ (Fig. 4) in order to examine whether some of this function's properties could be used as a tool for assessing average neuronal population activity. The result allowed a qualitative detection of the direction of neuronal population average activity changes. This was achieved simply by measuring the corresponding change of $\overline{\text{Amp}_{\text{RBA}}}$, such as before and after an experimental intervention. Quantitative aspects of this approach, such as assessing percentage of changes in the population activity, based on recorded changes in $\overline{\text{Amp}_{\text{RBA}}}$, would require a more precise modeling of the probability density function of spike intensities forming the RBA (work in preparation). Uniform distribution could therefore be regarded as a first approximation in search for a quantitative method.

Through our approach, using only one site recording, it may become possible not only to evaluate the discharge rate of one target Purkinje cell, but detect changes of the average neuronal population discharge activity. The problem of specific discharge patterns in time domain can not be achieved by our approach as it is possible by at least two or multichannel recordings and correlation functions analysis in the cerebellum (10, 11, 13), or in other brain structures (1).

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REFERENCES


