Corticotropin Releasing Factor (CRF) Impairs Sustained Attention in Male and Female Rats

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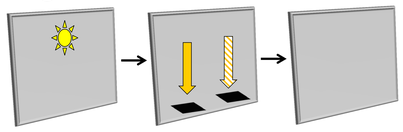
Abstract

Background: Stress can disrupt a variety of cognitive processes, including attention. Moreover, patients with stress-related psychiatric disorders, such as depression, often report difficulty in sustaining attention. Despite these well documented effects, the neurobiological basis for stress regulation of attentional processes remains underexplored. During a stressful event, corticotropin releasing factor (CRF) is released centrally to modulate cognitive and behavioral stress responses. Previous research identified sex differences in the CRF_1 receptor that increase neuronal sensitivity to CRF in female compared to male rats. The present study was designed to examine whether CRF alters sustained attention—a subject's ability to monitor a situation for a prolonged period of time in order to respond to rare and unpredictable events—and, if so, whether there are sex differences in this effect.
Methods: See adjacent panels.
Results: See adjacent panels.
Discussion: See adjacent panels.

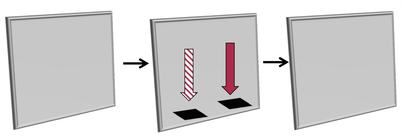
Sustained Attention Task

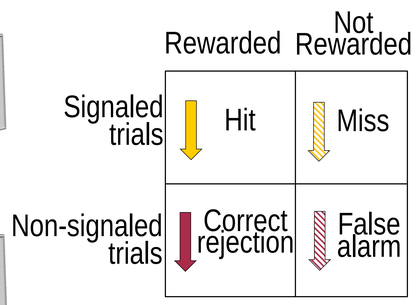
Rats were trained on an operant Sustained Attention Task (SAT) in which they had to discriminate visual signals (25-500 ms in duration) from non-signaled events (Demeter et al. 2008, St Peters et al., 2001 and Parikh et al., 2013).

Signaled trial



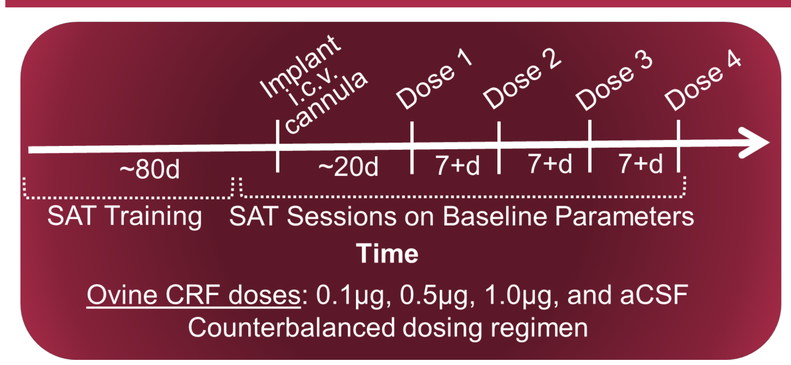
Non-Signaled trial





- **Percent Hits:** The percentage of correct responses on a signaled trial
- **Percent Correct Rejections:** The percentage of correct responses on a non-signaled trial
- **Vigilance Index:** Measure of hits and false alarms thought to reflect the construct of vigilance
- **Omissions:** Trials during which neither lever is pressed

Experimental Design



CRF Causes a Dose-Dependent Impairment of Hits and Correct Rejections

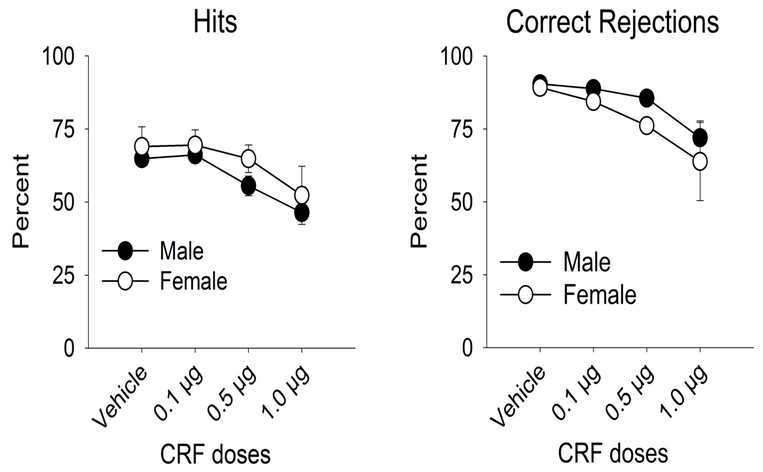


Figure 1. CRF dose-response curves for hits and correct rejections in male (n = 7) and female (n = 6) rats. There was a main effect of dose for both percent hits [$F(1, 11) = 4.4$, $p < .05$] and percent correct rejections [$F(1,11) = 7.5$ $p < .01$]. However, there were no significant main effects of sex or any sex by dose interactions.

CRF Causes a Dose-Dependent Impairment in Vigilance

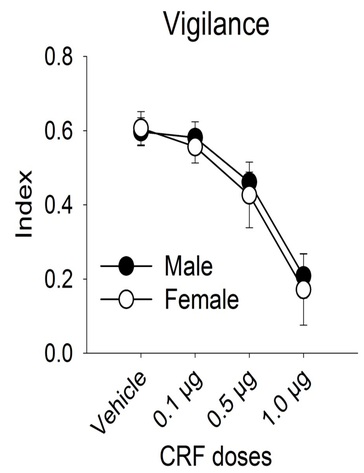


Figure 2. CRF dose-response curve for vigilance. There was a main effect of dose for the vigilance index [$F(1, 11) = 17.2$, $p < .001$]. However, there was no significant main effect of sex or a sex by dose interaction.

CRF Increases Omissions in Female Compared to Male Rats

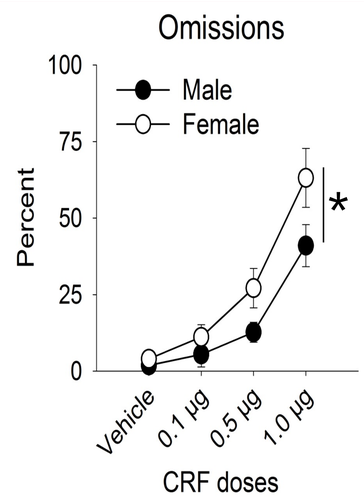


Figure 3. CRF dose-response curve for omissions. There was a main effect of dose for omissions [$F(1, 11) = 42.8$, $p < .001$]. Interestingly, there was also a main effect of sex for this measure [$F(1,11) = 125.1$, $p < .001$]. However, there was no significant interaction.

The Ability to Sustain Vigilance Declines in Females at the 0.5 µg CRF dose

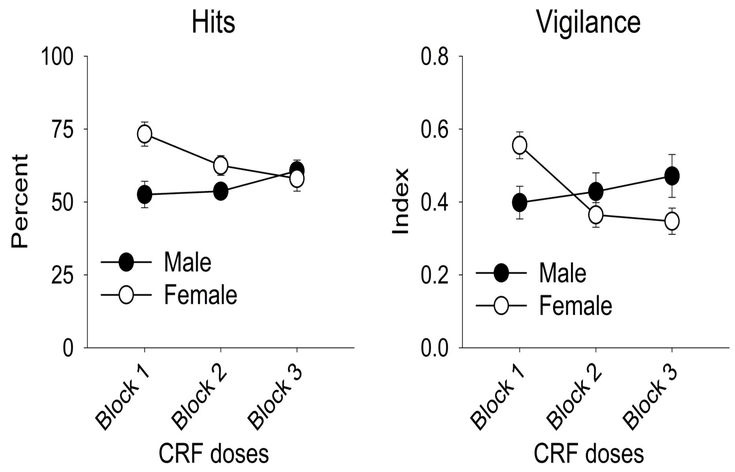


Figure 4. Attention declines over time in females but not males at the 0.5 µg dose of CRF. There were block by dose by sex interactions for percent hits [$F(6, 66) = 3.8$, $p < 0.01$] and the vigilance index [$F(6, 66) = 3.4$, $p < 0.01$] that prompted further analyzes of attention over time (e.g., across three trial blocks) at different doses. Of interest, at the 0.5 µg CRF dose there was a trend for a dose by sex interaction [$F(2, 22) = 3.3$, $p = .057$]. For the vigilance index, there was a significant dose by sex interaction [$F(2, 22) = 3.5$, $p < .05$].

Conclusions

- In both male and female rats, CRF significantly reduced accuracy and vigilance in a dose-dependent fashion, with the highest dose of CRF causing the largest deficits.
- The ability to sustain vigilance declined in female rats at the 0.5 µg CRF dose, while the performance of male rats remained stable across the session at this dose.
- Although the number of omissions increased with the CRF dose in both males and females, female rats omitted more trials, presumably reflecting a lower motivation to perform under stressful conditions than males.
- Together, the results reveal that sustained attention is disrupted under stressful conditions in both male and female rats. However, on some measures, attention deficits are greater in females than in males, an effect that may be linked to sex differences in CRF_1 receptors.

Acknowledgements, References, Disclosures

Acknowledgements:
The authors wish to thank Alexa Fritz and Hamidou Keita for their technical assistance. Supported by PHS grant MH092438 to DAB

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Disclosures:
The authors have nothing to disclose.