Identifying the Optimal Parameters for Neuromodulation in Epilepsy

Epilepsy is the most common neurological disease in the world. As of 2021, according to the National Institute of Health, around 3 million people in the US have been diagnosed with epilepsy. Of these people, only ⅔ respond to medications and many are not candidates for resection. Neuromodulation is an innovative approach for those with refractory epilepsy; devices directly send electrical pulses intracranially to disrupt epileptiform activity, consequently preventing seizures and/or lessening the severity. Devices include Deep Brain Stimulation (DBS) and Responsive Neurostimulation (RNS). DBS constantly sends stimulation, with patient-specific parameter settings, whereas RNS reads the brain activity and sends simulations based on a detection. While innovative, neuromodulation poses limitations as well. Efficacy studies have shown that attaining the patient-specific parameters for either the RNS or DBS is a time-consuming process as it's done through an ad hoc approach, and even after the optimal parameters are attained, neuromodulation is not at its highest potential in terms of efficacy immediately. Its efficacy improves over time, taking several months, even a couple of years, for patients to achieve severity and abundance in seizures. In addition to the time limitation, the parameters of stimulation, including frequency, amplitude, and duration of stimulation, are not well known, meaning all patients must start from the same baseline when finding their specific parameters. Strategic changes cannot be made based on the behaviors of both the parameters and the patient's epileptiform activity. This, too, prevents patients from getting closer to a better quality of life quickly. This study, conducted in the Department of Neurology at Massachusetts General Hospital, analyzed different frequencies and their effects. Subjects with intracranial depth electrodes were simulated with 5 different frequencies (1 Hz, 20 Hz, 40 Hz, 140 Hz, and 200 Hz) in a randomized paradigm to the epileptogenic zone (EZ) channel, determined by the highest spike ripple rate. Both the stimulation amplitude at 1 milliamp and stimulation duration at 100ms, remained constant for all stimulation bursts. Rates of spikes, the canonical biomarker for the EZ, and spike ripples, the most accurate biomarker for the EZ, were detected during the 900 ms after each individual stimulation burst for analysis. Detections were made using the automated, validated Spike detector, Persyst. Spike ripple and spike definitions within the detector were adjusted based on pre-stimulation data for each subject. Comparisons between the rates from different frequencies were conducted using a mixed linear effects model. Results show that higher frequencies (>20Hz) are significantly more disruptive to spike ripples than lower frequencies (<20Hz). This suggests that higher frequencies are more disruptive to epileptiform activity in general. With more knowledge and understanding of one of the parameters of stimulation, the time consumption in the process of determining the optimal patient-specific parameters for neuromodulation will decrease, allowing patients to achieve a better quality of life faster with lessened seizure severity and/or abundance.

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