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. retrieval[5]; animal studies have leveraged closed-loop, phase-aligned stimulation to selectively evoke these mechanisms.[6,7]

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2. Inman et al. *PNAS*. 2018.
3. Hanslmayr et al. *Trends in Neuro*. 2019.
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5. Hasselmo et al. *Neural Comp*. 2002.
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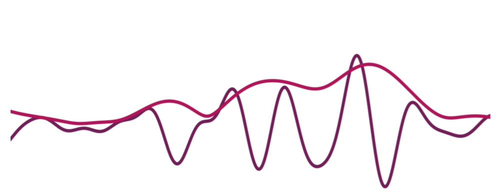
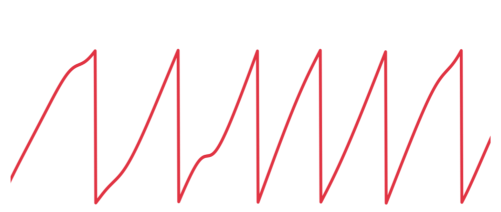
Phase Alignment

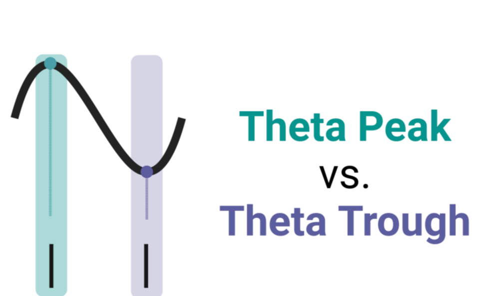
Continuous recording of intracranial local field potentials (LFP) in 500ms sliding window



Isolate hippocampal channel(s) with high SNR, compute theta power via Fourier transform in Hann window

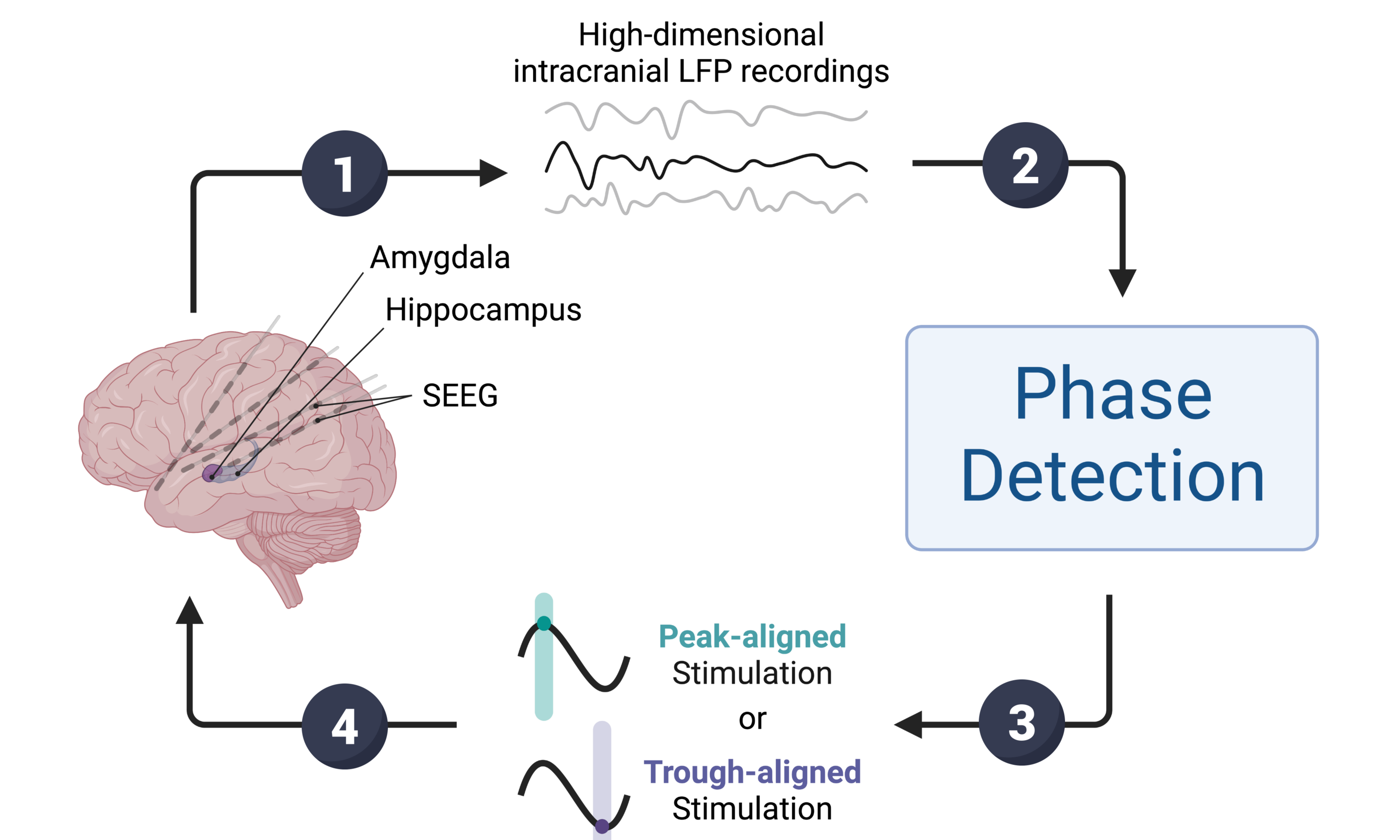


Calculate phase via Hilbert transform, use real-time phase to predict theta cycles (**peak** vs. **trough**)



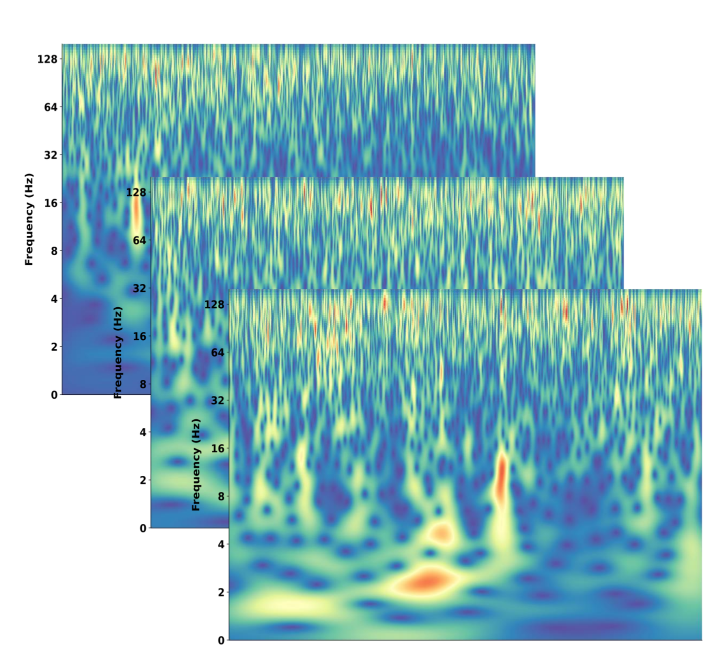
Deliver closed-loop, phase-aligned TBS to BLA

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

Personalized **theta-burst stimulation** (**TBS**)



Isolate hippocampal LFP, calculate average power spectra across 60s baseline (Welch's method)

↓

Parameterize spectra with *FOOOF*[8] to determine individual theta frequency (**ITF**, 3-8 Hz)

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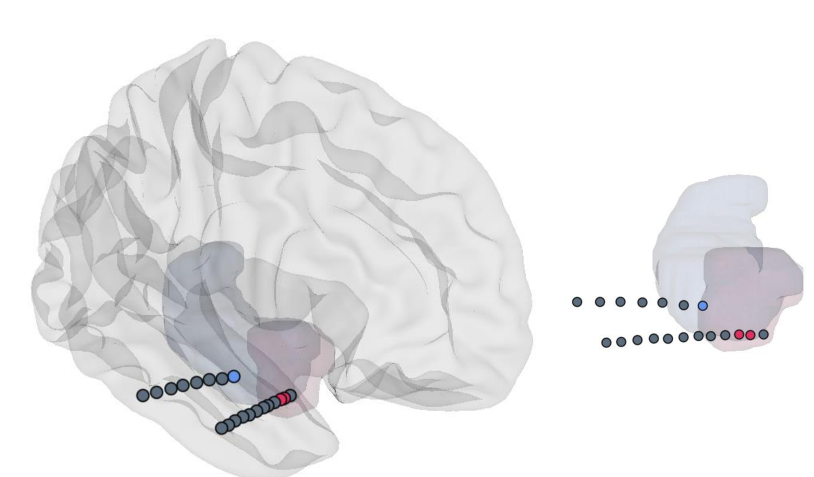
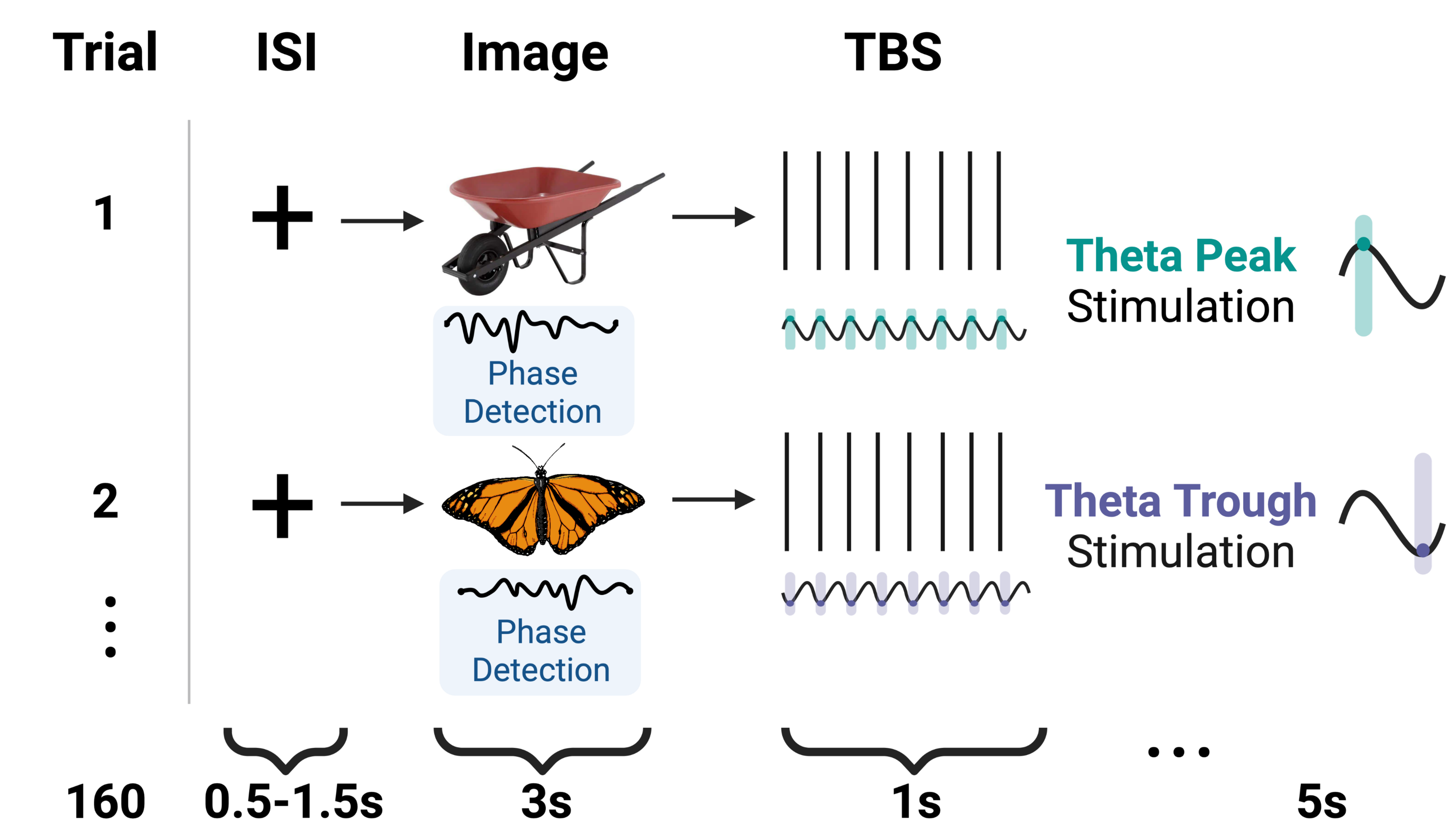
Calibrate TBS burst frequency to match ITF for phase alignment

(Bipolar, charge-balanced pulses (1 mA) delivered at 50 Hz in 3-8 trains [ITF] for 1s)



Declarative Memory Task



- **Visual Recognition Memory Task** adapted from prior work[2]
- 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

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)

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