Testing for Operant Self-Administration of Aggression in Female Mice

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Introduction

1. Appetitive aggression is reward-motivated and self-administered by the perpetrator.[1]

2. Highly aggressive male mice lever-press to gain access to a subordinate intruder male to attack in a resident-intruder paradigm.[2]

3. There is a lack of literature on aggression in female mice beyond maternal and hierarchical contexts.

Question

Do female mice (specifically retired dams) exhibit appetitive aggression as revealed by operant self-administration of aggression in a resident-intruder paradigm?

Methods and Tests

Animals: The residents were 12 retired dams (females formerly used as breeders; 27-41 weeks old); 30 young (10–15-week-old) intruder females were also used.

1. Aggression Screening: Assessed residents' baseline aggression by introducing intruder into home cage. 5 sessions (5 min each) per resident.

2. Fixed-Ratio 1 Testing (FR1): Residents could press either an inactive or an active lever. Active lever-pressing resulted in the delivery of the intruder (reward) into the operant chamber. 7 sessions with 10, 4-minute-long trials (40 min total) across 7 days per resident.

3. Aggression-Seeking Test: Residents' active lever-pressing resulted in no reward delivery. 1 session (30 min each) per resident.

4. Progressive-Ratio Testing (PR): Residents were required to make an increasingly greater number of active lever-presses for reward delivery. 1 session (up to 2 hours each) per resident.

Measurements

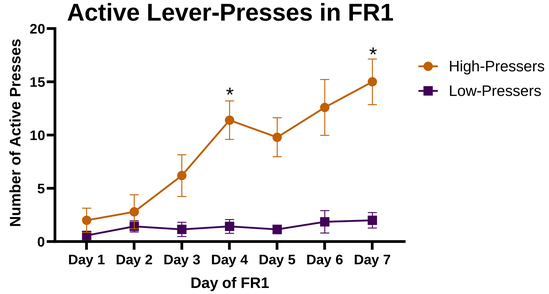
- The number of active/inactive presses
- The number of rewards earned
- Attack, allogrooming (social grooming), sniffing, and self-grooming durations during FR1

Fixed-Ratio 1 (FR1) Trial Structure
(1) At the start of each trial, an active and an inactive lever was available to the resident for up to 2 minutes. **(2)** When the resident pressed the active lever, the cue-light flashed, and the active lever retracted. The intruder was then introduced. **(3)** This was the reward phase. The intruder remained in the chamber until the house light turned off (3 minutes into the trial). The house light remained off for 1 minute. Then the next trial started.

Results

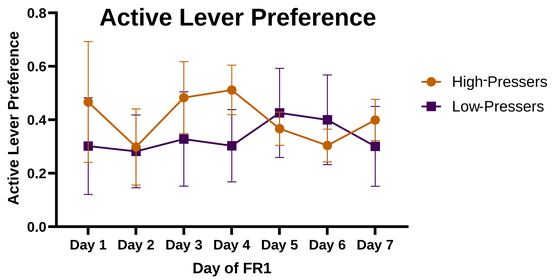
No aggression was observed (!) during any of the behavioral tests ran (aggression screening, fixed-ratio 1 testing, and progressive-ratio testing). Residents were thus divided into "high-presser" and "low-presser" groups. Lever-pressing behavior, the number of rewards earned, and a behavioral ethogram was compared between the two groups in supplementary analyses to explore what may have motivated some residents to lever-press.

Active Lever-Presses in FR1



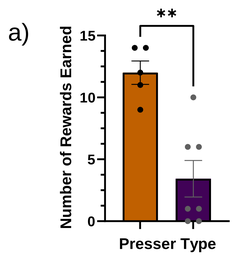
The number of active lever presses made between high-pressing and low-pressing residents differed on 2 days of FR1. There was also a main effect for group on the number of active presses over time. $*$ = $p < .05$.

Active Lever Preference

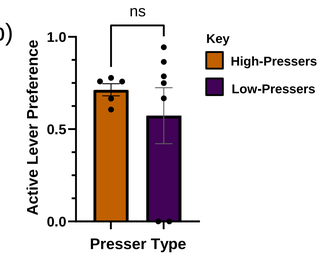


Active lever preference between high-pressing and low-pressing residents did not differ on any day of FR1.

Rewards Earned in PR

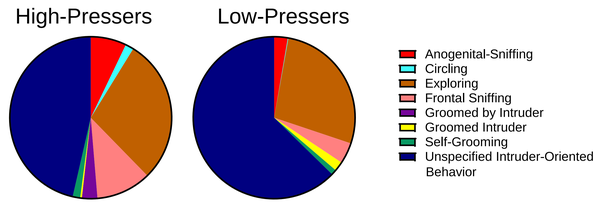


Active Lever Preference in PR



a) High-pressers earned significantly more rewards than low-pressers during progressive-ratio testing ($**$ = $p < .01$).
b) High-pressers showed an active lever preference greater than random chance ($p = .003$).

FR1 Testing Behavioral Ethograms



Pie charts show behavior distribution during the reward phase. High-, but not low-pressers, were groomed by intruders. Anogenital sniffing differed significantly between high and low-pressers ($p < .05$). Frontal sniffing tended to differ ($p = .09$).

Summary and Conclusions

1. No aggressive behavior exhibited by resident females was observed towards the young intruder females throughout the entire study. However, some mice still acquired lever-pressing behavior.

2. Therefore, residents were split into two groups (using a median-split) to investigate why residents lever-pressed. Residents that more frequently pressed the active lever were considered "high-pressers," while the rest of the residents were considered "low-pressers."

3. High-pressers did not show a preference for pressing the active lever over the inactive lever during fixed-ratio 1 testing. Thus, high-pressing residents may have found indiscriminate lever-pressing to be rewarding.

4. However, high-pressers earned significantly more rewards than low-pressers during progressive-ratio testing. This may have been because the active lever did not retract upon being pressed in this test, allowing residents ample opportunity to active lever-press compared to FR1.

5. Notably, high- and low-pressers differed in their distribution of behaviors during the reward phase of FR1. Frontal-sniffing and anogenital sniffing occurred more often in high-pressers, and only high-pressers were groomed by intruders.

Future Study Directions

Were the high-presser resident mice lever-pressing because lever-pressing itself was rewarding?

References

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2. Golden, S.A., Heins, C., Venniro, M., Caprioli, D., Zhang, M., Epstein, D.H., & Shaham, Y. (2017). Compulsive addiction-like aggressive behavior in mice. Biological Psychiatry, 82, 239-248.

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