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K_{IR} currents suppress neuronal spiking for unsynchronized distal synaptic inputs in striatal medium spiny neurons: a computational study

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Dendritic active conductances are known to powerfully modulate the integration of subthreshold synaptic inputs and thereby, neuronal excitability in central neurons. A suitable candidate for this modulation in medium spiny (MS) neurons of nucleus accumbens (NAc) is the K_{IR} currents. We predict that K_{IR} currents may differentially affect the temporal integration of synchronized and unsynchronized inputs from distal and proximal synapses and consequent neuron spiking. In this study, using a 189-compartment computational model of the neuron, built using NEURON simulation platform and based on Wolf *et al.* (2005) [1], we investigate this issue.

Eighty co-localized NMDA-AMPA synapses were used to mimic physiological synaptic inputs which were distributed either distally or proximally. Randomness of the inputs was varied using an adjustable parameter called "noise fraction" whose value varied between 0 (synchronized) and 1 (completely random) [2]. The synapses were redistributed within each region for each value of noise fraction. 30 trials were done for every combination of noise fraction and synapse position, recording the number of spikes elicited in each trial.

In the presence of K_{IR}, probability of spiking progressively decreased with randomness for distal synaptic inputs (0.2 for completely random inputs) whereas in all other cases the probability was almost 1 (probability = 0.94 for Proximal inputs (Control); Figure 1A). Furthermore, the average number of spikes was greater for

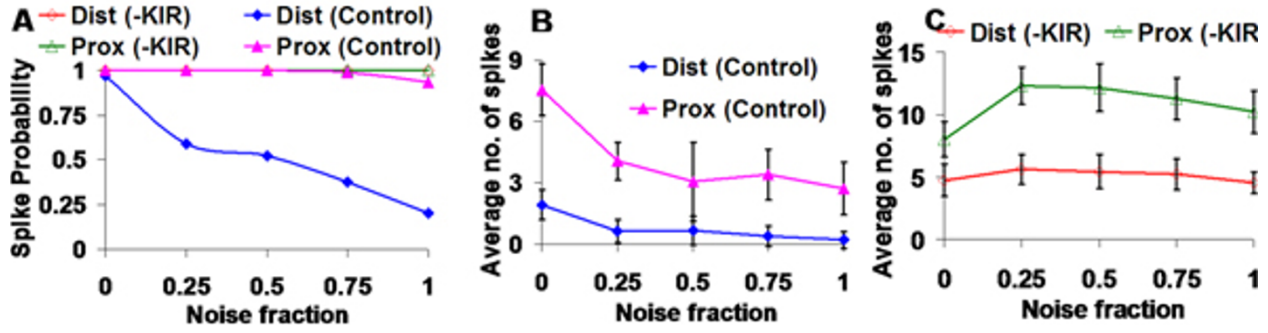

Figure 1 Effect of K_{IR} on MS neuron spiking. (A) Presence of K_{IR} progressively decreased spike probability with randomness for distal inputs (probability = 0.2 for fully random inputs), while, in their absence, probability was always 1. Proximal inputs, synchronized or unsynchronized, and synchronized distal inputs showed spike probability ~ = 1 irrespective of the presence or absence of K_{IR}. (B) In presence of K_{IR}, the number of spikes decreased with input randomness, while it first increased and then decreased, in their absence (C).

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proximal inputs (Figure 1B & C). In the presence of K_{IR}, the number of spikes decreased with the randomness of the input (Figure 1B) while in its absence, the number of spikes first increased and then decreased (Figure 1C) with input randomness.

Thus, K_{IR} currents appear to differentially affect the temporal integration of unsynchronized distal inputs in NAc MS neurons, reducing cell excitability in their presence. Since, synchronous inputs are likely to be of greater functional significance than asynchronous inputs, K_{IR} conductance, which in turn is powerfully modulated by external factors such as dopamine, may play an important role in discriminating functionally relevant/irrelevant events.

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