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BIOMEDICAL ENGINEERING

Ph.D. Dissertation Defense

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"Fiber Tract Stimulation of the Corpus Callosum for Focal Cortical Epilepsy"

By

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ABSTRACT:

Epilepsy is one of the most common neurological disorders. Many patients that suffer from epilepsy do not respond to traditional regimens of anti-epileptic drugs (AEDs). These same patients are often not candidates for surgical resections due to the location of the seizure focus. Recently, several deep brain stimulation (DBS) technologies have become available as an alternative to surgical resection for patients with refractory epilepsy. These devices utilize stimulation of grey matter targets using high-frequency electrical current to suppress seizures. These methods have shown some success in large clinical trials. However, there is a great deal of room for improvement in terms of both efficacy and understanding of how DBS suppresses seizures. Previous studies involving low-frequency stimulation (LFS) of the ventral hippocampal commissure (VHC) have demonstrated an alternative approach to seizure suppression. Based off of the success of these studies in mesial temporal lobe epilepsy (mTLE) we developed and tested LFS of an analogous fiber tract for focal cortical epilepsies. The corpus callosum (CC) much like the VHC provides numerous interhemispheric axonal projections that are essential to the spread of neural activity across large portions of the brain.

The goals of this study were: (i) to develop and test the efficacy of CC-LFS in suppressing seizures by (a) developing an acute focal cortical model of seizures and (b) to determine the necessary parameters such as frequency range and location to suppress seizures, (ii) to compare CC-LFS to other clinically available DBS technologies for epilepsy in the same model of focal cortical seizures by (a) comparing the seizure suppression rates directly and by (b) evaluating the effect of stimulation frequency vs stimulation target as well as (c) through a comparison to a transection of the CC.

To achieve these aims a novel acute focal cortical seizure model was developed that allowed us to evaluate the efficacy of CC-LFS as well as to compare this new technique to well-established methods of seizure suppression in patients using DBS. The main metric that was evaluated in this study was the percent time spent seizing before, during, and after stimulation. Seizures were identified and the duration of each was summated and normalized to assess the relative severity of seizures during each period of time.

CC-LFS significantly reduces the seizure percentage during the time that it is applied. The effect of CC-LFS in our model of seizures is comparable only to a partial transection of the CC. No other DBS technique had any effect on seizure suppression. CC-LFS optimally suppresses seizures when applied to regions of the CC that directly innervate the seizure focus. Furthermore, the stimulation frequency range is limited to between 10 – 20 Hz.

The knowledge gained from this study supports the hypothesis that low-frequency stimulation of fiber tracts provides a uniquely effective method for reducing neural excitability and suppressing seizures. This study builds off of the previous work by others that has demonstrated the mechanisms and effect of LFS to the VHC in mTLE. Our study demonstrates that much of what was discovered in the VHC could potentially apply to the CC and serve as a template for investigating the potential for CC-LFS to be used to treat cortical epilepsies.