Differential response to cocaine in mice exposed to stress

Gavin Vaughan, Melissa Herman, Isabel Ross, Katie Bugbee, April Rowell, Jennifer Bodzon, Allison R. Bechard Ph.D.

Department of Psychology and Neuroscience, SUNY Geneseo

Introduction

- PTSD and substance abuse disorder are two of the most commonly co-occurring disorders
- Among people being treated for substance abuse disorder, 70% have experienced some form of traumatic stressor
- The issue of substance abuse in the United States is highly prevalent, with an estimated 18.7 million adults having been treated for substance abuse in their lives. This represents a major health crisis that need to be addressed
- In this study, we seek to investigate the relationship between exposure to a traumatic stressor and responses to drug prime tests in mice
- We hypothesize that mice exposed to stress will be more likely to show increased preference for cocaine in a CPP paradigm

Method

- TMT is a synthetic fox pheromone used once in adulthood to simulate trauma. Control mice were not exposed to TMT.
- A locomotor test was run to measure the physiological effects of cocaine. This is a one hour test, preceded by an hour baseline test.
- The Conditioned Place Preference (CPP) test is a paradigm that tests mouse preference for cocaine over a week long protocol. Mice that spend more time in the cocaine associated side (CS+) are said to show preference for cocaine. Mice that spend more time in the saline associated side (CS-) are said to not show preference for cocaine.
- CPP uses both a 15 minute cue prime (saline only) and a 15 minute drug prime (small dose of cocaine) during preference testing.

Results

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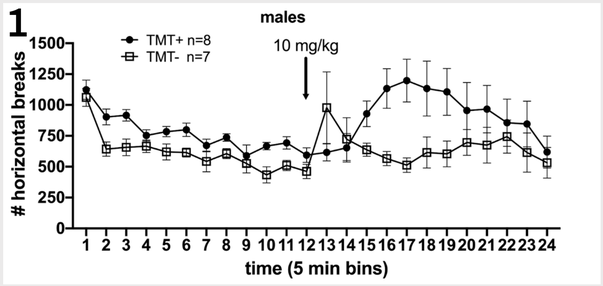

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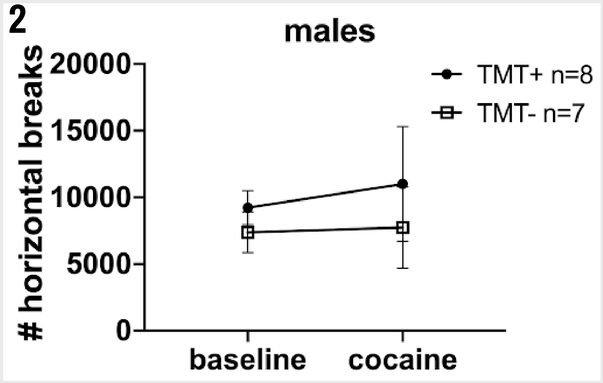

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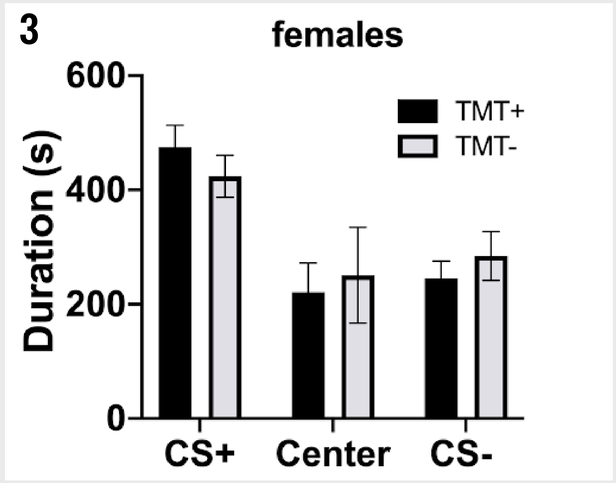

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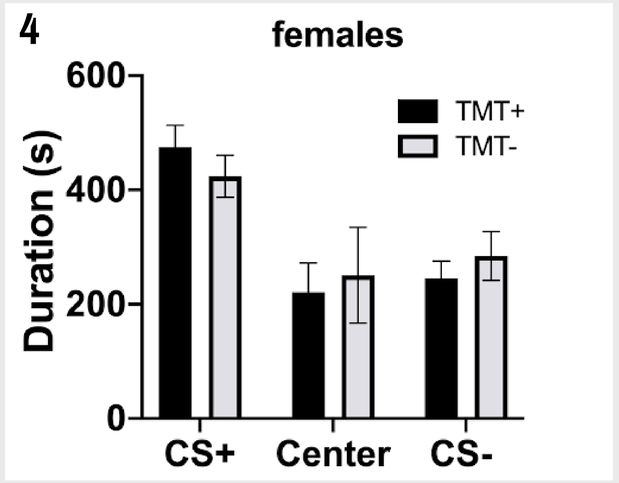

- Male mice exposed to TMT showed greater locomotor response to cocaine over time ($F(23, 299) = 2.16$, $p = 0.002$) (Fig 1).
- Male mice exposed to TMT also showed more beam breaks total when compared to control mice, indicating overall increased locomotor behavior ($F(1, 13) = 5.0$, $p = 0.042$) (Fig 2).
- These effects were not observed in female mice
- In a CPP paradigm utilizing both a cue primed test (Fig 3) and a cocaine primed test (Fig 4), no significant group differences were observed as an effect of TMT treatment. Interestingly, these mice showed increased cocaine preference during the cue prime trial as compared to the cocaine primed trial

Discussion

- Results indicated sex differences in locomotor behavior in response to TMT treatment. Males exposed to TMT exhibited much greater overall locomotor behavior, implying potentially increased susceptibility to the physiological effects of cocaine
- This research could be valuable in evaluating the causes of substance use and abuse among humans and its potential correlation with past traumas. This research also illuminates the potential for sex diffrences to play a role in drug seeking behavior in response to trauma

Future Directions

- Future directions include investigating the results in regards to the cue prime test. Our experiment showed an larger preference for cocaine during cue primed testing but not during cocaine primed testing, which was unexpected. Future studies will focus more on the differences between these tests and why the results varied so significantly
- Additionally, differences between sex were present when looking at locomotor tests, and priming tests. These sex differences may need to be investigated in later studies. Practical limitations only allowed for CPP testing of females in this study, however female and male locomotor behavior differed, so it is possible that female and male preference behavior may also differ as well.