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### Background

Direct electrical stimulation is a widely used therapy to treat various neurological disorders (Benabid et al., 2009).

There is increasing interest in applying direct electrical stimulation to modulate cognitive functions such as memory (Suthana & Fried, 2014).

Stimulation's mechanisms of action and the ideal parameters to affect memory networks remain unclear (McIntyre & Hahn, 2010; Kim et al., 2016).

We applied direct electrical stimulation via intracranial electrodes in humans, to test how stimulation modulates neural activity in the memory network.

# Experimental Design

### **Stimulation Parameters**

Pulse Frequency (10, 25, 50, 100, 200 Hz) Pulse Amplitude (three levels, up to 1.5/3.5 mA [depth/surface])) Targeted Area (hippocampus, MTL, lateral TC, DLPFC) Train Duration (500 ms)



Jittered ISI (min 2750 ms)



Data Collection and Analysis: intracranial EEG / SR = 500,1000 or 1600ms / wavelet decomposition / 8 log-spaced freqs 3 - 180 Hz / Mirrored buffers / PreStim epoch [-1100 to -100 ms] / PostStim epoch [100 to 1100 ms] rel. stim onset Stimulation Details: 300 µs biphasic charge-balanced pulses / bipolar electrode pair / Max amplitude identified via pre-task calibration session to avoid ADs

# Large-scale assessment of the effects of direct electrical stimulation on brain network activity

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# Stimulation Frequency and Amplitude





# Aggregate Effects of Stimulation Location



High-frequency power (65-180 Hz) modulation across the cortex



Verbal Task: 1600ms presentation / 750-1000ms jittered ISI / 20s distractor / 30s recall / 25 lists per session / 12 words per list Classifier Details: L2 penalized logistic regression / spectral power over 1600ms encoding interval / z-scored input patterns / x-validation leave-one-out by session

### Across all sessions, stimulation frequency positively affects classifier output

### Effect of stimulation frequency varies by stimulated brain region

### CA1 stimulation tends to reduce classifier estimates of successful memory states



Classifiers applied to neural activity before and after stimulation show modulation in classifier estimates of memory states.

Across all stimulated regions, higher frequencies led to increased classifier estimates.

CA1 stimulation decreased the spectral tilt, a marker of successful memory function, while stimulation of DG, DLPFC and TC increased it.

References Benabid at al. (2009). Lancet Neurology / McIntyre & Hahn (2010) Neurobiol Disease Kim et al (2016). Neurobiol Learn & Mem / Suthana & Fried (2016). NeuroImage

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