Impulse Coding of Electrical and Synaptic Input Actions by Nucl. Abducens Motoneurons with Active Dendrites: A Simulation Study

S. M. Korogod,1 I. B. Kulagina,1 and V. I. Kukoushka2

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The study was carried out on models of nucl. abducens motoneurons with dendritic arborizations reconstructed with a high spatial resolution. The arborizations had membranes with nonlinear electrical properties due to the presence of glutamatergic NMDA-type synaptic conductivity with voltage-dependent kinetics of ligand activation. We studied rules governing the transformation of electrical influences on the soma and of tonic excitatory synaptic actions on dendritic arborizations into output discharges of action potentials (APs), i.e., the processes of formation of “intrinsic” neuronal codes. The electrical action was a depolarizing current applied to the soma, and the synaptic action was a tonic synaptic excitation homogeneously distributed over the dendrites; this excitation was simulated by introducing a synaptic conductivity, which was homogeneous over the dendritic membrane surface and constant in time. We recorded impulse patterns generated at different intensities of the applied current or synaptic excitation. The only pattern generated in response to the current application was a continuous rhythmic discharge of APs with equal interspike intervals (ISIs); increases in the mean frequency of AP firing with increasing current intensity obeyed the logarithmic law. An increase in the synaptic activation intensity also led to an increase in the mean firing frequency, but in this case the “intensity-to-frequency” conversion obeyed the polynomial law. A feature of the patterns generated under these conditions was the existence of essential dissimilarities in the type and complexity observed at three ranges of the synaptic intensity, low, medium, and high. The medium range corresponded to complex multiburst output patterns, both periodical and non-periodical. At intensities corresponding to the low and high ranges, continuous AP discharges were generated with constant (or slightly varying) ISIs similar to those observed upon application of the depolarizing current. In the complex patterns, the interburst intervals demonstrated the greatest variability. Their duration was mainly determined by processes in the dendrites, whereas the variability of the intraburst ISIs was mostly due to fast processes in the trigger zone and was an order of magnitude smaller. Electrical states of the dendritic arborization were essentially heterogeneous during generation of AP bursts in the multiburst patterns, less heterogeneous during generation of simple patterns, and practically homogeneous within interburst time intervals.

Keywords: nucl. abducens, motoneurons, tonic synaptic activation, dendritic arborization, output impulse electrical activity, heterogeneity of the electrical states.

INTRODUCTION

Elucidation of the laws governing the conversion of input electrical and synaptic actions into neuronal codes, i.e., discharges of action potentials (APs), at the output of a neuron possessing dendritic arborizations, which are characterized by complex geometry and nonlinear active membrane properties, is a topical problem in biophysics, physiology, and functional morphology of nerve cells. The presence of voltage-dependent conductances in the dendritic membrane is shown in almost all main types of central neurons examined to date [1]. On models of cells with reconstructed dendritic arborizations, it was demonstrated that the complex geometry of active dendrites substantially affects the characteristics of the discharge patterns generated at the neuronal output [2-4]. Also, a high diversity of different output patterns generated during tonic synaptic excitation distributed over the dendrites and the dependence of the pattern complexity on the characteristics of synaptic activity were shown [4-7]. These data obtained within recent years allow one again, on a new basis, to address the problem of the principles, by which neurons code
the intensity of external electrical and synaptic actions applied to them into the output discharge patterns, and to direct attention previously focused mainly on the neuron’s trigger zone to the role of the dendrites in this process. This is, in particular, the role of the dendrites in the origin of the complex, especially stochastic, output spiking patterns. The characteristics of the latter were previously interpreted exclusively as the effects of complex spatial and temporal combinations of actions received from the partner neurons in the common neural network. According to the new statement of the problem, the most important role in shaping the intrinsic (i.e., not imposed by some external pacemakers) complex spiking patterns (neural codes including stochastic ones) is attributed to the dendrites with active nonlinear membrane properties and complex, metrically asymmetrical geometry [4, 6, 7]. The resolution of this problem requires one to be not limited by the approach aimed at finding common “input-output” conversion phenomena in different types of neurons. A profound quantitative analysis of the rules governing such conversions is necessary for understanding the relationships between intrinsic and evoked impulse activities of neurons, i.e., the intrinsic and induced codes.

The aim of our study was to elucidate in detail quantitative characteristics of the conversion (encoding) of constant homogeneous electrical and tonic synaptic influences performed in neurons possessing complex metrically asymmetrical dendritic arborizations with nonlinear electrical properties of the membrane. Motor neurons of the nucl. abducens nucleus have been selected as the object of such a study performed with the use of computer modeling techniques. This choice was justified by the availability of several specimens of the cells whose dendritic arborizations have been successfully reconstructed with a high spatial resolution [8, 9], with demonstration of the marked metrical asymmetry of the arborizations and existence of a significant effect of the latter on both the passive transfer properties [9, 7] and the output AP discharge patterns [6, 7]. The fact that the type of changes in the discharge pattern with change in the intensity of synaptic activation in these neurons [6, 7] is rather common to those found in other types of neurons was also demonstrated [4]. The typical pattern of spike activity of nucl. abducens motor neurons looks like interleaved AP bursts, in particular those related to saccades (see [10]). In addition, nucl. abducens motoneurons are perhaps the most suitable for such studies of the rules governing formation of the “intrinsic” patterns (codes) when the network effects are minimized. Motoneurons of the nucl. abducens differ from other representatives of the class of motoneurons (e.g., spinal motoneurons) by a lack of recurrent inhibitory circuits [11] and by the fact that the discharge patterns of all motoneurons in the nucleus are qualitatively similar (homogeneous) [12].

**METHODS**

This study was performed on models of rat nucl. abducens motoneurons built in the NEURON software environment [13]. For the simulated neurons described in detail in earlier reports [6, 7], reconstruction of their complex dendritic arborizations was performed with a high spatial resolution; active nonlinear electrical properties of the dendritic membrane were provided by the presence of the voltage-dependent conductivity of glutamatergic (NMDA-type) synaptic currents with a prevailing calcium component, as well as of the potassium conductivity dependent on the dynamically changing intracellular Ca\(^{2+}\) concentration. Using the earlier described protocol of computational experiments [6, 7], we obtained AP discharge patterns (neuronal codes) of different complexities at the neuronal output by varying the intensity of 10-sec-long tonic synaptic activation homogeneously distributed over the dendrites. Such activation was simulated by introducing a spatially homogeneous and constant-in-time specific synaptic conductance, whose maximum value \(G_s\) was changed within the range of 0 to 50 \(\mu S/cm^2\) (reversal potential of the synaptic current, \(E_s\), 0 mV). Moreover, a conventional electrophysiological protocol was used in the study of the neuron discharge characteristics under conditions of such electrical action. A direct depolarizing current, \(I_{st}\), was applied to the soma with the intensity varying from 0 to 50 nA (stimulus duration 3 sec), and long-lasting discharges of APs evoked by this current application were recorded from the distal end of the axon.

The AP discharge patterns generated at the neuronal output under the actions of depolarizing current or tonic synaptic activation were characterized quantitatively by the dependences of the mean AP firing rate \(f\) and mean interspike interval (ISI) \(\theta =1/f\) on the intensity of the applied current \(I_{st}\) (“current-to-frequency,” \(f–I\), and “current-to-