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Stress, Decision-Making and Reward Value: Effects of Intermittent Social Stress on Delay Discounting Behavior

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STRESS, DECISSION-MAKING AND REWARD VALUE: EFFECTS OF INTERMITTENT SOCIAL STRESS ON DELAY DISCOUNTING BEHAVIOR

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INTRODUCTION

The intermittent exposure to social defeat stress (ISD) promotes drug-seeking behavior (i.e., cocaine self-administration) (1), which ultimately can increase the risk for developing substance use disorders. Previous studies suggest that drug-seeking behavior is associated with a distortion in the brain processing of rewards that leads to choice impulsivity (2). Here, based on these studies, we investigated whether ISD alters performance in a delay discounting task. Delay discounting is a decision-making task in which animals need to make a choice between an immediate small reward and a delayed large reward. The subjective value of a reward decreases as the delay to receive it increases.

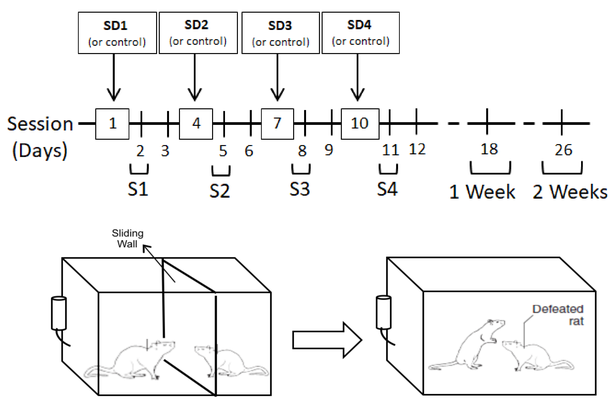
METHODS

Delay discounting task. First, we trained 24 male Long Evans rats (3 months of age) to discriminate between a High-Reward lever (HR) and a low-Reward lever (LR) associated with a cue light. Pressing the HR delivered 3 sugar pellets while pressing the LR delivered 1 sugar pellet. Then, delay discounting sessions begun. The delay discounting task consisted of three blocks of 20 trials each (60 trials total per session). In each block, the first 10 trials were forced choice trials in which both levers were extended but only one of the two levers was active (cue light on), HR or LR, pseudo-randomly. The remaining 10 trials of the block were free choice trials in which both levers were active (both cue lights on), and animals had to make a choice between the HR and the LR. The three blocks were different in the delay to receive the large reward after pressing the HR: 1 s (block 1), 10 s ((block 2) and 20 s (block 3). The delay to receive the small reward after pressing the LR was always the same in the three blocks (1 s). After stable performance, rats were divided into two groups (Control, n= 12; Stress, n= 12) and exposed to ISD (or handling). Rats were tested in the task twenty-four hours after every stress episode, and one and two weeks after the end of the last stress episode.

Intermittent social defeat stress (ISD). The rats assigned to the ISD group underwent 4 sessions of social defeat via the resident/intruder paradigm (3), each separated by 3 days (Figure 1). The intruder rats were placed in the resident's cage (70L x 70W x 50H cm) separated by a divider wall for 10 minutes, allowing sensory exposure, but no physical interaction. Next, the divider wall was removed, allowing the rats to interact. The interaction was stopped when either 6 attacks were witnessed, the intruder was in supine position for 5 seconds, or 5 minutes had elapsed. At that point, the divider wall was reinserted, and the intruder remained in the cage for 10 more minutes. Control rats were moved to a different room for the same amount of time and handled for 1-2 minutes.

Statistics. Two-three way ANOVAs with repeated measures (Group x Block) (Group x Block x Session) were performed to analyze the number of HR and LR choices during force and free trials, and choice latency (time to press the HR lever) during free choice trials.

1. Intermittent social stress protocol.



2. Delay discounting task. Rats shift their preference from a large (HR) delayed reward to a smaller (LR) immediate reward.

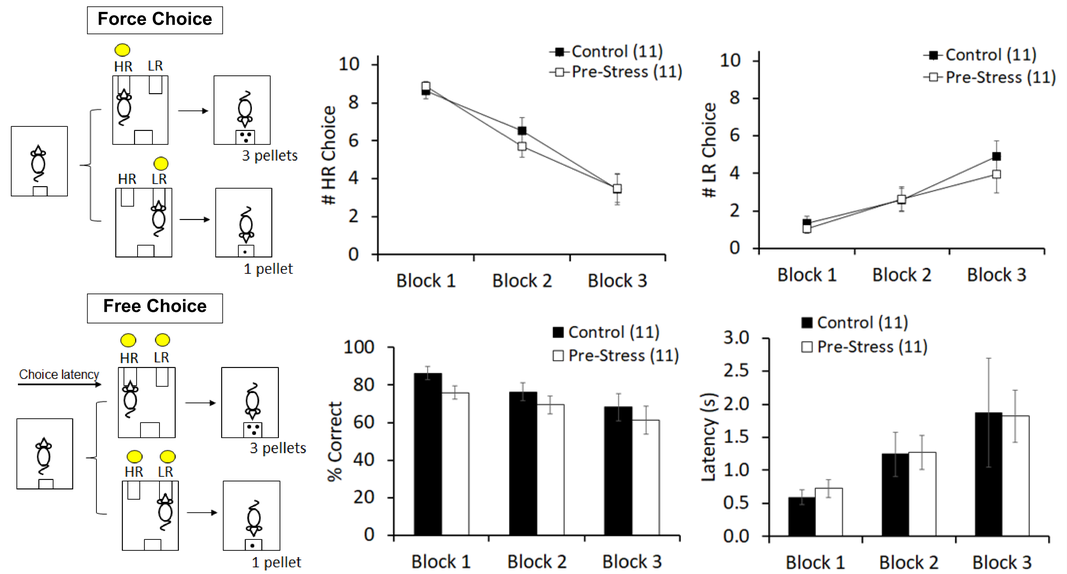


Figure 2. (Top left) HR lever presses per block before stress. [Block: F(2,40)= 55.56, p< 0.001; Group: F(1,20)= 0.090, p= 0.760]. **(Top right)** LR lever presses per block before stress. [Block: F(2,40)= 21.87, p< 0.001; Group: F(1,20)= 0.31, p= 0.580]. **(Bottom left)** Accuracy per block before stress. [Block: F(2,40)= 9.10, p< 0.001; Group: F(1,20)= 3.26, p= 0.080]. **(Bottom right)** Latency to HR per block before stress. [Block: F(2,40)= 5.23, p= 0.010; Group: F(1,20)= 0.04, p= 0.840].

3. Rats can be grouped as low impulsive (LI) and high impulsive (HI) according to their basal preference for HR.

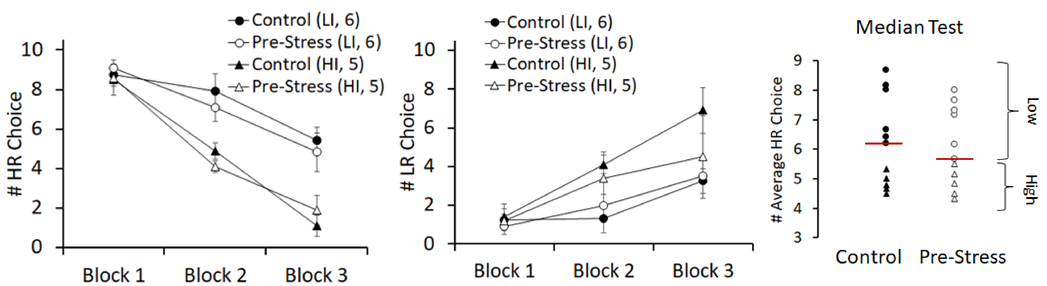


Figure 3. (Left) HR lever presses per block before stress according to choice impulsivity. [Block: F(2,16)= 46.87, p< 0.001; Impulsivity: F(1,8)= 68.15, p< 0.001: Block x Impulsivity: F(2,16)= 13.25, p< 0.001]. **(Middle)** LR lever presses per block before stress according to choice impulsivity. [Block: F(2,16)= 20.91, p< 0.001; Impulsivity: F(1,8)= 3.08, p= 0.117: Block x Impulsivity: F(2,16)= 3.85, p= 0.043]. **(Right)** Median test (red line) to group low and high impulsive animals (every dot is an animal).

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4. Social stress decreases the preference for a delayed HR in low impulsive rats.

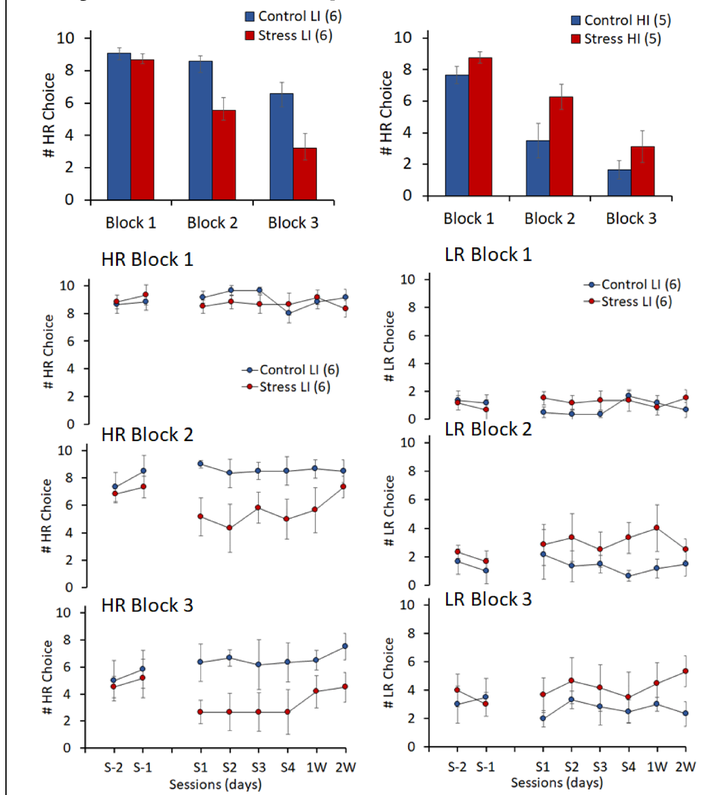

Figure 4. (Top left) HR lever presses per block after stress. [Block: F(2,20)= 40.67, p< 0.001; Group: F(1,10)= 14.50, p= 0.003]. **(Top right)** LR lever presses per block after stress. [Block: F(2,16)= 53.75, p< 0.001; Group: F(1,8)= 5.99, p= 0.040]. **(Bottom left)** HR lever presses per block and session after stress. [Block: F(2,20)= 47.83, p< 0.001; Group: F(1,10)= 10.39, p= 0.009]. **(Bottom right)** LR lever presses per block and session after stress. [Block: F(2,20)= 22.20, p= 0.010; Group: F(1,10)= 2.20, p= 0.170].

SUMMARY AND CONCLUSIONS

1. Rats shift their preference from a large delayed reward to an smaller immediate reward, which shows that they make a choice according to the subjective value of rewards. Opposite to LR, rat's preference for HR decreased as delay increased (Blocks 2 and 3).
2. Intermittent social stress decreases the preference for HR. Stressed animals pressed the HR lever less times compared to controls when the delay to receive the reward increased (Blocks 2 and 3). These results suggest that social stress alters the brain processing of rewards.
3. The effects of social stress on delay discounting behavior depend on the basal level of choice impulsivity. These results suggest that ISD produces long-term changes in the neurobiological substrates that regulate decision-making and reward-seeking behavior.

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