

Sex Differences in Immediate Early Gene Expression within Retrosplenial Cortex following Contextual Fear Conditioning

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Introduction

- Sex differences are prevalent in anxiety-related psychiatric disorders. Anxiety disorders can be modeled in the lab using the classical conditioning paradigm where animals learn to associate a neutral conditioned stimulus (CS), which is paired with an aversive unconditioned stimulus (US). Following a few CS-US pairings, presentation of the CS alone elicits conditioned responses (CR).
- Female mice show stronger context fear conditioning and generalization compared to male mice (Keiser, et al., 2017). Female rats outperform males during trace eye blink conditioning (Dalla et al., 2009).
- Male rats show better long term retention of contextual fear conditioning than females (Gresack et al., 2009). Hippocampal Extracellular signal-regulated kinase (ERK) activation following fear conditioning is higher in male rats than female rats (Gresack et al., 2009). ERK is critical in the formation and maintenance of cellular changes associated with learning and memory (Peng et al., 2010).
- The Retrosplenial Cortex (RSC) is known to be involved with navigational memory (Vann et al., 2017).
- Lesions in the RSC lead to spatially impaired memory in both rats and primates (Vann et al., 2017).
- In a study done on female humans with an MRI, there was a correlation between RSC activity and navigational ability (Auger et al., 2012).



Results

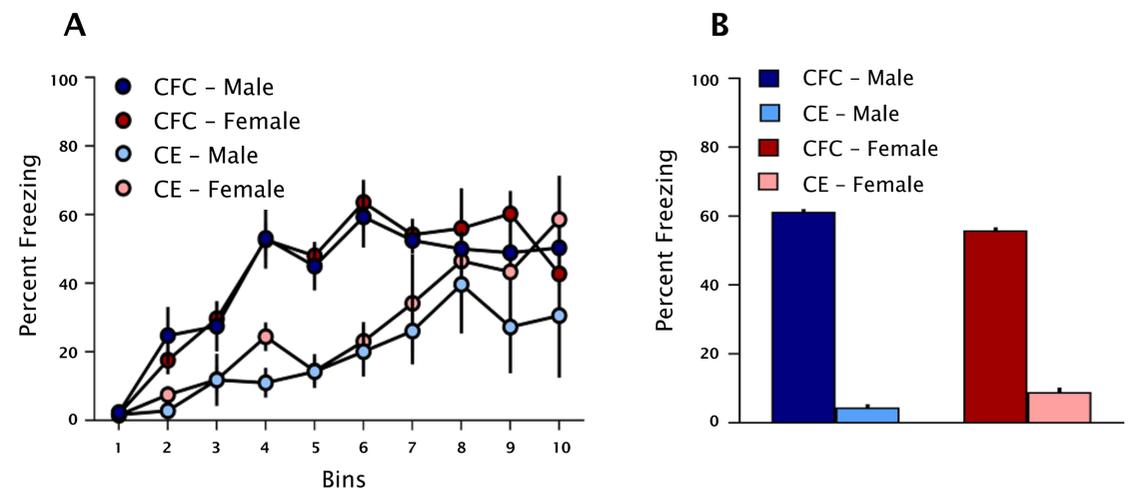


Figure 1A) Behavioral responses of contextual fear conditioned (CFC) males (n = 8), context exposed (CE) males (n = 4), contextual fear conditioned females (n = 6) and context exposed females (n = 4). The group of CFC males and CFC females froze at similar levels. The group of CE males and females froze at similar levels. Figure 1B) Conditioned responses of the subjects. The group of CFC males and CFC females froze at similar levels comparable to their baseline. Similarly the group of CE males and CE females does not vary from the baseline.

Methods

Subjects:

Animals in the current study included 22 F344 rats (12 males and 10 females) of approximately 3 months age. All animals were handled for 4 days, caged and handled for 4 days, and then received one session of contextual conditioning. Animals were then separated into their experimental groups by an individual uninformed with every day handling.

Animals that received contextual fear conditioning included 8 males and 6 females. Control animals that received only exposure to the context included 4 males and 4 females.

Paradigm:

The contextual conditioning lasted 35 minutes. The training phase included six presentations of an aversive stimuli. Each trial period included the presentation of a 1mA shock that lasted for 1 second as an aversive stimuli approximately every 300 seconds for a total of 6 shocks.

Animals were tested 24 hours later. Animals were placed in the same chamber as they were trained in for 10 minutes. Contextual testing protocols did not include any aversive stimuli. Animals were euthanized 1 hour after the start of the testing period. Brain tissue was collected via rapid decapitation under isoflurane anesthesia and flash frozen for a later experiment.

Analysis:

Videos were reviewed once all the experimentation was completed using FreezeFrame 4 software. The software analyzed the amount of time animals spent freezing. The data was then exported and analyzed using SPSS.

Conclusions and Future Directions

Summary:

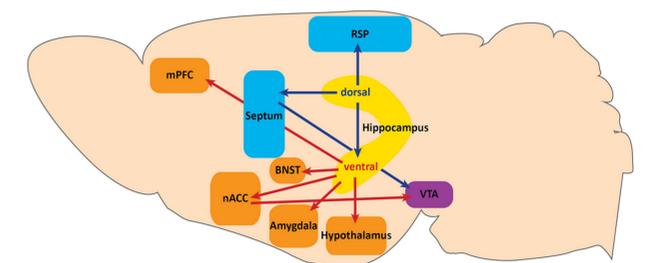
- No sex differences in contextual fear conditioning were observed.

Implications:

- Despite similar contextual fear learning in males and females, there may be differences in the molecular mechanisms underlying fear learning.
- Investigating the neurological mechanisms could help explain differences seen in the human population.

Future Directions:

- By using Western Blots, we will measure different immediate early gene expression (c-fos, ARC, Zif-268) in the RSC.



(Tannenholz, L., Jimenez, J. C., & Kheirbek, M. A, 2014)

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