**Affective Bias and Electrophysiology as Biomarkers of Treatment Resistant Depression**

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Depression is a debilitating illness that affects over 21 million American adults each year and is characterized by symptoms such as low self-esteem, suicidal thoughts, and changes in behavioral patterns. Nearly 2.3 million patients do not respond to therapeutic strategies and are diagnosed with treatment-resistant depression (TRD). The use of surgically implanted electrodes in Deep Brain Stimulation (DBS) has shown promise in treating TRD. TRD patients often exhibit an affective bias in which they perceive positive or neutral emotional stimuli more negatively than non-depressed populations. This suggests that any assessments of mood that rely on the patient's perspective may be inaccurate due to dysfunction in processing emotional content rather than favoring one interpretation over another. Affective Bias may serve as an accurate cognitive biomarker of mood than traditional mood assessments.

The research participants, patients with TRD undergoing DBS (n=4), are part of a clinical trial employing intracranial stereo-electroencephalogram (sEEG) to characterize the underlying electrophysiological abnormalities in TRD and to monitor the brain activity changes associated with different therapeutic stimulation parameters. sEEG recordings are used to select the stimulation settings that optimally activate the network of brain regions believed to be dysfunctional during depressed states. Stimulation is targeted to the white matter of the subcallosal cingulate and ventral capsule/ventral striatum, known to be abnormal in TRD. We administered the Affective Bias Task (ABT) to track mood state; patients assess the emotional valence and intensity of static human face stimuli using a sliding scale ranging in emotional intensity (sad, neutral, happy).

Our planned analyses include 1) computing the ABT score per run, as well as evaluating it as a function of valence and analyzing it to evaluate the changes in AB scores before vs. after DBS stimulation and 2) extracting spectral features from the sEEG recordings during the ABT and focusing on two aspects of neural activity. First, we will expand upon recent findings in our lab demonstrating modulation of theta and alpha-band power during the ABT. Second, we will explore the 1/f feature of the power spectrum, which captures the ratio between low and high-frequency signals in brain activity. The 1/f slope is believed to be related to the excitation and inhibition balance across brain circuits and is a possible biomarker for depression. We aim to test whether changes in the ABT score covary with changes in these two metrics.

By characterizing the relationship between changes in emotional bias behavior and intracranial electrophysiological markers, we move the field toward a more nuanced understanding of the pathophysiological underpinnings of TRD and test individualized treatment approaches in the future.

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