August 29, 2016

Letter from the research team…

Dystonia is a movement disorder characterized by sustained or intermittent muscle contractions causing abnormal, often repetitive, movements and postures that are typically patterned, twisting and may be tremulous. Symptoms are often initiated or worsened by voluntary action and associated with overflow muscle activation.

Two of the more common forms of dystonia are primary generalized dystonia (affecting multiple body regions) and focal dystonia (affecting a single region of the body). For example, cervical dystonia is a common focal dystonia that predominately affects the neck muscles.

Pharmacological therapy for dystonia has largely been ineffective and botulinum toxin, while effective for some patients with focal dystonia such as cervical dystonia, requires repeated visits, often every 2-3 months, and patients may eventually develop antibodies that limit its effectiveness.

Deep brain stimulation has been effective in reducing dystonic symptoms in some forms of dystonia such as primary generalized and cervical dystonia. However, the degree of improvement for those treated with deep brain stimulation may vary significantly, with some treatment centers reporting reductions in severity as high as 90% while others may show limited or no improvement. Reasons for this variability are not clear. Some explanations offered include co-morbidities, dystonia phenotype (observable characteristics), or underlying pathophysiology in the brain. Related to the stimulation, some explanations for the variability in outcomes may lie in the complexity of the programming parameters for delivering stimulation (such as the frequency or intensity of stimulation) or the location of the lead placed within the brain and its proximity to very specific structures and neuronal pathways.

The programming parameters by which electrical stimulation is delivered through the lead to the brain are particularly difficult to define for dystonia patients given the number of parameters from which to choose, the complexity of these parameters and the numerous differences in signs and symptoms between individual patients. Furthermore, there are significant delays of days, weeks or months before patients see any benefit following onset of stimulation, which makes determining optimal therapeutic stimulation parameters even more difficult. For patients, this can be exceptionally frustrating and problematic given the amount of time required to be in the clinic over the course of this “onset period” in order to optimize the stimulation parameters.

The University of Minnesota has an interdisciplinary team of physicians and scientists with a vast amount of experience and expertise in the field of movement disorders and neuromodulation that are committed to elucidating these areas of uncertainty. One of the goals of our team is to develop patient-specific treatments, particularly related to deep brain stimulation programming strategies in order to improve outcomes for dystonia patients. More specifically, we are trying to improve our understanding of the changes in neuronal activity that occurs in dystonia patients and how these changes relate to dystonic movement and how they are affected by deep brain stimulation.

Our team also has the unique opportunity to capture ultra-high resolution magnetic resonance images of the deep brain structures we are targeting for deep brain stimulation therapy. If we can understand the changes in neuronal activity, we can then combine this information together with these high resolution images in order to predict the exact location to place the lead for each individual patient and also predict the most effective stimulation parameters.

Leveraging the broad range of expertise of our team and unique state-of-the-art equipment available to us here at the U of M, this work will eventually lead to reduced clinic time for

patients, improved outcomes and ultimately a better quality of life. We are sincerely grateful for the significant contribution provided to us by The Kurt B. Seydow Dystonia Foundation and will use this contribution to address these questions and improve the lives of patients with dystonia.

Sincerely,

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