Measuring Cognitive Function of DAT-KO Mice

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Introduction

- The dopamine transporter (DAT) aids in reuptake of dopamine into a presynaptic cell
- Mice without DAT have elevated dopamine levels in the extra cellular space[1]
- The over activation of the dopamine system is important to understanding mechanisms that may underlie diseases characterized by inflexible behavior
- Spatial discrimination and reversal learning were to measure the mice's cognitive flexibility[2]

Methods

Subjects: C57BL/6J male and female mice were generated from breeding pairs purchased from The Jackson Laboratory, Bar Harbor, ME. DAT-KO mice came from the laboratory of Dr. Scott Hall at the University of Toledo. Of 16 total mice, 8 were WT(5 males) and 8 HET(2 males).

Behavioral Testing:

Free-feeding weight was taken and food restriction weight calculated (90%) for each mouse. Mice were weighed daily and fed to maintain the restricted weight throughout the study. Operant chambers were powered by MedPC software, and each session lasted 15 minutes. Each chamber contained two nose-poke sensors labeled left and right, with the food-dispenser between them.

Pretraining: 30 grain pellets were given in home cages.

Autoshaping:

- 30 grain pellets were dispensed in operant chambers.
- To progress, the mice had to consume all pellets.

"*Both*":

- Both the right and left sensors were activated and nose-pokes to either resulted in grain pellet reward.
- To progress, the mice had to have 30 responses.

Discrimination:

- All mice were randomly assigned to begin with either the left or right sensor resulting in reward. Incorrect nose-pokes to the opposite sensor produced no reward.
- Two consecutive days of 85% correct responses were needed to progress.

Reversal:

- The opposite sensor was assigned as correct.
- Two consecutive days of 85% correct responses were needed to progress.

Measures of correct and incorrect responses

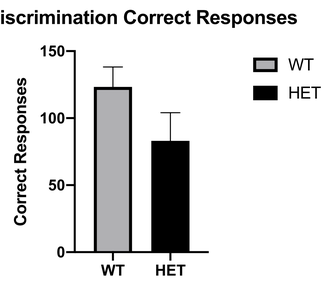


Figure 1: p = 0.1332; t = 1.611

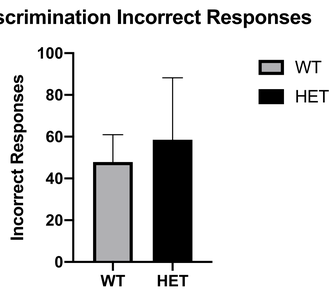


Figure 2: p = 0.7256; t = 0.3593

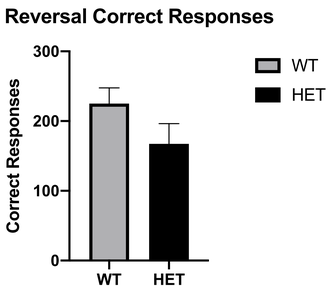


Figure 3: p = 0.1545; t = 1.572

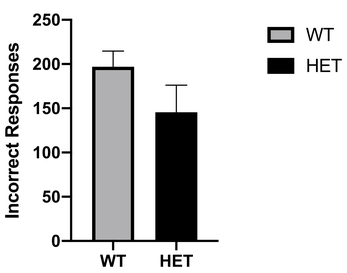


Figure 4: p = 0.1841; t = 1.454

Measures with sex as a factor

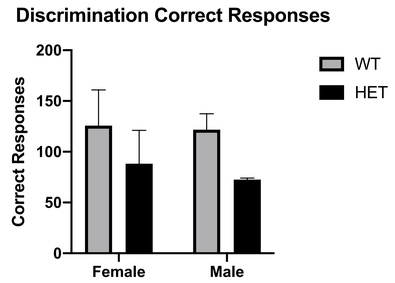


Figure 5: The interaction of sex and genotype was not significant, F(1,10) = 0.043, p = 0.839.

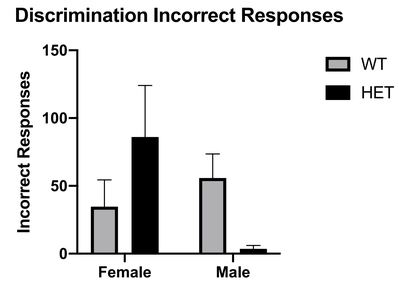


Figure 6: The interaction of sex and genotype was not significant, F(1,10) = 3.2, p = 0.1034.

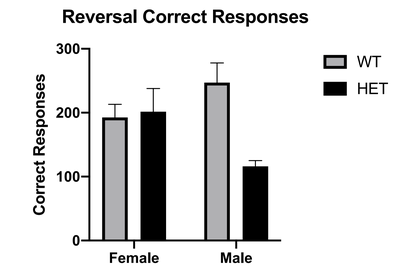


Figure 7: The interaction of sex and genotype was not significant, F(1,6) = 4.825, p = 0.070.

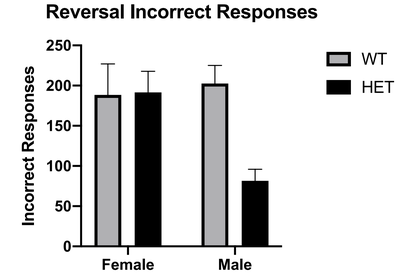


Figure 8: The interaction of sex and genotype was not significant, F(1,6) = 5.27, p = 0.0614.

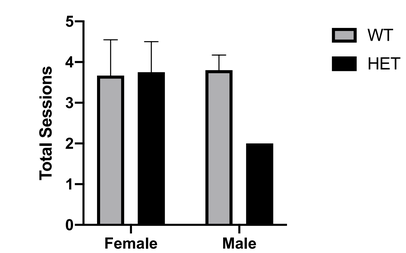


Figure 9: The interaction of sex and genotype was not significant, F(1,10) = 1.9, p = 0.1934.

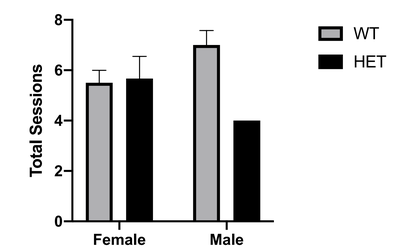


Figure 10: The interaction of sex and genotype was not significant, F(1,10) = 5.03, p = 0.0659.

Total sessions for discrimination and reversal

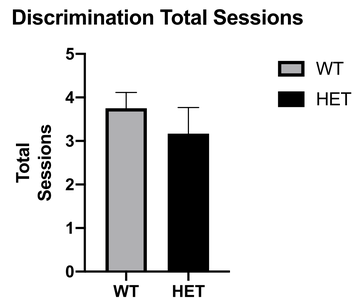


Figure 11: p = 0.3993; t = 0.8739

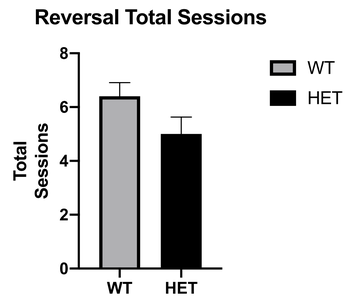
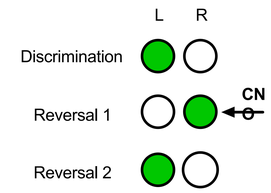


Figure 12: p = 0.1231; t = 1.723



Results

- The average number of correct responses for both discrimination and reversal were calculated for both wild-type and heterozygous mice
- The average total number of sessions for both discrimination and reversal was also calculated
- Repeated the same measures with sex as a factor and performed a 2-way ANOVA

Conclusions

- Among discrimination and reversal, we saw no statistical difference between wild-type and heterozygous responses
- Figure 7 has an almost significant difference (p = 0.07) of the interaction of sex and genotype when looking at the number of correct responses during reversal
- Figure 8 has an almost significant difference (p = 0.0614) of the interaction of sex and genotype when looking at the number of incorrect responses during reversal
- In the future, we would like to see if these results remain in future discrimination and reversal tasks when using more mice
- We would also like to investigate adding a re-reversal in the future

References

1. Wise, R. (2004). Dopamine, learning and motivation. *Nature Reviews: Neuroscience*, *5*, 1-12.
2. Radke, A., Zweifel, L., Holmes, A. (2019). NMDA receptor depletion on dopamine neurons disrupts visual discrimination and reversal learning. *Neuroscience Letters, 699*, 109-114

Acknowledgements

Research supported by the Department of Psychology at Miami University.