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NMDA driven spikes modulate plateau potentials in D1 and D2 Spiny Neurons

The striatum receives and integrates excitatory inputs from the cortex and thalamus and outputs inhibitory signals to the thalamus and other subcortical structures via the globus pallidus. It also receives strong dopaminergic innervation from the substantia nigra pars compacta; degeneration of the input dopaminergic input contributes to the hypokinesia observed in Parkinson's Disease (PD). Around 95% of the striatum is composed of GABAergic cells known as Spiny Projection Neurons (SPNs) or MEdium Spiny Neurons (MSNs). Around half of these SPN's exclusively present D1 type metabotropic dopaminergic receptors (D1Rs) while the other half exclusively presents D2 type receptors (D2Rs). The D1R cells are involved in the 'go' or direct pathway, promoting motor movement, the D2R cells are considered to be part of the 'no go' pathway or indirect pathway, inhibiting motor movement. In anesthetized model animals, SPN's have been observed to display a cyclic state of depolarization from a somatic resting membrane potential of a 'DOWN state' of about -85 mV to a relatively depolarized -55mV 'UP state'. Evidence indicates similar regenerative dendritic plateaus exist in dendrites.It is hypothesized that the 'UP states' and plateaus create a spatio-temporal window allowing for integration of input information. Understanding of the generative mechanisms of these states is severely limited. Determining the factors could help determine targets for the treatment of PD. We performed computer simulations of neurons using physiologically plausible multi-compartment cell models to explore the generation of plateaus in SPN dendrites using the NEURON simulation software. Our simulations showed that NMDA-generated dendritic plateau potentials could occur in dendrites. Width of the plateaus differed between D1 and D2 neurons, which are morphologically different. Further modeling and simulation of the SPN will help identify specific channels and potential drug targets for PD.