Movement Disorders
CLINICAL PRACTICE
CASE SERIES

Phenomenology and Management of Subthalamic Stimulation-Induced Dyskinesia in Patients With Isolated Dystonia

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Abstract: Background: The pallidum has been the preferred DBS target for dystonia, but recent studies have shown equal or greater improvement in patients implanted in the STN.[1] Transient stimulation-induced dyskinesia (SID) is frequently observed when stimulating this novel target, and there are no previously published video case reports of this phenomenon.

Cases: We describe in detail the SID phenomenology experienced by 4 patients who had been implanted with STN DBS for isolated dystonia.

Conclusions: SID can occur in focal, segmental, axial, or generalized distribution, can resemble levodopa-induced dyskinesia choreiform or dystonic movements observed in Parkinson's disease, and is generally transient and resolves with customized DBS programming. Providers should be aware that SID can occur after STN DBS when treating isolated dystonia and not assume movements are the result of worsening or spread of the underlying dystonia.

Historically, the pallidum has been the preferred target for DBS for isolated dystonia, but in recent years, the STN has emerged as a potential alternative target.[1,2] In a 3-year prospective study of isolated dystonia patients treated with STN DBS,[1] the improvement in symptom severity was shown to be similar to that reported in pallidal DBS clinical trials.[2–4] The most common limiting side effect reported in this trial was the presence of stimulation-induced dyskinesia (SID).

SID in dystonia patients represents a novel phenomenon. SID is often observed in Parkinson's disease (PD) patients with STN DBS and shares a similar phenomenology with levodopa-induced dyskinesia (LID). Some have incorrectly assumed that SID after STN DBS occurs only in PD because of presynaptic denervation of the striatum and use of replacement L-dopa. SID has also been noted in STN DBS in other settings, including obsessive-compulsive disorder[5] and Huntington's disease,[6] but it remains a poorly recognized side effect outside of PD. Here, to improve awareness and recognition of this clinical phenomenon, we describe in detail the heterogeneity, clinical features, and presentation of SID in 4 cases of isolated dystonia, all exhibiting unique forms of SID following STN DBS.

Three of the cases included in this series (Patients 1, 2, and 4) were part of a larger cohort of 20 patients who participated in a prospective clinical trial examining the long-term safety and efficacy of STN DBS as a novel target for isolated dystonia at Uni-

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versity of California San Francisco.[2] Patients 1 and 2 also participated in a substudy assessing 60- versus 130-Hz stimulation.[7] All patients in this series were implanted in the STN with Medtronic devices (Medtronic, Minneapolis, MN), using standard stereotactic techniques, and experienced SID. Three of the 4 were videotaped while experiencing the stimulation-induced movements, which represent excellent examples of the phenomenology for publication.

Cases

Case 1 was a 66-year-old man with a 3-year history of painful craniocervical dystonia, characterized by retrocollis, lingual and jaw-opening dystonia, and blepharospasm (Video 1.1). He had only partial response to botulinum toxin injections and underwent bilateral STN-DBS surgery. During monopolar review, he quickly developed mild SID affecting the right arm and leg with activation of left (L) STN contacts 1 or 2. SID was observed at various settings through the next 18 months of programming. Three months after DBS implantation, SID consisted of rapid asynchronous flexion/extension and athetoid movements in the right fingers, with a "piano-playing" appearance (Video 1.2 and 1.3). He additionally developed new stimulation-induced dystonic posturing of the right forearm and wrist, noted when performing heel stomps (Video 1.4) and dystonic pulling of the arm behind his back when walking. Finally, he developed choreiform movements in both legs (Video 1.5). All these movements abated when stimulation was turned off and were generally worse at higher voltage. They were present at both lower (60 Hz) and higher (130–140 Hz) frequencies. The addition of L STN contact 3 had a slight antidyskinetic effect. Ultimately, stimulation settings were identified that led to 52.2% improvement in the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS), and 29.6% improvement in the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS), without significant ongoing dyskinesia (not shown in the video).

Case 2 was a 48-year-old woman with a 3-year history of isolated cervical dystonia (Video 1.6). She had inadequate benefit from medications and botulinum toxin injections and underwent bilateral STN DBS. During initial programming, SID was immediately noted in her left arm and leg (Video 1.7). Movements consisted of a complex mixed phenomenology in the arm and hand, with rapid jerks overlying irregular flexion/extension movements of the fingers. There were occasional rapid jerks in the leg and shoulder overlying more sustained periods of posturing with a dystonic appearance (Video 1.7). SID was noted with monopolar stimulation of R STN contacts 9, 10, or 11 at different pulse widths and frequencies when voltage exceeded 5 V, but resolved at lower voltage.

Six months later, she developed new stimulation-induced dystonia in her right arm with unwanted humeral abduction, and elbow and finger flexion (Video 1.8), and had difficulty elevating her arms above her shoulders (Video 1.9). The difficulty was interpreted as stimulation-induced dystonia given that it reversed when stimulation was turned off (Video 1.10). The right arm and hand dystonia improved by adding a more dorsal contact and changing L STN stimulation to bipolar configuration. Ultimately, she had marked improvement in dystonia, with 100% reduction in both BFMDRS and TWSTRS scores at 36-month follow-up, without significant dyskinesia.

Case 3 was a 57-year-old woman with a 14-year history of cervical dystonia with diminishing benefit of botulinum toxin injections who therefore underwent bilateral STN DBS. During initial programming, she developed right leg choreiform SID with monopolar stimulation using L STN contacts 1, 2, and 3 and less prominent left leg SID with right (R) STN monopolar stimulation at contact 2. She was programmed with monopolar stimulation on contact 1 bilaterally at 1.8 mA (60 μs, 130 Hz) with fairly immediate improvement in head tremor, but several days later developed right arm and leg SID at any L STN current >1 mA. Video 2 shows evolution of dyskinesia, which is absent on initial settings (0.7-mA L STN contact 1 and 0.8-mA R STN contact 1). With R STN current held constant and L STN current increased to 1 mA, she developed repetitive, stereotyped elevation of the right shoulder. With a further increase to 1.3 mA, SID evolved into a more random choreiform pattern with spread to the right leg. With increase to 1.9 mA, the movements become higher amplitude and more dramatic, at times flinging and ballistic in the right arm with spread to the left leg. SID resolved rapidly when stimulation was turned off on both sides. Given that she has only recently been implanted, additional programming strategies to circumvent occurrence of SID are ongoing.

Case 4 was a 15-year-old male with a 1-year history of dystonia, initially affecting neck and right hand with workup revealing DYT1 mutation. He underwent bilateral STN DBS. During monopolar review, he developed SID consisting of internal rotation of the right arm and athetoid movements in the left fingers. Initially, these were circumvented by slowly increasing voltage at home accompanied by improvement in dystonia. Six months later, he developed new mild dyskinesia in his left shoulder and arm with R STN at C + 1-2-, 1.2 V, 60 μs, 130 Hz, which resolved by lowering voltage. He has remained sensitive to the development of SID with increases in voltage and has required intensive reprogramming to optimize dystonia control without causing SID. Ultimately, the best control has been achieved using interleaved settings bilaterally. At 36-month follow-up, he had a 91.1% improvement in his BFMDRS score and 100% improvement in his TWSTRS score (video not included).

Discussion

Here, we describe the phenomenology of SID in 4 patients who underwent bilateral STN DBS for isolated dystonia. We encountered considerable heterogeneity in the phenomenology of SID, including athetotic movements in the fingers, choreiform movements, more sustained dystonic posturing, and clusters of fast, irregular jerks. Body regions affected involved primarily the arm and leg. Often, SID consisted of complex phenomenology with mixtures of different types of movements. Whereas all patients in this series experienced SID at initial programming, they also developed different forms of SID after several months, even in the absence of preceding programming changes. The mechanism for such delayed SID is unclear and warrants future investigation. The delayed clinical effect often observed in DBS for dystonia invites speculation that sensitivity to dyskinesia may also change along with reorganization of motor networks with prolonged stimulation.

Our series highlights the complexity of phenomenology of SID in this setting, including the precipitation of dystonic movements in regions not affected by dystonia preceding DBS. It is important to recognize this as a potential stimulation-induced phenomenon rather than assuming that it constitutes a spread of the underlying dystonia. In all cases in this series, the possibility of spread of dystonia was ruled out by observing resolution of the dystonic movements when stimulation was turned off. This is important to consider so that stimulation-induced symptoms are not missed or misinterpreted.

The strategies used to improve SID in dystonia patients who have undergone STN DBS are highlighted. We typically recommend lowering voltage and increasing it slowly over several days, trying bipolar stimulation settings, or using a more dorsal contact.[2] Antidyskinetic properties of dorsal contact stimulation have been observed also in STN DBS in Parkinson's disease, including use of an interleaving strategy, with a postulated mechanism relating to stimulation of pallidofugal fibers.[8] Additional studies are needed to evaluate other potential strategies for mitigation of SID in STN DBS for dystonia, such as use of directionally segmented leads.

When considering DBS target choice for dystonia, it is important to set appropriate expectations with patients regarding the complexity of programming. Targets should be chosen based on potential benefit and the side-effect profile that would be best tolerated by the patient, given that stimulation-induced side effects are observed in both STN and pallidal DBS (including stimulation-induced bradykinesia and gait difficulty in the latter).[9] Knowledge of these side effects may influence DBS target choice, and a customized treatment approach is necessary until a definitively superior target is identified.

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Author Roles

(1) Research Project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript Preparation: A. Writing of the First Draft, B. Review and Critique.

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K.A.D.: 1A, 1B, 2A, 2B, 3A, 3B
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P.A.S.: 1A, 1B, 2A, 2B
L.C.M.: 2A, 2B
J.L.O.: 1A, 1B, 2A, 2B, 3A, 3B

Disclosures

Ethical Compliance Statement: The patients described in this case series were part of a research study that was approved by the University of California San Francisco Institutional Review Board. Verbal and written consent was obtained and documented by study and/or clinical staff. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

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Supporting Information

Supporting information may be found in the online version of this article.

Video 1. Segment 1.1: Preoperative baseline dystonia in Case 1. Segments 1.2 to 1.5: SID affecting the arms and legs in Case 1. Segment 1.6: Preoperative baseline dystonia in Case 2. Segments 1.7 to 1.10: SID and dystonia affecting the arms in Case 2.

Video 2. Evolution of SID with successive increases in current to left STN in Case 3.