The effect of normal aging on extinction learning.

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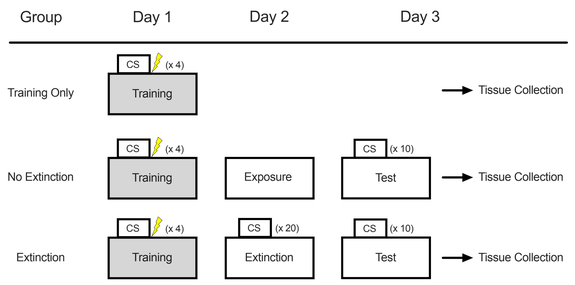
Introduction

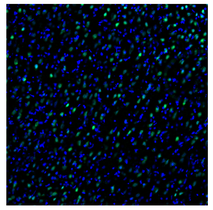
Healthy aging often coincides with cognitive deficits, including impairments in cognitive flexibility.

Cognitive flexibility can be assessed through extinction learning, in which a previously reinforced conditional stimulus is presented without an aversive outcome (Bonanno et al, 2023).

Further, dysfunction in memory-related regions like the hippocampus and retrosplenial cortex has been implicated in age-related memory impairments (Trask & Fournier, 2022).

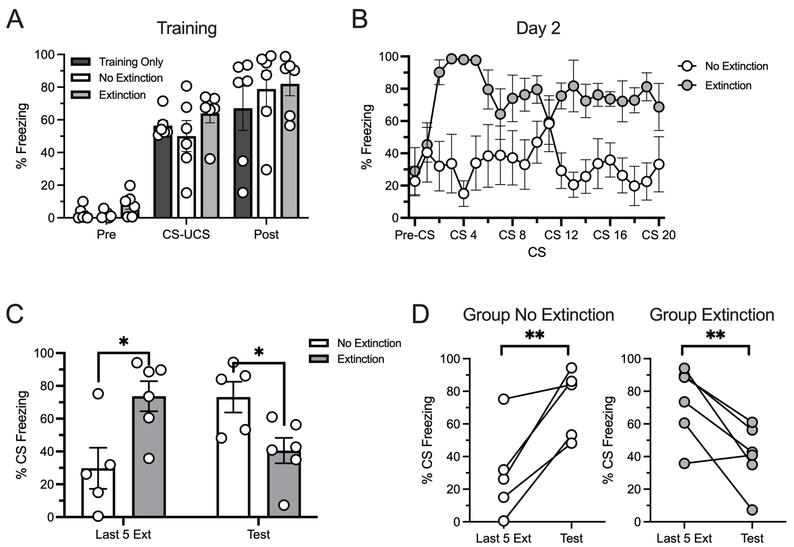
We extinguished a delay fear memory in young (3-month) and aged rats (20-month) to investigate how aging might affect extinction learning capabilities.



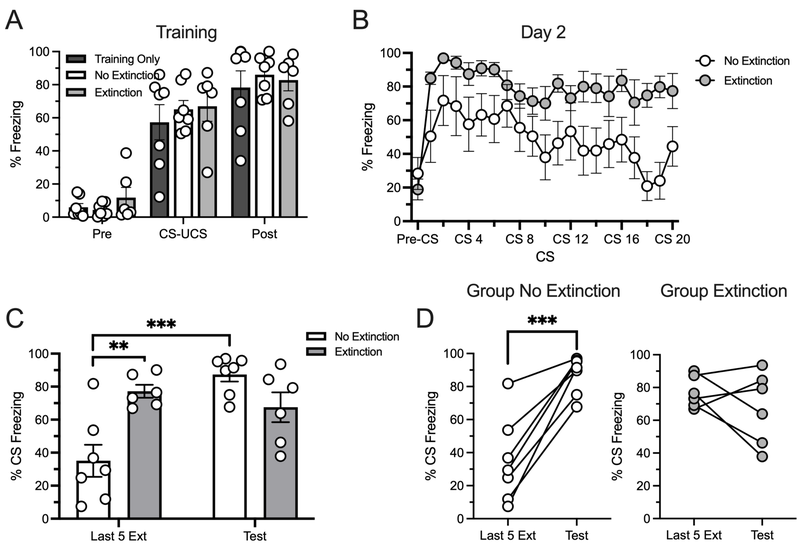


Example image in the anterior retrosplenial cortex.

Young rats decreased freezing following extinction.



Aged rats did not decrease their freezing following extinction.



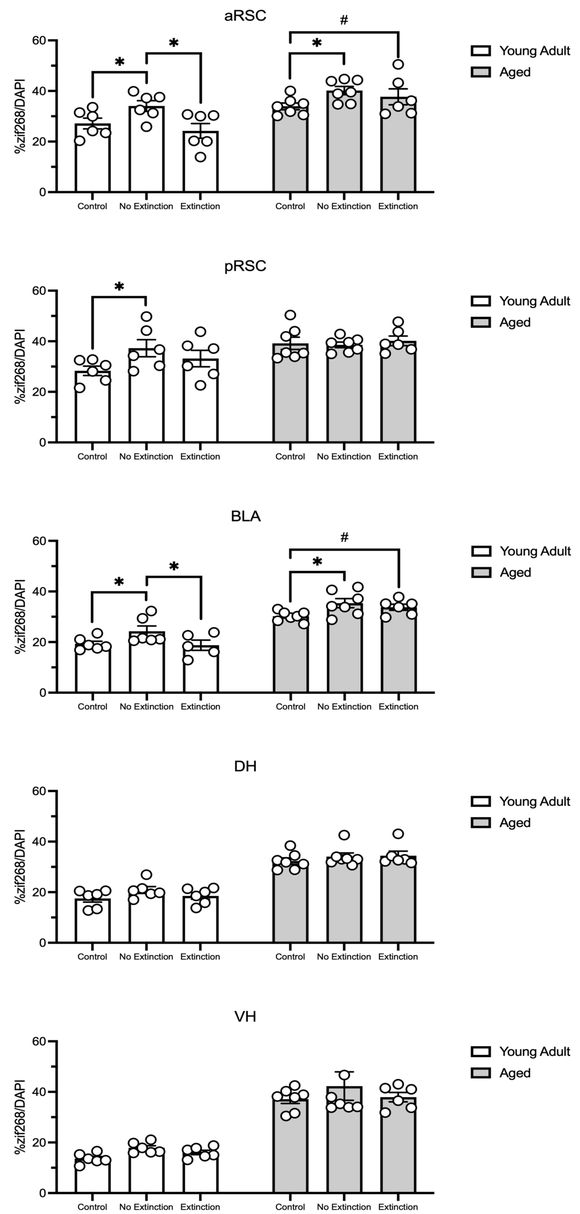
Young rats that received extinction had decreased zif268 protein expression in the aRSC; aged rats did not.

Fear retrieval in the young rats that did not receive extinction was associated with increased zif268 in the pRSC. This pattern was not observed in aged rats.

Young rats who received extinction had decreased zif268 protein expression in the BLA; aged rats did not.

Within each age group, no group differences in zif268 were observed in the DH.

Within each age group, no group differences in zif268 were observed in the VH.



Conclusions

Young rats extinguished their fear responding, showing decreased freezing following extinction. Aged rats failed to show extinction, suggesting a reduced cognitive flexibility in this group.

Distinct patterns of neural activity assessed using zif268 were observed in each age group. In the aRSC and BLA, the extinction group less similar zif268 protein expression than the No Extinction group, tracking with behavioral performance.

Overall, aged rats had higher zif268 protein expression regardless of the group or brain region (similar to Trask et al., 2020), suggesting overall dysfunction in protein regulation and accumulation in aged rats.

Future and ongoing work will assess proteolytic function in these regions, with the hypothesis being that proteolytic function will be reduced in aged animals leading to an increased protein accumulation.

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References

Bonanno, G.R., Met Hoxha, E., Robinson, P.K., Ferrara, N.C., & Trask, S. (2023). Fear reduced through unconditional stimulus deflation is behaviorally distinct from extinction and differentially engages the amygdala. *Biological Psychiatry: Global Open Science.*

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Trask, S., & Fournier, D. I. (2022). Examining a role for the retrosplenial cortex in age-reimpairment. *Neurobiology of Learning and Memory,* 189, 107601

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