

Introduction

Throughout our lives we are put through different situations in life, which tend to leave us with memories. Memories of fear are often found to be acquired fast and temporally enduring. Meanwhile procedures that are aimed to reduce fear and anxiety like exposure therapy, often produce fear suppression that develops slowly or is short-lived⁽¹⁾. A recent study on rats has revealed that mPFC inputs to RE are involved in fear inhibition, which could mean that fear could become a thing of the past⁽²⁾.



Figure 1. Photo of person in fear⁽¹⁾.

Testing on rats to inhibit fear

Rats were put in an experiment to assess if it was possible to inhibit fear. Due to the important role for mPFC-HPC interactions in emotional memory retrieval, researchers proposed that RE serves as a center by which HPC is regulated by mPFC to suppress the retrieval of memories containing fear. Researchers then aimed to manipulate mPFC projections to RE, to inactivate mPFC terminals with the goal of inhibiting fear in the rats⁽²⁾.

How was it done?

1. Surgically rats were bilaterally infused with AAV8-hSyn-eGFP into PL and IL, then were left for 4 weeks.
2. After the first surgery the rats were put under a second surgery to implant cannula targeting the RE.
3. 10 minutes before testing, the rats were given intraperitoneal injections of either saline (3mg/kg) in the vivarium or CNO and then were put back into their cages.
4. Rats underwent auditory fear conditioning which consisted of a five tone footshock in 60s interstimulus intervals (ISIs).
5. Fear extinction also took place which consisted of receiving a 3 min stimulus-free BL, which is followed by 45 tone-alone presentations in 30s (ISIs).
6. Half of the rats underwent fear extinction and conditioning in a different order and each session was recorded.⁽²⁾

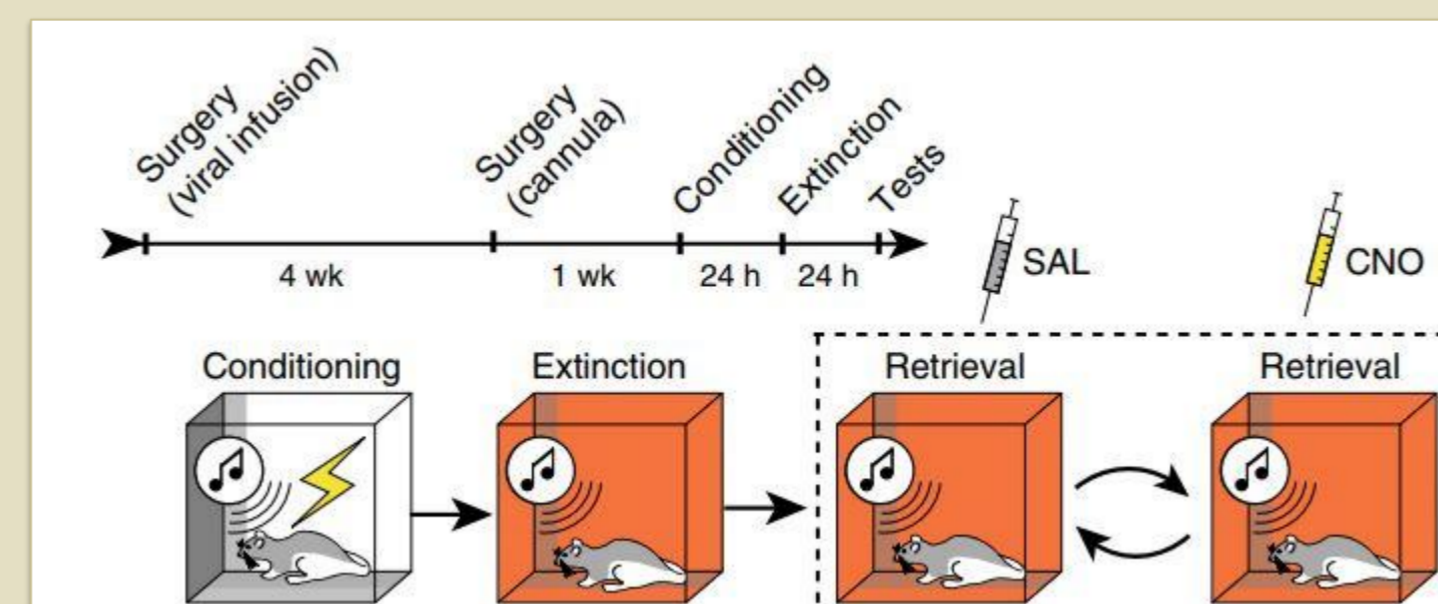


Figure 2. Visual summarization of steps taken during the experiment⁽²⁾.

Results

Through the experiment It was revealed that direct HPC-mPFC projections were not able to inhibit fear, but actually contributed to the excitation of fear. Also by impairing both extinction encoding and retrieval, it lead to excessive fear in safe situations⁽²⁾.

Conclusion

Before fear could possibly be inhibited more studies would be needed to completely understand how dysfunction in mPFC-RE circuits underlies psychopathology associated with stress and trauma related events. Hopefully with today's advanced technology researches will be able to provide a way to inhibit fear soon, which could significantly change people who deal with PTSD or Anxiety lives.

References

1. Maren S, Holmes A. Stress and Fear Extinction. *Neuropsychopharmacology*. 2015;41(1):58–79. doi:10.1038/npp.2015.180
2. Ramanathan KR, Jin J, Giustino TF, Payne MR, Maren S. Prefrontal projections to the thalamic nucleus reuniens mediate fear extinction. *Nat Commun*. 2018;9(1):4527. Published 2018 Oct 30. doi:10.1038/s41467-018-06970-z