Gamma-Tetha Local Field Potentials as Biomarkers in Treatment Resistant Depression on Bilateral Subgenual Corpus Callosum Deep Brain Stimulation. Integrated Behavioral, Neurophysiological and Clinical Effects

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Abstract

Introduction: Treatment-resistant depression (TRD) remains a significant therapeutic challenge globally. Although (DBS) has been an option for treatment, some suggests that a personalized approach base on main symptomatology and individual biomarkers, may yield more efficacious outcomes. Since 2013, our center at Rionegro San Vicente Fundacion Hospital Colombia, South America, has implemented a multidisciplinary neurofunctional program and performed bilateral subcallosal cingulate DBS (SCC-DBS) in 7 patients. Recently, 3 of these patients underwent device replacement with the PerceptTM RC neurostimulator Brain SenseTM technology, enabling advanced local field potential (LFP) recordings and behavioral and neurophysiological assessments. This study focuses on these 3 patients, each representing a distinct depressive phenotype: hypersensitive, stable, and anhedonic. We conducted comprehensive evaluations integrating emotional perception tasks, local field potential recordings, and longitudinal clinical profiling to elucidate the mechanisms and effects of SCC-DBS.

Method: EMOTIONAL PERCEPTION TASK Patients viewed 10 standardized images 5 happy 5 sad in randomized order during two conditions stimON Chronic therapeutic stimulation and stim-OFF: 1 hour washout period. For each image, patients provided: Happiness rating 1 very sad to 10 very happy semantic association single-word descriptor and response latency measurement.

Results: Behaviorally, SCC-DBS significantly enhanced positive image perception +9.5% and reduced negative bias −28% with a 34% improvement in emotional discrimination capacity. Neurophysiologically, stimulation led to increased gamma oscillations up to +175% suppressed theta activity up to −41.9% strongly correlated with affective improvements r = 0.76 and r = 0.71 respectively). Clinically 49.3% overall improvement in QofL with phenotype specific responses beta/gamma ratio was most effective in the hypersensitive patient theta-alpha phase-amplitude coupling relevant in the stable phenotype and high gamma power was a key biomarker in the anhedonic patient.

Discussion: Our observations suggest that deep brain stimulation (DBS) of the (SCC) achieves therapeutic effects through frequency-specific, dissociable mechanisms. Gamma oscillations may facilitate long-term synchronization between the SCC and the nucleus accumbens, enabling positive valence encoding. Pathological theta hyperactivity during StimOFF states may reflect limbic-cortical dysrhythmia, consistent with the Broadway model of depressive hyperarousal. Theta suppression correlated with reduced connectivity between the amygdala and SCC may suggest normalized threat processing. All of this could have clinical application when programming real life patients, but more cases and scenarios are required for applicability across all individuals.

Conclusions: We can suggest that SCC DBS may modulates affective circuits through frequency specific mechanisms gamma enhancement may facilitates positive affect and

reward processing, while theta suppression may mitigates negative cognitive bias. The therapeutic response varies by depression phenotype, supporting a personalized neuromodulation approach guided by electrophysiological biomarkers. The use of Percept RC technology may enable real-time monitoring and biomarker identification. This optimized programming framework may have the potential to improve clinical outcomes in TRD and maybe establish SCC DBS as a targeted, phenotype-driven therapy.

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