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Tremor and Other Hyperkinetic Movements

Case Reports

High-voltage VIM Region Deep Brain Stimulation Mimicking Progressive Supranuclear Palsy

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Abstract

Background: Deep brain stimulation (DBS) for essential tremor (ET) can cause unwanted side effects.

Case Report: A patient with ET underwent unilateral dual-lead thalamic DBS. He later developed parkinsonism with atypical features and was diagnosed with progressive supranuclear palsy. During presentation for a second opinion, stimulation-induced side effects were suspected. Inactivation of DBS resolved atypical features and superimposed idiopathic Parkinson disease (PD) was diagnosed.

Discussion: This case illustrates the importance of recognizing the possible influence of stimulation-induced side effects and discusses when to utilize dual-lead DBS for ET and the co-occurrence of ET and PD.

Keywords: DBS, VIM, ET, stimulation side-effect

Citation: Patterson A, Okun M, Hess C. High-voltage VIM region deep brain stimulation mimicking progressive supranuclear palsy. Tremor Other Hyperkinet Mov. 2017; 7. doi: 10.7916/D80G3QWB

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Editor: Elan D. Louis, Yale University, USA

Received: January 5, 2017 **Accepted:** March 1, 2017 **Published:** March 20, 2017

Funding: None.

Financial Disclosures: None.

Conflict of Interest: The authors report no conflict of interest.

Ethics Statement: This study was reviewed by the authors' institutional ethics committee and was considered exempted from further review.

Introduction

Thalamic deep brain stimulation (DBS) is a generally well-tolerated therapy for medically refractory essential tremor (ET). Side effects of stimulation can include changes in speech, gait, and cognition and are more likely to occur with higher voltages due to spread of current to surrounding structures. It is important to consider the possibility of stimulation induced side effects when new symptoms arise.

Case Report

An 81-year-old male with a 15-year history of ET underwent DBS surgery at an outside institution 6 years before presentation. Initially, a left ventralis intermedius (VIM) DBS failed to produce a reduction in tremor, so the decision was made to place a second DBS lead into the left VIM region during the same operative procedure. Tremor reduction was observed intraoperatively and deemed to be sufficient after the second lead was placed. Both leads were connected to a dual-channel implantable pulse generator. Over the subsequent 4-year period, the voltage settings of both leads were gradually increased to address incomplete tremor control. Two years before presentation to our center, the patient gradually developed significant cognitive impairment, speech difficulty, and abnormal eye movements associated with parkinsonism. Previous records documented severe gait impairment, square wave jerks with saccadic pursuits, as well as slow and incomplete vertical and horizontal saccades. The patient underwent neuropsychological testing, which demonstrated significant frontal-subcortical dysfunction and he was diagnosed with PSP (Progressive Supranuclear Palsy), although at no time during his neurologic or neuropsychological evaluation was his stimulation turned off. Levodopa was initiated and titrated up to 200 mg administered three times per day. The medication trial was complicated by mild visual hallucinations that resolved with the addition of quetiapine 50 mg administered at bedtime. He presented to the North Florida South Georgia VA Medical Center/University of Florida for a second opinion of the diagnosis of PSP. On his initial examination, he was non-ambulatory with marked inattention,

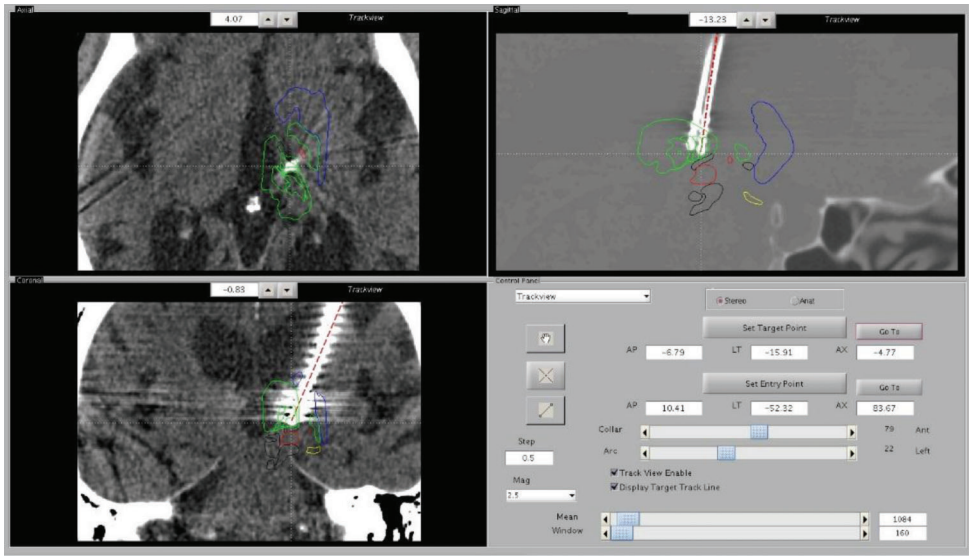

Figure 1. **Lead Location**. The anterior lead is 6.8 mm posterior, 15.9 mm lateral, and 4.7 mm ventral to the mid-commissural point using the AC–PC line as a reference system. The posterior lead is 10.1 mm posterior, 16.5 mm lateral, and 3.3 mm ventral. Both leads were lateral based on lead measurement.

decreased responsiveness, and expressive aphasia. The presence of supranuclear gaze palsy could not be confirmed, because of inattention and poor cooperation; however, there were clear abnormalities of vertical gaze on smooth pursuit. Both thalamic region DBS leads were confirmed as activated during the evaluation: lead A 1-2-C+ 5.0 V, 150 μs, 200 Hz; lead B 4-5-C+ 5.0 V, 120 μs, 200 Hz. A lead localization scan was performed using computed tomography imaging (Figure 1).

The prior neurologic evaluation and neuropsychiatric evaluation resulting in the diagnosis of PSP were conducted without regard to DBS status or settings. The high-voltage settings raised the possibility that at least some component of his neurologic abnormalities could be stimulation related. A complete neurologic examination was subsequently performed with both DBS leads turned off. A few minutes following inactivation, the patient was observed to have an immediate and dramatic improvement in his level of alertness, cognition, speech, and his ability to ambulate. He had normalization of his eye movements with full horizontal and vertical saccades. He was able to speak in full sentences and walk independently. Although he remained moderately parkinsonian, immediate resolution of many of his symptoms suggested that the atypical PSP-like features were stimulation induced. His Unified Parkinson Disease Rating Scale Part III motor score was performed on medication and off stimulation and the score was 35. Moderate postural and action tremor consistent with the initial diagnosis of ET was noted on testing, including spiral drawing and pouring water. Collectively, the examination findings off stimulation suggested that the initial preoperative diagnosis of ET was correct and that the patient had developed parkinsonism since DBS implantation. DaTSCAN was performed and demonstrated asymmetrically decreased radiotracer uptake in the posterior right basal ganglia, consistent with a neurodegenerative etiology of parkinsonism as well. The lack of atypical features in the off-stimulation state suggested that the cause of his parkinsonism was idiopathic PD rather than PSP, and that much of his cognitive, language, and gait abnormalities were secondary to gradual increases in his DBS settings resulting in excessive stimulation of VIM and surrounding structures (e.g., the internal capsule).

The DBS settings for lead 1 (the anterior lead) were reduced and lead 2 (the posterior lead) was completely inactivated. This decision was based on the clinical responses from empirical bedside programming. Although it is counterintuitive to turn off the posterior (VIM) lead and program using solely the anterior (ventralis oralis anterior/ventralis oralis posterior (VOA/VOP)) lead, we suspect that the posterior (VIM) lead was causing capsular side effects because of its lateral placement. The final settings after this initial consultation were lead 1 1-2-C+ 4.0 V, 90 μs, 160 Hz; lead 2 off. Following the re-programming session, the patient's speech was fluent and the ability to walk independently was restored.

The patient continued with carbidopa–levodopa 25/100 mg, two tablets three times per day. Throughout his follow-up visits, the patient has continued to ambulate independently and resumed driving. He reports that he does his grocery shopping and banking independently. No atypical features have recurred and he has a positive response to levodopa therapy.

Discussion

This case brings up several interesting issues.

The most salient point is to recognize that high-voltage stimulation within the VIM can result in side effects and that these side effects can be a source of diagnostic errors. VIM DBS is in general an effective and well-tolerated therapy for medication refractory essential tremor (ET).[1,2] The usual preferred lead location within the VIM target places the tip of the lead 1–2 mm anterior to the VC (ventralis caudalis) border with the 0 (deep) contact at or below the ventral boundary of the VIM.

These coordinates can vary depending on lead trajectory and many surgeons place the deepest contact below the AC–PC (anterior commissure–posterior commissure) line into the zone incerta region. If the lead is laterally placed, fibers of the posterior limb of the internal capsule can be stimulated, resulting in side effects similar to those seen in the above case: dysarthria, facial pulling, eye movement abnormalities, or limb pulling. If the lead is posteriorly placed, the VC nucleus can be stimulated, resulting in paresthesia. These are the most common side effects; however, changes in gait and cognition have also been reported.[3] Postoperative imaging can be useful to predict potential side effects based on the anatomical lead location. We suggest obtaining postoperative imaging and performing lead measurement before the initial programming to help guide setting adjustments.

It is well established that side effects from stimulation are more likely to occur when utilizing higher voltages, presumably because of spread of the electrical current outside the target and into the larger surrounding area. We suggest performing monopolar threshold testing for side effects and benefits at each electrode contact at the time of the initial programming. Even when programming is optimal, disease progression often results in a perceived loss of benefit over time and a gradual increase in stimulation parameters (though in rare cases tolerance to the DBS has been hypothesized).[4–6] As a result, it is not uncommon that DBS voltage will be slowly increased over the course of many outpatient visits and the gradual onset of stimulation-induced side effects can be overlooked, resulting in unintended overstimulation,[3,7] as occurred in this patient. In any patient who has undergone DBS implantation, it is important to consider the possibility of stimulation-induced side effects when new complaints develop. Some side effects (such as gait dysfunction) may not be immediately apparent during or after a programming session. Finally, it is critically important that neurologic and neuropsychological evaluations in patients with DBS occur off stimulation to control for possible stimulation-induced side effects.

In this case, side effects from overstimulation were likely compounded by the immediate addition of a second DBS lead. Details regarding this decision are not known, but in a majority of cases a well-placed VIM lead is sufficient for tremor suppression. If tremor suppression cannot be obtained intraoperatively, the next step should be to consider suboptimal lead placement. This information can be obtained from the microelectrode recording data, and the side effect thresholds obtained during macrostimulation. If the lead is suboptimally placed, the lead should be adjusted, negating the need for a second lead. In exceptional cases of refractory tremor, especially for proximal severe tremor, dual-lead DBS for ET, either in the initial surgery or as rescue therapy, has been proposed.[8–10] Proposed locations for the second lead include the VOA nucleus of the thalamus, which is a pallidal receiving area,[8] the prelimniscal radiations, which contain cerebello-thalamic afferents,[11] and the zona incerta. This approach might improve tremor control by increasing the total volume of tissue activation or by differentially affecting two separate tremor-generating circuits.[10] There is evidence that this strategy can be effective;[8,12] however, there is no clear consensus on when this strategy should be utilized. There is also no evidence comparing dual intraoperative leads versus initial VIM placement followed by a rescue lead in select cases when benefit from the VIM lead is deemed unsatisfactory. A general approach to programming simultaneous intraoperative thalamic leads at our center is to perform monopolar thresholds to identify side effects and benefits for each electrode contact and then to activate and optimize one lead, over a period of months. After a period of initial optimization with the first lead, if needed, the second lead is additionally activated and optimized. In a small published case series of dual VIM/VOA leads, combined voltages ranged from 5 V to 7.1 V.[12] The patient above was receiving a significantly higher combined voltage of 10 V. Despite higher voltages it remains reasonable to expect that having dual leads in close proximity, each at high voltage, would increase the overall risk for side effects simply because of an overlapping, and also wider, dispersal of the electrical current.

A final interesting aspect of this case is the development of superimposed idiopathic PD in a patient with DBS for ET. Both ET and PD are common movement disorders and may co-occur by chance alone. However, epidemiological studies support the idea that there may be an association between ET and the development of PD in select cases.[13–15] One review suggests that the magnitude of the increased odds/risk is on the order of 3–13.[13] This epidemiological link is not well understood despite clinical, imaging, genetic, and pathological study, and the link remains somewhat controversial among the experts.[16] In this case, parkinsonism developed long after the onset of action tremor and after DBS surgery; however, initial misdiagnosis of PD as ET has been considered as a factor in the relationship between the two diseases. There is currently no evidence to suggest that patients with ET who undergo DBS surgery are at greater risk of developing idiopathic PD than their non-DBS cohort.

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