

Binghamton University

The Open Repository @ Binghamton (The ORB)

Research Days Posters Spring 2020

Division of Research

2020

Neonatal Clomipramine Rat Model of Obsessive Compulsive Disorder (OCD) Demonstrates Neurochemical Differences in Prefrontal and Motor Cortices and Behavioral Differences in Elevated Plus Maze and Hole Board

Rebecca Nussbaum

Binghamton University--SUNY

Maylin Vititow

Binghamton University--SUNY

Juan Mato

Binghamton University--SUNY

Kristen Coletti

Binghamton University--SUNY

Dana Silberstein

Binghamton University--SUNY

Follow this and additional works at: https://orb.binghamton.edu/research_days_posters_spring2020

Recommended Citation

Nussbaum, Rebecca; Vititow, Maylin; Mato, Juan; Coletti, Kristen; and Silberstein, Dana, "Neonatal Clomipramine Rat Model of Obsessive Compulsive Disorder (OCD) Demonstrates Neurochemical Differences in Prefrontal and Motor Cortices and Behavioral Differences in Elevated Plus Maze and Hole Board" (2020). *Research Days Posters Spring 2020*. 60.

https://orb.binghamton.edu/research_days_posters_spring2020/60

This Book is brought to you for free and open access by the Division of Research at The Open Repository @ Binghamton (The ORB). It has been accepted for inclusion in Research Days Posters Spring 2020 by an authorized administrator of The Open Repository @ Binghamton (The ORB). For more information, please contact ORB@binghamton.edu.

Neonatal Clomipramine Rat Model of Obsessive Compulsive Disorder (OCD) Demonstrates Neurochemical Differences in Prefrontal and Motor Cortices and Behavioral Differences in Elevated Plus Maze and Hole Board

Kristen Coletti, Juan Mato, Rebecca Nussbaum, Dana Silberstein, Maylin Vititow, and Dr. Deborah Kreiss
First-Year Research Immersion Program, Binghamton University, Binghamton, NY 13902

BACKGROUND

Obsessive Compulsive Disorder (OCD)- psychiatric disorder characterized by uncontrollable thoughts and maladaptive behaviors

- 2.5-3% of population diagnosed¹

Predominant Treatment- Serotonin Reuptake Inhibitors (SRIs)

- Only 40-60% of patients experience symptom attenuation after a 8-10 week period and side effects are problematic²

Current Animal Models

- A valid animal model is analogous the neurobiology, symptoms, and response to drug treatments of the human disorder
- Current animal models of OCD are lacking face and construct validities³
- The neonatal clomipramine (neoCLOM) model induces OCD-like behaviors in adulthood⁴ by altering maturation of the hypothalamic-pituitary-adrenal (HPA) axis⁵

Neurotransmitters and Brain Structures

- Patients with OCD typically have more norepinephrine (NE)⁶, and dopamine (DA)⁷ than individuals without this disorder
- OCD patients have abnormal activity in the Prefrontal Cortex (PFC)⁸ and Motor Cortex (MC)⁹

Objectives:

- Evaluate face validity of the neoCLOM model via a combination of Hole Board (HB) and Elevated Plus Maze (EPM) behaviors
- Evaluate construct validity via High Performance Liquid Chromatography analysis of monoamine concentrations in post-mortem brain tissue homogenate samples
- Assess sex differences in experimental and control rats

BEHAVIORAL METHODS

Subjects and Neonatal Injections

- 36 female and 36 male Sprague-Dawley rats received 15 mg/kg clomipramine or 0.09% saline vehicle twice per day on neonatal Days 9-16

Behavioral Testing assessed on Days 83-92

- HB: Total number of pokes and repeat pokes¹⁰
- EPM: Seconds in open arms and total arm entries¹¹

NE and DA Analysis via High Performance Liquid Chromatography (HPLC)

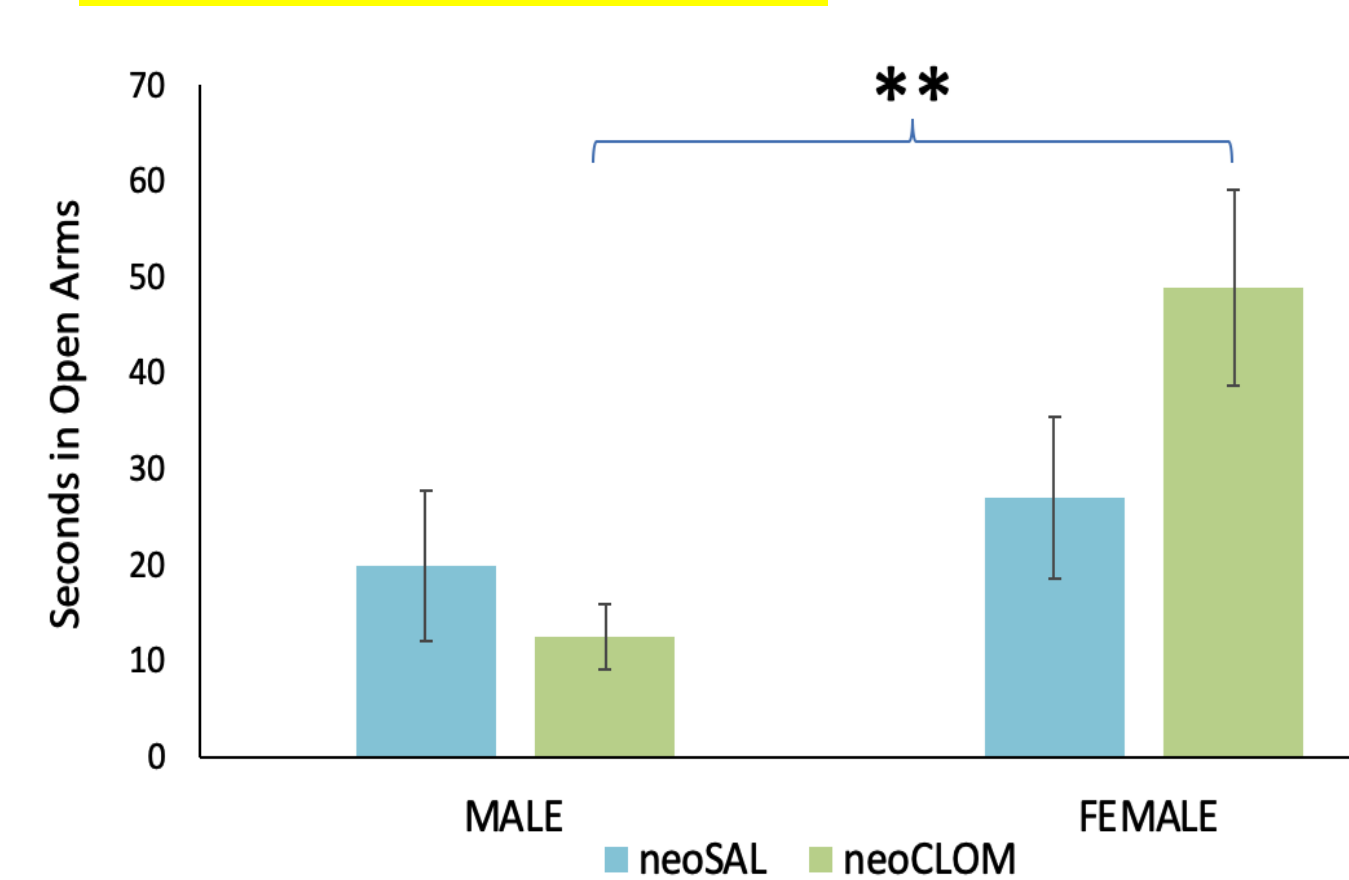
- Supernatants from tissue homogenates of micropunches were analyzed via HPLC
- PFC: 1.0 mm lateral from the midline, 2.8 mm ventral from the skull, and interaural 13.70 mm¹²
- MC: 1.5 mm lateral from the midline, 1.5 mm ventral from the skull, and interaural 8.70 mm¹²

Data Analysis

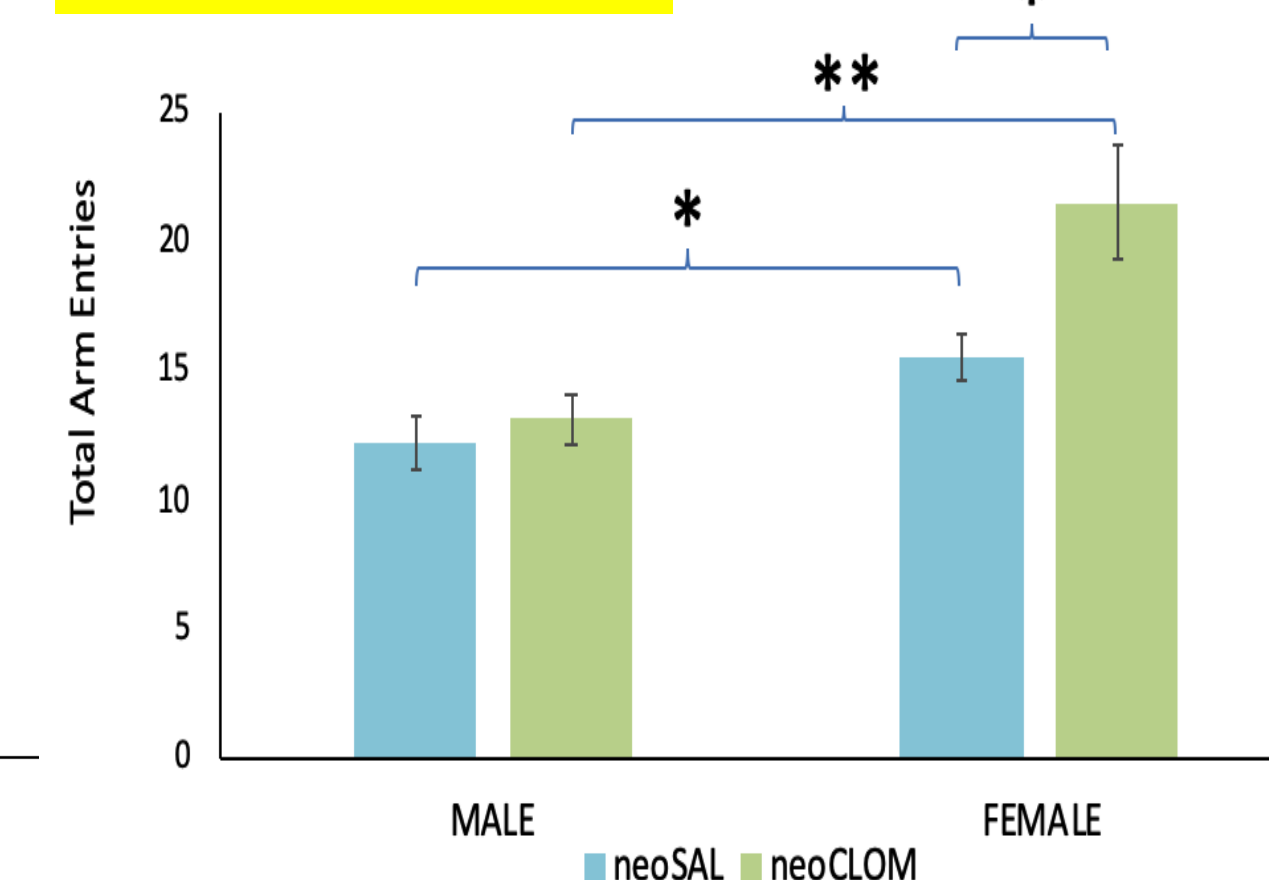
Data were expressed as mean \pm standard error of the mean (SEM). Outliers (>2.5 STD) were eliminated. Analysis was conducted using ANOVA and Student's t-test (* indicates $p < 0.05$, ** indicates $p < 0.01$, *** indicates $p < 0.001$)

RESULTS

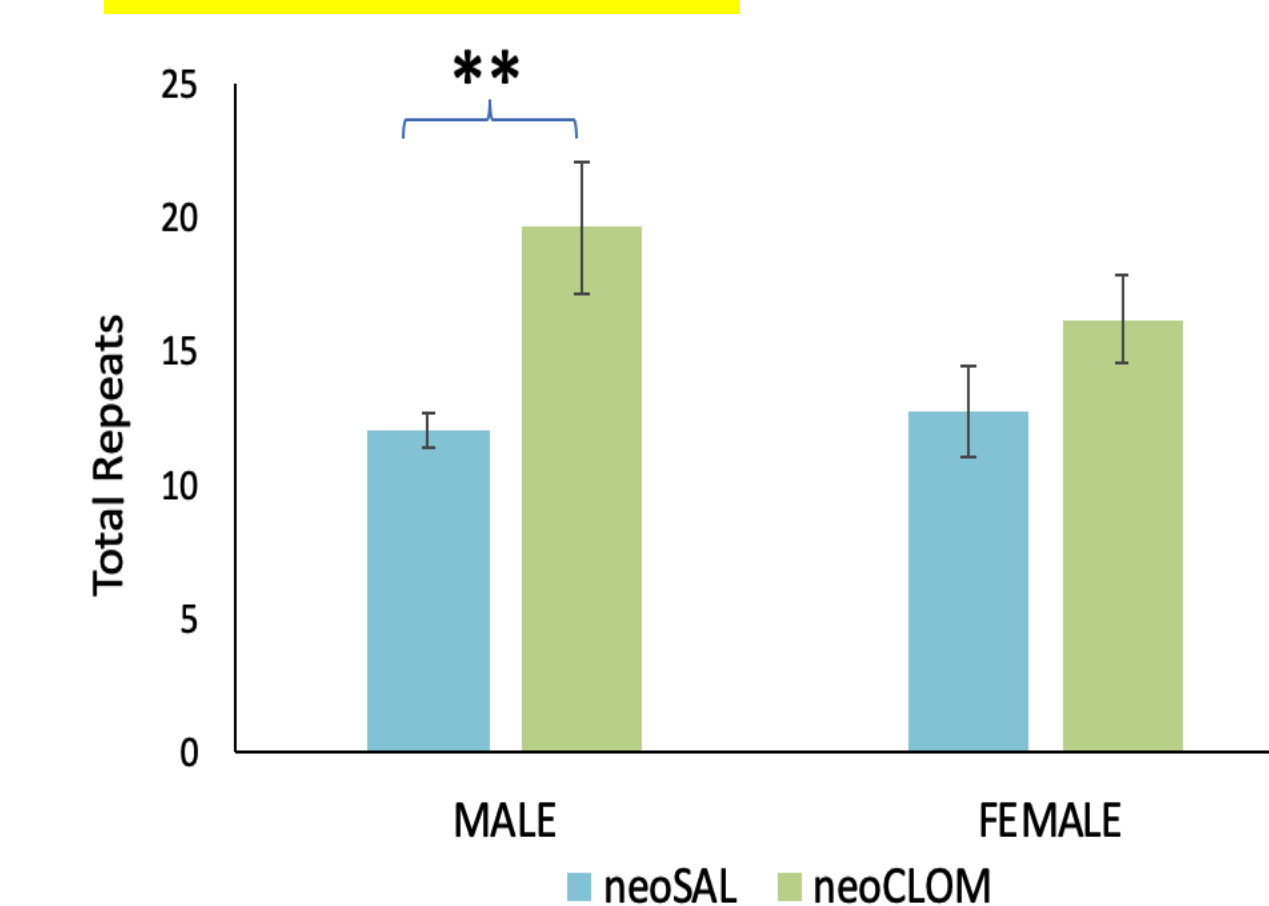
SECONDS IN OPEN ARMS



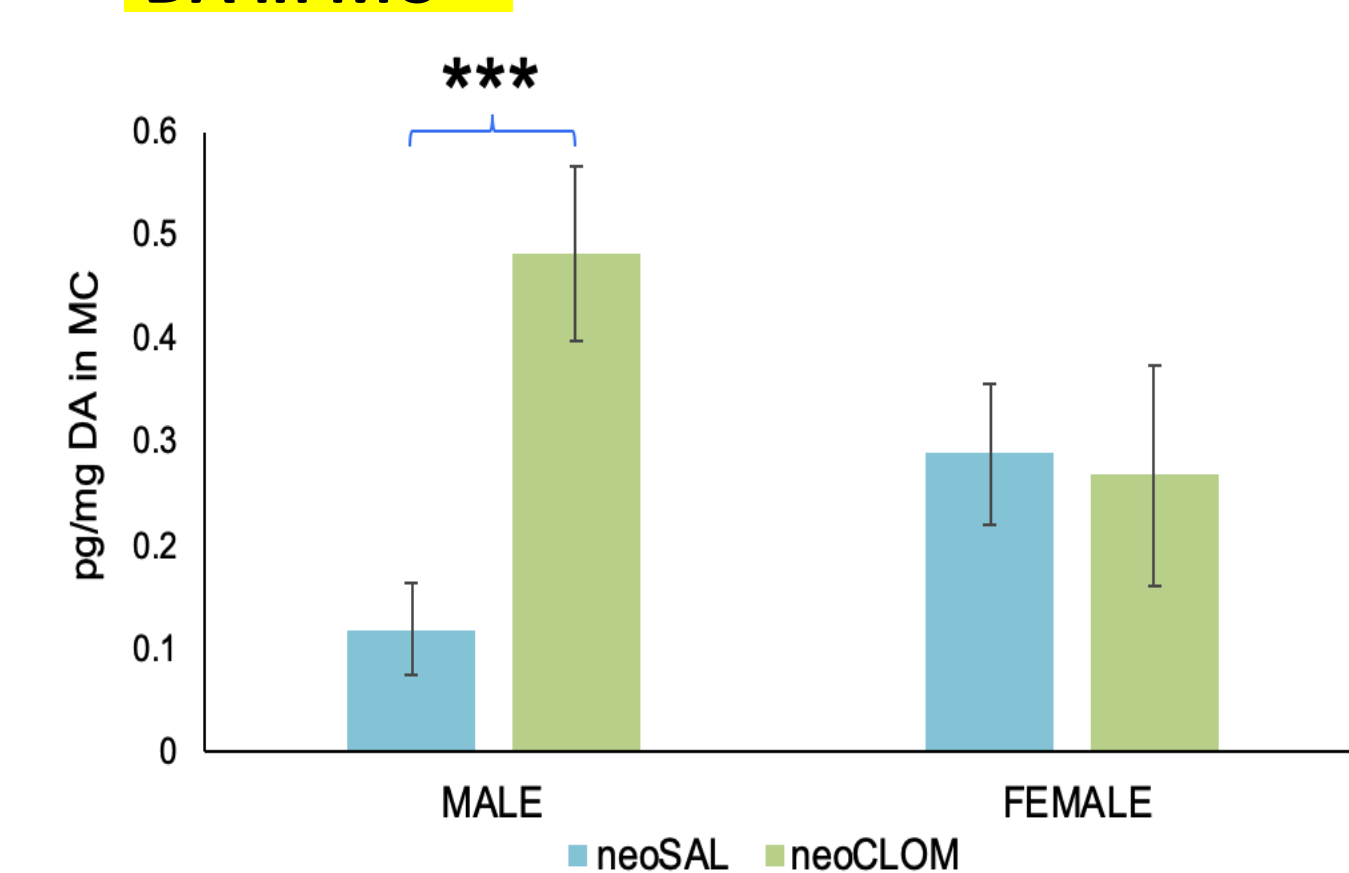
TOTAL ARM ENTRIES



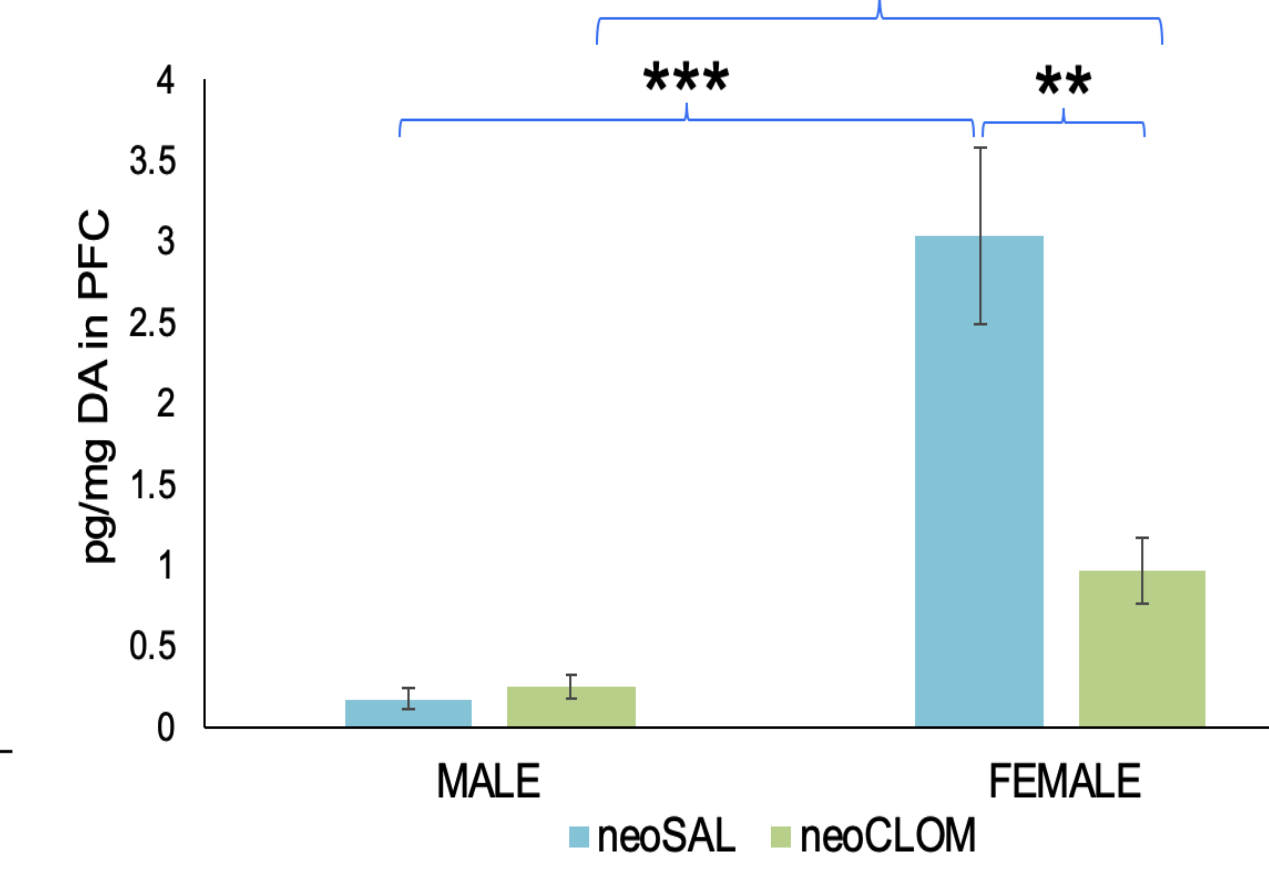
REPEAT HOLE POKES



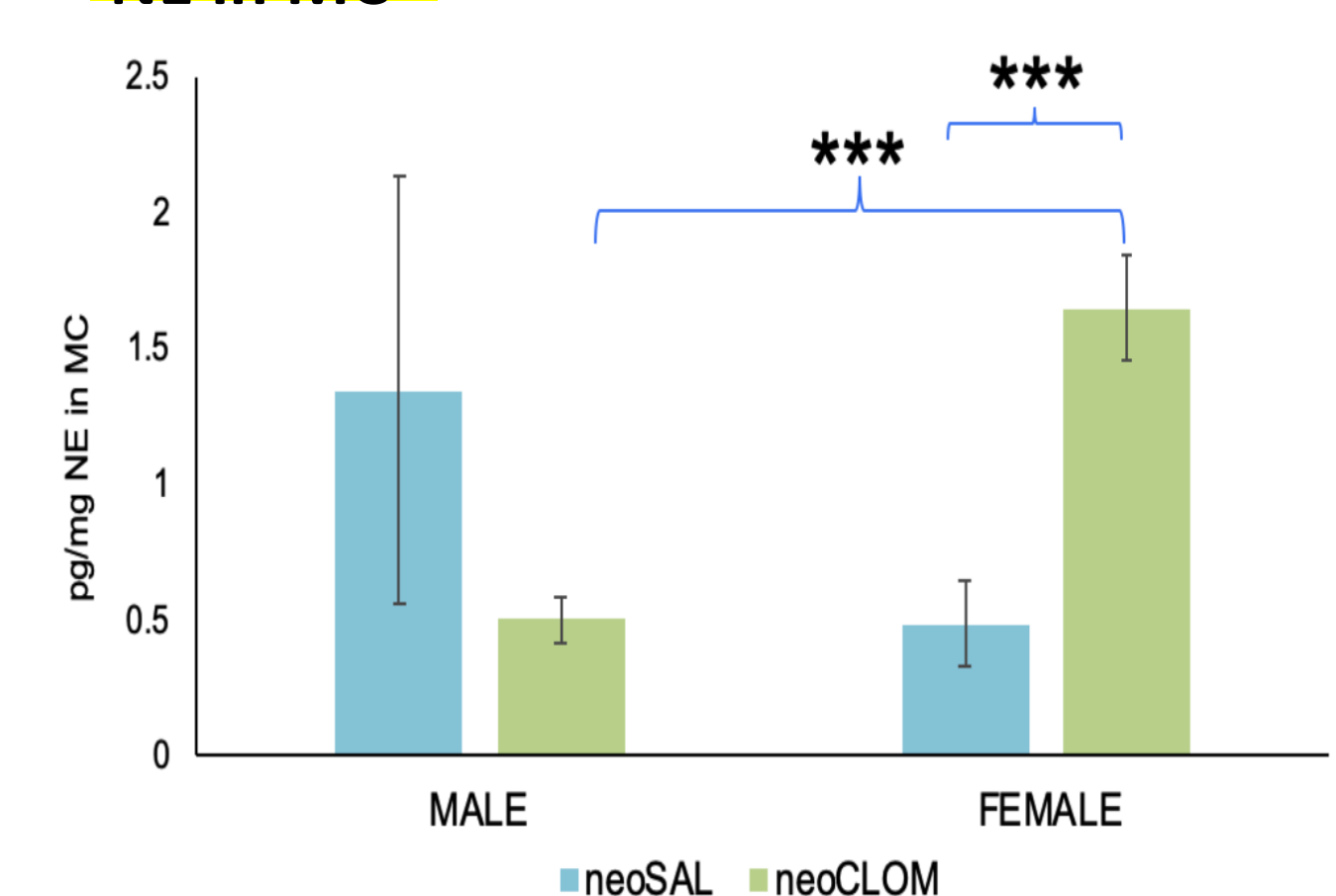
DA in MC



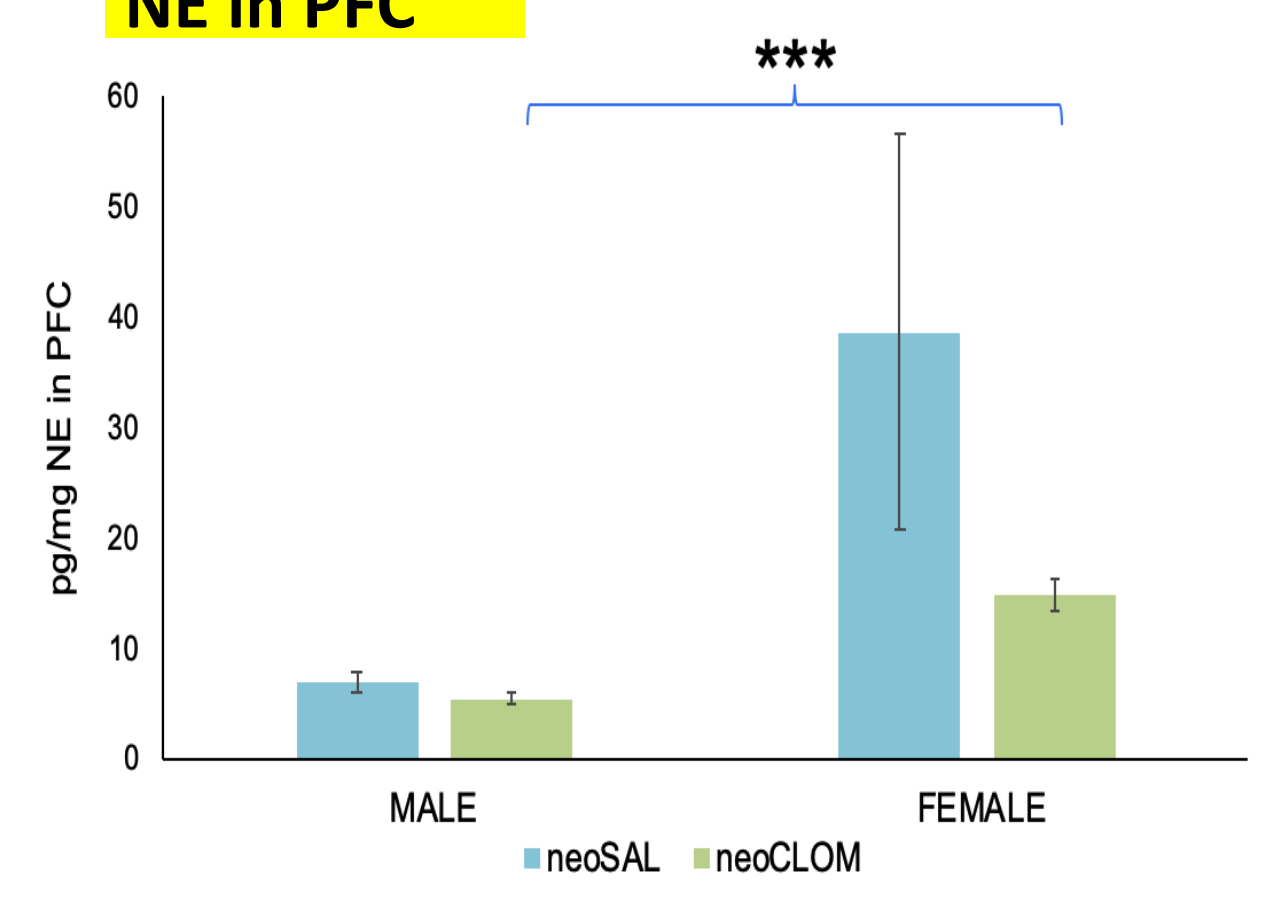
DA in PFC



NE in MC



NE in PFC



- NeoCLOM males had higher DA in the MC than neoSAL males
- NeoCLOM females had lower DA in the PFC than neoSAL females
- Female groups had higher DA in the PFC than male groups
- NeoCLOM females had higher NE in the MC than neoSAL females
- NeoCLOM females had higher NE in the MC than neoCLOM males
- NeoCLOM females had higher NE in the PFC than neoCLOM males

CONCLUSIONS

Behavioral

- Elevated Plus Maze behaviors do not support validity of neoCLOM model
- Inherent sex differences in locomotion require alternative interpretations of female behavior in the Elevated Plus Maze
- Hole Board Behaviors suggest neoCLOM model has good face validity for male rats
- Open arm and head poking behaviors assess different aspects of the rats' psychological state

Neurochemical

- Neurochemical differences in the MC support construct validity of the model
- Sex differences in NE and DA levels in the MC and PFC may underlie behavioral differences

FUTURE WORK

- Evaluation of predictive validity of the neoCLOM model
- Further evaluation of face validity using spontaneous alternation and open field tests
- Control for effect of estrous cycle

ACKNOWLEDGEMENTS

The authors would like to acknowledge the Binghamton University Laboratory Animal Resources Staff for their husbandry, the First-Year Research Immersion Program, the Binghamton University PSYC 364 class of Fall 2019, Jovannah Gerisma, Ben Morrison, Kate Lerner, Trevor Towner and Kim Papastrat for euthanization aid, and Gina Rizzo for obtaining brain punches.

REFERENCES

- Pittenger C, Kelmendi B, Bloch M, Krystal JH, & Coric V. (2005) Clinical treatment of Obsessive-Compulsive Disorder. *Psychiatry*, 2: 34-43.
- Koran LM, Mcelroy SL, Davidson JR, Rasmussen SA, Hollander E, & Jenike MA. (1996) Fluvoxamine versus clomipramine for Obsessive-Compulsive Disorder. *Journal of Clinical Psychopharmacology*, 16: 121-129.
- Willner P. (1991) Behavioural models in psychopharmacology. *Behavioural models in psychopharmacology: Theoretical, industrial and clinical perspectives* (pp. 3-18). New York, NY, US: Cambridge University Press.
- Andersen SL, Greene-Colozzi EA, & Sonntag KC. (2010) A novel, multiple symptom model of Obsessive-Compulsive-like behaviors in animals. *Biological Psychiatry*, 68: 741-747.
- Levine S. (2002) Regulation of the hypothalamic-pituitary-adrenal axis in the neonatal rat: the role of maternal behavior. *Neurotoxicity Research*, 4: 557-564.
- Vitrac C, & Benoit-Marand M. (2017) Monoaminergic modulation of motor cortex function. *Frontiers in Neural Circuits*, 11: 72.
- Harsányi A, Csizgó K, Demeter G, & Nemeth A. (2007) New approach to Obsessive-Compulsive Disorder: dopaminergic theories. *Psychiatria Hungarica*, 22: 248-258.
- Manning EE, & Ahmari SE. (2018). How can preclinical mouse models be used to gain insight into prefrontal cortex dysfunction in Obsessive-Compulsive Disorder? *Brain and Neuroscience Advances*, 2.
- Mantovani A, Rossi S, Bassi BD, Simpson HB, Fallon BA, & Lisanby SH. (2013) Modulation of motor cortex excitability in Obsessive-Compulsive Disorder: an exploratory study on the relations of neurophysiology measures with clinical outcome. *Psychiatry Research*, 210: 1026-1032.
- Brown GR, & Nemes C. (2008) The exploratory behaviour of rats in the hole-board apparatus: Is head-dipping a valid measure of neophilia? *Behavioural Processes*, 78: 442-448.
- Walf AA, & Frye CA. (2007) The use of the elevated plus maze as an assay of anxiety-related behavior in rodents. *Nature Protocols*, 2: 322-328.
- Paxinos G, & Watson C. (1986) *The Rat Brain in Stereotaxic Coordinates*: second edition. Academic press, INC, New York.

