Modeling the Lowering of Motoneuron Voltage Threshold during Fictive Locomotion

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The excitability of lumbar motoneurons in the cat is increased during fictive locomotion induced by stimulation of the mesencephalic locomotor region (MLR). This change in excitability has previously been demonstrated experimentally. During fictive locomotion (1) the afterhyperpolarization (AHP) is reduced1, 2 and (2) the voltage threshold for production of an action potential is lowered.3

The excitability of motoneurons is determined by intrinsic properties of the cells that are modulated by the premotoneuronal locomotor network. In this computer-simulation study we focus on the lowering of the voltage threshold for an action potential and the accompanying reduction of the AHP. The purpose of this paper is to explore the potential ionic conductances responsible for the increase in motoneuron excitability during fictive locomotion.

COMPUTER MODEL

A single-cell model with three compartments (initial segment, soma, and dendrite) was built using the GENESIS software (Fig. 1A). The active ionic currents were taken from Traub,4 Jones and Bawa5 and Takahashi.6 Ramp current was injected into the soma following a reduction of 70% of the $g_{\text{K(AHP)}}$ that was used to simulate the reduction of AHP during fictive locomotion. Membrane potential of the soma compartment was solved to investigate the relationship between voltage threshold and varying specific conductances in the soma and initial segment.

RESULTS

Decreasing somatic conductance of various potassium channels and increasing somatic conductance of the sodium channel readily produced changes in current threshold, but changes in voltage threshold were small and were accompanied by gross changes in the action potential shape. Increasing $g_{\text{Na}}$ by 100% in the initial segment (Fig. 2) produced a lowering of the voltage threshold in the soma by 6.7 mV (compared to a mean value of 6.3±3.9 recorded in the cat experiments), while the size and shape of the somatic action potential were minimally affected (Fig. 2C), as in the experimental results. Alternatively, decreasing $g_{\text{K(DR)}}$ by 60% in the initial segment was also able to produce a lowering of the

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voltage threshold in the soma by 6.4 mV, but this caused a change in shape of the repolarization phase of the somatic action potential (Fig. 2D).

CONCLUSION

Simulation results suggested that (1) altering currents ($I_{K(AHP)}$, $I_{K(A)}$, $I_{K(DR)}$, and $I_{NA}$) in the soma could readily enhance repetitive firing of the cell, but had only small effects on the voltage threshold for somatic action potentials, and that (2) increasing sodium current ($I_{NA}$)
or decreasing fast potassium current ($I_{K(DR)}$) in the initial segment could readily enhance repetitive firing and cause a lowering of the voltage threshold for a somatic action potential comparable to the experimental data. Therefore, modulation of sodium channels or potassium channels or both within the initial segment could be a potential mechanism producing voltage-threshold lowering during fictive locomotion. The simulation results predicted that the lowering of voltage threshold by 6.7 mV would be accompanied by a 5 mV increase in the size of the initial segment spike during locomotion. We tried to verify this hypothesis experimentally by measuring the initial segment spike amplitude in a cat motoneuron before and during fictive locomotion when the soma–dendritic spike was blocked with hyperpolarizing current. However, in two motoneurons tested we observed no change in the size of the initial segment spike, although the voltage threshold lowered by 2 mV. Other mechanisms of voltage-threshold lowering continue to be assessed using this model.

REFERENCES


