

Binghamton University

The Open Repository @ Binghamton (The ORB)

Research Days Posters Spring 2020

Division of Research

2020

Neonatal Clomipramine Model of Obsessive-Compulsive Disorder (OCD) Demonstrates Treatment and Sex Differences

Allison Radin

Binghamton University--SUNY

Lenah Midani

Binghamton University--SUNY

Samantha Paley

Binghamton University--SUNY

Eliana Safer

Binghamton University--SUNY

Emily Walters

Binghamton University--SUNY

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

Recommended Citation

Radin, Allison; Midani, Lenah; Paley, Samantha; Safer, Eliana; and Walters, Emily, "Neonatal Clomipramine Model of Obsessive-Compulsive Disorder (OCD) Demonstrates Treatment and Sex Differences" (2020). *Research Days Posters Spring 2020*. 72.

https://orb.binghamton.edu/research_days_posters_spring2020/72

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.

INTRODUCTION

- Obsessive-compulsive disorder (OCD)
 - Affects both sexes equally¹
 - Characterized by repetitive, uncontrollable thoughts and actions
- Current treatments
 - Serotonin reuptake inhibitors (SRIs)
 - Ineffective for 40-60% of patients²
 - Delay in onset, severe side-effects²
- Importance of animal models
 - Ethical and practical benefits
 - No universally accepted model
 - Face and construct validities used to evaluate animal models³
- Neonatal clomipramine (neoCLOM) model⁴
 - Rats treated with clomipramine from Day 9-16
 - Lifelong behavioral and neurochemical alterations
- Etiology of OCD: Neurotransmitters and structures
 - Amygdala (AMY): Hyperactive fear response of the limbic system⁵
 - Hypothalamus (HYP): Hyperactive hypothalamic-pituitary-adrenal gland⁶
 - Elevated levels of norepinephrine (NE) and dopamine (DA)^{7,8}
 - Lower levels of serotonin (5-HT)⁹

OBJECTIVE

Evaluate the face and construct validity of the neoCLOM model of OCD by analyzing elevated plus maze and hole board behaviors and neurochemical analysis of DA, NE, and 5-HT concentrations in post-mortem tissue homogenates of the HYP and AMY using high performance liquid chromatography.

METHODS

Neonatal injections:

- 36 male and 36 female Sprague-Dawley rats
- Clomipramine was dissolved in 0.9% NaCl at 15 mg/mL and injected intraperitoneally twice daily at 15 mg/kg body weight

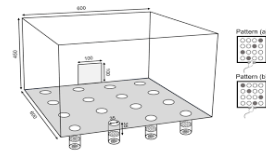


Figure 1. Hole Board

Behavioral Trials: Took place on Days 83-92

Hole board (HB, Figure 1):

- Clear plexiglass arena had 16 evenly spaced holes in the floor
- Hole poke defined as when the rat's nose cleared the maze bottom and ended when nose went above hole¹⁰



Figure 2. Elevated Plus Maze

Elevated plus maze (EPM, Figure 2):

- 2 closed and 2 open arms in a plus shape
- Arm entry scored when 3 paws crossed into arm¹¹

Tissue Extraction (Figure 3): Punches 2-2.5 mm diameter and 1-1.5 mm deep obtained on Days 87-93.

- Amygdala (AMY): ML 4.8 mm lateral from midline, DV 8.6 mm ventral of skull, and interaural 6.20 mm¹²
- Hypothalamus (HYP): ML 0.6 mm lateral from midline, DV 10 mm ventral of skull, and interaural 6.20 mm¹²

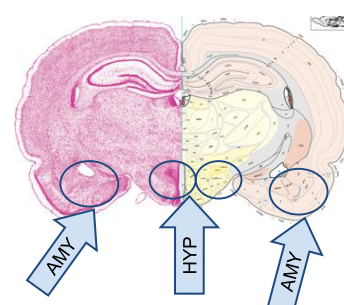


Figure 3. Location of Tissue Punches

Tissue Analysis (Figure 4):

- Samples weighed, homogenized and centrifuged for 45 mins at 14,000 rpm at 4°C temp. Results expressed as pg/mg brain tissue. Samples analyzed using High Performance Liquid Chromatography.

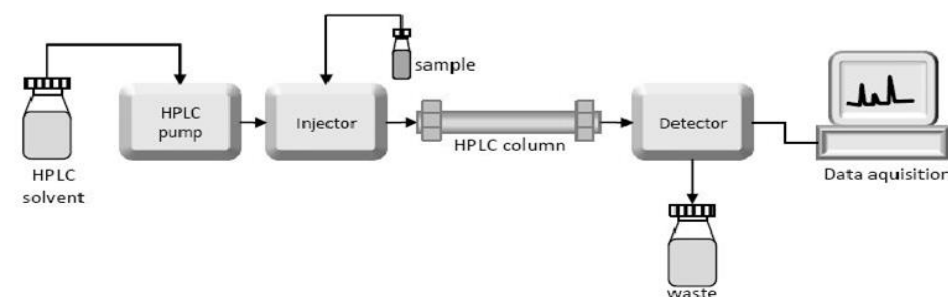
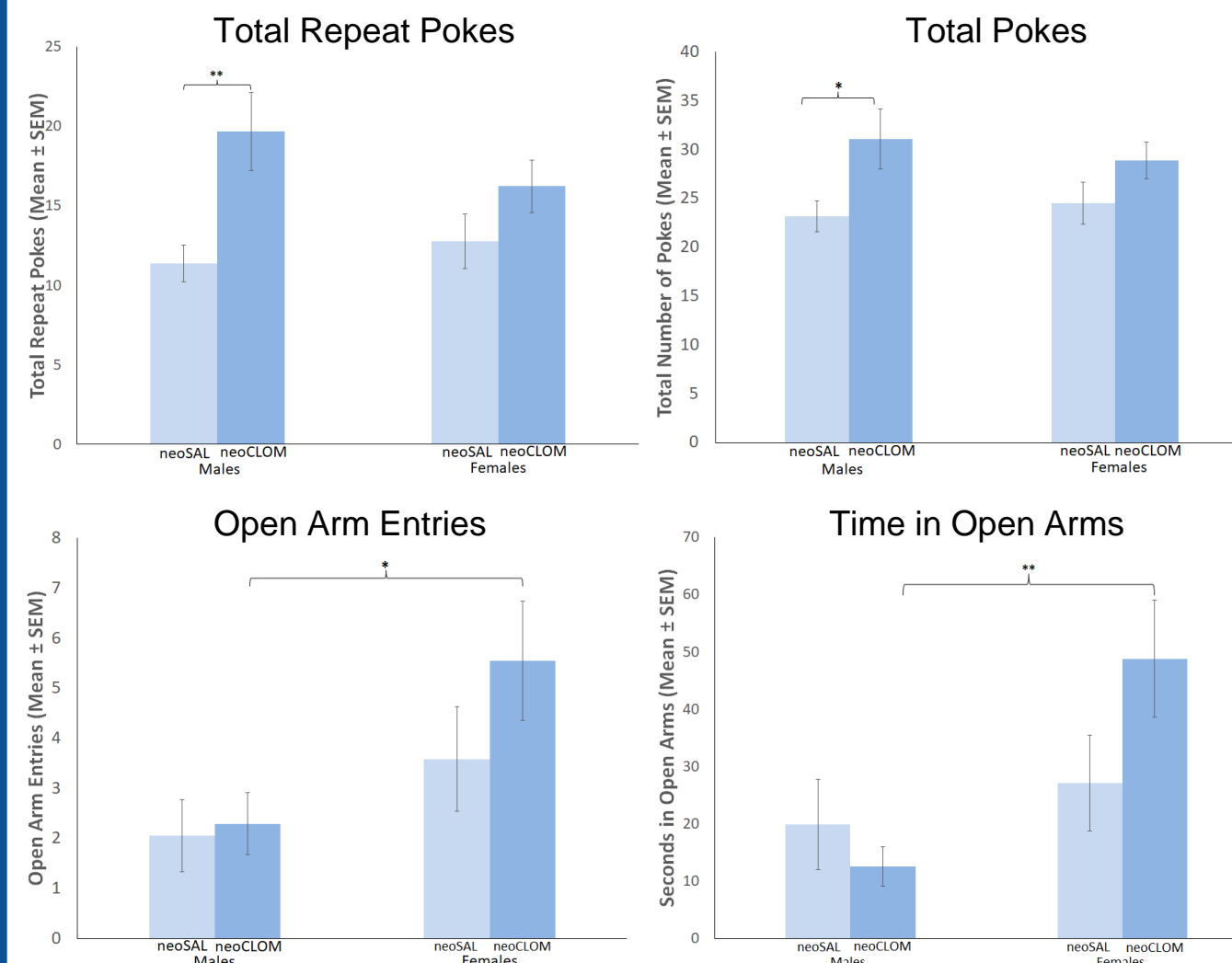


Figure 4. High Performance Liquid Chromatography

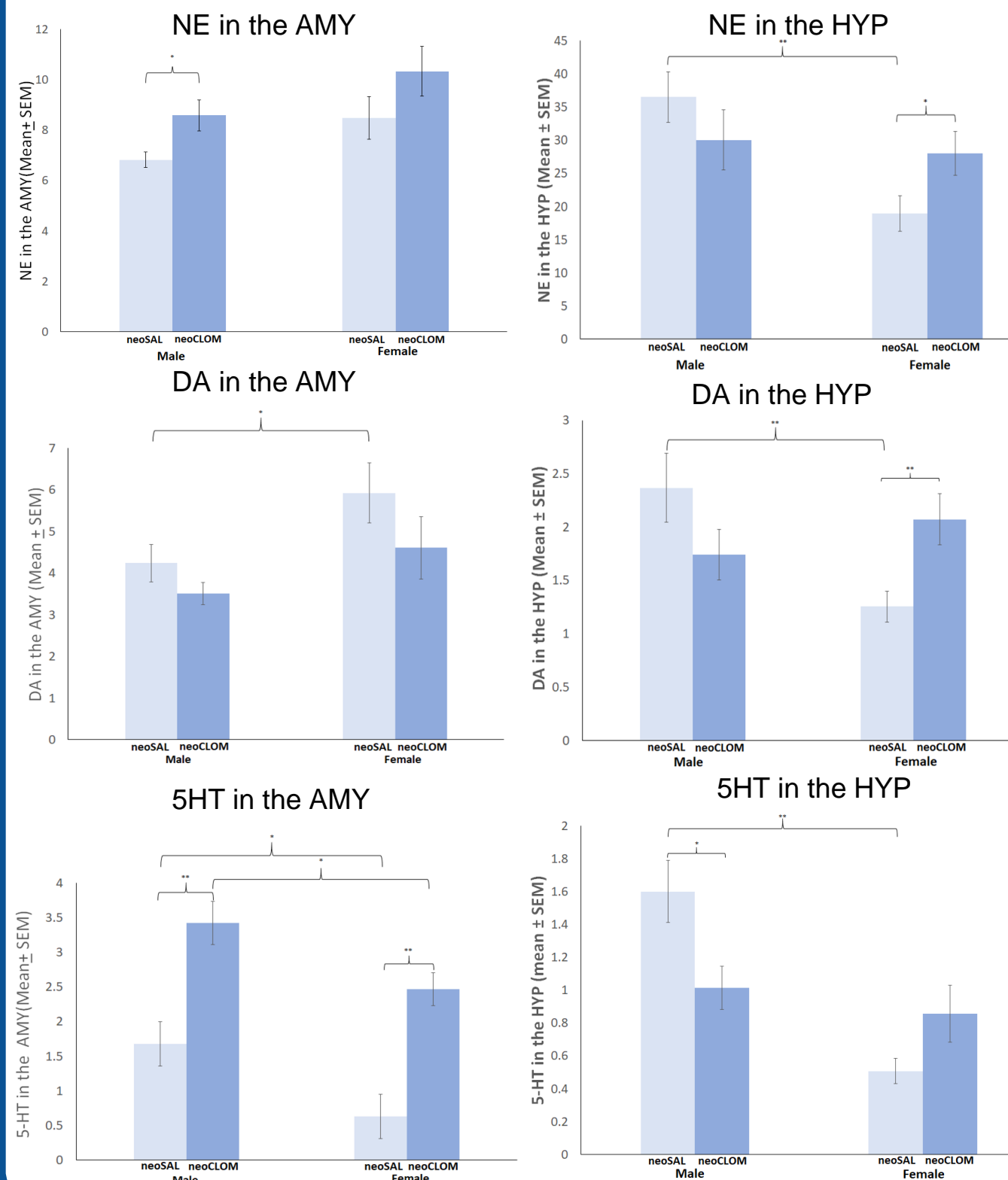
Statistical analysis:

- SPSS was used to perform two factor ANOVAs. Student's two-tailed t test utilized for pairwise comparisons
- Data expressed as mean ± 1 Standard Error of the Mean (SEM). *p < .05; **p < 0.01
- Outliers (values > 2.5 standard deviations from the mean) were eliminated.

BEHAVIORAL RESULTS



NEUROCHEMICAL RESULTS



DISCUSSION

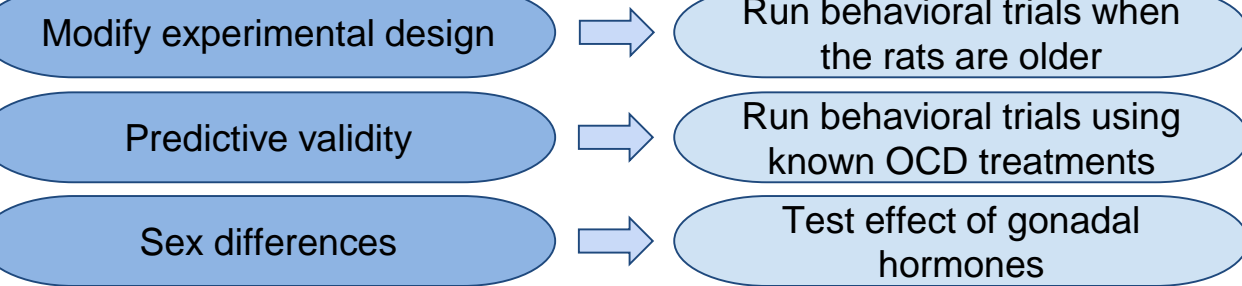
Behavioral Conclusions:

- Hole Board (HB) results suggest model has good face validity for males.
- Elevated Plus Maze (EPM) results indicate model has poor face validity for females, maze is poor assay for female anxiety, or both.
- Sex influences open arm behaviors, whereas Treatment influences poking behaviors.
- HB and EPM behaviors do not correlate, demonstrating that they represent differing assessments of OCD-like behaviors.

Neurochemical Conclusions:

- Results supports construct validity of the model.
 - NE & DA alterations correspond to OCD literature^{7,8}
 - 5-HT alterations in males correspond to OCD literature⁹
- Both Sex and Treatment influence monoamine levels

FUTURE WORK



ACKNOWLEDGMENTS

Thank you to Dr. Kreiss, the First-Year Research Immersion Program, the BU Animal Resources Staff for their animal husbandry, Neuroscience Stream Cohort 5, Cristal Finkenberg, Jovannah Gerisma, Linie Li, Hannah Rockwood, Trevor Towner, Kim Papastrat, May Vititow, and Gina Rizzo.

REFERENCES

1. The National Institute of Health (2019) Obsessive Compulsive Disorder. Retrieved from <https://www.nimh.nih.gov/health/topics/obsessive-compulsive-disorder-ocd/index.shtml>. Accessed online 2019 October 5.
2. Pigott TA and Seay SM (1999) A review of the efficacy of selective serotonin reuptake inhibitors in obsessive-compulsive disorder. *J Clin Psychiatry*. 60:101-106.
3. Willner P (1984) The validity of animal models of depression. *Psychopharmacology*. 83:1-16.
4. Andersen SL, Greene-Colozzi EA and Sonntag KC (2010) A novel, multiple symptom model of obsessive-compulsive-like behaviors in animals. *Biol. Psychiatry*. 68:741-747.
5. Simon D, Adler N, Kaufmann C, and Kathmann N (2014) Amygdala hyperactivation during symptom provocation in obsessive-compulsive disorder and its modulation by distraction. *Neuroimage Clin*. 26:549-57.
6. Kluge M et al. (2007) Increased nocturnal secretion of ACTH and cortisol in Obsessive Compulsive Disorder. *Journal of Psychiatric Research*. 41:928-933.
7. Tanaka M, Yoshida M, Emoto H and Ishii H (2000) Noradrenaline systems in the hypothalamus, amygdala and locus coeruleus are involved in the provocation of anxiety: basic studies. *European Journal of Pharmacology*. 405:397-406.
8. Koo MS, Kim EJ, Roh D and Kim CH (2010) Role of dopamine in the pathophysiology and treatment of obsessive-compulsive disorder. *Expert Review of Neurotherapeutics*. 10: 275-290.
9. Joel D, Doljansky J, Roz N and Rehavi M (2005) Role of the orbital cortex and of the serotonergic system in a rat model of obsessive compulsive disorder. *Neuroscience*. 130:25-36.
10. Brown GR and 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.
11. Walf AA and Frye CA (2007) The use of the elevated plus maze as an assay of anxiety-related behavior in rodents. *Nature Protocols*. 2: 322-328.
12. Paxinos G and Watson C (1986) *The Rat Brain in Stereotaxic Coordinates*. New York: Academic Press, Inc.