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Evaluation of a Novel Reduced Enrichment Rat Model of Depression Using Elevated Plus Maze and Cortical Monoamine Analysis

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INTRODUCTION

Depression

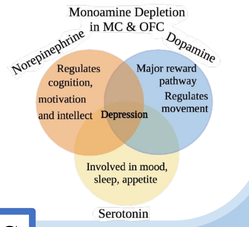
- A mental health disorder compromising thoughts, feelings and actions.[1]
- Affects approximately 6,150 students at Binghamton University in a given year.[2]
- Twice as prevalent in women than men.[3]
- Up to 60% of Major Depressive Disorder patients have an inadequate response to antidepressant treatments.[4]

Rat Animal Model

- Rats' behavior mimic social behavior seen in humans.[5]
- Brain structures and physiology analogous to those of humans.[5]

Reduced Enrichment Model

- Rats are significantly affected by removal from high enrichment which can represent aspects of depression.[6]
- Open and Closed arm entries in the Elevated Plus Maze (EPM) were used to analyze the effects of reduced enrichment.

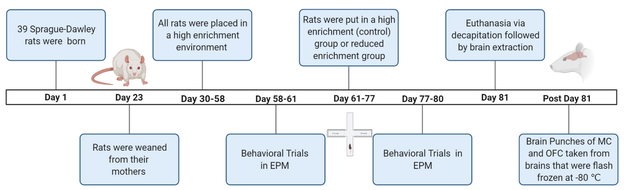


OBJECTIVES

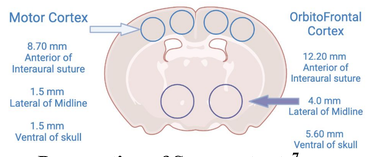
Assess the validity of a reduced enrichment rat model of depression through behavioral analysis in the EPM and monoamine analysis of norepinephrine (NE), serotonin (5-HT), and dopamine (DA) in the Motor and OrbitoFrontal Cortices

METHODS

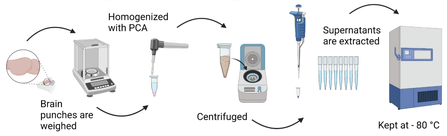
Behavioral Analysis Timeline



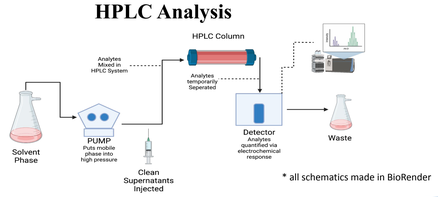
Acquisition of Tissue Samples[6]



Preparation of Supernatants[7]



HPLC Analysis



* all schematics made in BioRender

Reduced Enrichment Increased Anxiety-Like Behaviors in the EPM for Female Rats

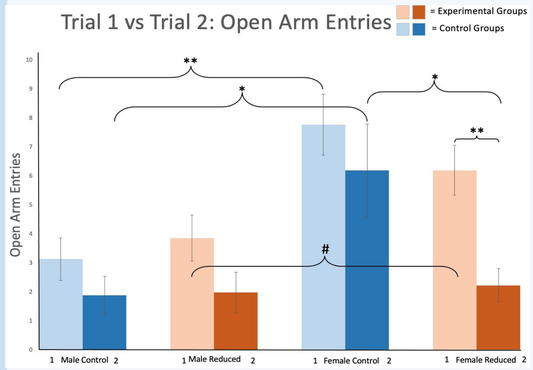


Figure 1. Comparison of the Number of Open Arms Entered in 5 minutes by Male Control Trial 1 and Male Control Trial 2, Male Reduced Trial 1 and Male Reduced Trial 2, Female Control Trial 1 and Female Control Trial 2, and Female Reduced Trial 1 and Female Reduced Trial 2. *represents p< 0.05, **represents p<0.01, and # represents 0.05<p<0.08.

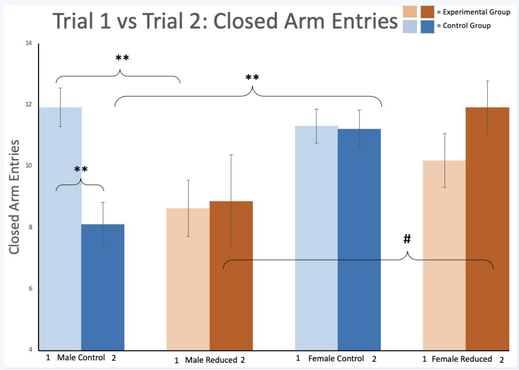


Figure 2. Comparison of the Number of Closed Arms Entered in 5 minutes by Male Control Trial 1 and Male Control Trial 2, Male Reduced Trial 1 and Male Reduced Trial 2, Female Control Trial 1 and Female Control Trial 2, and Female Reduced Trial 1 and Female Reduced Trial 2. ** represents p<0.01 and # represents 0.05<p< 0.08.

NE and 5-HT Levels in the OrbitoFrontal Cortex may Underlie EPM Open Arm Behavioral Differences in Female Rats

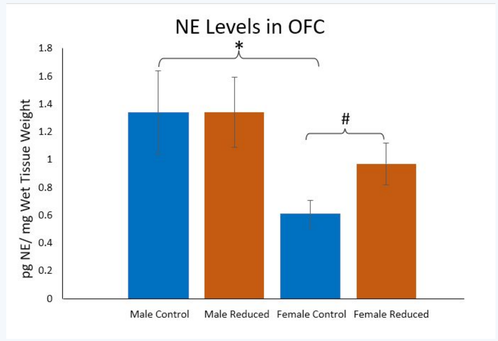


Figure 3. Comparison of the levels of NE in Male Control, Male Reduced, Female Control, and Female Reduced *represents p< 0.05, and # represents 0.05<p<0.08.

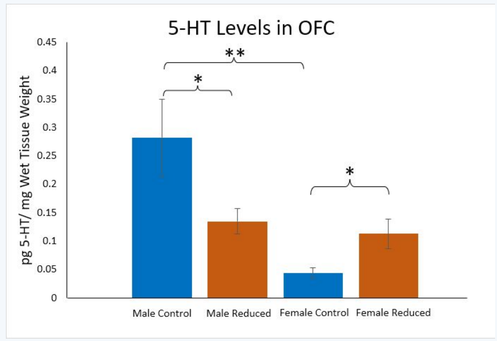


Figure 4. Comparison of the levels of 5-HT in Male Control, Male Reduced, Female Control, and Female Reduced. *represents p<0.05, and **represents p<0.01.

CONCLUSIONS

EPM: Open Arm Entries

- Reduced enrichment decreased open arm entries by female rats
- Sex differences were observed initially between male and female rats
- Sex differences were observed in Male and Female Control Trial 2 as a result of age

EPM: Closed Arm Entries

- Male controls entered a fewer number of closed arms as a result of age
- Sex differences were observed as a result of age

Two-Way ANOVA

Open Arms

- Two-Way ANOVA indicated the effect of trial is significant [F(1,34)=23.06, p<0.01]
- Two-Way ANOVA indicated a significant effect of Trial [F(1,34)=23.54, p<0.01] and of Sex [F(1,34)=10.68, p=0.002]

Closed Arms

- A two-way ANOVA indicated that the effect of Enrichment [F(1,33)=1.41] and the interaction between Enrichment and Trial [F(1,33)=4.77, p=0.036] were significant

Neurochemical Analysis

- 5-HT levels in the OFC were higher in Reduced Females compared to Control Females
- NE levels in the OFC trended to be higher in Reduced Females compared to Control Females

In combination, the behavioral and neurochemical results suggest the reduced enrichment model has validity for females

FUTURE DIRECTIONS

- Evaluate alternate neurotransmitters in the MC and OFC
- Evaluate different behaviors to observe anxiety-like behaviors
- Evaluate neurochemistry in alternate structures in the brain
- Use *in vivo* microdialysis with HPLC to analyze monoamines

ACKNOWLEDGEMENTS

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