

POSTER PRESENTATION

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Role of low and high-voltage activated Ca^{2+} -dependent K^{+} currents in the control of alpha-motoneuron discharge and its implication in hyperreflexia

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Specificity of calcium-activated potassium (K^{+}) currents to different sources of calcium has been noted in many neurons (e.g.¹). Recently, in spinal alpha-motoneurons (α -MN), it was shown that the low-voltage activated L-type calcium currents (also known as persistent calcium currents) activate an exclusive subset of small conductance K^{+} currents (SK_L)². The SK_L currents were distinct from the medium after-hyperpolarization (mAHP) producing N/P-type calcium activated K^{+} currents (SK_{AHP} currents). The same study further suggested that an enhancement of persistent calcium current often observed after chronic spinalization can in part be due to reduced availability of the SK_L channels albeit mAHP remained unchanged. While mAHP has been suggested to be integral in controlling motoneuron firing frequencies and grading L-Ca activation, the role of SK_L currents in motoneuron discharge is unknown. The goal of this study is to characterize the influence of SK_{AHP} and SK_L currents on motoneuron firing frequencies. Here we test the hypothesis that SK_{AHP} and SK_L currents play differential roles in the control of persistent inward currents that are key determinants of motoneuron excitability.

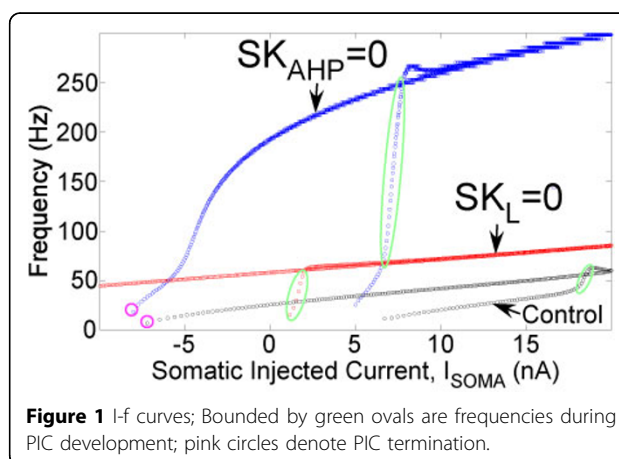
Methods

The α -MN is modeled with two compartments (soma and dendrite) using conductance-based Hodgkin-Huxley formalism. The persistent L-Ca and SK_L are located in the dendrite along with persistent sodium current. The mAHP causing high-voltage activated Ca^{2+} and SK_{AHP}

currents are confined to the soma along with action potential causing fast sodium and delayed rectifier K^{+} currents. Model simulations are performed using the XPPAUT software.

Results

The model α -MN shows counter-clockwise hysteresis in the injected current-frequency (I-f) relationship (Fig. 1, control) as observed in many chronic spinal sacrocaudal motoneurons. This hysteresis is mediated by the dendritic L-Ca and persistent sodium currents (together termed PIC). A selective blockade of somatic SK_{AHP} greatly increases the spike frequencies consistent with experimental findings that mAHP is integral for controlling α -MN frequencies. On the other hand, eliminating SK_L resulted in uncontrolled L-Ca activation with virtually no deactivation of the persistent inward currents



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even with large hyperpolarization (self-sustained discharge for $I_{SOMA} \leq 0$ does not terminate; compare with $SK_{AHP} = 0$ and control traces).

Conclusions

Chronic spinal cord injury often results in spasticity (hyperreflexia). Intrinsic hyper excitability of α -MN has been attributed to underlie hyperreflexia. The uncontrolled and abrupt PIC activation due to reduction in SK_L currents implicates rapid development and sustenance of muscle contraction forces such as during spasms, thus delineating a possible mechanism for α -MN hyper excitability that could lead to hyperreflexia following injury.

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