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Modeling motoneurons after spinal cord injury: persistent inward currents and plateau potentials

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Abstract

A single-compartment conductance-based computational model to mimic the behavior of rat tail motoneurons after acute and chronic spinal cord injury (SCI) was developed. The model includes a calcium-dependent potassium current, $I_{K(Ca)}$, that contributes to after hyperpolarizations. In the chronic SCI model, the presence of sodium and calcium persistent inward currents (PICs) causes plateau potentials resulting in prolonged self-sustained firing. The interaction between the calcium PIC and $I_{K(Ca)}$ affects the magnitude and duration of plateau potentials as well as the hysteresis seen during injected current ramps. The model responses mimic experimental observations and may explain the spasticity observed after chronic SCI.

Keywords: Hysteresis; Rat; Self-sustained firing; Calcium current; Spasticity

1. Introduction

Spasticity is a major complaint of people with chronic spinal cord injury (SCI) as well as an impediment to the recovery of functional locomotion after SCI [7,8,14],

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but the mechanisms underlying spasticity are poorly understood. Recent studies with a rat sacral spinal cord transection model suggest that after chronic SCI, changes in the membrane properties of spinal motoneurons lead to plateau potentials that may play a large role in spasticity [1–3]. Although normal motoneurons may use plateau potentials to amplify synaptic input and have been shown to develop plateau potentials in response to the application of certain neurotransmitters [9,10], after acute SCI, rat motoneurons lose the endogenous ability to generate plateaus [3]. After chronic SCI in rats, plateau potentials appear in almost all motoneurons and have been found to be caused by voltage-dependent calcium and sodium persistent inward currents (PICs) [2,3,13]. In the presence of these PICs brief stimuli can trigger prolonged self-sustained firing [13], much as spasticity increases following sensory stimuli in human SCI patients [7]. Recent evidence indicates that plateau potentials are also present in human motoneurons [5].

Here, we have developed a computational model to mimic the behavior of rat motoneurons after acute SCI as seen in Ref. [3]. We utilize this model to examine the effects of calcium and sodium PICs in altering the behavior of the motoneurons after chronic SCI.

2. The model

A single-compartment conductance-based model is developed to mimic the behavior of rat motoneurons after acute SCI by modifying a previous vertebrate motoneuron model [4]. The current balance equation for this "acute model" is given by

$$C_{\mathrm{m}}\frac{\mathrm{d}V}{\mathrm{d}t} = -I_{\mathrm{Na}} - I_{\mathrm{K-dr}} - I_{\mathrm{Ca}} - I_{\mathrm{K(Ca)}} - I_{\mathrm{L}} + I_{\mathrm{app}}, \tag{1}$$

where C_{m} is the membrane capacitance and V is the membrane voltage. I_{Na} and $I_{\mathrm{K-dr}}$ are Hodgkin–Huxley-like sodium and potassium delayed rectifier currents that produce action potentials. I_{Ca} and $I_{\mathrm{K(Ca)}}$ are calcium and calcium-dependent potassium currents, respectively, that have been found to contribute to after hyperpolarizing potentials (AHPs) in rat motoneurons [6,15]. I_{L} is a leak current and I_{app} is an applied (injected) current that takes the form of slow (0.5 nA/s) ramps or pulses. The currents are modeled as

$$I_{\mathrm{Na}} = g_{\mathrm{Na}} m_{\infty(\mathrm{Na})}^3(V) h_{\mathrm{Na}}(V - E_{\mathrm{Na}}), \tag{2}$$

$$I_{\mathrm{K-dr}} = g_{\mathrm{K-dr}} n^4 (V - E_{\mathrm{K}}), \tag{3}$$

$$I_{\mathrm{Ca}} = g_{\mathrm{Ca}} m_{\mathrm{Ca}}^2 h_{\mathrm{Ca}} (V - E_{\mathrm{Ca}}), \tag{4}$$

$$I_{\mathrm{K(Ca)}} = g_{\mathrm{K(Ca)}} \frac{[\mathrm{Ca}]}{[\mathrm{Ca}] + S_{\mathrm{Ca}}} (V - E_{\mathrm{K}}), \tag{5}$$

$$I_{\mathrm{L}} = g_{\mathrm{L}} (V - E_{\mathrm{L}}), \tag{6}$$