

Anterodorsal thalamus histamine signaling modulates object location memory via histamine H3 receptors

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Abstract: The histaminergic (HA) system has long been considered to be associated with learning and memory, fulfilling its functions mainly through the activation of both H1R, H2R and H3R. By whole-brain mapping of histaminergic projections in mouse brain, we find dense histaminergic projections to the anterodorsal thalamus (AD). AD contains a large proportion of head direction cells and has recently been identified as a critical nucleus in episodic memory regulation. However, the precise role of this histaminergic projection remains to be elucidated. By employing optogenetic technique, we found that TMN-AD histaminergic circuit bidirectionally modulates object location memory (OLM) but not other forms of memory including contextual fear memory and novel object recognition. Interestingly, histamine H3 receptor (H3R) but not H1R or H2R express densely in AD shown by fluorescence in situ hybridization (FISH). Therefore, we selectively delete H3R in AD by bilaterally injecting AAV-syn-cre-GFP into AD in *Hrh3^{fl/fl}* mice and found that OLM was impaired. By contrast, selective depletion of H1R in AD fails to affect OLM. Taken all, evidence so far indicate that AD-projecting histaminergic circuit mediating object location memory via downstream H3R-dependent signaling in AD glutamatergic neurons.

Keywords: histamine; anterodorsal thalamus; histamine H3R; object location memory