

Nicotine and the Nucleus Accumbens: a DREADDs and CPP Study of Addiction Behavior

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Background

- **The nucleus accumbens (NAc):** subcortical striatal structure implicated in modulating the addictive effects of drugs of abuse.
- **Nicotine:** addictive component in tobacco products, acts on receptors within the NAc to produce the rewarding effects associated with addiction, and drive drug seeking behavior.
- **Designer receptors exclusively activated by designer drugs (DREADDs):** a subfield of chemogenetics that allows for the activation of specific cell populations to determine their role in a given behavior.
- **Conditioned place preference (CPP):** a longstanding paradigm used to observe the effects of a substance of interest.

Using both excitatory hM3Dq DREADDs and CPP, I sought to further determine the role of the NAc in drug seeking behavior in a mouse model of addiction.

Methods

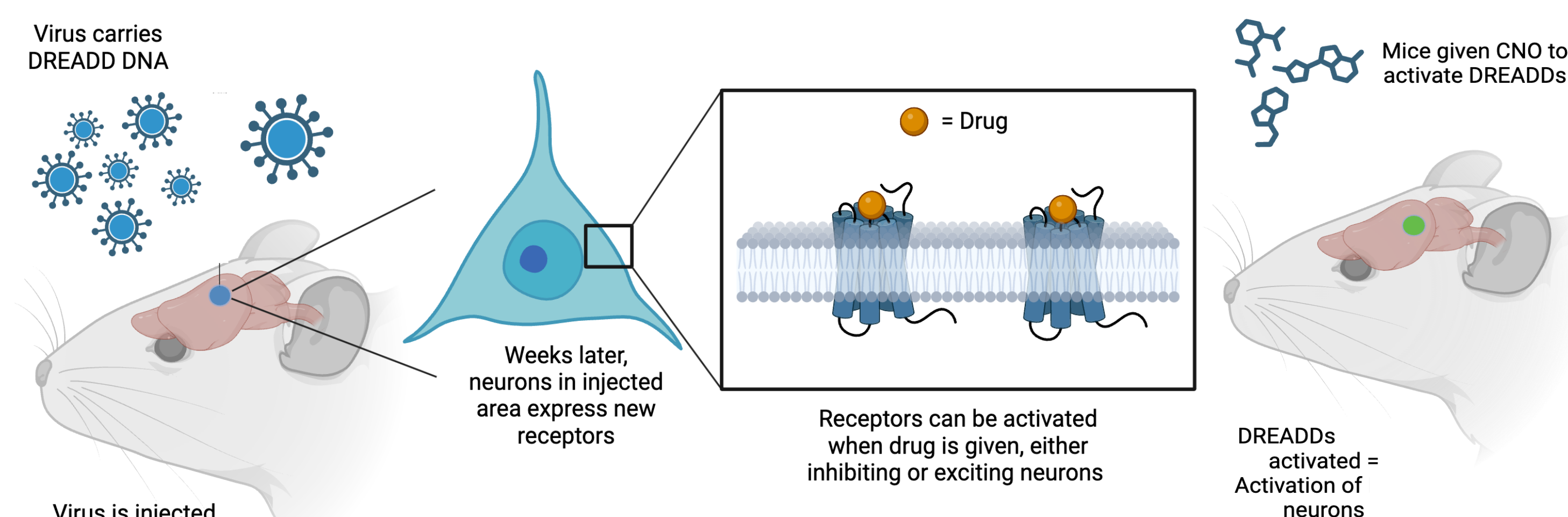


Figure 1. Mechanism and methods of DREADDs. DREADDs were stereotactically injected in the ROI and activated using CNO injection.

Conditioned Place Preference Timeline

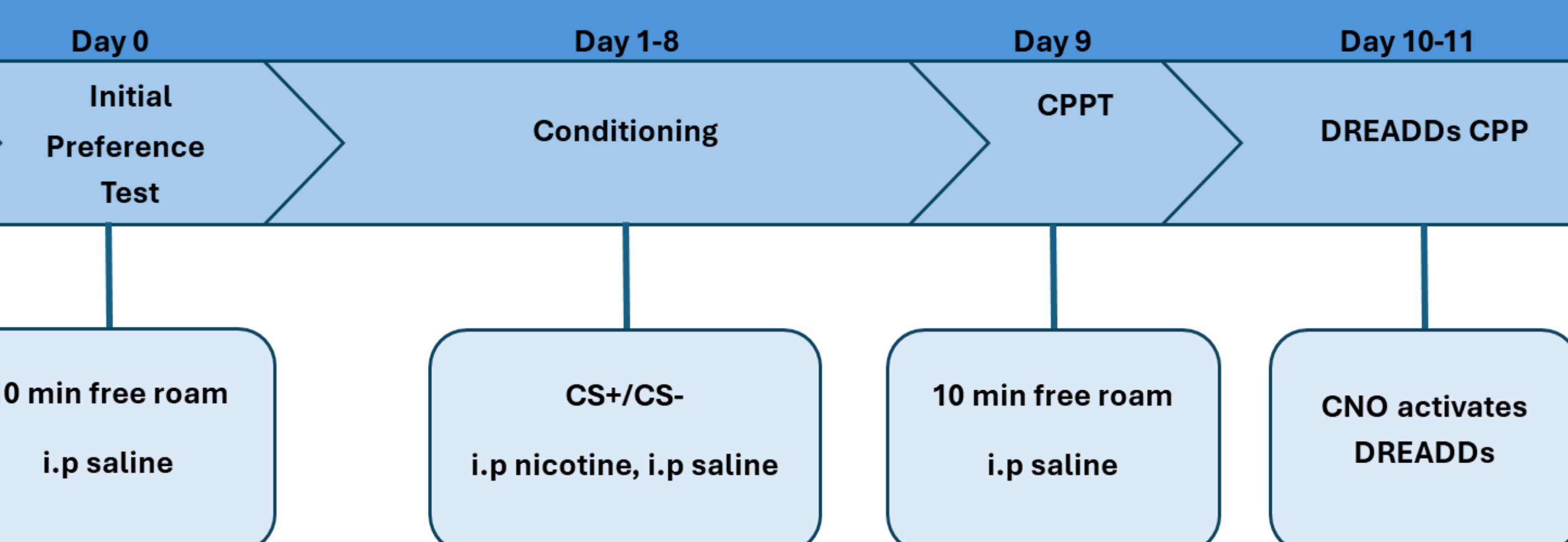


Figure 2. Timeline of CPP and DREADDs activation. After surgery, animals underwent standard CPP protocol, followed by activation of DREADDs.

Behavioral Changes and Viral Expression

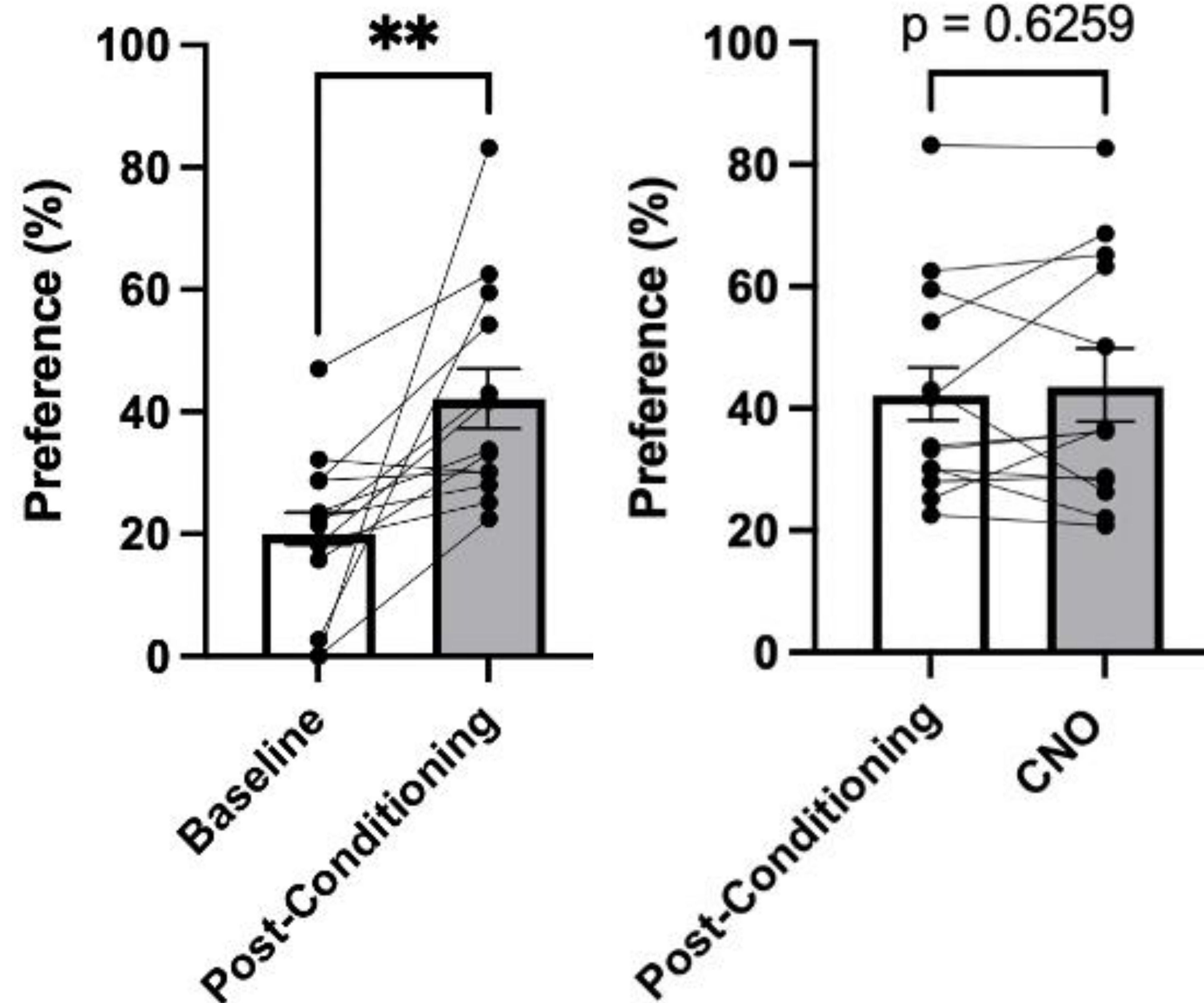


Figure 3. CPP scores after Conditioning and after DREADDs activation. C57BL/6J mice received either i.p. nicotine or saline during conditioning. Nicotine successfully increased time spent in context A ($p < .005$). During a final CPP test, animals received i.p. CNO to activate DREADDs prior to testing. There was no significant effect of CNO activation on time spent in the drug paired context ($p > .005$).

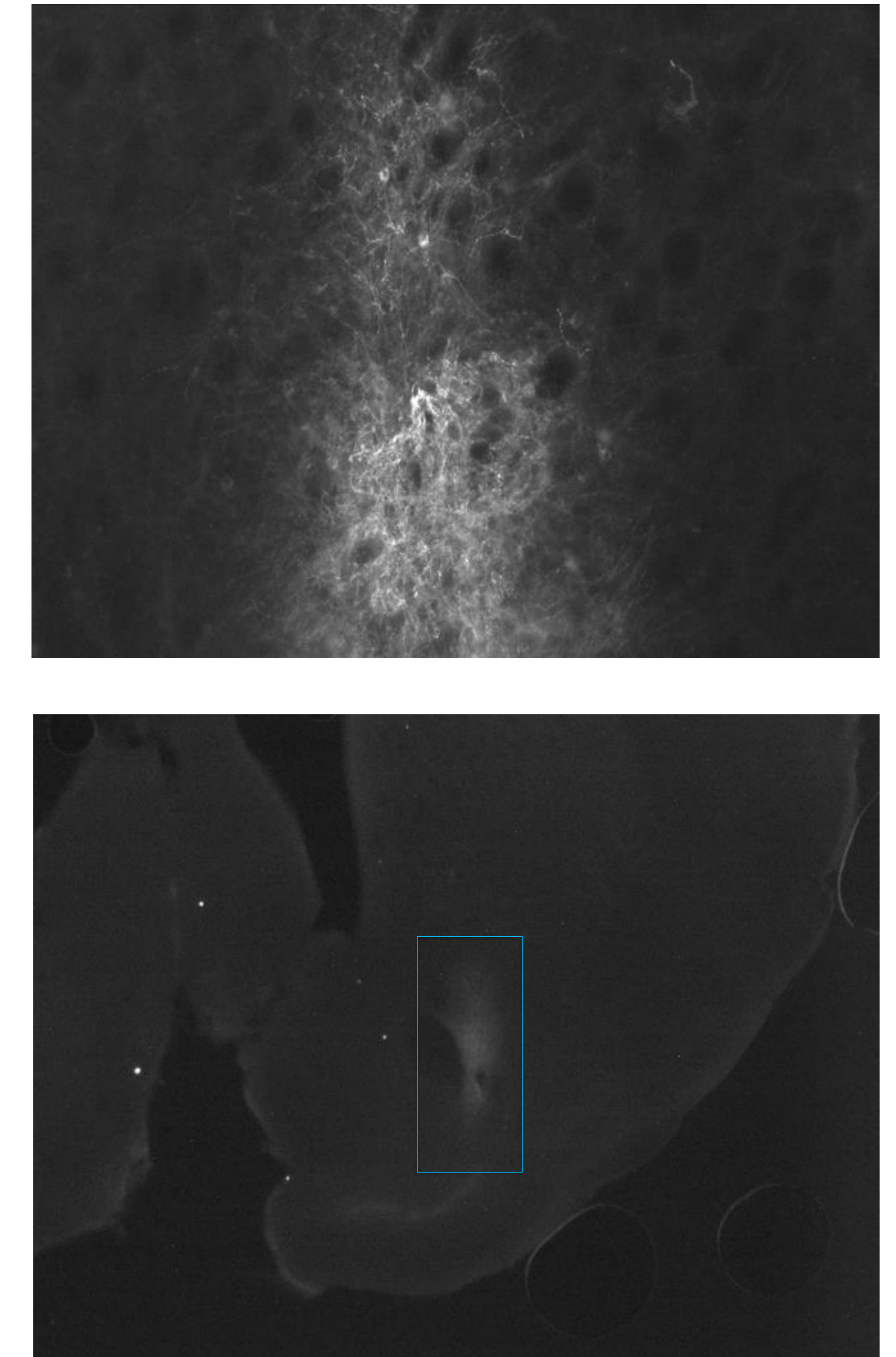


Figure 4. Viral expression of hM3Dq DREADDs in the NAc. DREADDs expression was shown in 8 out of 11 animals tested. Neurons expressing hM3Dq excitatory DREADDs are pictured at 10x magnification (top) and 2x magnification (bottom) within the NAc.

Further Research

- Successful expression of DREADDs without a concurrent behavioral change necessitates reevaluation of the activation process.
- Changes to habituation and conditioning may result in greater time spent in the drug paired context.

Acknowledgements

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References

- Abela, A. R., Li, Z., Lê, A. D., & Fletcher, P. J. (2019). Clozapine reduces nicotine self-administration, blunts reinstatement of nicotine-seeking but increases responding for food. *Addiction Biology*, 24(4), 565–576. <https://doi.org/10.1111/adb.12619>
- Calcagnetti, D. J., & Schechter, M. D. (1994). Nicotine place preference using the biased method of conditioning. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, 18(5), 925–933. [https://doi.org/10.1016/0278-5846\(94\)90108-2](https://doi.org/10.1016/0278-5846(94)90108-2)
- Grabus, S. D., Martin, B. R., Brown, S. E., & Damaj, M. I. (2006). Nicotine place preference in the mouse: Influences of prior handling, dose, and strain, and attenuation by nicotinic receptor antagonists. *Psychopharmacology*, 184(3–4), 456–463. <https://doi.org/10.1007/s00213-006-0305-7>
- Hori-Hayashi, N., & Nishi, M. (2021). Protocol for behavioral tests using chemogenetically manipulated mice. *STAR Protocols*, 2(2), 100418. <https://doi.org/10.1016/j.xpro.2021.100418>
- Salgado, S., & Kaplitt, M. G. (2015). The nucleus accumbens: A comprehensive review. *Stereotactic and Functional Neurosurgery*, 93(2), 75–93. <https://doi.org/10.1159/000368279>