Nicotinic and opioidergic modulation on inhibitory inputs to cholinergic interneurons in the striosomes and the matrix of the mouse striatum

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Striatal functions are strongly modulated by both cholinergic and opioidergic innervation; however, the modulations would be uneven between the compartments, the striosomes (or patches) and the extrastriosomal matrix. The striosomes and the matrix are anatomically and neurochemically distinct compartments. Acetylcholinesterase is expressed more abundantly in the matrix, and dopaminergic innervation is relatively dense in neonate striosomes. Furthermore, μ-opioid receptors are expressed exclusively in the striosomal projection neurons.

We examined γ-aminobutyric acidergic (GABAergic) inhibitory inputs to cholinergic interneurons in both compartments, and found that nicotinic receptor (nAChR)-mediated GABAergic responses were evoked more frequently in the matrix than in the striosomes. Most of the matrix cholinergic neurons received polysynaptic inhibitory post-synaptic currents, which had long latency and required the activation of nicotinic receptors. A single action potential of cholinergic neurons induced nAChR-mediated GABAergic inputs to the cholinergic neurons themselves, suggesting mutual connections that shape the temporal firing pattern of cholinergic neurons. The nAChR-mediated responses were attenuated by continuous application of acetylcholine or the acetylcholinesterase inhibitor eserine, and were enhanced by desformylflustrabromine, a positive allosteric modulator of the α4β2 subunit-containing nicotinic receptor. SCH-23390 and sulpiride, antagonists of dopamine receptors, had no effect on the nAChR-mediated responses. We also evaluated the opioidergic effects on the GABAergic inhibitory inputs in both compartments. Although an application of DAMGO, a μ-opioid receptor agonist, did not affect the nAChR-mediated GABAergic inputs, a frequency of mIPSCs of cholinergic interneurons was reduced by DAMGO only in the striosomes, suggesting that continuous inhibitory inputs were provided by the striosomal projection neurons.

As acetylcholine and opioid are important modulators of striatal functions, the differences in nicotinic and opioidergic effects between the striosomes and matrix might be involved in the physiology and pathophysiology of the striatal compartments.

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