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The role of mTOR signaling in enhanced fear extinction produced by acute, voluntary exercise

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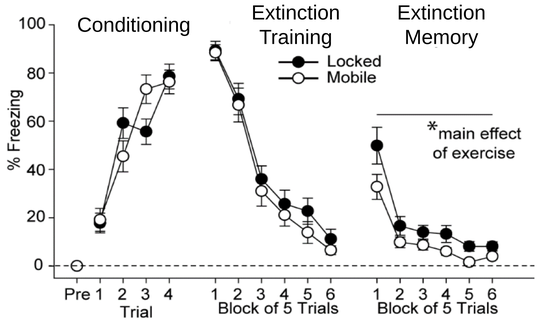
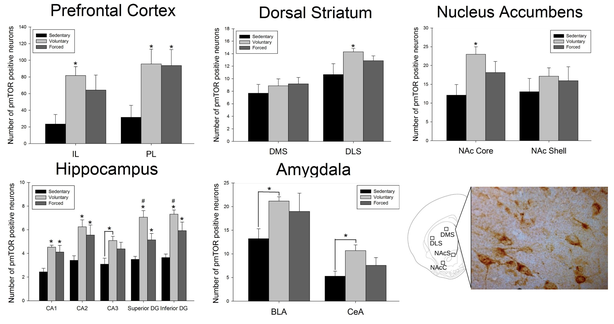
Background

- Exercise produces beneficial effects on cognition and mental health. In rats, these beneficial effects include enhancing fear extinction memory (Bouchet et al. *Learning and Memory* 2017).
- The mechanisms by which a single session of acute exercise (2 hours) enhances fear extinction are unknown.
- The mammalian target of rapamycin (mTOR) is a translation regulator involved in synaptic plasticity, cell growth, and proliferation. mTOR signaling is increased after chronic exercise (6 weeks) in brain areas involved in learning and emotional behavior (Lloyd et al. *Behavioural Brain Research*, 2017).
- mTOR is therefore a compelling potential mediator of the cognitive benefits of exercise.

A single bout of acute exercise after fear extinction training enhances fear extinction memory



Chronic exercise increases mTOR signaling



Experimental Goal

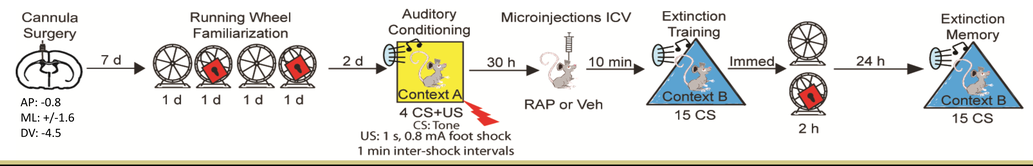
- The objective of this study was to determine whether mTOR signaling is necessary for enhanced fear extinction produced by acute, voluntary exercise.

Hypothesis

- It was hypothesized that blocking mTOR signaling would prevent the ability of acute exercise to enhance fear extinction memory.

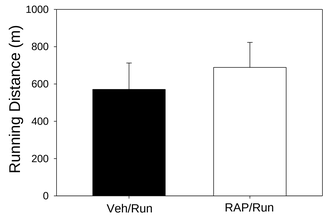
Methods

- mTOR was blocked with an intracerebral-ventricular (ICV) injection of rapamycin (50 µg/2 µL; Cota et al. 2006), while the control groups received a vehicle (DMSO) solution (rate of diffusion = 0.5 µg/1 minute).

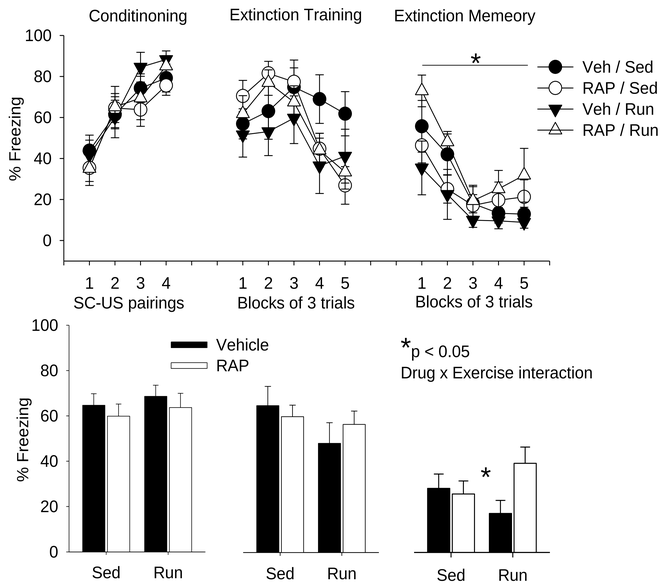


Results

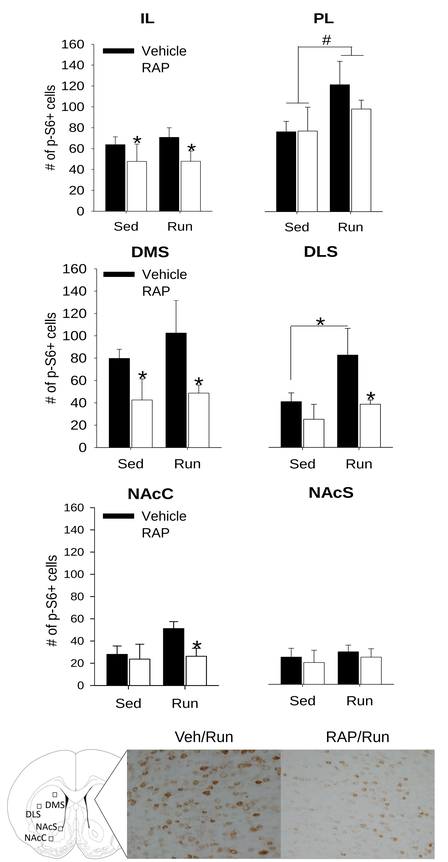
Rapamycin has no effect on voluntary exercise behavior



Blocking mTOR signaling eliminated the ability of acute exercise to enhance fear extinction memory



Rapamycin blocks acute exercise-induced increases in mTOR signaling



Conclusions

- Acute exercise enhances fear extinction through a mechanism involving mTOR signaling.
- Rapamycin blocks the acute exercise-induced increases in mTOR signaling without altering fear extinction learning or running behavior.
- Factors that increase mTOR signaling could be novel targets for the treatment of fear and anxiety-related disorders.

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