

## Histamine neurons in the tuberomammillary nucleus modulate memory retrieval

Hiroshi Nomura, Ayame Kubo, Kyoka Nishimura, Shohei Ohmori, Masabumi Minami

*Dept. Pharmacol., Grad. Sch. Pharmaceut., Hokkaido Univ.*

Brain histamine is produced mainly in the tuberomammillary nucleus (TMN) and is implicated in learning and memory as well as wakefulness and feeding. Previously, we demonstrated histamine H<sub>3</sub> receptor inverse agonists upregulate histamine release in the perirhinal cortex and promote the recall of forgotten object memories. However, since H<sub>3</sub> receptors are expressed in non-histaminergic neurons as well as histaminergic neurons, other neurotransmitter systems could be involved in the memory recovery. In this study, we examined whether chemogenetic manipulation of histamine neurons modulates memory retrieval in mice. We virally targeted hM3Dq, the excitatory DREADD receptor, to histamine neurons in the TMN of HDC-Cre mice. In a training session of the novel object recognition task, mice were placed in the field, in which two identical objects were positioned. One week later, they underwent a test session where one familiar and one novel object were presented. The pre-test injection of CNO to the mice receiving AAV-DIO-hM3Dq enhanced the discrimination between two objects as compared to controls. The activation of histamine neurons had no effect on anxiety-like behavior in the elevated plus maze test. These findings indicate that activation of histamine neurons enhances retrieval of a forgotten long-term object memory.