THE NEUROSURGICAL TREATMENT OF SPASMODIC DYSPHONIA: THINKING OUTSIDE THE VOICE BOX

by

Anujan Poologaindran

BSc., Queen's University, 2014

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF

THE REQUIREMENTS FOR THE DEGREE OF

MASTER OF SCIENCE

in

THE FACULTY OF GRADUATE AND POSTDOCTORAL STUDIES

(Experimental Medicine)

THE UNIVERSITY OF BRITISH COLUMBIA

(Vancouver)

August 2017

Abstract

Spasmodic Dysphonia (SD) is a neurological speech disorder characterized by sudden and involuntary contractions in the laryngeal musculature during speech production. In adductor SD (80-90% of cases), the vocal cords slam together and stiffen making it difficult to produce speech. As a result, an individual's quality of life is impacted due to significant social embarrassment and the inability to work. Since the 1980s, the standard of care for SD has been to inject botulinum toxin A (BTX) into the affected laryngeal muscles thereby diminishing the spasms. Unfortunately, this therapy is limited by the delayed-onset of benefits, wearing-off effects, and repeated injections required every 3 months. To make a quantum leap in treating SD and providing patients with long-term therapy, the central neurological problem needs to be addressed and not the resultant peripheral spasms. Deep Brain Stimulation (DBS) is a neurosurgical therapy that repairs malfunctioning neural circuits giving rise to pathological behavior; DBS is the standard of care for movement disorders such as Parkinson's disease and essential tremor (ET). In this thesis, we set out to investigate 1) which motor thalamic neural circuit required neuromodulation for SD, 2) if thalamic laryngeal control was lateralized, and for the first time, 3) if chronic subcortical electrical stimulation can provide long-term relief in SD. First, we systematically interrogated the pallidal and cerebellar inputs into the thalamus of an ET patient with coincident SD. Next, we studied n=6 with ET and coincident voice tremor to assessed if left, right, or both thalamic electrodes were crucial for vocal fold control. Finally, we launched a Phase 1 trial (DEBUSSY) on unilateral thalamic DBS for SD. Overall, we determined that unilateral left thalamic Vim DBS can safely and instantaneously abort laryngeal spasms in

n=4 SD. There were no serious complications or adverse events to report. If voltage increased above the therapeutic range, dysarthria and contralateral dysmetria was induced but resolved with stimulation adjustment. Finally, the dentato-rubro-thalamic tract appears to be preferentially affected during DBS treatment for SD. Future work will characterize the long-term benefit of DBS in SD and further elucidate the mechanism by which DBS mediates improvement.

Lay Summary

Spasmodic Dysphonia (SD) is a neurological speech disorder characterized by involuntary vocal cord spasms during speech production. With an average age of onset at 45, SD significantly affects an individual's quality of life due to social embarrassment and inability to work. Since the 1980s, SD has been treated as a muscular problem. To make a quantum leap in treating SD, we must think outside the voice box and repair the brain region involved in generating these spasms. Deep Brain Stimulation (DBS) is a surgical therapy that involves implanting an electrode deep in the brain to repair abnormal electrical circuits. For the first time ever, we applied DBS for SD and found that a single electrode in the left motor thalamus safely and instantaneously aborts laryngeal spasms in SD without complications. This work represents the first neurological treatment for SD and represents a viable long-term solution for patients with severe SD.