Role of the Anti-Inflammatory Cytokine IL-10 in Fear Learning

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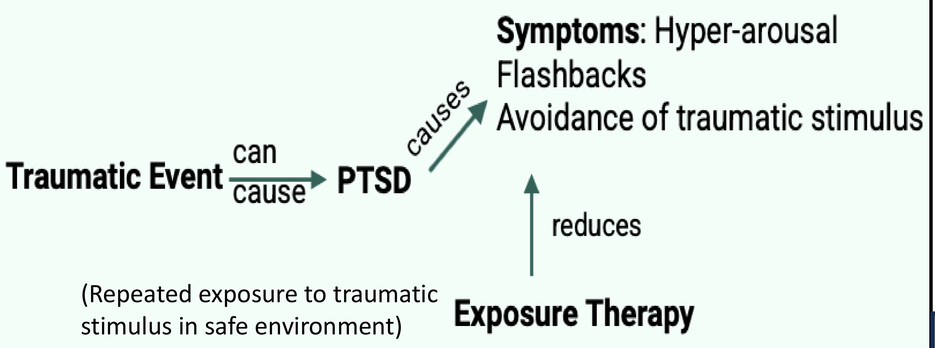
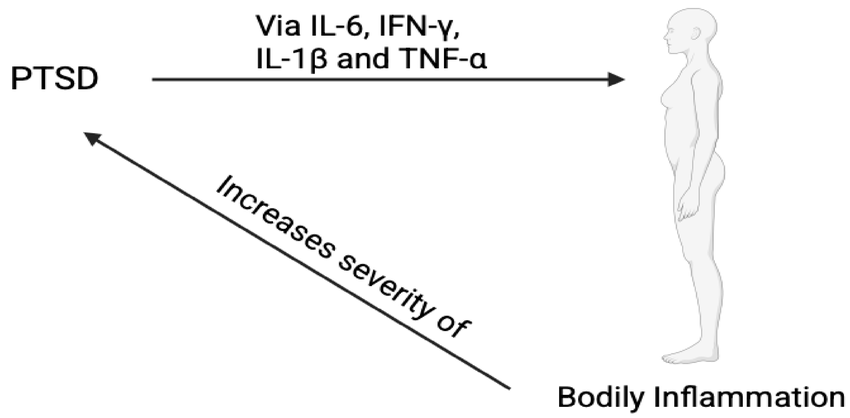
Introduction



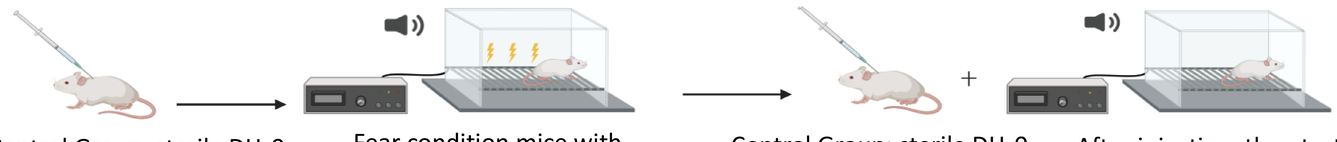
- PTSD afflicts over 13 million people in the U.S.A. and 6% of the population will acquire it at some point in their lives.
- Current treatment has high drop-out rates due to the distress caused by PTSD
- Finding adjunct treatments that may accelerate exposure therapy will significantly decrease suffering and improve people's lives.



- Higher levels of anti-inflammatory cytokines IL-10, IL-4, and TGF-B after a traumatic event correlate to decreased severity of PTSD symptoms.
  - IL-10 may do that by modulating IL-6.
- IL-10 in the brain can counteract effects of learned helplessness (Worthen et al., 2020). Injection of IL-10 peripherally can reduce depressive symptoms by counteracting IL-6 => peripheral IL-10 has a neuroactive effect (Voorhees et al, 2013)

Aim: Investigate if injection of anti-inflammatory cytokine IL-10 before fear learning/during extinction training decreases PTSD symptom severity and accelerates extinction learning.

Methods



Control Group: sterile DH_20
Pre Group: IL-10
Post Group: sterile DH_20
Throughout Group: IL-10

Fear condition mice with auditory cue

Control Group: sterile DH_20
Pre Group: sterile DH_20
Post Group: IL-10
Throughout Group: IL-10

After injection, then test mice for fear freezing/perform extinction training.

Results

Day 1 Freezing Due to Cue

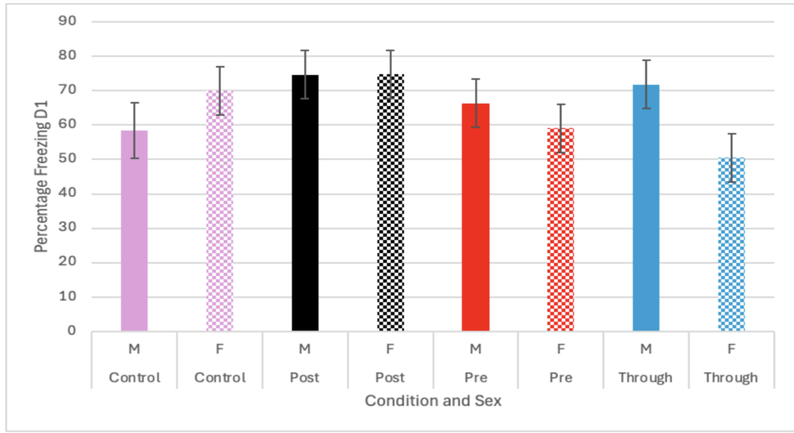


Figure 1: No significant difference found. All p-values > 0.092. Error bars indicate SEM

Freezing Across 4 Days of Extinction

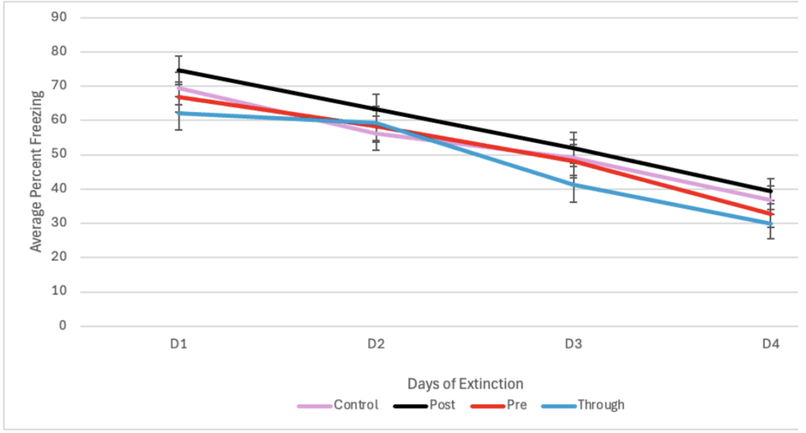


Figure 2: No significant difference found. Freezing decreases each day for all conditions ($p<0.01$). All other p values > 0.37. Error bars represent SEM.

Conclusions

- IL-10 at the chosen dosage does not modulate fear learning at any injection time point.
- This may be due to inadequate dosage, timing, or requirement to use multiple cytokines to show effect.
- IL-10 has been used alone successfully only for depression and restraint stress, which differ from fear learning
- Fear learning is an imperfect model of PTSD as it cannot model effects such as nightmares, flashbacks, etc., and IL-10 may influence the latter effects.

Future Directions

- Determine bioavailability of IL-10 and inject at the point of maximal anti-inflammatory effect.
- Use multiple anti-inflammatory cytokines instead of just IL-10
- Measure symptoms of depression, anxiety, etc. in parallel to see if IL-10 exerts effect there.

Literature Cited

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Acknowledgements: This study was supported by the Henry J. Copeland Fund