

Stress-induced Cognitive Changes in Female Rats



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Abstract

Women are disproportionately more affected by stress and are more prone to developing stress-related psychiatric disorders than men. Cognitive impairment is a key phenotype in such disorders. Literature about how stress affects female cognition is equivocal.

Using restraint stress model and attentional set shifting paradigm, we examined the effects of stress on cognitive flexibility in female Sprague Dawley rats. We hypothesized that more stressed female rats would be worse at the cognitive task than less stressed female rats. The results showed that while more stressed female rats were better at completing a simple cognitive task, they were worse at completing a more complex one, which suggests that stress can impair cognitive flexibility in female rats.

Introduction

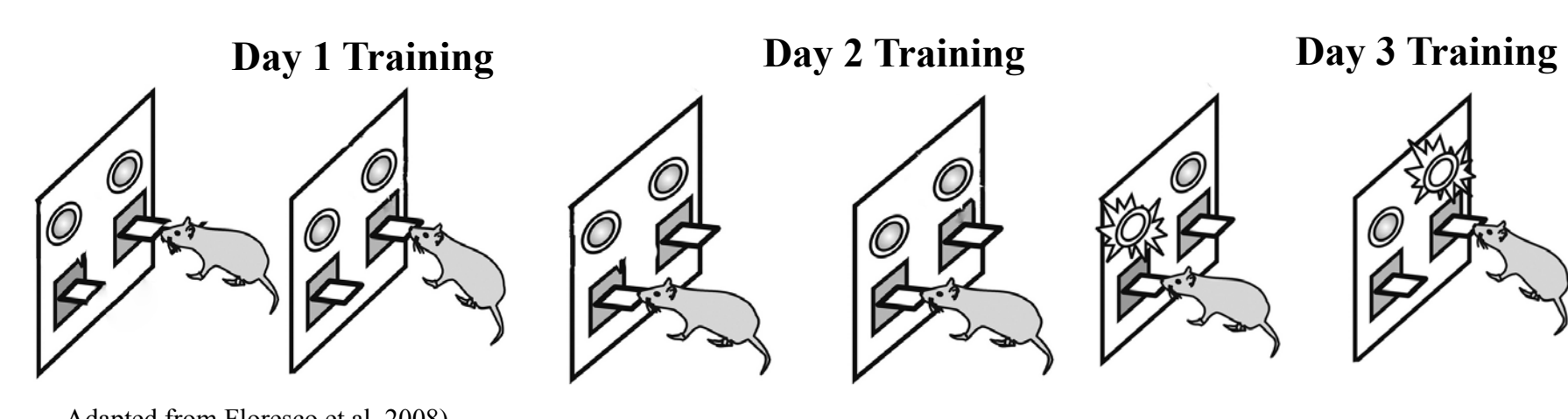
Women are disproportionately more affected by stress and are more prone to developing stress-related psychiatric disorders (Bagley, S. et al., 2011). Previous literature assessed cognitive function in response to stress, but not specifically cognitive flexibility which is a crucial part of decision making, especially in a stressful situation (Luine, 2016).

The present study examined the effects of restraint stress on cognitive flexibility in female rats using the restraint stress model and attentional set-shifting task (AST) which specifically assesses cognitive flexibility.

Methods

32 Sprague Dawley rats (16 males, 16 females) underwent 3 days of learning with right/left levers and light for the AST task before the test day (as illustrated in the image below). Half of the rats underwent 30 minutes of restraint stress (shown below) on the test day before performing the AST task, while the other half was control and did not undergo the restraint stress. The first 15 minutes of the restraint were recorded and coded for struggle behavior which is indicative of a larger stress response (Grafe et al., 2017)

Attentional Set Shifting Training



Restrain Device



Results

Restrain Stress and Attentional Set Shifting Task Correlation

We ran a series of Pearson correlations to determine the relationship between stress behavior and cognitive flexibility. An alpha level of $p < 0.05$ was used for all analyses.

A significant positive association between struggle time and % of correct responses on the side AST task in females was found, ($r(6) = 0.7726$, $p = 0.0246$), which indicates that the more stressed a female rat was, the better it performed on the side discrimination cognitive task. Another correlational analysis revealed a significant negative association between struggle time and % of correct responses on the reversed side AST task in females, ($r(6) = -0.8610$, $p = 0.006$), which suggests that the more stressed a female rat was, the worse it performed on the reversed side discrimination cognitive task.

The results indicate that female rats perform better at side discrimination task but worse at reversed side discrimination task when stressed, which suggests that stressed females perform better on a simple task but stress can impair their performance at a more complex task or when they need to shift rules.

Figures

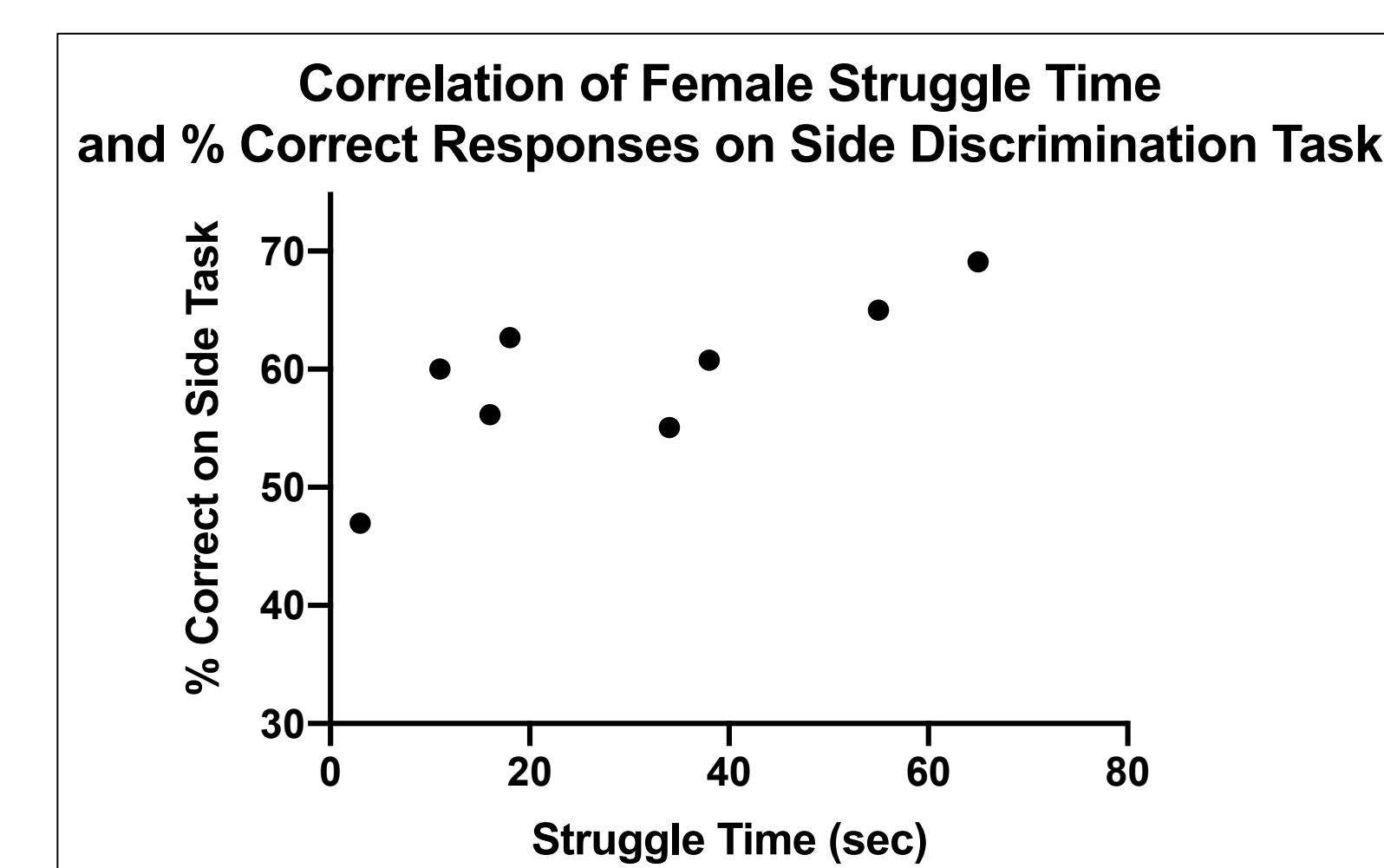


Fig. 1. Significant positive association was found between struggle time and % of correct responses on the side AST task in females, indicating that the more stressed a female rat was, the better it performed on the side discrimination cognitive task.

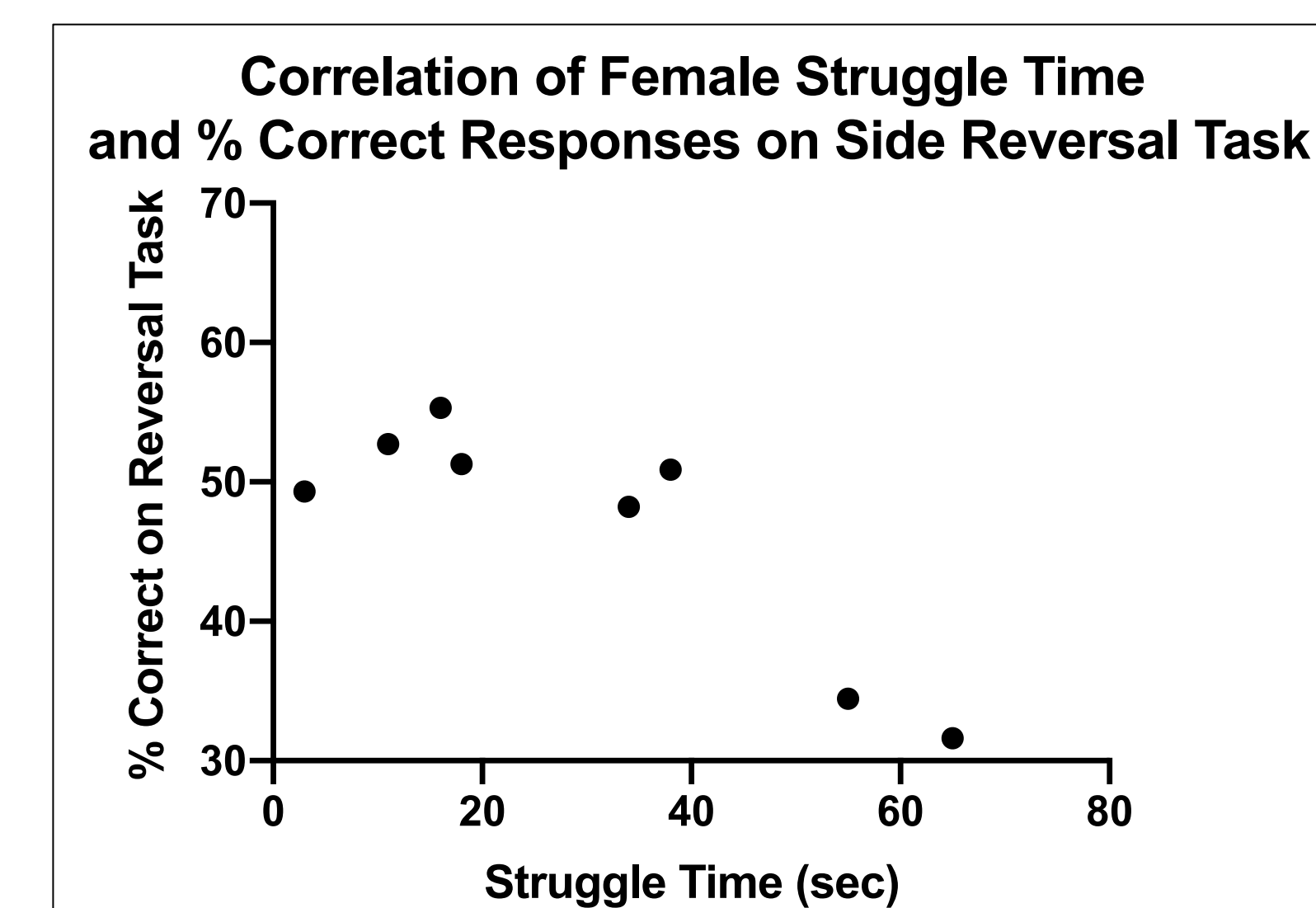


Fig. 2. Significant negative association was found between struggle time and % of correct responses on the reversed side AST task in females, indicating that the more stressed a female rat was, the worse it performed on the side reversal cognitive task.

Discussion

The present study has demonstrated the effects of restraint stress on cognitive flexibility in female rats. It showed that stress improved cognitive performance in females on a simple task but decreased it on a more complex task, which supports the hypothesis that stress impairs cognitive flexibility in female rats and aligns with previous literature that showed decrease in female cognitive flexibility following acute stress manifested in worse performance on side reversal task (Grafe et al., 2017). Moreover, better female performance on a simpler side discrimination task and worse at reversal when stressed could be explained by perseveration tendencies observed in female rats. Females usually perseverate on the first rule of the task which could enhance side discrimination and decrease side reversal performance (Grafe et al., 2017). Perseveration is observed in stress-related psychiatric disorders such as PTSD that disproportionately affect women, meaning that stress-induced decrease in cognitive flexibility in females shown in the present study could have clinical implications for prevention and treatment of such disorders (Bangasser et al., 2014).

Following this study, we are examining the neural substrates of these changes in cognitive flexibility, analyzing how neural activation in the prefrontal cortex or orbitofrontal cortex might underlie enhancements or impairments in the task performance.

Conclusions

The study has demonstrated that stress impairs cognitive flexibility in female rats as they perform worse at a more complex cognitive task when stressed.

This could be attributed to perseveration tendencies in female rats that are observed in stress-related psychiatric disorders largely affecting women.

References

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