

Introduction

Previous work demonstrated asymmetrical generalization of an active avoidance behavior based on visual cues (Oleksiak et al., 2021).

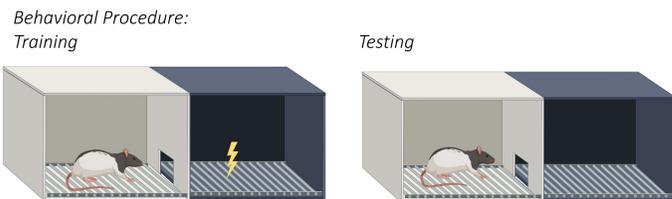
The basolateral amygdala (BLA) has a well-known role in avoidance behavior (Huff et al., 2013).

Less is known about how activity within the retrosplenial cortex (RSC), which has been implicated in fear learning (Trask & Helmstetter, 2022), might contribute to avoidance learning.

Here, we aimed to examine the role of the RSC in acquisition, retrieval, and generalization of inhibitory avoidance.

Methods

Animals: Age matched (~3-month) male and female Long Evans rats.
Apparatus: Behavioral procedures were conducted in two identical passive avoidance chambers housed in a separate room of the laboratory. The major distinction between the two rooms was that one had fluorescent lighting (light room) and the other had red LED lighting (dark room).

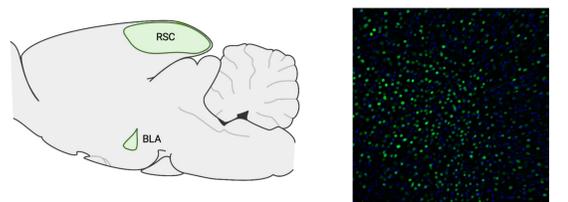


A subset of rats were sacrificed after training with either a weak (0.7 mA) or strong (1.5 mA) footshock.

The rest of the rats were either tested in the same context as training or a different context from training, creating four distinct behavioral groups:

- Group Light/Light (Same)
- Group Dark/Dark (Same)
- Group Light/Dark (Shift)
- Group Dark/Light (Shift)

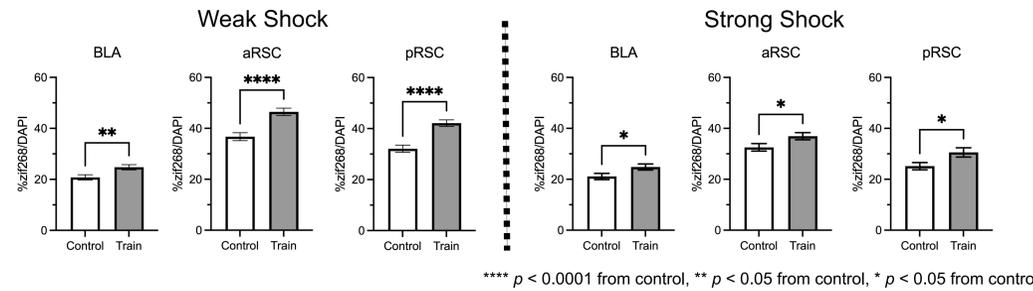
Tissue Collection: 65 minutes following behavioral training (Experiments 1 and 2), or testing (Experiment 3) animals were sacrificed and tissue was collected for immunofluorescence.



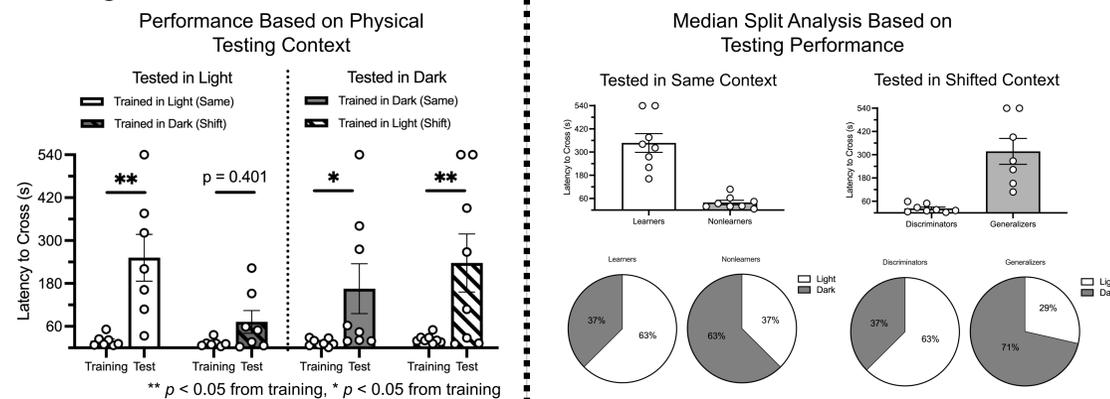
Median Split Analysis: Animals tested in the same context (regardless of context identity) were classified as learners or nonlearners according to a median split of testing performance. Similarly, animals tested in a shifted context (regardless of context identity) were classified as generalizers or discriminators according to a median split of testing performance.

Results

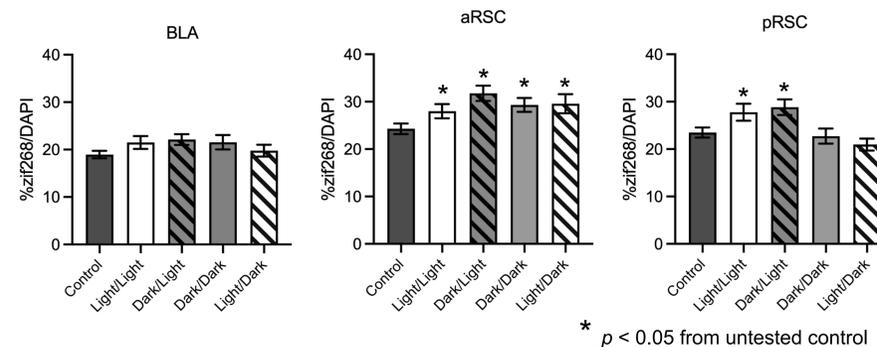
Training with a weak shock (0.7 mA) or a strong shock (1.5 mA) increases zif268 activity in the BLA, aRSC, and pRSC.



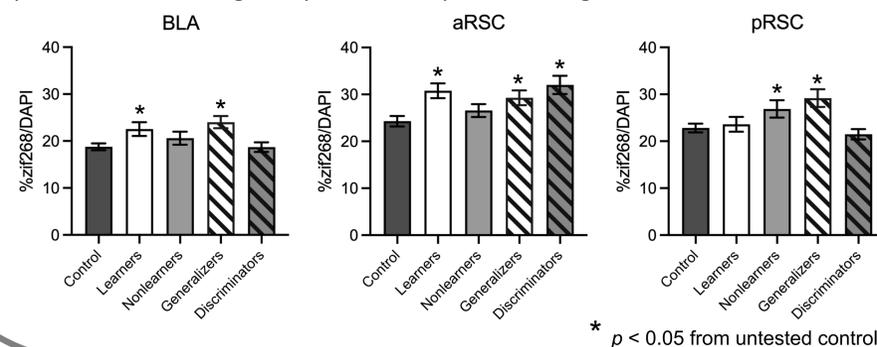
Animals tested in the light maintained context-specificity and animals tested in the dark generalized avoidance behavior.



Patterns of zif268 are generally elevated in the aRSC in tested animals, but zif268 expression is only elevated in the pRSC in animals tested in the light.



While BLA activity correspond with overall levels of avoidance behavior, aRSC activity corresponds with learning and pRSC corresponds with generalization.



Conclusions

Inhibitory avoidance training with both weak and strong shocks increases zif268 expression in the BLA and RSC.

Animals tested in a light context demonstrated the ability to discriminate, indicated by longer latencies to cross in the same context and shorter latencies to cross in a novel context. However, animals tested in a dark environment exhibited generalized avoidance behavior, indicated by similarly long latencies to cross when testing was in the same or a shifted context.

Zif268 expression was generally elevated in the aRSC in tested animals, but zif268 expression is only elevated in the pRSC in animals tested in the light. Following categorization of animals into discriminators, generalizers, learners, and nonlearners, we found elevated levels of zif268 in the BLA corresponded with higher levels of avoidance: only the learners and generalizers showed increased activity. Only discriminators and learners exhibited elevated levels of zif268 activity in the aRSC, while only generalizers showed elevated zif268 activity in the pRSC.

These findings suggest that visual cues can contribute to asymmetrical contextual generalization and discrimination, with differential engagement of retrosplenial subregions to these processes.

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References

Huff, M. L., Miller, R. L., Deisseroth, K., Moorman, D. E., & LaLumiere, R. T. (2013). Posttraining optogenetic manipulations of basolateral amygdala activity modulate consolidation of inhibitory avoidance memory in rats. *Proceedings of the National Academy of Sciences*, 110, 3597-3602.

Oleksiak, C. R., Ramanathan, K. R., Miles, O. W., Perry, S. J., Maren, S., & Moscarello, J. M. (2021). Ventral hippocampus mediates the context-dependence of two-way signaled avoidance in male rats. *Neurobiology of Learning and Memory*, 183, 107-158.

Trask, S., & Helmstetter, F. J. (2022). Unique roles for the anterior and posterior retrosplenial cortices in encoding and retrieval of memory for context. *Cerebral Cortex*, 32, 3602-3610.