The tight relationship between asymmetric signaling and locational excitability in motoneuron dendrites

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Spinal motoneurons possess large, highly branching dendritic structures that contain thousands of synaptic contacts and various voltage-gated ion channels (VGICs). Research has indicated that dendritic arborization and cable properties provide the basis for foundational dendritic processing, which is characterized by direction-dependent signal propagation and location-dependent channel activation in dendritic arbors. Due to these arbors' complex structure, signals attenuate differentially depending on whether propagation occurs from the soma to the dendrite or in the opposite direction. In addition, current thresholds for the activation of dendritic ion channels differ depending on the location of these channels within dendrites. However, whether and how these foundational properties for dendritic signaling and excitability are related in motoneurons remains unclear.

Based on our analyses of anatomically reconstructed motoneurons and novel reduced models, we propose that 1) directional signal propagation is similar across spinal motoneurons, regardless of cell type-specific structures; 2) reduced models that retain dendritic signaling asymmetry can accurately replicate anatomical dendritic excitability in both passive and active modes; and 3) asymmetric signal propagation and locational dendritic excitability are closely related, irrespective of motoneurons' arbor structures.

Signal Propagation Over Motoneuron Dendrites

The signal propagation properties of the dendrites have been analyzed by calculating voltage attenuation factors (the ratio of voltage at the measurement site to voltage at the stimulation site) between the soma and single points (i.e., a point-to-point condition) on the dendrites.1,2 However, in vivo, synaptic inputs and voltage-gated ion channels (VGICs) are distributed across many dendritic branches (i.e., a point-to-all condition).3-5 Thus, electrical signals are generated in parallel from individual dendritic branches and flow into the soma to initiate action potentials near the cell body. When propagated from the soma to the dendrites, direct current (DC) signals are exponentially attenuated along individual paths of dendritic trees. However, when transferred from the dendrites to the soma under point-to-all conditions, due to the summation effect of proximal dendritic branches on signal transduction into the soma, DC signals are attenuated in a manner similar to the way in which attenuation occurs for signals propagated from the soma to the dendrites in dendritic regions proximal to the soma. In distal dendrites, DC signals are attenuated much more rapidly as they travel from the dendrites to the soma than in the opposite direction (from the soma to the dendrites). Consequently, the attenuation of DC signals from the dendrites to the soma was best fit using an inverse sigmoidal function rather than an exponential function, which has previously been suggested for point-to-point conditions.6 Moreover, the shapes of fitting equations for signal attenuation data do not appear to vary as a function of cell type-specific structures, indicating that the direction-dependent signal attenuation is a generic feature of dendritic signal propagation in motoneurons.

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Channel Activation Over Motoneuron Dendrites

Historically, cable theory has been used to estimate dendritic excitability when injecting current into the soma. Under this stimulation protocol, the voltage response at the soma attenuates exponentially while propagating along dendritic paths. Thus, greater current input into the soma is expected to be required for the activation of more distal channels in the dendrites. From this viewpoint, dendritic excitability is expected to decrease as a function of path length from the soma. However, our analyses of anatomically reconstructed motoneurons with active channels at various locations along the dendrites produced findings opposite to this expectation. Although the voltage produced in response to somatic current injection attenuated exponentially when transferred from the soma to the dendrites, less current input to the soma was needed to activate channels located in distant dendritic regions than channels located in proximal dendritic regions. Consistent results were obtained when synaptic inputs were applied to the same site of active channels as these channels' dendritic locations were varied. In realistically reconstructed motoneurons, increases in dendritic excitability with increasing path length were partially attributable to increases in dendritic input resistance as a function of distance from the soma. These results suggest that the attenuation property for voltages traveling from the soma to the dendrite is insufficient to predict the spatial profiles of dendritic excitability for spinal motoneurons.

The Relationship between Dendritic Signaling and Excitability in Motoneurons

How are signal propagation and channel activation correlated for the dendrites? This fundamental question was investigated under point-to-point conditions. Yet, it has remained unresolved for point-to-all conditions; a likely cause of this issue is a lack of suitable modeling approaches in which reduced neuron models retain the directional signal attenuation properties of anatomically reconstructed motoneurons in physiological distribution of synaptic inputs or dendritic VGICs. Using a novel reduced neuron model that incorporates anatomical signal propagation properties, we found that the asymmetry in signal attenuation properties between the soma and the dendrites was directly related to the input resistances of the dendrites at all distances from the soma. Consequently, the reduced model (in which the directional signal attenuation characteristics of motoneuron dendrites were retained) accurately predicted both the activation of VGICs on the dendrites at all distances and the resulting current input-frequency output relationship of the motoneuron. Sensitivity analysis revealed that the attenuation property for DC signals from the dendrites to the soma was an essential determinant of channel activation in the dendrites. The attenuation of DC signals from the dendrites to the soma was positively correlated with dendritic channel activation, whereas the attenuation of DC signals from the soma to the dendrites was negatively correlated with dendritic channel activation. More importantly, the normal dendritic excitability profile (i.e., increased excitability with increasing distance from the soma) was completely reversed (i.e., decreased excitability with increasing distance from the soma) when the signal attenuation from the dendrites to the soma changed over a non-physiological range. These results all emphasize that attenuation properties for signals from the dendrites to the soma and from the soma to the dendrites are an important determinant of dendritic excitability. Therefore, to correctly predict channel activation in dendrites, the propagation properties of signals in both directions should be taken into account.

Implications for Reduced Modeling Approaches

Reduced modeling approaches have provided computational frameworks for many studies of the biological principles underlying neuronal signal processing and computation. To improve upon the accuracy of prior reduced neuron models, including models for active dendrites, methods of mapping the complex signal propagation and locational excitability of the dendrites must be incorporated into reduced modeling frameworks. Given this perspective, our new reduced modeling approach may provide a means of linking anatomical and reduced models that offers several advantages: 1) analyses have demonstrated that the cable parameters of our reduced model retain the directional signal attenuation properties of the anatomical model; 2) the dendritic excitability of the anatomical model can be automatically embedded into the reduced model using the direct relationship between dendritic signaling and excitability; and 3) channel locations can be expressed in terms of physical distance in the reduced model, allowing for direct comparisons between the reduced and anatomical models based on path length from the soma.

Conclusions

For spinal motoneurons, the signal attenuation in the dendrites differs depending on propagation direction. This directional signal attenuation over the dendrites is not dependent on type specific morphologies of motoneurons. The locational channel activation in the dendrites is directly related to the signal attenuation properties in both the soma-to-dendrite and dendrite-to-soma directions. The signal attenuation asymmetry between the soma and the dendrites is a key determinant of dendritic excitability at all distances from the soma and is essential for maintaining the normal firing behavior of motoneurons. The direct relationship between signal propagation and channel activation in motoneuron dendrites may not only provide fundamental insight into generic features of signaling and excitability in branching dendritic networks but also diminish the gap between reduced and anatomical neuron models.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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