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BACKGROUND & AIM OF THE STUDY

The hypothalamic histaminergic system is an important regulator of memory consolidation and retrieval in various learning paradigms[1,2]. However, DREADDs-induced modulation of histaminergic neurons in the tuberomammillary nucleus (TMN^{HA} neurons) during memory has not been investigated yet. In the present study, to functionally interrogate the histaminergic activity with a cell-specific accuracy on different memory tasks, we chemogenetically activated the histaminergic neurons in Hdctm1.1(icre)Wwis/J (hereafter HDC-Cre)mice.

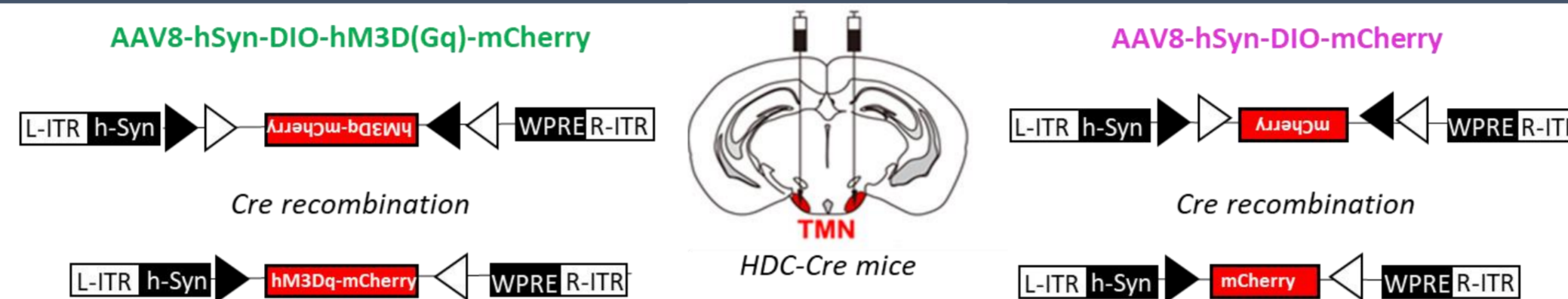
1.Provensi, G., et al., *Brain histamine modulates recognition memory: possible implications in major cognitive disorders*. Br J Pharmacol, 2018. 2.Provensi, G., et al., *Neuronal histamine and the memory of emotionally salient events*. Br J Pharmacol, 2018.

MATERIALS AND METHODS

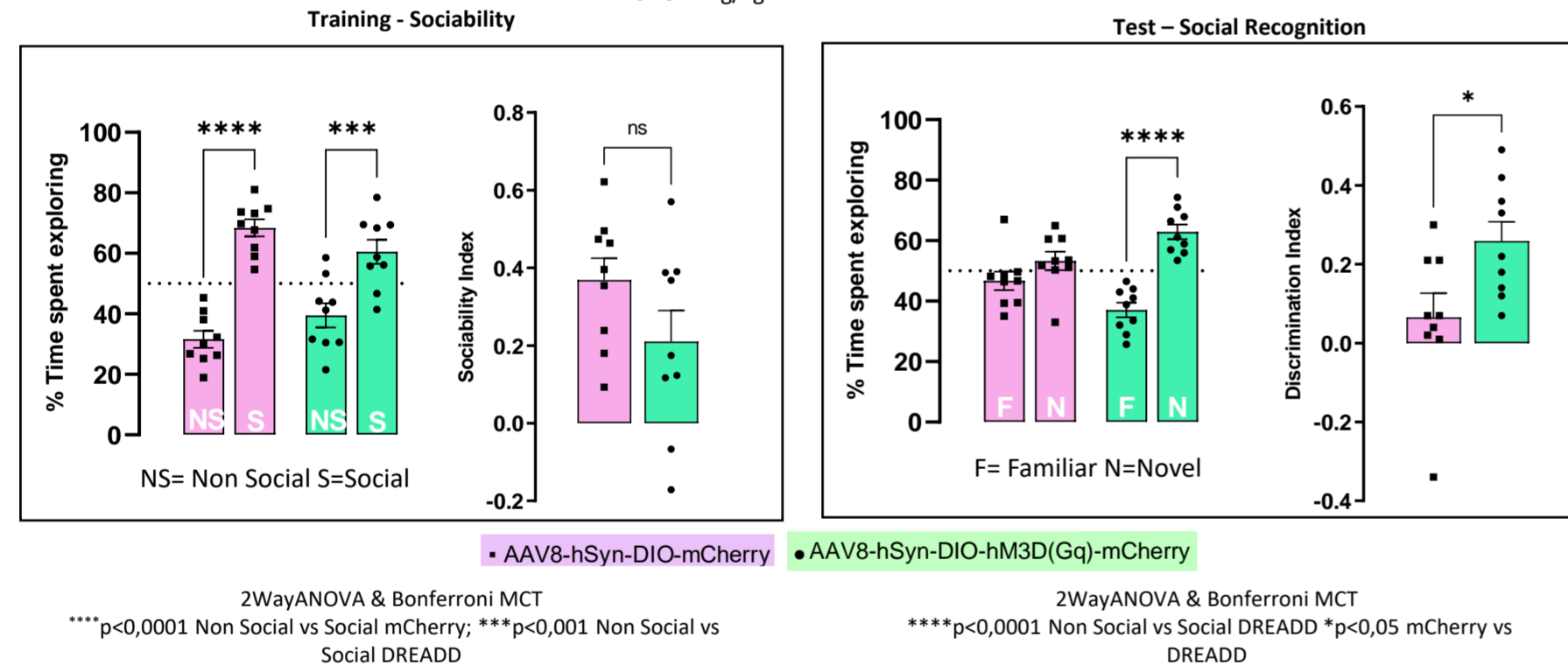
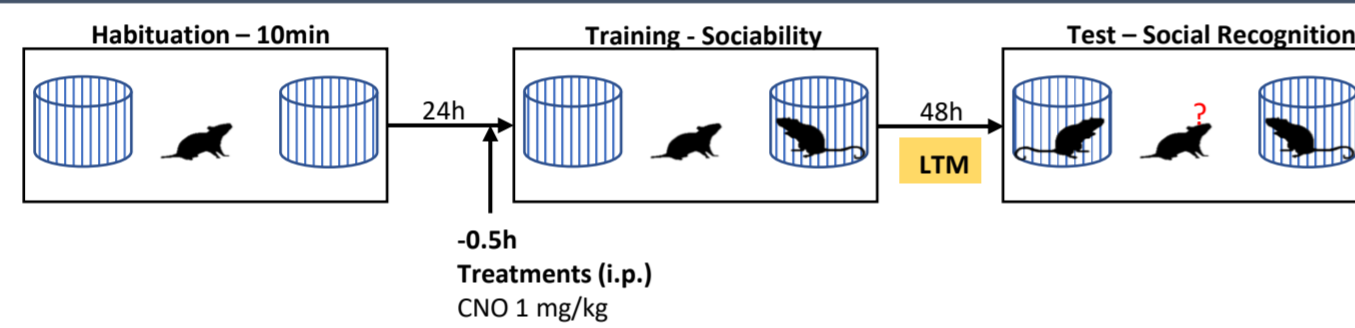
HDC-Cre mice were injected bilaterally into the TMN following stereotaxic coordinates (AP -2.4mm; ML ±0.6mm; DV -5.0mm from dura) with excitatory DREADD (AAV8-hSyn-DIO-hM3D(Gq)-mCherry) or related control (AAV8-hSyn-DIO-mCherry) to transfect histaminergic cells. All the animals were left 30 days undisturbed in their home cages for the correct viral expression and then tested for social, spatial and fear memories followed by DREADDs activator Clozapine-N-Oxide (CNO, 1mg/kg) i.p. injection. The accuracy of viral injections and transfections were then assessed in 20µm brain slices double stained for anti-HDC Ab and Cre-dependent mCherry Ab.

RESULTS

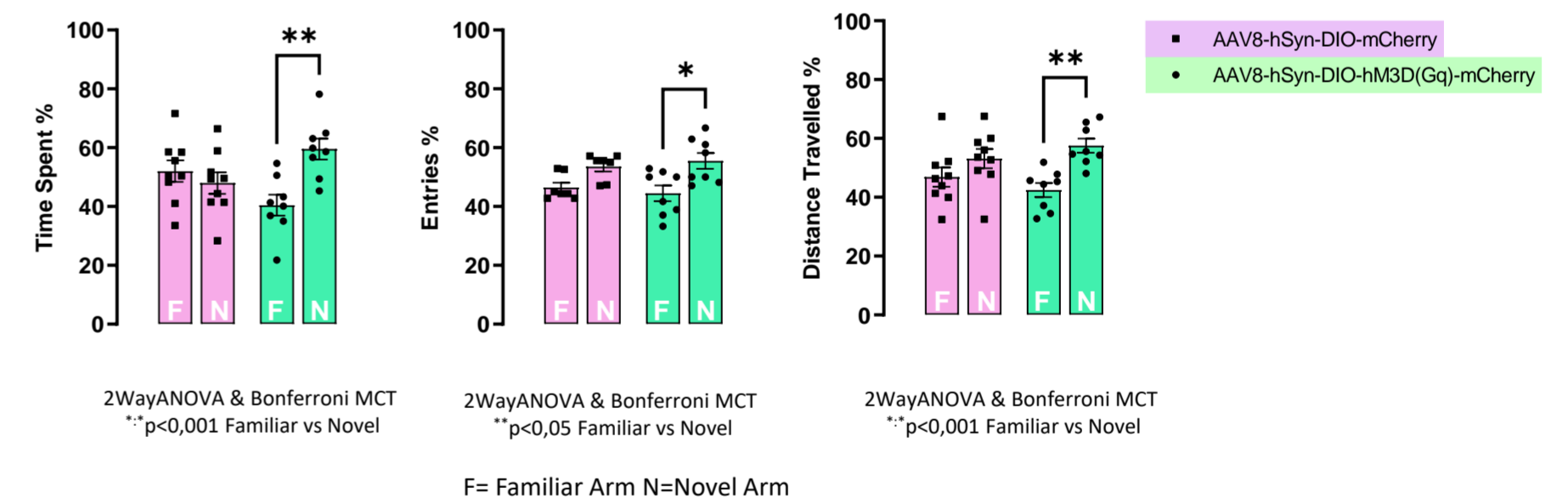
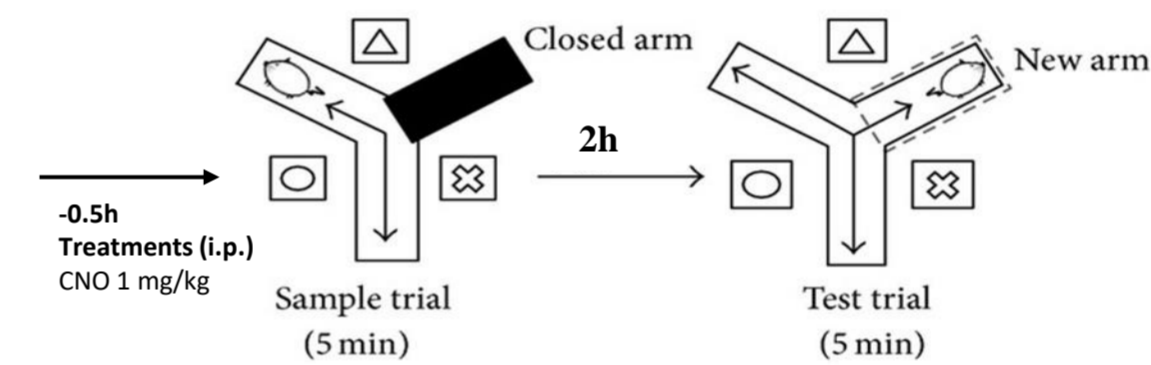
Viral injections and recombination in the TMN of HDC-Cre mice



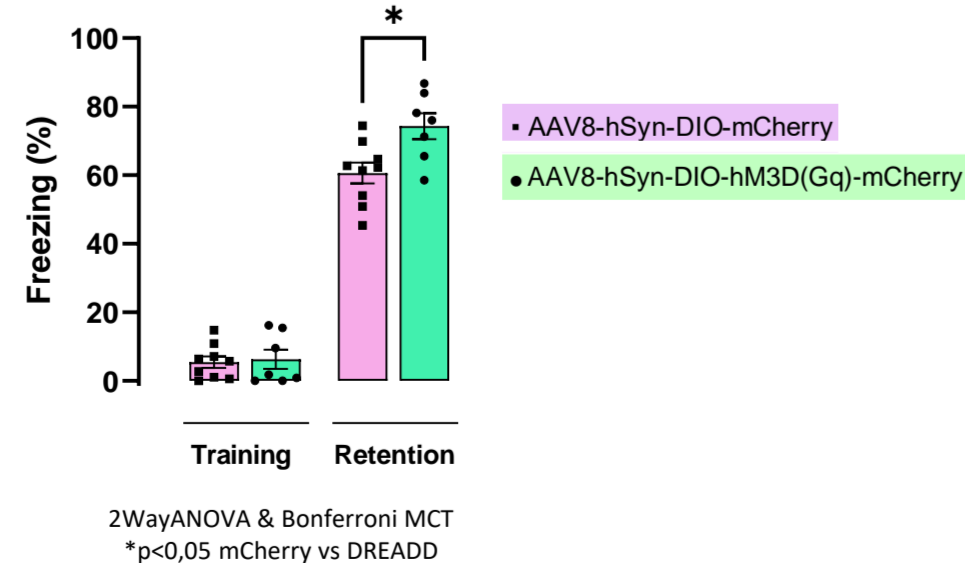
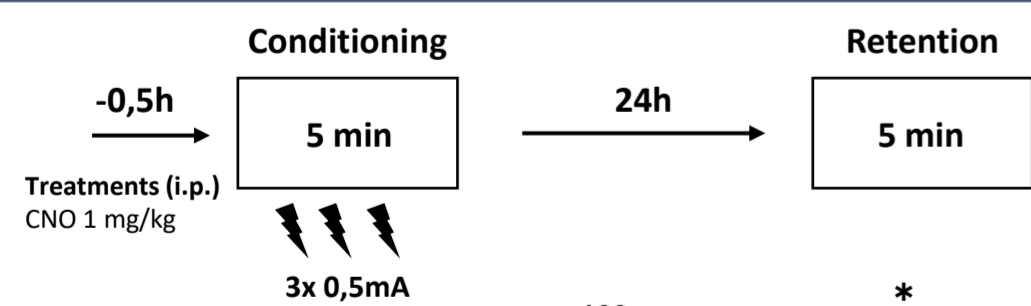
Chemogenetic activation of TMN^{HA} neurons improves social memory in HDC-Cre mice tested in the social recognition test



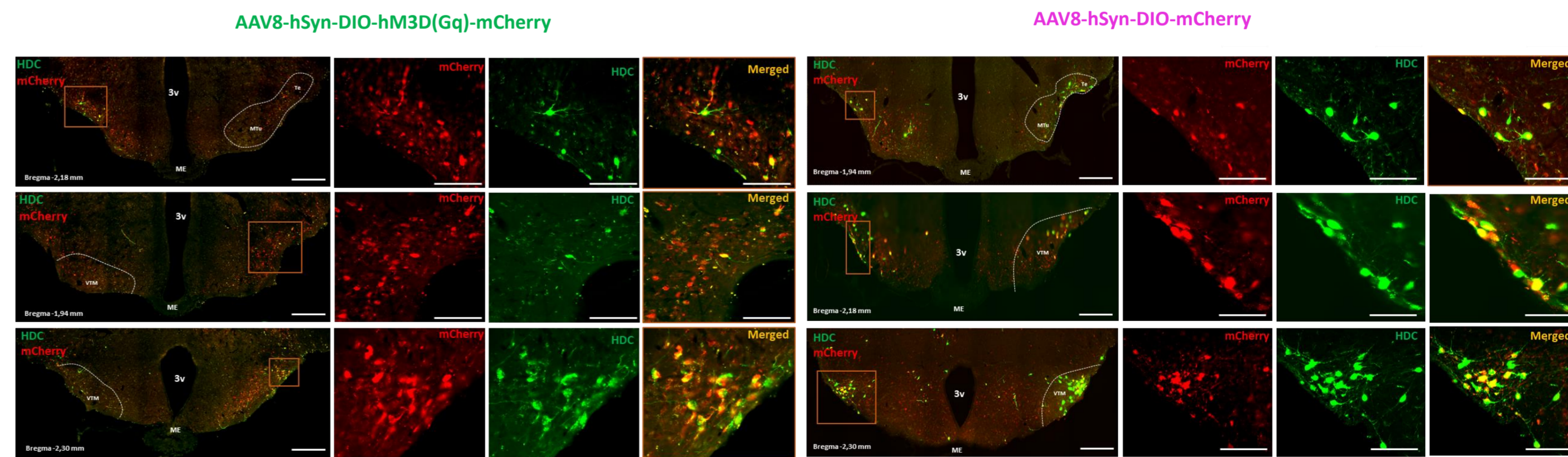
Chemogenetic activation of TMN^{HA} neurons improves spatial memory in HDC-Cre mice tested in the Y-maze spatial memory test



Chemogenetic activation of TMN^{HA} neurons improves retention memory in HDC-Cre mice tested in the fear conditioning test



HDC/mCherry Double Immunofluorescence for cellular detection and viral expression



CONCLUSION

In the present work, we showed an improvement of social, spatial and fear memories when TMN^{HA} neurons were activated by excitatory DREADD-driven mechanism. The results highlight the influence of histaminergic signalling on emotionally salient events. Further studies will elucidate in details the circuitries involved in such effects.

Acknowledgements

