Dopamine induced alterations in the subthreshold oscillations of the striatal cholinergic interneuron: a modelling study

Krisztina Szalisznyó and László Müller

Department of Biophysics, KFKI Research Institute for
Particle and Nuclear Physics of the Hungarian Academy of Sciences
H-1525 P.O. Box 49, Budapest, Hungary

Abstract

In this study we raised the question of dopamine induced single cell activity alterations in the striatal cholinergic interneurons (AchN). AchN-s are key elements of the striatal circuitry in associative learning and controlling and planning movement. These interneurons are tonically active *in vivo* and respond to sensory stimuli by transiently suppressing firing activity, and are able to fire in the absence of synaptic inputs. Some cholinergic interneurons exhibit large spontaneaous hyperpolarizations *in vitro* that result in transient spontaneaous activity. These pauses are associated with sensorimotor learning. The regular spiking is influenced by two hyperpolarization activated conductances (Wilson, 2005) and apamin-sensitive calcium dependent potassium currents (Wilson and Goldberg, 2006). The pause in tonic firing is dependent on dopaminergic activity; however its cellular mechanisms remained unclear. Recent experimental evidence has showed that dopaminergic inhibition of hyperpolarization-activated cation current I_h is involved in this process, and it seems that D2 receptor-dependent inhibition of I_h may be the mechanism for modulating the pause response in tonic firing in cholinergic interneurons (Deng et al., 2007). Given these motivations, we restricted our modelling analysis to the subthreshold membrane potential range (Wilson, 2005), (Wilson and Goldberg, 2006) and examined the parameter regime of this slow subthreshold oscillation in a single point neuron model. We have found, that subthreshold oscillatory behavior of the AchN can be attributed to a combination of inward rectifying outward (KIR) and inward potassium (Ih) currents (Wilson, 2005). We have implemented and analyzed the dopaminerg effect on both of the hyperpolarization activated conductances and followed several aspects of the subthreshold single cell excitability and behavior. We have found, that the G_{KIR} value and the half activation voltage of the G_h has very little effect on the amplitude of the subthreshold membrane potential oscillations and the dopaminerg effects widen the dynamic regime of the subthreshold oscillation. Furthermore we predict, that the hyperpolarizing synaptic events are not amplified intrinsically in these neurons by the two hyperpolarization activated conductances (Wilson, 2005).

References

Deng P, Zhang Y, Xu Z (2007) Involvement of I(h) in dopamine modulation of tonic firing in striatal cholinergic interneurons. *J. of Neurosci.* 27(12):3148–56.

Wilson C (2005) The mechanism of intrinsic amplification of hyperpolarizations and spontaneous bursting in striatal cholinergic interneurons. *Neuron* 45(4):575–85.

Wilson C, Goldberg J (2006) Origin of the slow afterhyperpolarization and slow rhythmic bursting in striatal cholinergic interneurons. *J.Neurophysiology* 95(1):196–204.