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K_{IR} channels in nucleus accumbens MS neurons modulate integration of excitatory synaptic inputs: a computational study

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Background

Nucleus accumbens (NAc) is a major site of action for many drugs of abuse and is implicated in brain disorders like schizophrenia [1]. NAc MS neurons possess an array of active channels (14 channels) that may influence their information processing [2]. Experimental studies on the electrophysiological properties of the dendrites of MS neurons are very sparse due to their tiny structure. Here we use a computational model of the NAc MS neurons to investigate the role of K_{IR} currents in the integration of excitatory synaptic inputs.

Methods

Using NEURON, a 189-compartment model of MS cell was built based on Wolf *et al*, 2005 [2]. Co-localized NMDA-AMPA synapses were used to generate EPSPs.

Results

50% reduction of dendritic K_{IR} conductance (gK_{IR}) augmented somatic and dendritic EPSP parameters such as amplitude, half-width, rise time and decay time (by 24%, 23%, 11%, and 53% respectively) (Figure 1A), indicating that the cell is driven towards temporal integration mode of action potential firing. Elevation of gK_{IR} had converse effects, thereby driving the cell towards coincidence detection mode. Additionally, 50% reduction of gK_{IR} enhanced

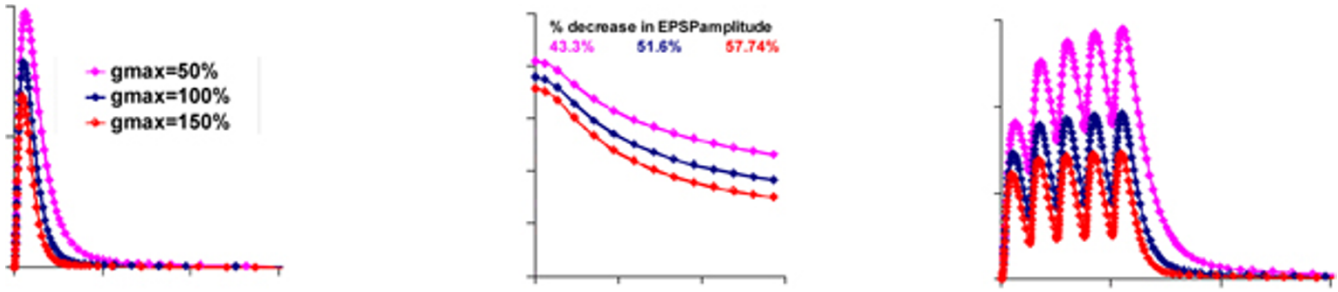

Figure 1
Reduction in gK_{IR} results in increase of EPSP amplitude, half width, rise time and decay time (A), increase in amplitude normalization (B), and increase in temporal summation (C).

EPSP amplitude normalization (from 43% in the native model to 52%) (Figure 1B) while it reduced normalization of EPSP temporal summation (summation increased from 31% in the native model to 60%, 50 Hz synaptic input) (Figure 1C), with the extent of normalization proportional to frequency of synaptic input. Our results indicated that cell excitability would increase with reduction in gK_{IR}, subsequently observed as increase in spiking frequency on reducing gK_{IR} (2 spikes in native model against 7 spikes for gK_{IR} = 50% for the same current injected at the soma).

Conclusion

Thus, K_{IR} currents significantly affect propagation and normalization of synaptic potentials in MS neurons. In view of the fact that dopamine powerfully modulates K_{IR} conductance in MS neurons K_{IR} channels may play an important role in setting the cell excitability in response to external modulatory influences.

References

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