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2. **Title**

   The Effects of Nicotinic Receptors in the Functional Compartments of the Caudal Striatum

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4. **Summary**

The striatum is densely innervated by intrinsic cholinergic interneurons, and therefore exert its physiological function under the powerful cholinergic control. On the other hand, in addition to dopamine, cholinergic interneurons themselves receive cholinergic control, and change their firing properties during reinforcement learning. The process is considered to involve the synaptic plasticity of excitatory inputs that depolarize neurons and initiate action potentials. Ionic mechanisms are also involved the depolarization and thereby modulate firing patterns. In this study, we investigate the effect of acetylcholine on the excitatory inputs and the ionic mechanisms that initiate action potentials. To identify the striatal compartment, we made electrophysiological recordings using striatal slices obtained from GFP- and/or YFP-expressing transgenic mice. Cholinergic interneurons are identified by their large somata and thick primary dendrites and, after recordings, expression of cholinergic marker is confirmed by immunostaining against choline acetyltransferase (ChAT). Immunohistological studies revealed that striatal cholinergic neurons distribute heterogeneously with caudo-rostral and medio-lateral axes. Electrical recordings revealed that hyperpolarization-activated cation current (Ih), an ATP-sensitive K+ channel and nicotinic receptor (nAChR)-mediated GABAergic inhibition modulate membrane potentials that shape the characteristic firing pattern of cholinergic interneurons. As expected from heterogeneous cholinergic innervation, nAChR-mediated GABAergic inhibition more prominently in the matrix compartment. Interestingly, high frequent stimulation with activation of μ opioid receptors induced long-term depression of excitatory inputs in the caudal striatum, especially in the medial area, and blocked by an α4β2 nAChR antagonist, suggesting the regional involvement of intrinsic acetylcholine. Considering the synergistic effect of intrinsic acetylcholine and opioid, there might be a regional diversity in the effect of acetylcholine on temporal and long-term synaptic plasticity via nicotinic receptors.