Simulating Direct Electrical Stimulation to Restore Fear-Extinction Balance in PTSD: Integrating Spiking Neural Networks and Mean-Field Models

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Introduction

Post-Traumatic Stress Disorder (PTSD) is a mental health condition commonly caused by traumatic experience recall that affects ~13 million people in the U.S.

One effect is heightened fear responses to conditioned stimuli in the basolateral amygdala (**BLA**) *Ref. (1)*

- Associated with following amygdala dysfunction: **hyperactivity**, **fear extinction**, decreased plasticity, and reduced inhibitory control
- Fear Extinction - neural process that suppresses the activity of fear-associated pathways
- Chronic stress impairs **top-down regulation** by the medial prefrontal cortex (mPFC) *Ref. (2)*

Direct Electrical Stimulation (**DES**) involves surgically implanted electrodes that deliver electrical currents to target regions in the brain.

- High-frequency stimulation (~130 Hz) can induce a **depolarization block**, where sodium channels stay open and prevent neuronal firing *Ref. (3)*
- Commonly used to treat psychiatric conditions such as Parkinson's and Epilepsy.
- Deep Brain Stimulation (**DBS**), a form of DES, has shown promise in preclinical trials and case reports as a potential treatment for PTSD *Ref. (4)*

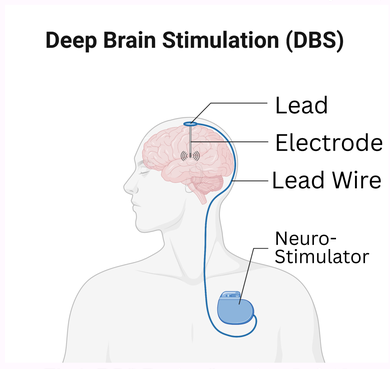

Fig 1. DBS Device Overview *Ref. (5)*

Goal: Understand and replicate PTSD-related neural dysfunctions underlying heightened fear responses and evaluate the impact of DBS across varying conditions.

Methods

Fear Learning Pathway

- **Thalamus** relays sensory input to the BLA.
- Dorsal hippocampus (dHPC) contributes precise spatial context; ventral hippocampus (vHPC) signals emotional/threat context.
- Intercalated cells (ITC) act as an inhibitory gate, suppressing activity in the central amygdala (CeA).
- The CeA drives the fear response (e.g., freezing, heart rate increase)

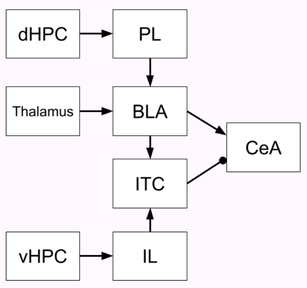

Fig 2. Fear Pathway Overview *Ref. (6-9)*

Model A - **Mean-Field Network** based on Fig 2.

- **Approach:** Rate-based equations simulate average population activity of each brain region
- PTSD modifications:
  - Reduced effectiveness of IL
  - Weakened vHPC-mediated inhibition of BLA
  - Diminished IL drive to ITC
- Applied low-frequency DES directly to the IL to stimulate enhanced cortical influence.

Model B - Adapted **Spiking Neural Network** *Ref. (10-11)*

- Architecture: 3200 excitatory and 800 inhibitory leaky-integrate-and-fire (**LIF**) neurons.
- Contextual Input simplified into CTX-A&B connections with **Hebbian synaptic plasticity**
- PTSD Modifications - reduced synaptic learning rate, increased background activity, and inclusion of CTX-A leakage during extinction phase
- DBS Modifications - Modeled 130 Hz stimulation, enhanced inhibitory synaptic conductance

Results

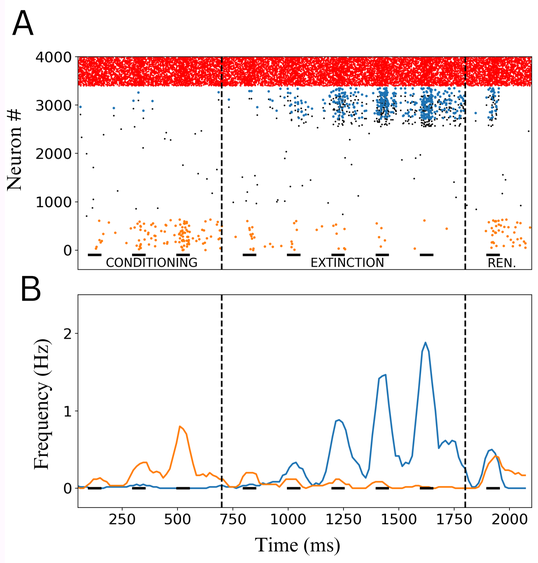

Fig 3. A) Raster plot of normal fear learning; red is inhibitory neurons, black is excitatory interneurons, orange is connected to CTX-A (popA), blue is connected to CTX-B (popB). **B)** Firing rate of popA and popB.

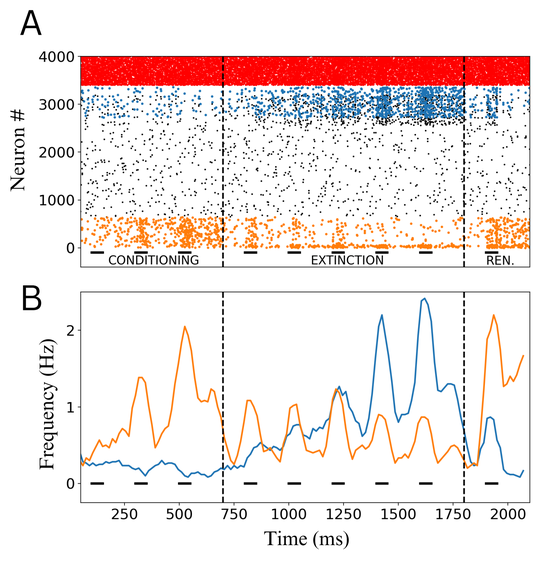

Fig 4. A) Fear learning with PTSD symptoms. Increased background activity causes denser excitatory population fire rates. **B)** PopA shows increased activity during extinction, and PopB learning rate decreases.

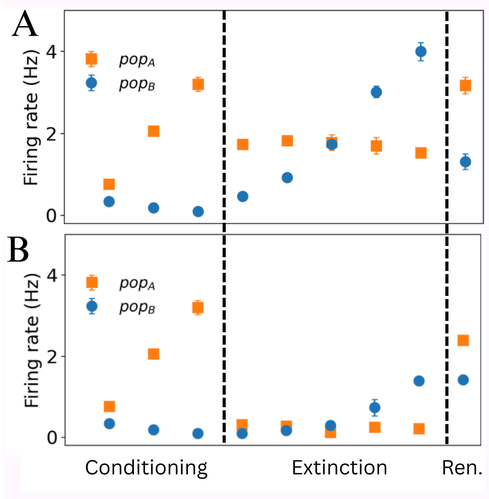

Fig 5. A) Firing rate with PTSD symptoms. **B)** Firing rate with DBS treatment during extinction

Parameter	alpha_synapse	w_syn (EXC->INH)	w_syn (INH->INH)	CTX-A Activation in Extinction	BKG Input EXC	BKG Input INH
Normal	0.002	1.25 nS	2.5 nS	0%	5.0 Hz	6.0 Hz
PTSD	0.001	1.125 nS	2.25 nS	10% of neurons	6.0 Hz	6.6 Hz

Fig 6. Parameter changes of the SNN

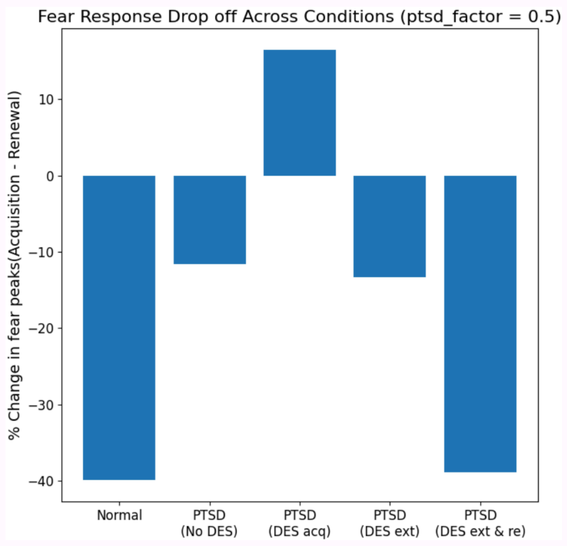

Fig 7. Bar graph showing % change in fear peaks from acquisition to renewal across different scenarios

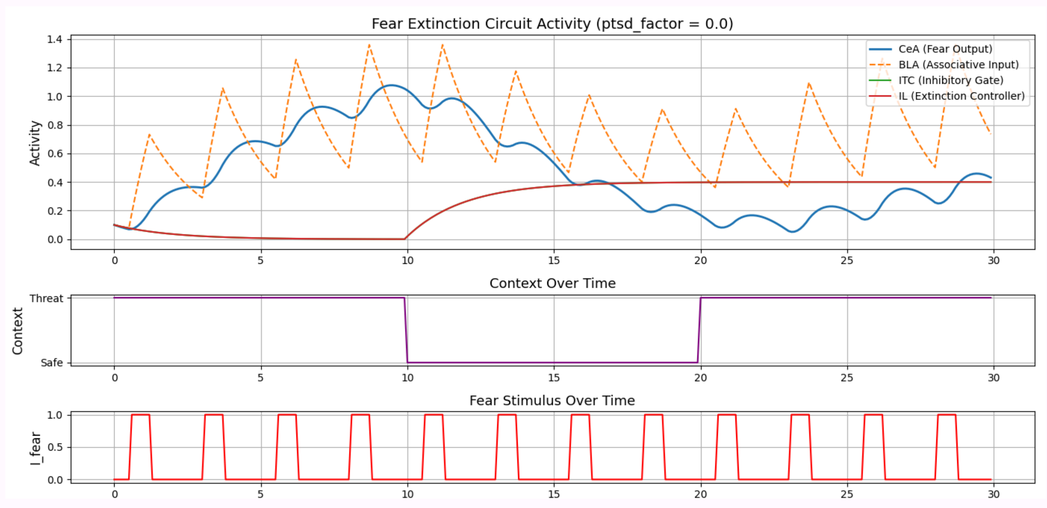

Fig 8. Neural activity in a person simulated with severe PTSD (ptsd_factor = 0.0) with DES applied during extinction and renewal phases.

Discussion

Conclusions

- DBS stimulation is most effective when applied during extinction and potentially during renewal
- DBS during extinction decreases hyperactivity of the amygdala and increases synaptic plasticity in connections to the mPFC
  - DBS during conditioning decreases hyperactivity; however, it may strengthen connection to the vHPC.
- In severe cases, fear regrows during renewal
  - That's why DBS during renewal can further normalize fear
- DES to the IL is most effective during the extinction and renewal phases.

Applications

- **Optimize** DES/DBS timing for PTSD treatments
- **Personalized PTSD therapies** depending on PTSD severity (ptsd_factor in the mean-field model)
- Serve as a testbed for **pharmacological interventions**
  - Simulate effects of different drugs on different brain regions

Limitations

- Mean-Field Model is **oversimplified**
  - Arbitrary numbers, DES is simplified current, brain regions realistically have other activity, and context weight is too weak
- **Large size of SNN** computationally limits complexity of modifications
- Implementation of CTX-A during extinction as a constant lesser current unintentionally limits synaptic depreciation during extinction phase.
- Cannot directly model a depolarization block **biologically** with an LIF model, requires hybrid solutions

Future Research

- Integrate a **hybrid model** that directly represents the opening of calcium channels in depolarization blocks.
- Model neurons in **3D space** to represent the decay of current over space.
- Implement **fear overgeneralization** and effects of **NTs** (i.e., serotonin and dopamine) into the models
- **Expand models** for other disorders like OCD and depression
- Test DBS timing and placement

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-- Github --

-- References --