Histaminergic system

The histaminergic system modulates different processes including wakefulness, feeding, and learning and memory consolidation. Histamine receptors (H1R, H2R, H3R, and H4R) belong to the rhodopsin-like family of G protein-coupled receptors, present constitutive activity, and are subjected to inverse agonist action

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The dorsolateral striatum (DLS) is the critical neural substrate that plays a role in motor control and motor learning. A past study revealed a direct histaminergic projection from the tuberomammillary nucleus (TMN) of the hypothalamus to the rat striatum. However, the afferent of histaminergic fibers in the mouse DLS, the effect of histamine on DLS neurons, and the underlying receptor and ionic mechanisms remain unclear.

Peng et al. demonstrated a direct histaminergic innervation from the TMN in the mouse DLS, and histamine excited both the direct-pathway spiny projection neurons (d-SPNs) and the indirect-pathway spiny projection neurons (i-SPNs) of DLS via activation of postsynaptic H1R and H2R, albeit activation of presynaptic Histamine H3 receptor suppressed neuronal activity by inhibiting Glutamatergic synapse on d-SPNs and i-SPNs in DLS. Moreover, sodium-calcium exchanger 3 (NCX3), potassium-leak channels linked to H1R, and hyperpolarization-activated Cyclic nucleotide-gated channel 2 (HCN2) coupled to H2R co-mediated the excitatory effect induced by histamine on d-SPNs and i-SPNs in DLS. These results demonstrated the pre- and postsynaptic receptors and their downstream multiple ionic mechanisms underlying the inhibitory and excitatory effects of histamine on d-SPNs and i-SPNs in DLS, suggesting a potential modulatory effect of the central histaminergic system on the DLS as well as its related motor control and motor learning [1)]

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Peng JY, Shen KL, Fan XJ, Qi ZX, Huang HW, Jiang JL, Lu JH, Wang XQ, Fang XX, Yuan WR, Deng QX, Chen S, Chen L, Zhuang QX. Receptor and Ionic Mechanism of Histamine on Mouse Dorsolateral Striatal Neurons. Mol Neurobiol. 2022 Oct 17. doi: 10.1007/s12035-022-03076-y. Epub ahead of print. PMID: 36245064.