Closed-loop direct electrical stimulation to optimize amygdala-mediated memory enhancement in humans


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Background

- Emotional memories tend to be more robust—a mechanism dependent on interactions between the amygdala and medial temporal lobe (MTL) networks.¹
- Recently, we reported that direct stimulation of the basolateral amygdala (BLA) in humans can evoke these prioritization mechanisms to enhance declarative memory.²
- Robust encoding is supported by dynamic, multiregional co-modulation of theta and gamma oscillations.³,⁴
- The Separate Phases of Encoding and Retrieval (SPEAR) model highlights how different phases of hippocampal theta preferentially support encoding vs. retrieval⁵; animal studies have leveraged closed-loop, phase-aligned stimulation to selectively evoke these mechanisms.⁶,⁷

Closed-Loop Approach

1. Continuous recording of intracranial LFP
2. Real-time calculation of theta power and phase
3. Predict delay for theta peak/trough alignment
4. Deliver theta phase-aligned TBS to BLA

Phase Detection

- Amygdala
- Hippocampus
- SEEG

Closed-Loop Memory Task

- Visual Recognition Memory Task adapted from prior work²
- 160 trials of neutral object images (3s each) followed by phase-aligned peak/trough stimulation (1s)
- Self-paced retrieval at ~24 hours post-encoding

Next Steps

- Personalized theta-burst stimulation (TBS)
- Isolate hippocampal LFP, calculate average power spectra across 60s baseline (Welch’s method)
- Parameterize spectra with FOOOF² to determine individual theta frequency (ITF, 3-8 Hz)
- Calibrate TBS burst frequency to match ITF for phase alignment (Bipolar, charge-balanced pulses [1 mA] delivered at 50 Hz in 3-8 trains [ITF] for 1s)

Data-driven characterization of amygdala-mediated memory enhancement from prior experiments of open-loop BLA stimulation (n = 60; Emory University, Washington University, University of Utah)

Continued testing, refinement, and validation of closed-loop system (offline implementation)

Collect data from closed-loop experiments with neurosurgical patients who have refractory epilepsy (target n = 12, ~ Fall 2023)

This research is supported by the National Institute of Neurological Disorders and Stroke (R01NS115723) and the National Institute of Mental Health (R01MH120194).

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