Initial inhibitory avoidance training produces changes in neural activity in the retrosplenial cortex

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Introduction

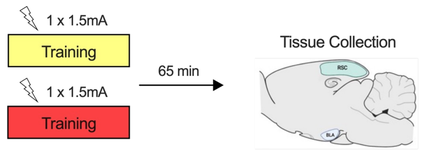
- Studying the neural basis of fear-driven avoidance behavior can better inform and aid in the development of treatments for those with anxiety disorders.
- In inhibitory avoidance learning, rats are placed in a two-compartment chamber in which one side is paired with a shock. Using distal contextual cues of the room and proximal cues of the chamber itself, the animals learn to avoid the side associated with the shock.
- While previous work has implicated regions such as the basolateral amygdala (BLA) in avoidance learning (Huff et al., 2013), less is known about the retrosplenial cortex (RSC) and its subregions, the anterior and posterior retrosplenial cortices (aRSC and pRSC), which also play an important role in Pavlovian fear conditioning (Trask & Helmstetter, 2022).

Here, we examined neural activity in the BLA and RSC (including expression of the immediate early gene zif268 and perineuronal nets) during inhibitory avoidance memory formation.

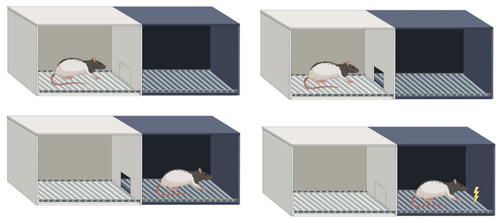
Methods

Subjects: Age matched (~3-months) male (n = 6) and female (n = 6) Long Evans rats.

Behavioral Design: Animals received training in either a well-lit or dark environment.

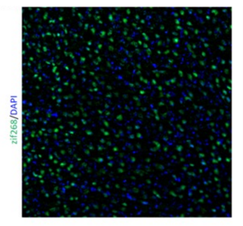


Behavioral Procedure: Animals were placed on the white side of the chamber. Following 30 s, the door opened. Once the animal crossed to the black side of the chamber, they received a 2-s 1.5mA footshock.

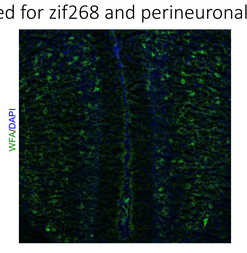


Tissue Collection: 65 minutes following training, animals were sacrificed, and brain tissue was collected.

Immunofluorescence: Tissue was stained for zif268 and perineuronal nets



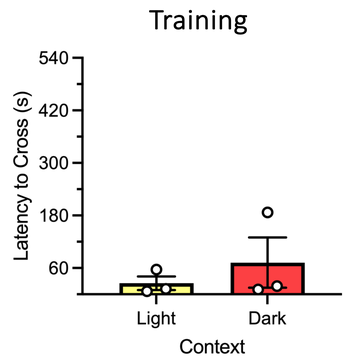
Zif268 (green) expression in the RSC.



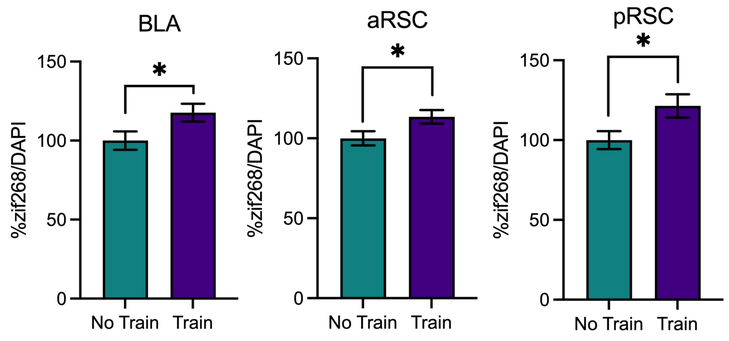
PNNs (green) in the RSC.

Results

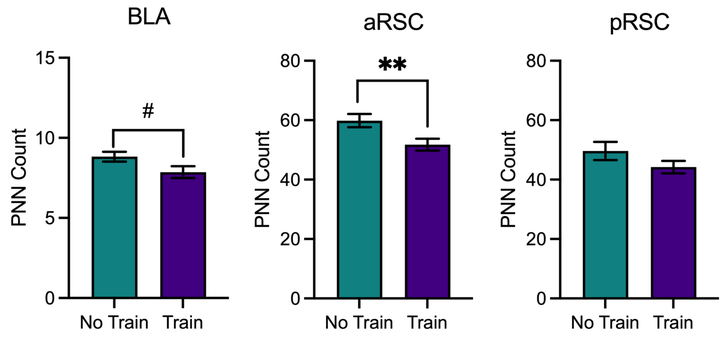
As expected, animals that received training did not differ in their latency to cross when training occurred in the light or in the dark environments.



Training with a strong shock increased neural activity in the BLA and both subregions of the RSC.



Trained animals showed a decrease in perineuronal nets (PNNs) in the aRSC and BLA.



Conclusions

Inhibitory avoidance training increases zif268 activity in the anterior retrosplenial cortex, posterior retrosplenial cortex, and BLA compared to homecage controls. It also decreases perineuronal net (PNN) counts in the aRSC and BLA.

These findings suggest that the RSC is involved in inhibitory avoidance memory formation, similar to its role in associative memory formation (Kwapis et al., 2015).

Reductions in PNNs in the aRSC and BLA suggest increased synaptic plasticity within these regions. The degradation of PNNs is typically associated with memory formation (Carulli et al., 2020), further supporting the idea that the RSC plays an important role in initial acquisition of inhibitory avoidance memory.

Follow-up experiments should look further into how memory retrieval and consolidation of inhibitory avoidance learning affects neural activity in the retrosplenial cortex and test a necessity of activity within this region for both memory formation and retrieval.

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