Fear reduced through unconditional stimulus deflation is behaviorally distinct from extinction and differentially engages the amygdala

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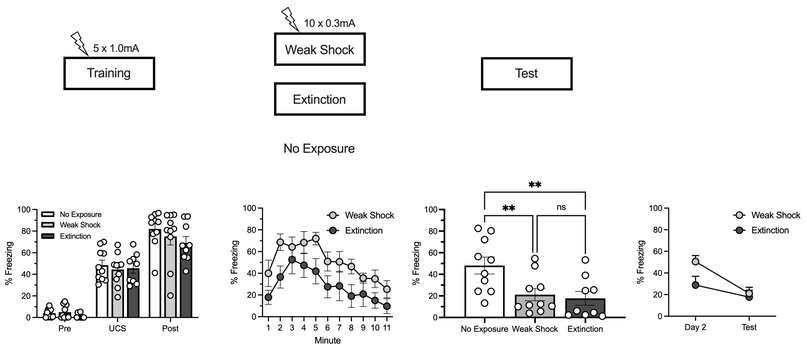
Introduction

Previous work has demonstrated that while exposure to 2 weak shocks following context fear conditioning increases freezing evoked by that context, 10 weak shocks decreases freezing (Ferrara et al., 2019).

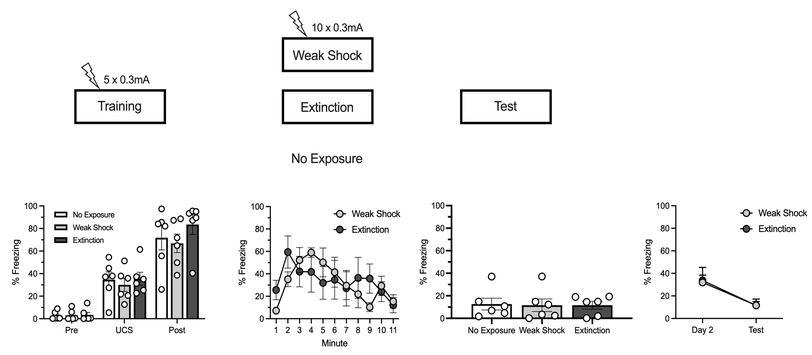
Behaviorally, this reduction in freezing following the weak shock exposure resembles performance observed following extinction learning (Bouton et al., 2021; Pavlov, 1927).

Here, we aimed to directly compare this 10 weak shock procedure to extinction both behaviorally and molecularly using male and female adult Long Evans rats.

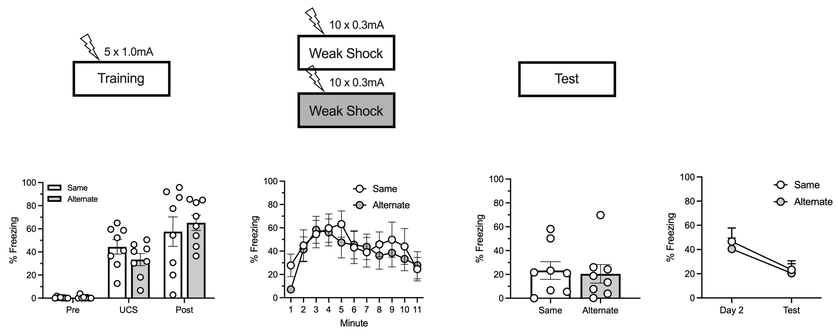
The weak shock and extinction conditions both reduce freezing relative to animals who received no behavioral intervention.



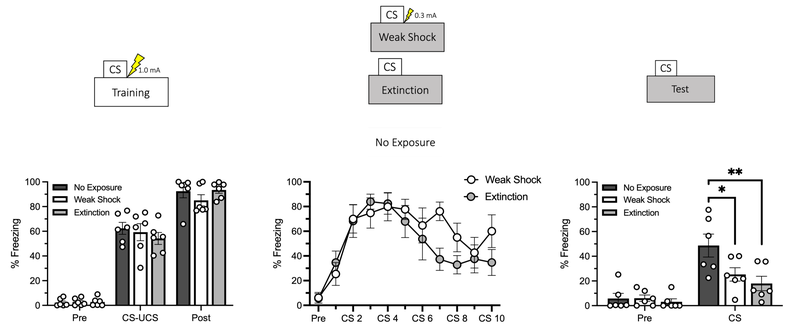
Conditioning with the weak shock does not create a fear memory.



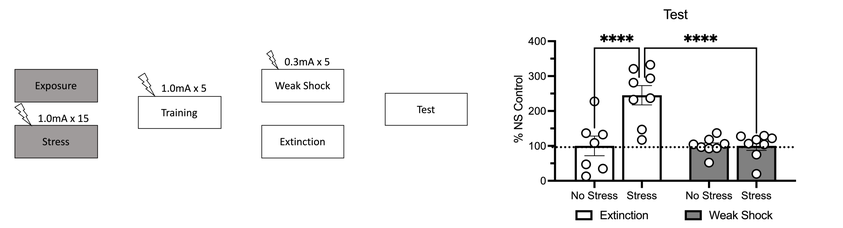
Presenting the weak shock in either the training (Same) or shifted (Alternate) context reduced freezing during testing.



The weak shock and extinction conditions both reduce freezing relative to animals who received no behavioral intervention following delay (cued) fear learning.



UCS deflation, but not extinction, is unaffected by prior footshock-induced stress.

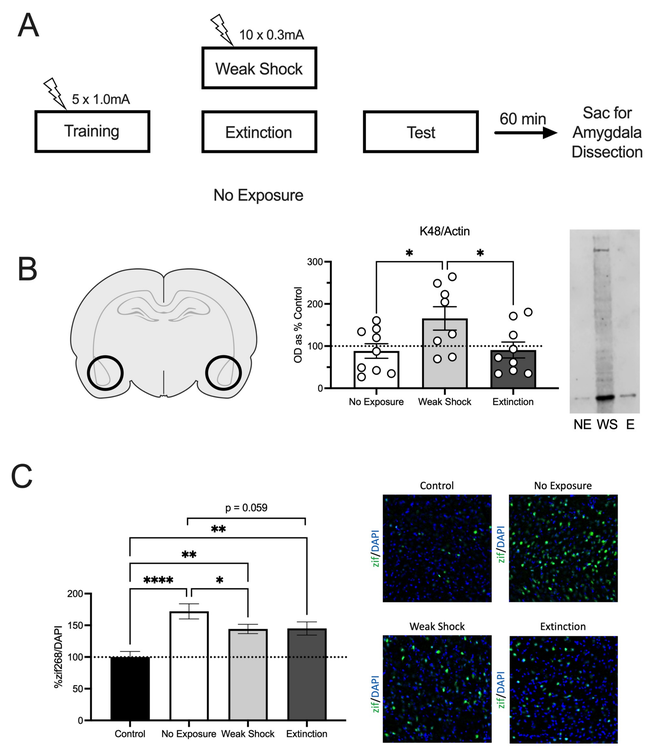


Differential patterns of neural activity are associated with weak shock and extinction.

A) Experimental design for Western blotting and immunofluorescence.

B) The weak shock increased K48 expression in the basolateral amygdala (BLA) relative to the extinction and no exposure conditions following testing.

C) The weak shock and extinction conditions showed decreased zif268 expression in the BLA compared to the no exposure condition following testing.



Conclusions

Weak shock exposure and extinction decreased context fear relative to a group that received no exposure on the second day in both context and cued paradigms. Unlike in extinction, the decrease produced by weak shock exposure was not context-dependent and was unaffected by prior stress. Zif268 expression in the BLA was reduced in the weak shock and extinction groups relative to the no exposure group, but synaptic K48 levels in the BLA were only increased in the weak shock group.

These results are similar to previous work in which habituation to an unconditional stimulus (UCS) alone following conditional stimulus (CS)-UCS pairings resulted in reduced responding to the CS (Rescorla, 1973). However, we did not use the same intensity of UCS during the second phase making habituation to the original UCS unlikely. Therefore, our findings might align more closely with work demonstrating that animals will modulate their response to a CS based on the current value of the UCS it predicts (e.g., Holland, 1990).

Together, our results suggest that the weak shock procedure does not rely entirely on the creation of a new inhibitory memory like that created in extinction and instead might alter the original representation of the shock to reduce fear responding.

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