Effects of Stress on Behavioral Inhibition in Male and Female Rats Tested via Operant Touchscreen Chambers

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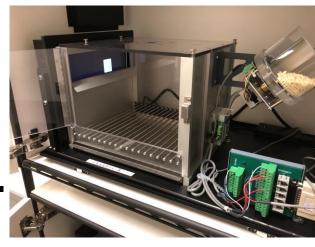
INTRODUCTION

- Addiction negatively impacts behavior and neuronal function, and defeating addiction requires an individual to inhibit reward-seeking behaviors (NIDA, 2014).
- Sex differences in addiction relapse may be stress-dependent (Lynch et al. 2002; McKay et al, 1996).
- The purpose of the present study was to examine the effects of acute stress on inhibition of an appetitively conditioned touchscreen response in male and female rats.
- Extinction training was used because it is known to produce inhibition of a reward-seeking responding (Todd et al, 2014).
- A spontaneous recovery test was used to measure behavioral inhibition (Brooks & Bouton, 1993).

METHODS

Subjects & Apparatus

Sprague Dawley rats (16 male; 16 female) were trained and tested in Layfette Touchscreen Chambers using ABET II software.



Pre-training

During a 60 min pre-training session, rats were presented with a conditioned stimulus (CS; i.e., a white square) every 30 secs followed by one 45 mg sucrose pellet. However, if the rat touched the CS it received three sucrose pellets.

<u>Acquisition</u>

During acquisition, rats were given 100 presentations of the CS per daily session. If the rat touched the CS it received a sucrose pellet. Incorrect responses were followed by the house-light turning on for 10 secs and no reward was given. The acquisition criterion was 80% correct conditioned touch responses (CR) within a single session.

Extinction & Spontaneous Recovery

During extinction, the rats were not reinforced (i.e., no food was given) for a touching the CS. Extinction consisted of 60 trials per session. The criterion was 77% no-CRs within a single session. Spontaneous recovery was tested two weeks after the rat reached extinction criterion.

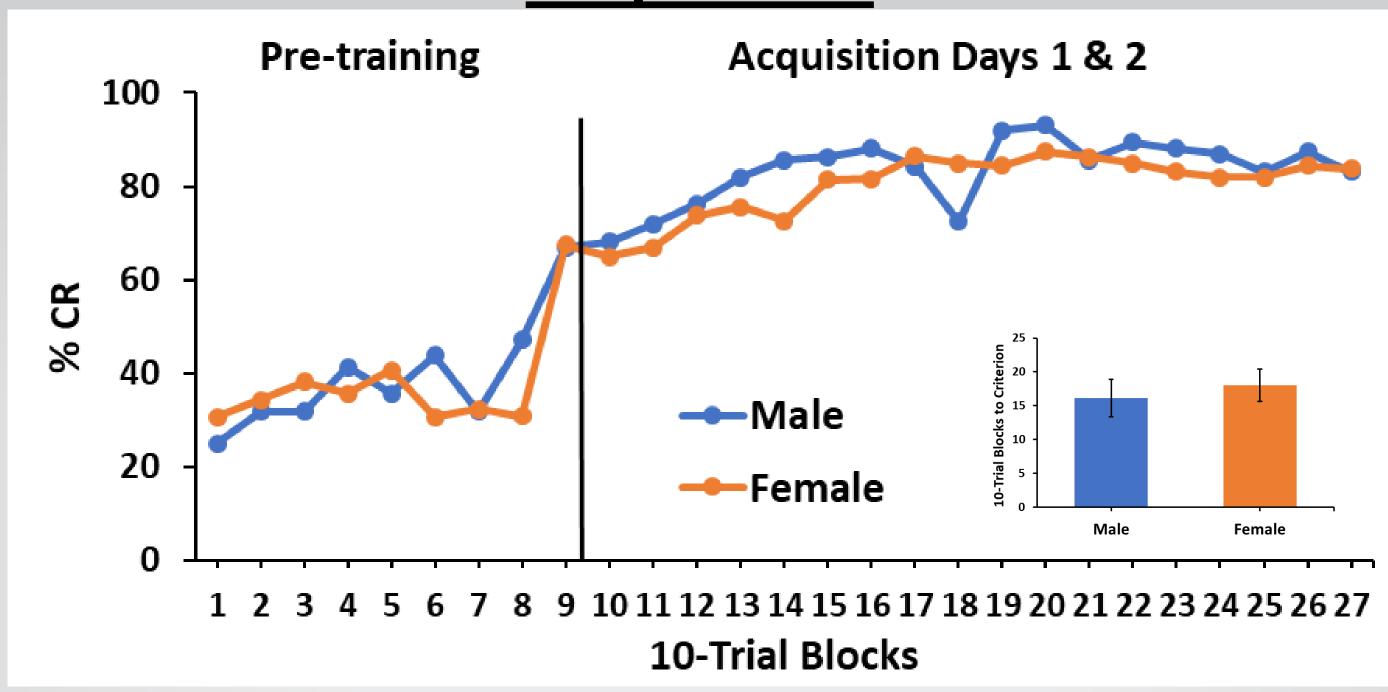
Acute stress administration

Half of the male and half of the female rats received a 30 min acute restraint stress (outside of the training chambers) immediately prior to the spontaneous recovery test.

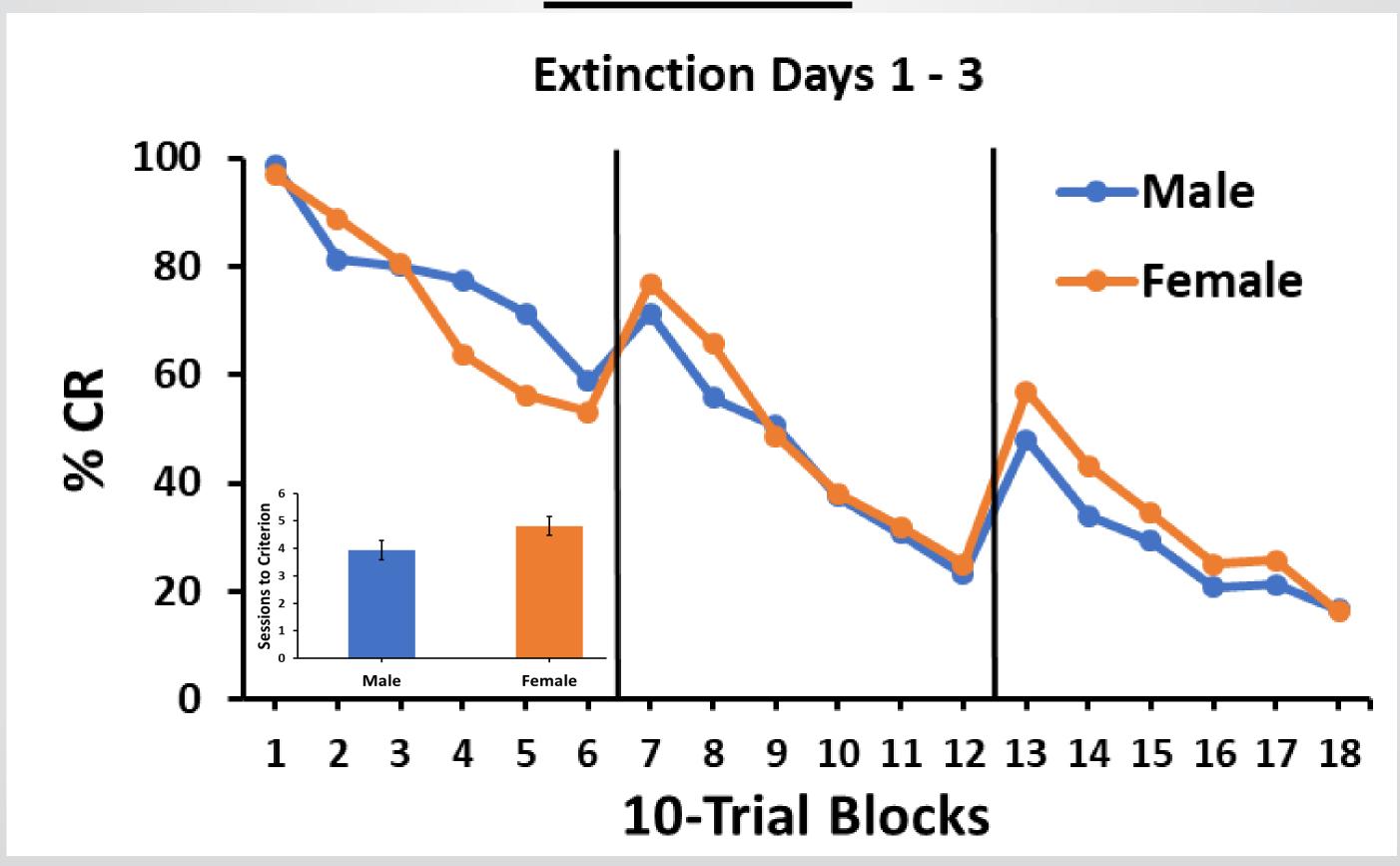


RESULTS

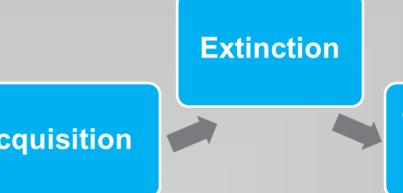
Acquisition



Extinction



Pre-Training





Spontaneous Recovery

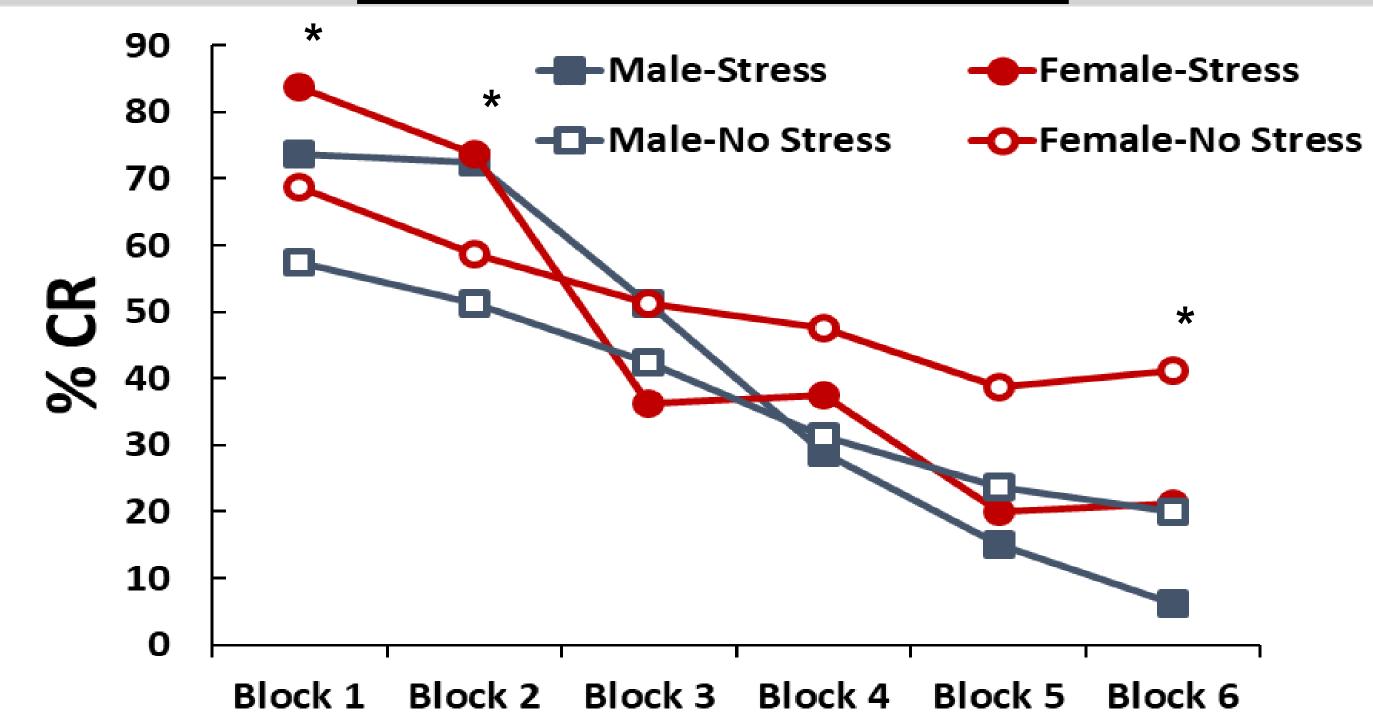
RESULTS AND DISCUSSION

- All rats successfully acquired and extinguished a conditioned touch response to the CS that was presented on a touchscreen.
- There were no sex differences in the rate of acquisition or extinction.
- Stressed rats showed greater spontaneous recovery than non-stressed controls.
 - A repeated measures mixed ANOVA revealed a significant Block X Stress interaction [F (5, 140) = 5.1, p < 0.01].
 - 2 x 2 ANOVAs revealed significant main effects of stress on Block 1 [F (1, 28) = 5.25, p = 0.03] and Block 2 [F (1, 28) = 5.98, p = 0.02].
- Stressed female rats showed the greatest spontaneous recovery overall, however their performance was highly variable.
- Our results show that stress decreases inhibition, which may be a possible mechanism that contributes to stress-induced drug relapse.

Future Studies

We plan to use a similar experimental approach to determine if fluctuations in estrogen levels differentially affect the magnitude of spontaneous recovery in stressed and non-stressed female rats.

Spontaneous Recovery



REFERENCES

- Bouton, M. E., Winterbauer, N. E., & Todd, T. P. (2012). Relapse processes after the extinction of instrumental learning: Renewal, resurgence, and reacquisition. *Behavioural Processes*,
- 90(1), 130-141.
 Brooks, D. C., & Bouton, M. E. (1993). A retrieval cue for extinction attenuates spontaneous recovery. Journal of Experimental Psychology: Animal Behavior Processes, 19(1), 77-89.
- Bussey, T. J., Padain, T. L., Skillings, E. A., Winters, B. D., Morton, A. J., & Saksida, L. M. (2008). The touchscreen cognitive testing method for rodents: How to get the best out of your rat. *Learning & Memory, 15*(7), 516-523.
- Lynch, W. J., Roth, M. E., & Carroll, M. E. (2002). Biological basis of sex differences in drug abuse: Preclinical and clinical studies. *Psychopharmacology*, 164(2), 121-137.
- Mar, A. C., Horner, A. E., Nilsson, S. R., Alsiö, J., Kent, B. A., Kim, C. H., Holmes, A., Saksida, L. M., & Bussey, T. J. (2013). The touchscreen operant platform for assessing executive function in rats and mice. *Nature Protocols*, 8(10), 1985-2005.
- McKay, J. R., Rutherford, M. J., Cacciola, J. S., Kabasakalian-McKay, R., & Alterman, A. I. (1996). Gender differences in the relapse experiences of cocaine patients. *The Journal of Nervous and Mental Disease*, 184(10), 616-622.
- National Institute on Drug Abuse. (2007, April). Drugs, Brains, and Behavior The Science of Addiction. Retrieved from https://www.drugabuse.gov/sites/default/files/soa_2014.pdf
- Todd, T. P., Vurbic, D., & Bouton M., E. (2014). Behavioral and neurobiological mechanisms
 of extinction in Pavlovian and instrumental learning. Neurobiology of Learning and Memory,
 108, 52-64.