

Dorsolateral striatum

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.

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