

# The effects of direct brain stimulation in humans depend on frequency, amplitude, and white-matter proximity

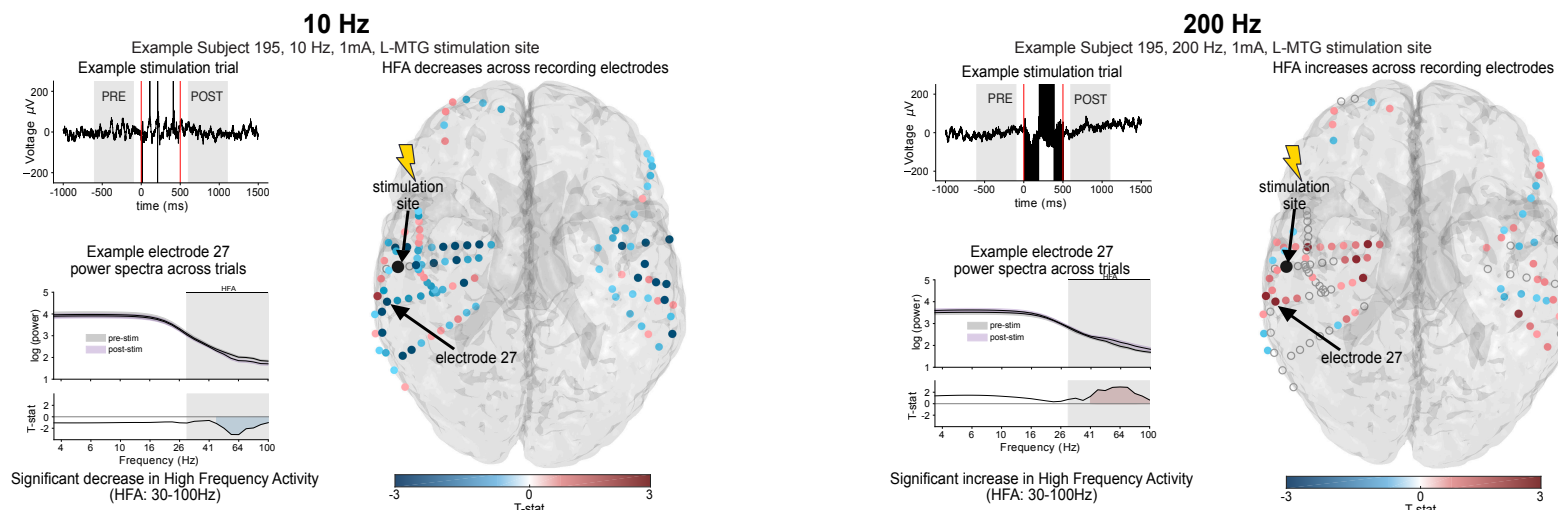
Mohan, U.M., Watrous, A.J., Miller, J.F., Lega, B.C., Sperling, M.R., Worrell, G.A., Gross, R.E., Zaghloul, K.A., Jobst, B.C., Davis, K.A., Sheth, S.A., Stein, J.M., Das, S.R., Goniak, R., Wanda, P.A., Rizzuto, D.S., Kahana, M.J., Jacobs, J.



## Introduction

- Mixed literature on excitatory (Hashimoto et al. 2003) and inhibitory (Dostrovsky & Lozano 2002, Welter et al. 2004) effects of stimulation
- Microstimulation in primates induced frequency dependent BOLD changes; local neuron populations show immediate excitation and prolonged inhibition (Logothetis et al. 2010)
- Unexplained variability of stimulation effects on memory (Penfield & Perot, 1963)

## High and low frequency stimulation have inverse effects on neuronal activity



## Methods

### Recordings

Intracranial EEG recording and stimulation:

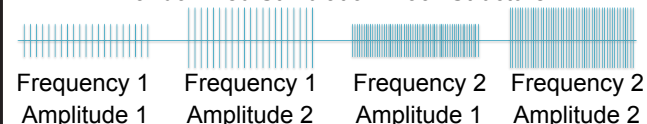
- 106 epilepsy patients
- 354 sessions
- 319 distinct stimulation locations
- 54-173 bipolar recording pairs (mean = 108, total 10,266 electrodes)

### Task Design

Varied parameters:

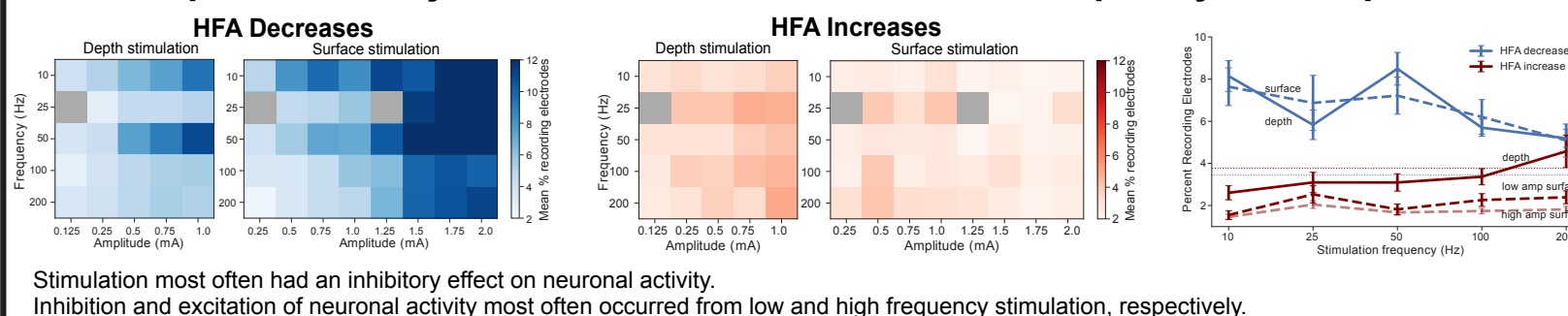
- Pulse frequency: varied over 10, 25, 50, 100, 200 Hz
- Pulse amplitude: varied over 0.25-2 mA
- Pulse duration: 500ms
- ~25min sessions

### Randomized Stimulation Block Structure



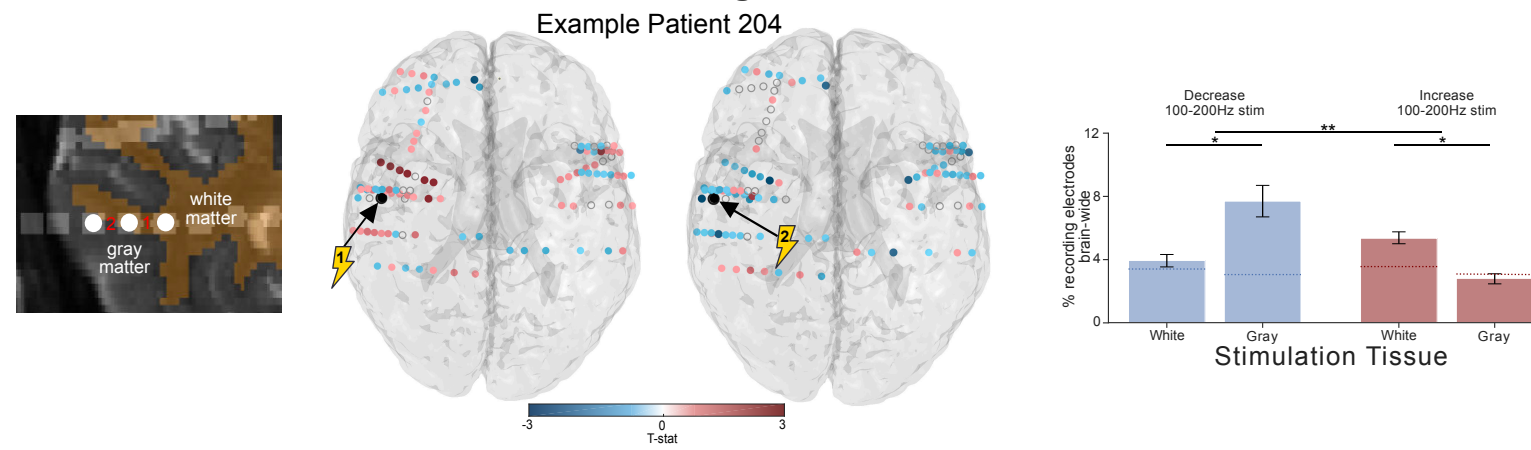
**Objective:** To comprehensively evaluate the effects of stimulation at different parameters and locations on neuronal activity across the human brain on a large-scale.

## Population analysis of the effects of stimulation frequency and amplitude



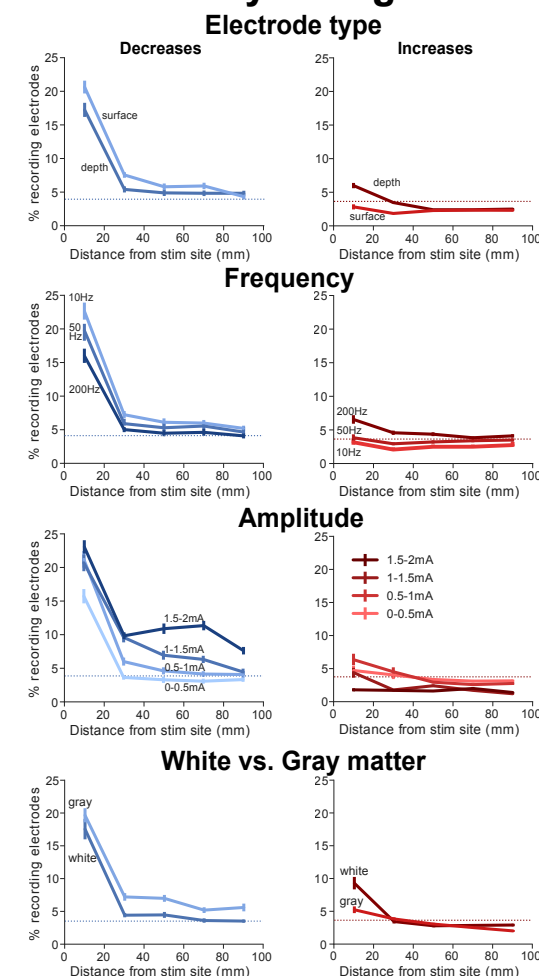
Stimulation most often had an inhibitory effect on neuronal activity. Inhibition and excitation of neuronal activity most often occurred from low and high frequency stimulation, respectively.

## Distance to white matter and region mediate the effects of stimulation



Stimulation sites near white matter more likely to excite, and stimulation near gray matter more likely to inhibit neuronal activity.

## Spatial spread of neuronal activity changes



## Summary

High-frequency stimulation was most likely to excite while low-frequency stimulation was most likely to inhibit neuronal activity.

Responses depended on stimulation proximity to white-matter tracts.

Comprehensive characterization of parameter space can help with stimulation protocols design.

For details: Mohan et al., 2020, *Brain Stimulation*