Identification of Tic Onset Biomarker from Chronic Recordings in Centromedian Thalamus and Globus Pallidus Interna for Closed Loop Deep Brain Stimulation in Tourette Syndrome

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Introduction: Tourette Syndrome (TS) is a neuropsychiatric disorder characterized by repetitive and involuntary motor and phonic tics. Most cases present symptoms that start and stop during childhood, but for up to 23% of cases, symptoms remain and can get progressively worse during adulthood [1], [2]. Multicenter retrospective studies have reported a 45.1-52.7% average decrease in tic severity [2] in patients with Deep Brain Stimulation (DBS), indicating it could offer an alternative therapy when symptoms become refractory. The most common nuclei targeted for conventional DBS are the Centromedian (CM) Nucleus of the Thalamus and the anterior Globus Pallidus Interna (aGPi) [3]. However, the paroxysmal nature of this disorder leads us to believe patients would benefit from closed-loop DBS therapy.

Materials, Methods, and Results: To test this, we implanted four patients (3 males, and 1 female) with bilateral macro electrodes targeting the CM, both connected to a rechargeable investigational neurostimulator from Medtronic (Summit RC+S, Medtronic PLC). This device, apart from delivering electricity to the region of interest, is also capable of streaming Local Field Potentials (LFP) and performing a linear discriminant analysis. After implantation, patients visit the center periodically for up to 24 months. During each visit we collect video, LFPs, electromyographic, and acceleration data while the patients are at rest (or holding the urge to tic as much as possible), voluntarily moving their hands when shown a cue, or freely ticking. Later, we align and mark down the data to separate each condition. After averaging across the runs where we stream data from sense-friendly configurations for the CM, we have identified a low-frequency (3-10 Hz) power increase occurring after tic onset. Using only this biomarker, we were also able to start closed-loop DBS in one subject thus far, reporting similar benefits to continuous stimulation with potentially fewer side effects and longer battery life.

Discussion: There are still many challenges left to find the optimal settings for each patient, due to the variable presentation of the tics and the psychiatric components of TS. These can make programming sessions time-consuming and tedious for the patient. Shortly, image and electrophysiological-informed decisions along with the adaptive capabilities embedded in new neurostimulators could make this process faster. To evaluate this, we just started a Brain Initiative-funded project, where we will be implanting 8 patients with bilateral Percept PC neurostimulators with BrainSense Technology (Medtronic PLC) along with bilateral directional leads targeting the CM and the aGPi. Identifying physiological features in both nuclei can help us understand intersubject variability, as well as which nucleus does a better job at detecting tics, and which one at suppressing tics. This could reveal valuable information about the pathophysiology of this disorder and could guide the development and improvement of neuromodulation therapies for Tourette.

References

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