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Introduction

Exposure to extreme stress can negatively impact behavior and lead to prolonged fear sensitization and the development of various anxiety disorders such as PTSD (Milad et al., 2008). This can be studied using **stress-enhanced fear learning (SEFL)**, where prior exposure to stress exacerbates later context fear conditioning and renders it resistant to extinction (Rau et al., 2005). Previous research shows extinction may not be as effective at reducing fear behavior in prior stress exposed rodents, with aged rodents also displaying impairments in extinction (Kaczorowski et al., 2012; Robinson et al., 2024).

US deflation (weak-shock exposure following contextual fear conditioning; Bonanno et al., 2023) may be a better alternative than extinction at reducing fear behavior under normal conditions; however, it has yet to be determined if US deflation can effectively reduce stress-enhanced fear.

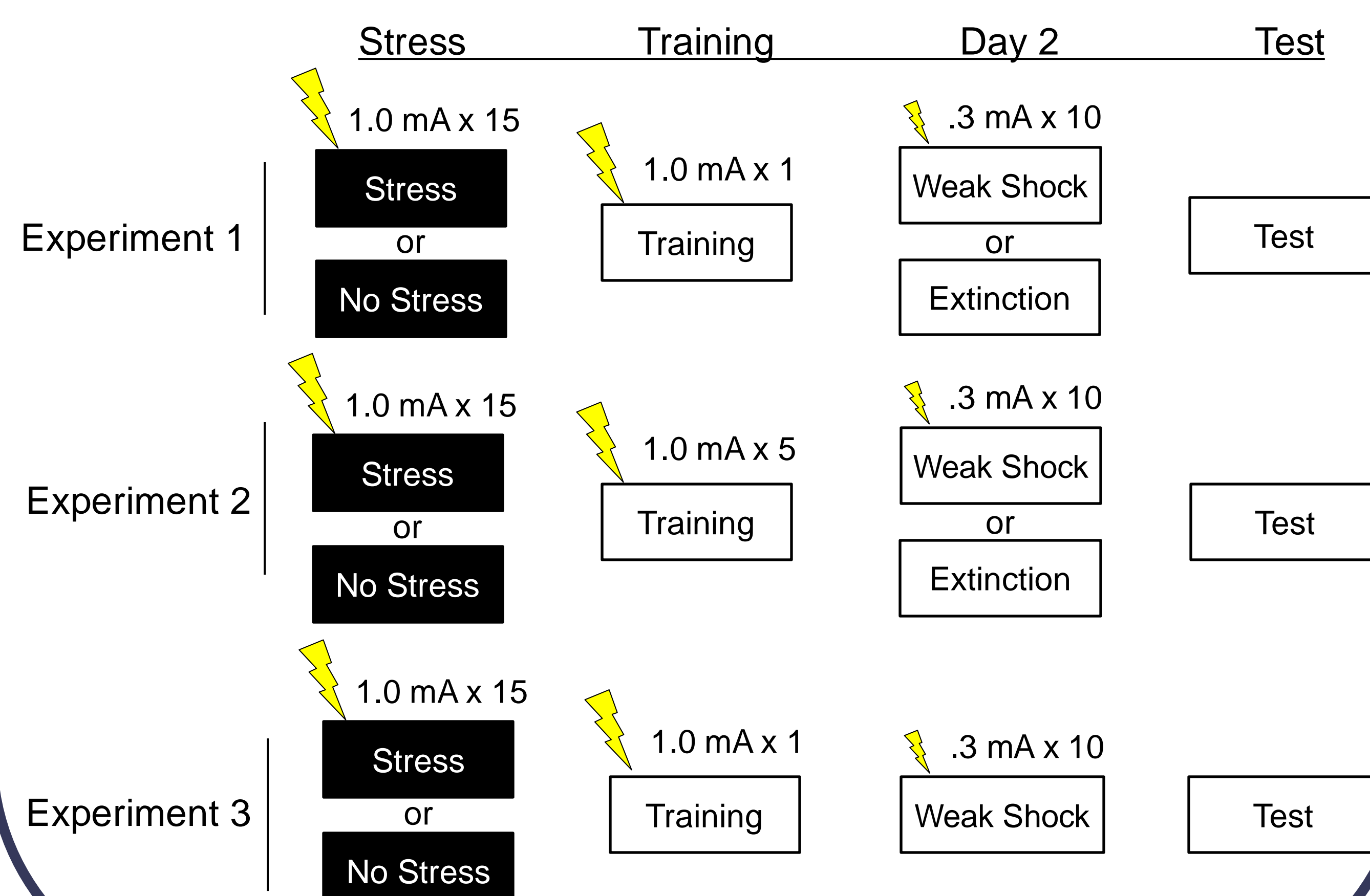
We aimed to test if US deflation could reduce contextual fear in a SEFL paradigm as well as to test if this procedure was effective in aged rodents.

Methods

Male and female Long Evans rats were used in Experiments 1 and 2, and males were used in Experiment 3 due to the limited availability of aged rats. Behavioral design for all three experiments is depicted below.

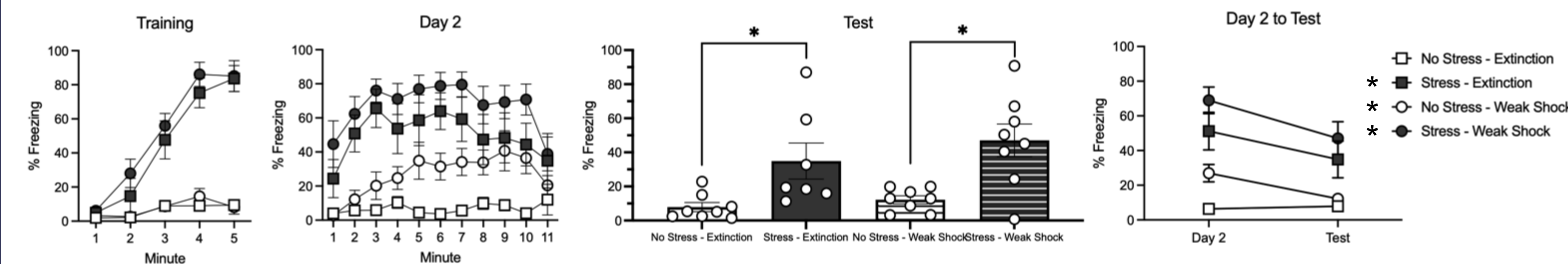
Sessions took place in Colbourn conditioning chambers with stainless-steel sides and plexiglass front and rear. For stress, rodents were placed in conditioning chambers consisting of red LED light and cleaned with ammonium hydroxide-based cleaner. On subsequent days, rodents were placed in conditioning chambers with white LED light, white noise, and cleaned with lemon-scented Lysol.

FreezeFrame was used to automatically score freezing in real time. Freezing was defined as the absence of movement except for that which was necessary for respiration (Rajbhandari et al., 2018).



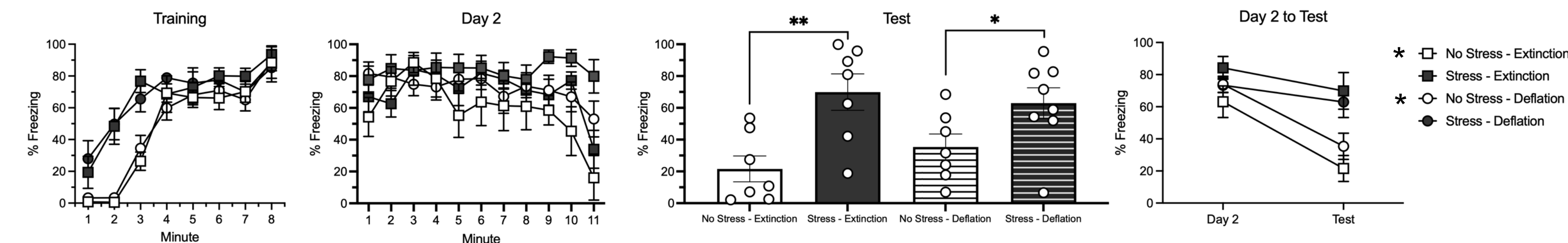
Results

Experiment 1: US Deflation reduces SEFL.



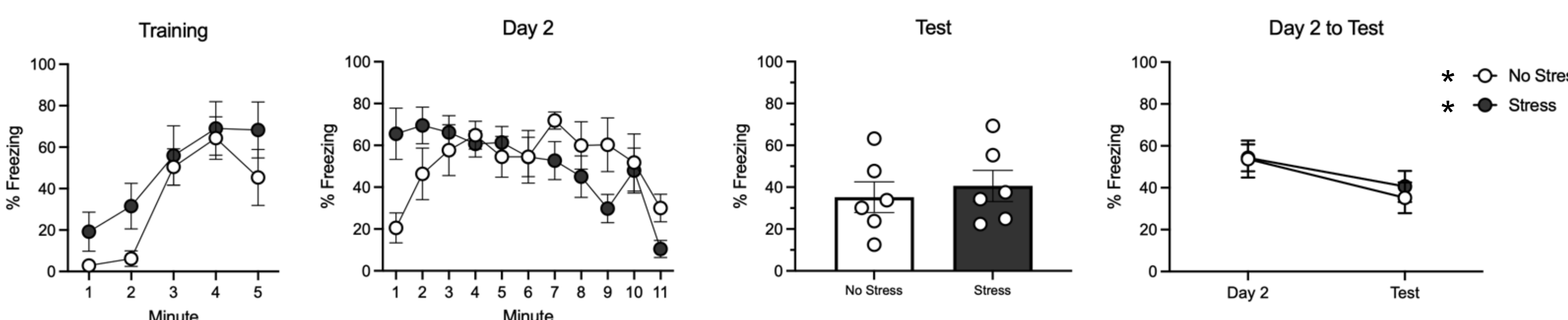
- Only animals that received prior stress increased freezing to the single shock.
- On day 2, prior stress exacerbated freezing levels before shocks began in the novel context.
- Both US deflation and extinction reduced freezing behavior of rats who had received prior stress.

Experiment 2: US deflation does not reduce SEFL following extended training.



- Following 5 context-shock pairings, neither US deflation or extinction worked to decrease fear in previously-stressed rats; only No Stress rodents displayed a significant decrease in fear behavior.

Experiment 3: US deflation reduces SEFL in aged rats.



- Aged rodents displayed a strong SEFL effect with prior stress enhancing fear learning, evidenced by increased freezing on Day 2.
- Despite showing impairments in traditional extinction, aged rodents showed a significant decrease in freezing behavior following US deflation.

* Next to group name indicates groups that decreased freezing between Day 2 and testing.

Conclusions

- US deflation reduced fear behavior using a SEFL paradigm.
- Additional shock presentations renders US deflation ineffective, possibly sensitizing the response to the weak shock to exacerbate fear responding.
- Stress-enhanced fear learning can be replicated in aged rodents.
- SEFL can be effectively decreased in aged rodents via US deflation following a single context-shock pairing.

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References

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