



# Role of the Cortical Projections to the Caudate Putamen in Associative Learning with Nicotine in Female Rats

J. HENSLEY, T. ALLEN, R. GRZESZKIEWICZ-O'NEILL, E. RIZZO, L. WAREING, S. CHARNTIKOV

Department of Psychology, University of New Hampshire, Durham NH

## Introduction

- Nicotine addiction: global health crisis resulting in 8 million deaths and 1.4 trillion USD of costs each year (WHO).
  - Limited interventions due to gaps in knowledge on mechanisms
  - Significant treatment obstacle in nicotine addiction: behaviorally reinforcing properties
  - Aim: investigate how a specific neural pathway plays a role in nicotine-associated learning
- Hypothesis:** inhibition of the corticostriatal pathway projecting from the prefrontal cortex to the dorsomedial caudate-putamen will result in decreased goal-tracking behaviors associated with nicotine.

## Methods

**Training:** Rats (n=24) were trained to self-administer nicotine and retrieve a sucrose solution from a dipper.

- 4 phases: magazine training, autoshaping, lever training, self-administration

**Surgery:** performed between sets of lever training sessions for pathway inhibition and nicotine delivery abilities.

1. Stereotaxic surgery to inject Designer Receptors Activated by Designer Drugs (DREADDs) or saline into the pathway
2. Implantation of IV catheter for nicotine delivery

**Testing:** Inhibition of corticostriatal pathway before nicotine self-administration sessions.

- CNO (DD) administered pre session for pathway inhibition
- Latin-square design used for dose assignment (0, 1, 3, 9 mg/kg)
- Dipper entry count and duration was measured to quantify goal-tracking behavior

**Immunohistochemistry (IHC):** procedure adapted from Falcy et al. (2020) used to visualize DREADDs receptors.

- Brain tissues were cryosectioned and stained using mCherry
- Imaging with a Nikon A1R HD confocal microscope used to confirm DREADDs placement and expression (Figure 1)

A portion of this study phase is still ongoing.

## Results

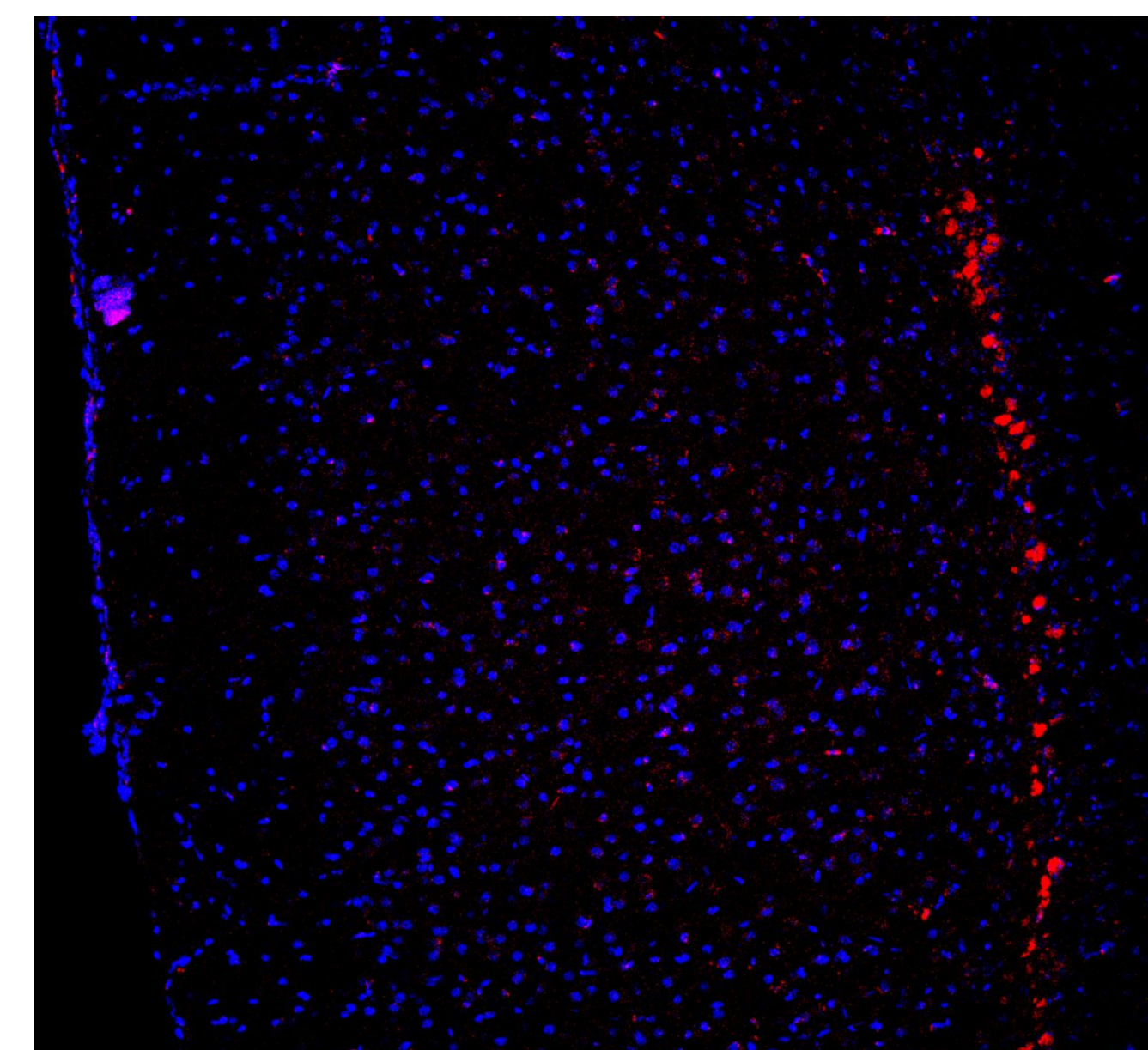


Figure 1. An image of a pre-frontal cortex section, showing cell bodies in blue and DREADDs at an injection site in red.

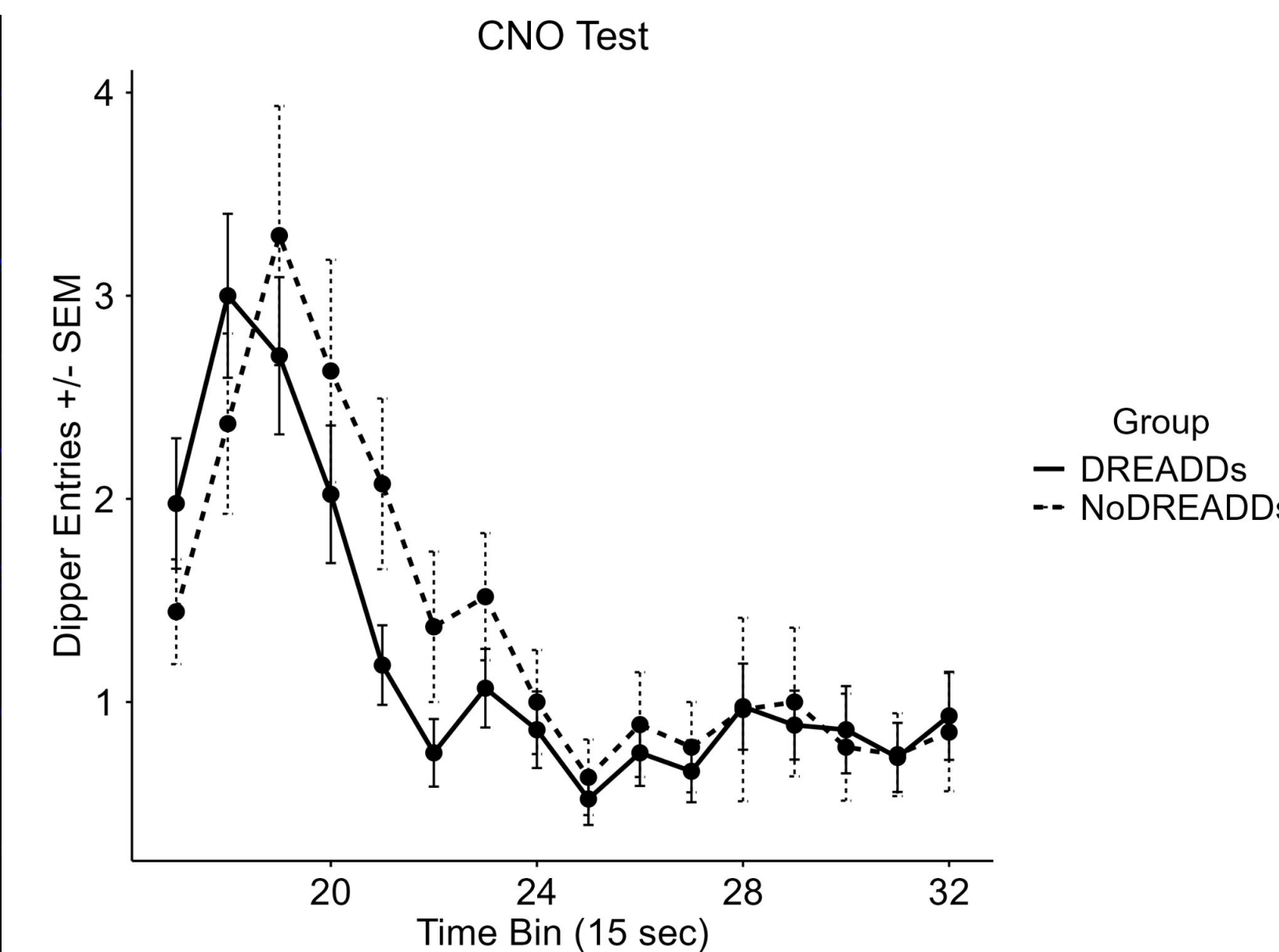


Figure 2. Performance of each group (saline control vs DREADDs) on self-administration during CNO testing

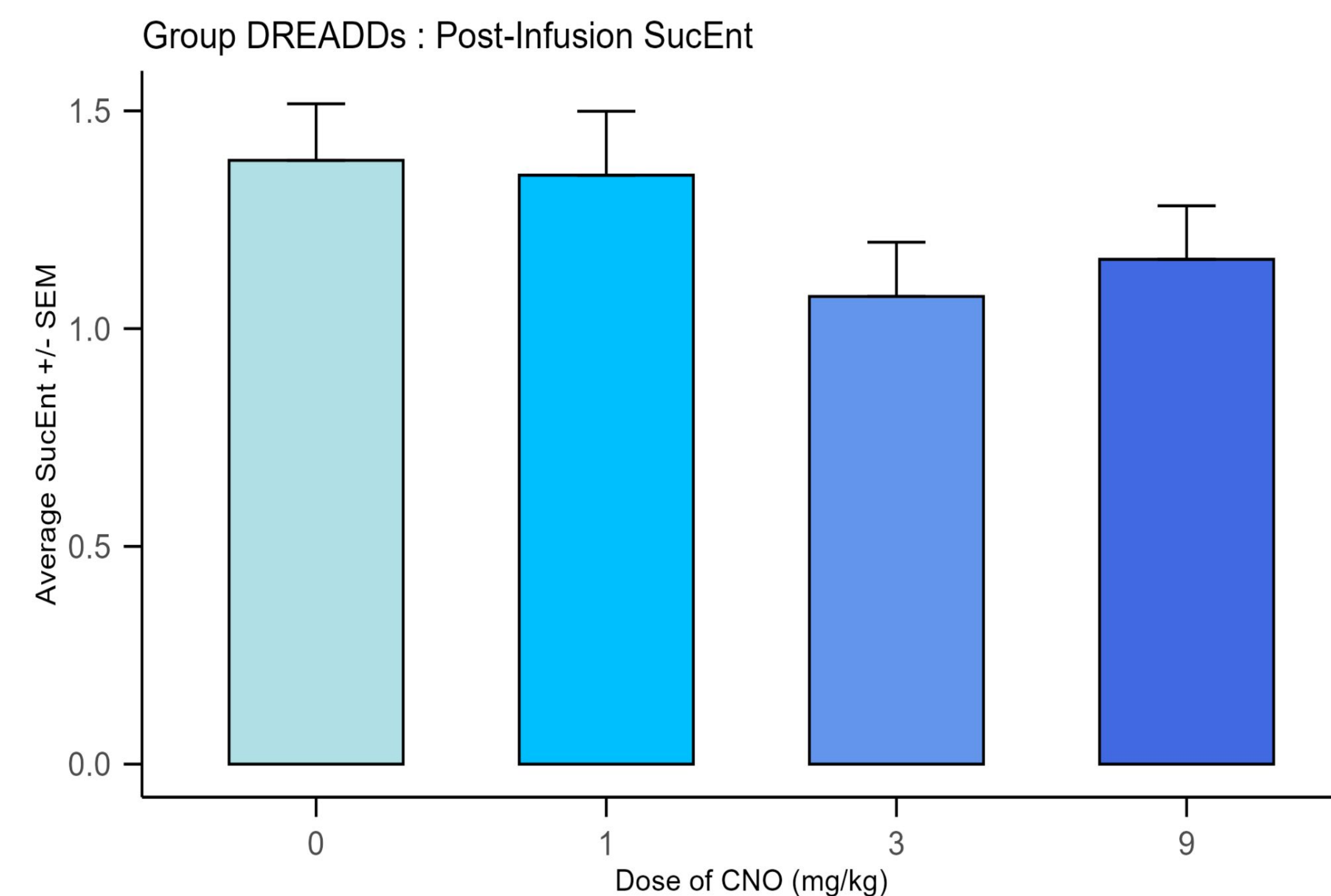


Figure 3. Number of sucrose dipper entries by dose of CNO in the DREADDs group

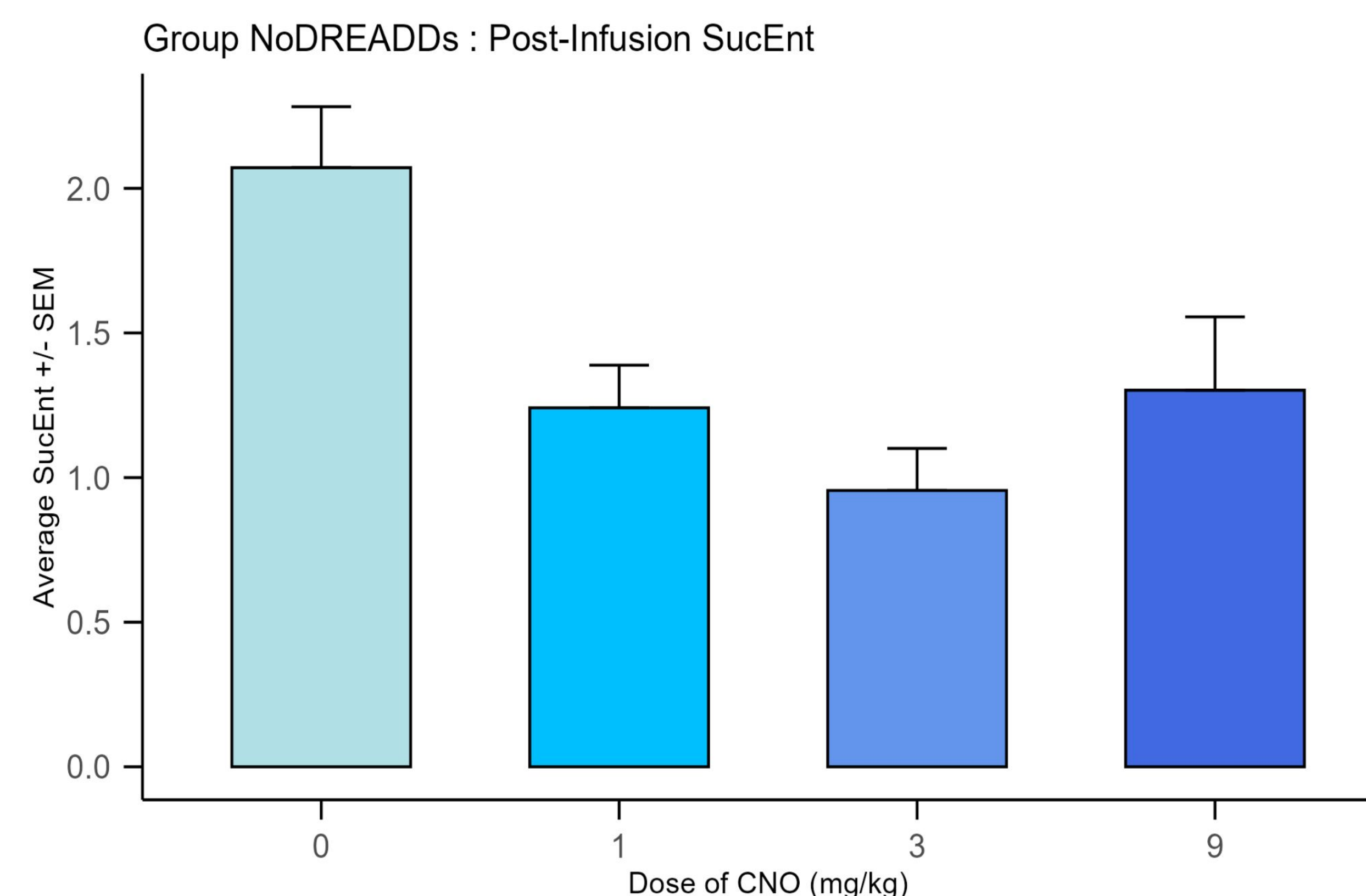


Figure 4. Number of sucrose dipper entries by dose of CNO in the saline control group

## Discussion

- Inhibition of the dmCPU does not appear to decrease nicotine-associated goal-tracking. Results are currently considered inconclusive.
- 6 rats withdrawn from results based on exclusion criteria, lowering statistical power
  - In-progress status of IHC limits interpretation
  - Results may yield different findings once combined in larger dataset including other project iterations
  - Current display of similar (non-significant) trends in the treatment and control group indicate that behavioral changes may be due to non-specific effects of CNO rather than DREADDs manipulation (Figure 2, 3, 4)

## Acknowledgements

My work on this project was funded by a Summer Undergraduate Research Fellowship (SURF) award, which was supported by the generosity of the late Dana Hamel.

Research reported in this publication was supported by the University of New Hampshire's Center for Integrated Biomedical and Bioengineering Research (CIBBR) through a grant from the National Institute of General Medical Sciences of the National Institutes of Health under Award Number P20GM113131.

## References

Falcy, B. A., Mohr, M. A., & Micevych, P. E. (2020). Immunohistochemical amplification of mCherry fusion protein is necessary for proper visualization. *MethodsX*, 7, 100946. <https://doi.org/10.1016/j.mex.2020.100946>

World Health Organization. (2023, July 31). Tobacco. <https://www.who.int/news-room/fact-sheets/detail/tobacco>