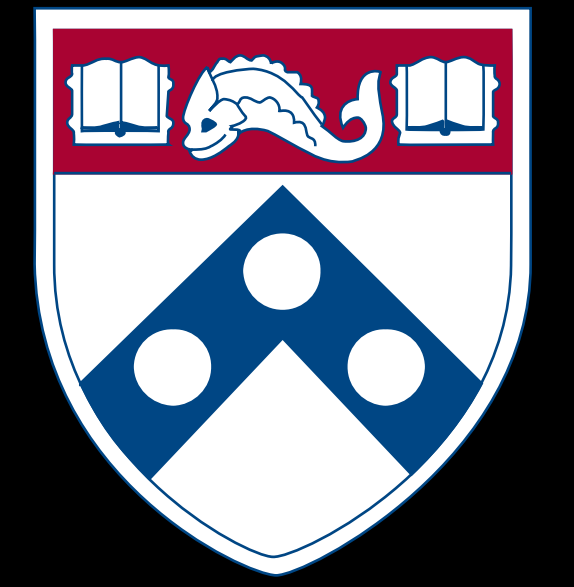


Characterizing the Efficacy of a GLP-1R Agonist to Reduce Cocaine Seeking in Female Rats



Austin Pothikamjorn^{1,2,3}, Suraj Neelamagam^{2,3}, Riley Merkel^{2,3}, and Heath D. Schmidt^{2,3}

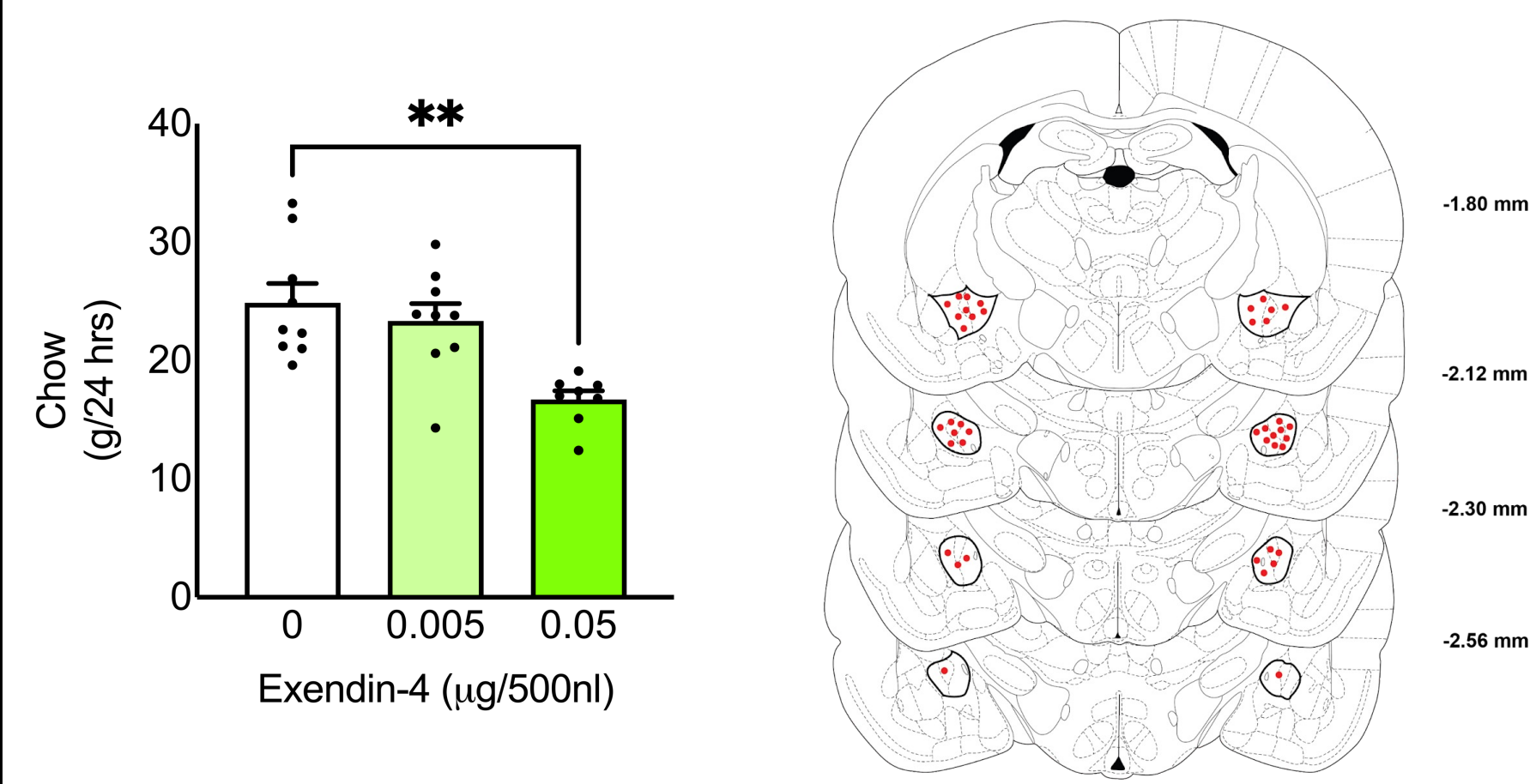
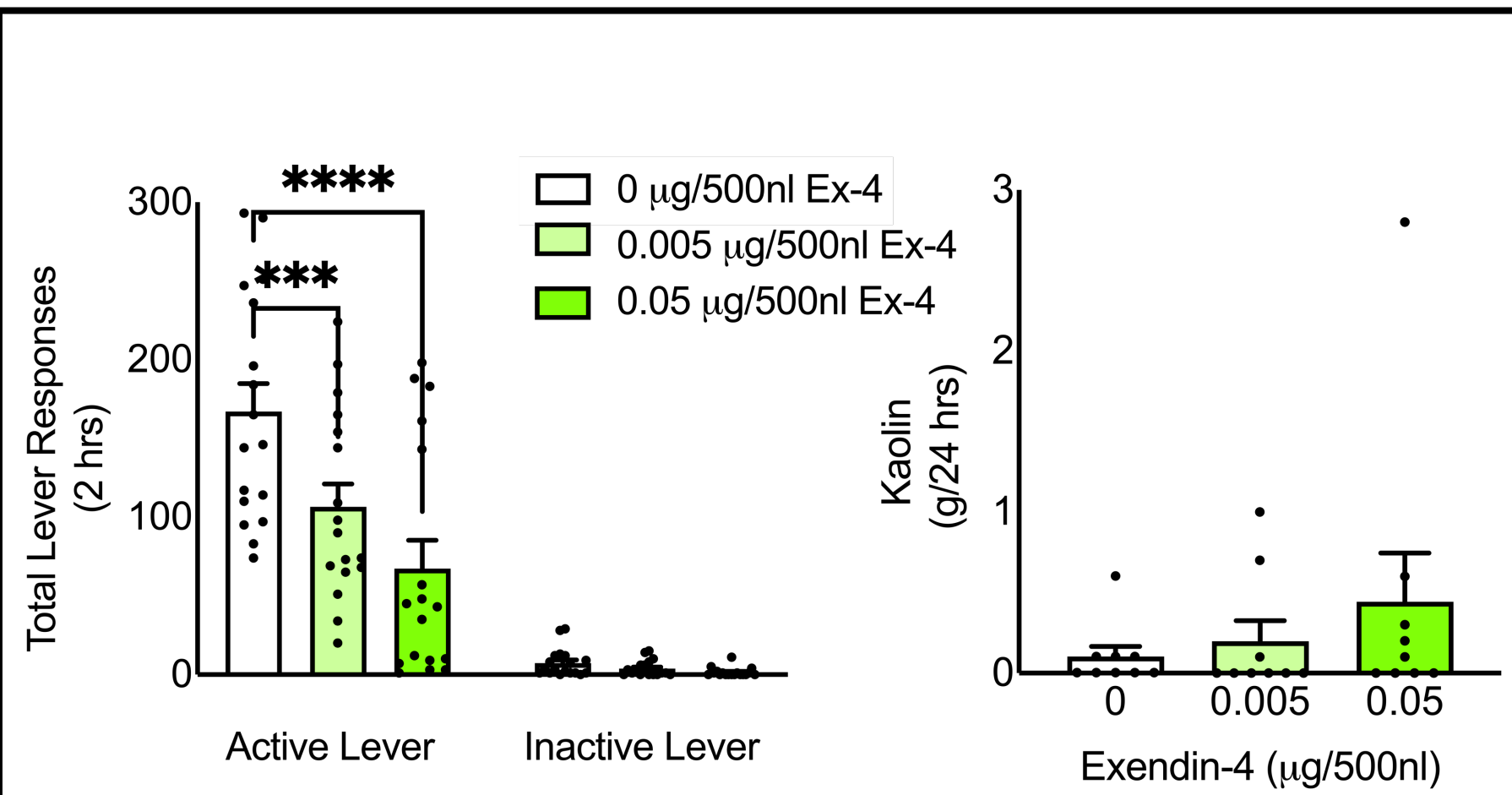
¹Department of Neuroscience, College of Arts and Sciences (2025); ²Department of Biobehavioral Health Sciences, School of Nursing; ³Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA

INTRODUCTION

- There are no FDA-approved pharmacotherapies to treat cocaine use disorder (CUD)¹.
- Intra-central amygdala (CeA) injection of the glucagon-like peptide-1 receptor (GLP-1R) agonist exendin-4 (Ex-4) attenuates cocaine reinstatement in male rats.
- However, the efficacy of GLP-1R agonists in the CeA to reduce cocaine seeking in female rats remains to be determined.
- Emerging literature highlights important sex differences in preclinical and clinical studies of CUD^{2,3}, including lower membrane capacity in GLP-1R-expressing CeA neurons in female mice⁴, suggesting potential influence on GLP-1R agonist efficacy.
- This study aimed to identify effective doses of Ex-4 that reduce cocaine seeking and are well-tolerated in female rats.

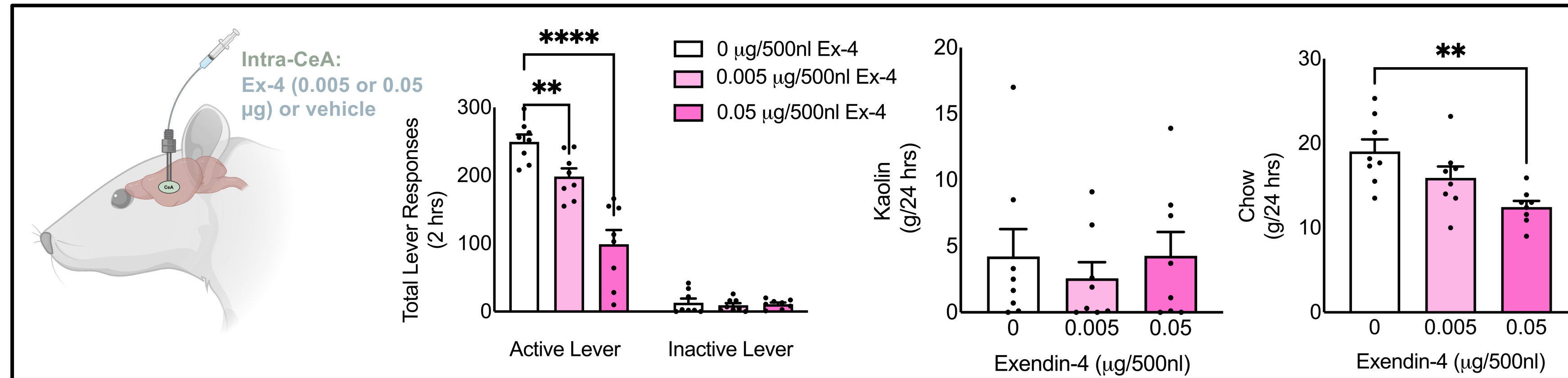
PRELIMINARY FINDINGS

Activation of GLP-1Rs in the CeA attenuates cocaine reinstatement at doses that do not affect food intake or produce pica in male rats

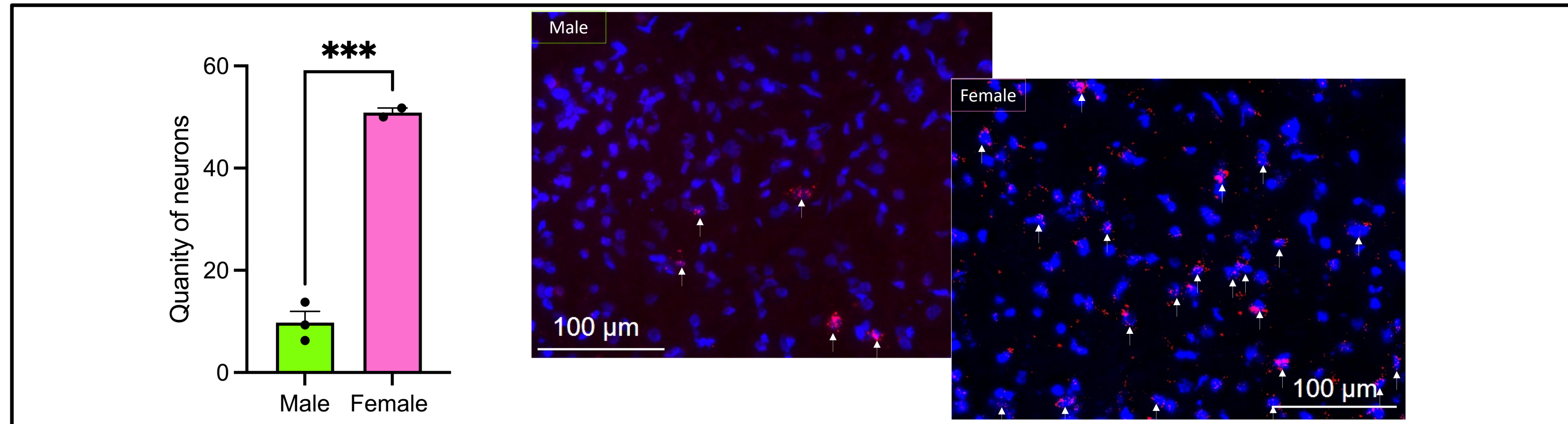


METHODS & RESULTS

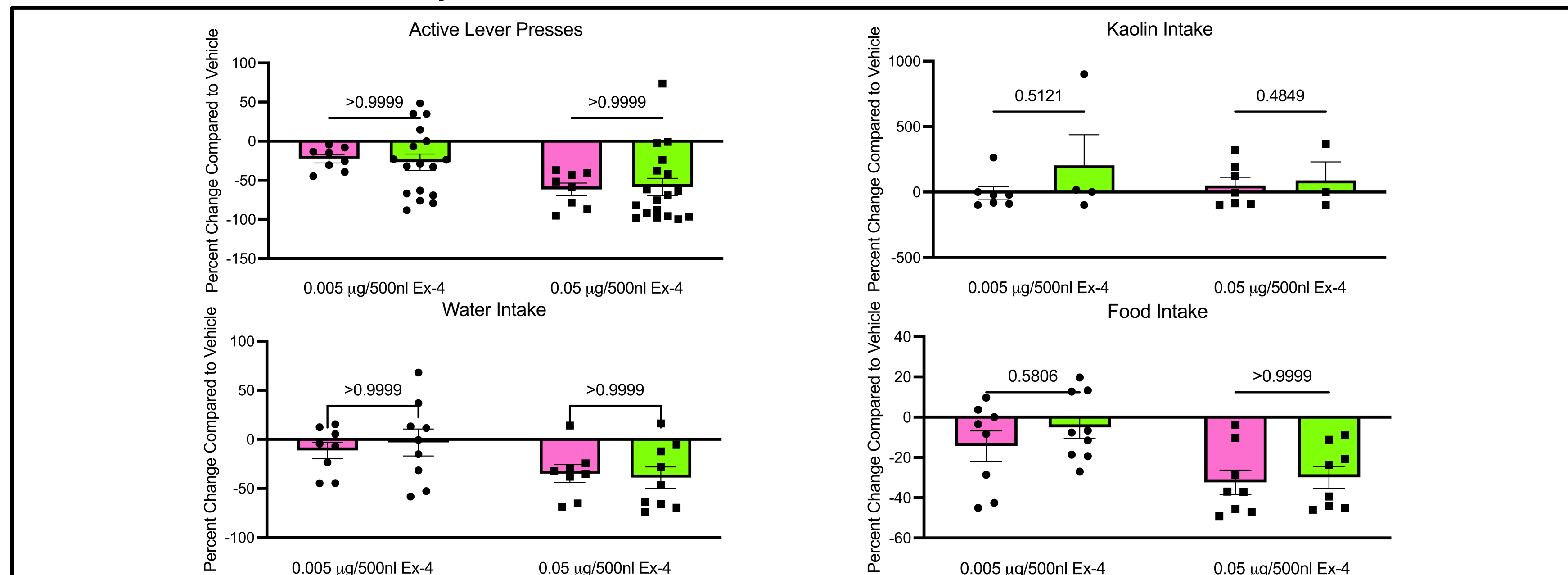
Activation of GLP-1Rs in the CeA attenuates cocaine reinstatement at doses that do not affect food intake or produce pica in female rats



Female rats have more GLP-1R-expressing neurons in the CeA



Exendin-4 produces similar behavioral effects in male and female rats

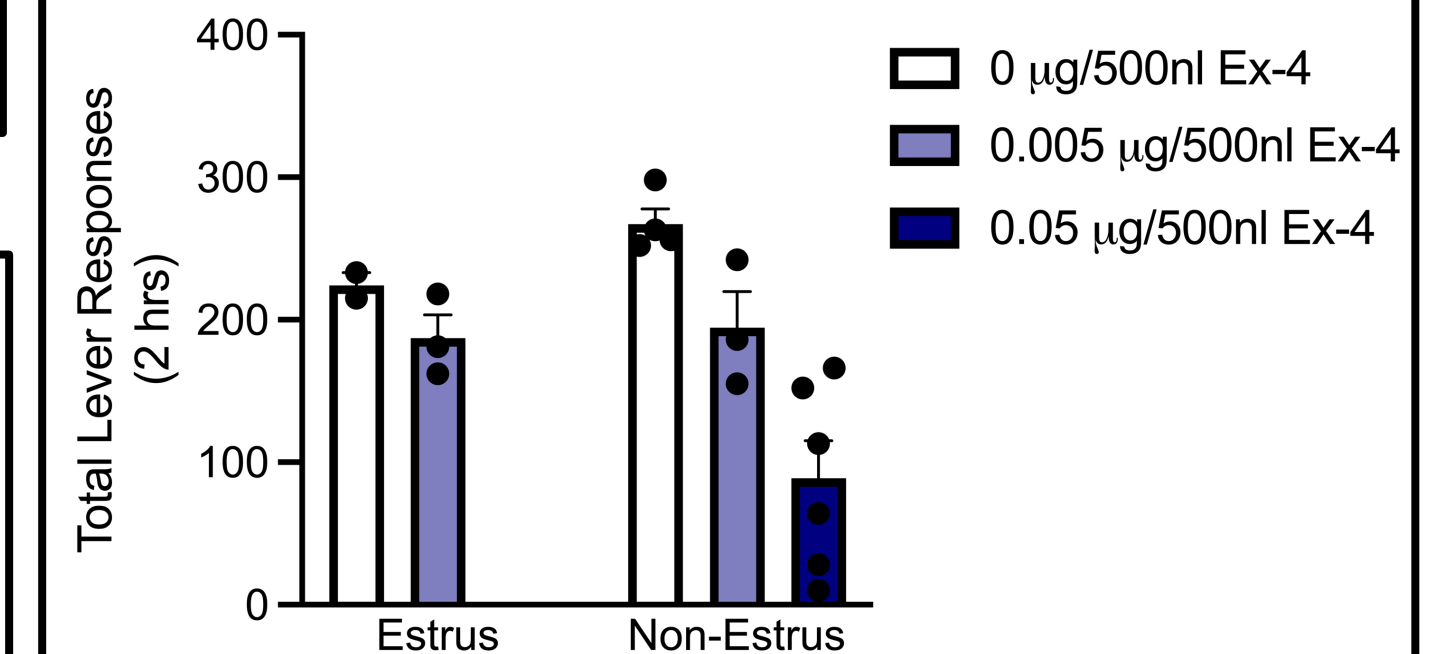


SUMMARY

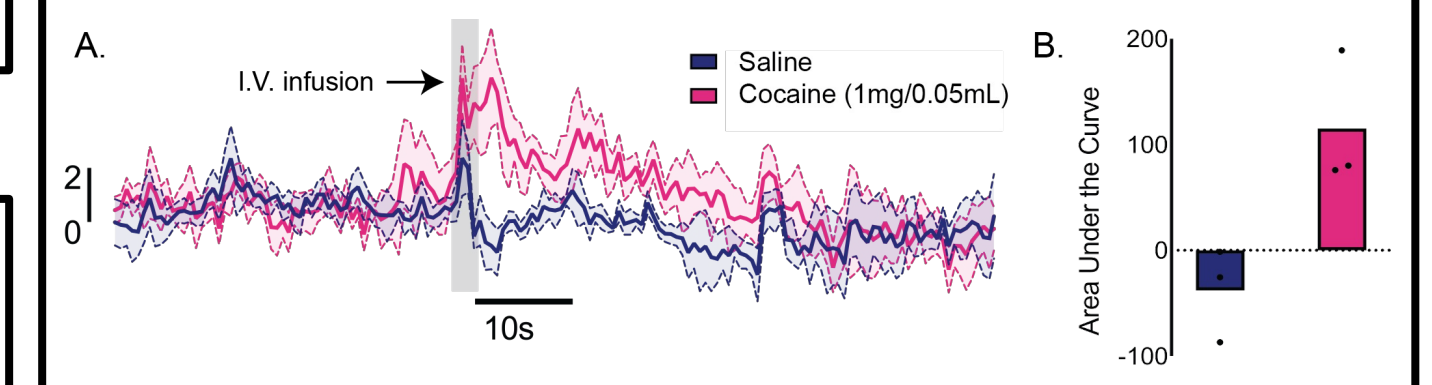
- Activating CeA GLP-1Rs reduced cocaine seeking in both female and male rats during reinstatement
- There are a greater number of GLP-1R-expressing neurons in the CeA of female rats

Future Directions

- RNA sequencing to further characterize and explore potential differences between sexes in CeA GLP-1R-expressing neuron subpopulations
- Explore the potential effects of female estrous cycles on the efficacy of Ex-4



- Use fiber photometry to determine how GLP-1R activation via Ex-4 alters CeA neuron dynamics to reduce cocaine seeking
→ Preliminary studies indicate that cocaine increases activity of CeA GABA neurons



REFERENCES

- Kampman K. M. (2019), *Science Advances*. 5(10).
- Becker, J. B., & Koob, G. F. (2016). *Pharmacological Reviews*, 68(2), 242–263.
- Radke, A. K., Sneddon, E. A., & Monroe, S. C. (2021). *Current Protocols*, 1(4), e119.
- Zeng N., et al. (2021), *Frontiers in Behavioral Neuroscience*. 15, 724030.

ACKNOWLEDGEMENTS

I would like to express my gratitude to my advisor Dr. Heath D. Schmidt, Riley Merkel, and everyone at the Schmidt Lab for their invaluable guidance and unwavering support. I would also like to thank the Ernest M. Brown, Jr. College Alumni Society Undergraduate Research Grant and CURF for funding my research.