Spasmodic Dysphonia and Thalamic Deep Brain Stimulation: Long-term Observations, Possible Neurophysiologic Mechanism and Comparison of Unilateral Versus Bilateral Stimulation

Mark K. Lyons1*, Orland K. Boucher1 and Virgilio G. H. Evidente2

1Departments of Neurological Surgery, Mayo Clinic, Arizona
2Department of Neurology, Mayo Clinic, Arizona

Abstract

The co-existence of essential tremor and spasmodic dysphonia has been reported in the literature. Spasmodic dysphonia is a primary focal dystonia manifested by loss of control of the vocal muscles during speech secondary to laryngeal muscle spasms. The pathophysiology is not well understood. Deep brain stimulation surgery (DBS) for other focal dystonias has been well reported. Voice and laryngo-videostroboscopic examinations can aid in confirmation of spasmodic dysphonia as opposed to voice tremor due to the underlying essential tremor. We report the long term follow up of a patient who underwent bilateral thalamic deep brain stimulation surgery for essential tremor and coincident spasmodic dysphonia, and report the effects of unilateral versus bilateral stimulation on her dysphonia. The topic literature is reviewed and the potential neuroanatomical pathophysiologic mechanisms of this finding are also discussed..

Keywords: Deep brain stimulation; Thalamus; Essential tremor; Spasmodic dysphonia

Introduction

The association of upper extremity essential tremor and several types of other dystonias, including spasmodic dysphonia, have been reported in the past [1,2]. We previously reported a brief case description of a patient with essential tremor (ET) of the hands and adductor spasmodic dysphonia (SD) with vocal tremor who responded to bilateral thalamic DBS with six month follow up [3]. Our patient is now 44 months postoperatively with sustained improvement in both her essential tremor and spasmodic dysphonia symptoms. There are no other reports of thalamic deep brain stimulation surgery improving spasmodic dysphonia in patients with or without essential tremor. Given the sustained response of our patient’s SD to chronic thalamic stimulation, we discuss the current literature and explore the possible mechanisms of action.

Materials and Methods

The review by Schweinfurth et al. found a well defined association between spasmodic dysphonia and essential tremor with a 79% female preponderance [2]. In addition, they noted a strong correlation between psychological stressors and spasmodic dysphonia [2]. We previously reported a 72 year old female with severe medically refractory ET involving the upper limbs presenting to our institution. In addition she also had moderate to severe adductor SD for which she was receiving regular botulinum toxin (BoNT) injection. The patient underwent bilateral thalamic ventralis intermedius (Vim) nucleus deep brain stimulation surgery for her limb tremor. The targeting parameters for both electrodes were based upon the anterior and posterior commissures, calculation of the thalamic height and 11.5 millimeters lateral to the third ventricular wall. The trajectory was adjusted to intersect in a parallel fashion the border between the ventralis nucleus intermedius and ventralis caudalis utilizing an overlay of the Guiot diagram. Determination of optimal final targeting was based upon awake intraoperative nuclear mapping with micro- and macrostimulation. The patient’s major morbidity was her essential tremor and therefore the thalamic target was chosen as opposed to the globus pallidus internus, which is the target used at our institution for DBS treatment of dystonia. The patient is now 44 months postoperative and has maintained significant improvement in her ET and SD. Blinded assessments of her phonation were conducted using the Unified Spasmodic Dysphonia Rating Scale (USDRS) at 6 and 44 months postoperatively. At six months post-DBS her stimulation off and stimulation on USDRS scores were 47 and 22, respectively. At 44 months post-DBS her USDRS scores were as follows: 51 with both stimulators off; 23 with both stimulators on; 34 with only the left stimulator on; and 36 with only the right stimulator on (audio recordings are attached as supplementary data). The implanted pulse generator (IPG) settings at 44 months post-DBS were as follows: left IPG: 2+, 0-, 3.3 volts, pulse width 90 microseconds, and frequency 130 Hz; right IPG: 3+, 0-, 2.5 volts, pulse width 90 microseconds, and frequency 130 Hz.

Discussion

Spasmodic dysphonia is considered a primary focal dystonia. Involuntary laryngeal muscle spasms resulting in loss of voluntary control of the vocal cords during speech production is the hallmark of the disease [4]. The disorder most commonly presents as the adductor type (AdSD) manifested by spasmodic bursts especially during vowel pronunciation [5,6]. There have not been previous reports of deep brain stimulation of any target resulting in improvement in spasmodic...
dysphonia. In addition, investigators have reported that thalamic DBS appears to activate cerebellolateralcortical pathways [7]. Our patient presented with AdSD. The focal dystonias are generally believed to be due to basal ganglia abnormalities; however, the pathophysiology of spasmodic dysphonia is poorly understood [8,9]. Simonyan and colleagues, using a combined diffusion tensor imaging with neuropathological study, have suggested altered microstructural integrity of the corticobulbar and corticospinal tracts [10]. They postulated that spasmodic dysphonia is associated with alterations in the anatomical connectivity of the corticobulbar tract as it descends from the laryngeal motor cortex to the brainstem phonation nuclei. The laryngeal motor cortex inputs to the putamen which then relays back to the laryngeal motor cortex via the globus pallidus and ventral lateral thalamus. This relay loop forms part of the striato-pallido-thalamo-cortical loop. Projections from the laryngeal motor cortex to the phonation nuclei (nucleus ambiguous) occur via the corticobulbar and corticospinal pathways. Microstructural neuropathological alterations may in turn affect the voluntary laryngeal control in patients with spasmodic dysphonia.

Speech deterioration has been reported by several authors after subthalamic DBS [11-13]. However, others have reported improvement in speech following DBS surgery [14,15]. Researchers have reported the preferential activation of the corticobulbar tract over the corticospinal tract with high frequency stimulation of the subthalamic nucleus [16]. Klostermann et al. observed that STN deep brain stimulation can result in the development of dysarthrophonia in Parkinson’s disease patients and significantly worsened speech performance [12]. Putzer noted that thalamic DBS resulted in glottal and supraglottal articulation reduction with stimulation and that phonation was increased with stimulation [17]. The findings of Putzer et al. concluded that the high frequency electrical impulses to the thalamus with deep brain stimulation in patients with multiple sclerosis affected the phonation subsystems differently [17]. The balance of excitation and inhibition of the thalamo-cortical circuit involving motor control by the basal ganglia may offer possible explanation of the effect seen in our patient. If thalamic DBS appears to activate cerebellolateralcortical pathways, as suggested by Molnar and colleagues, it may help explain the potential mechanism of improvement in spasmodic dysphonia observed in our patient as the stimulation impacts the striato-pallido-thalamo-cortical circuit.

Essential tremor patients who undergo thalamic DBS generally have a sustained long-term response to chronic stimulation. Although we initially reported the initial short-term benefit at 6 months post-DBS of SD with bilateral thalamic DBS, we were uncertain of its long-term effects on dysphonia, and whether there were any differences between unilateral versus bilateral stimulation. Our patient has had a sustained improvement of her SD on blinded assessments using the USDRS for SD at 44 months post-DBS. Additionally, bilateral thalamic stimulation exerted a more profound benefit on her SD compared to unilateral stimulation. Thus, similar to other midline symptoms, SD may require bilateral stimulation in order to achieve maximal improvement. Further studies are needed to confirm these observations, particularly in patients with pure spasmodic dysphonia or SD in the setting of segmental or generalized dystonia.

Conclusions

Bilateral stimulation of the Vim nucleus of the thalamus may be a viable long-term treatment for patients with severe spasmodic dysphonia who experience inadequate improvement with pharmacotherapy including botulinum toxin injections. Although unilateral thalamic stimulation had some effect on SD in our patient, bilateral stimulation resulted in more profound improvement of vocal quality. Further studies are required.

References