

Rapid assessment of gait and speech after subthalamic deep brain stimulation

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Abstract

Background: Describe a rapid assessment for patients with idiopathic Parkinson's disease (PD) and deep brain stimulation of the subthalamic nucleus reporting worsening speech and/or gait problems.

Methods: We retrospectively reviewed 29 patients that had improvement in gait and/or speech within 30 min after turning stimulation off. Clinical data analyzed include unified PD rating scale motor scores and stimulation parameters before and after adjusting stimulation. All patients received electrode efficacy and side effect threshold testing. Stimulation parameters were adjusted to maximize efficacy, avoid side effects, and maximize battery longevity.

Results: Turning stimulation off revealed reversible speech and/or gait stimulation side effects within 30 min. Focusing on six factors revealed stimulation modifications that improved motor symptoms, eliminated stimulation side effects, and reduced battery drain. Primary stimulation parameters modified were cathode selection and pulse width reduction.

Conclusions: Stimulation-induced side effects impacting gait and speech can be identified within 30 min. A systematic evaluation can distinguish disease progression from reversible stimulation side effects and improve motor outcomes over the long term.

Key Words: Deep brain stimulation, Parkinson's disease, side effects, subthalamic nucleus

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INTRODUCTION

Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is an effective treatment for idiopathic Parkinson's disease (IPD).^[3,11,23] Rigidity, bradykinesia, dyskinesia, and tremor show sustained improvement.^[8,11,23] Gait, speech, and postural stability follow a natural continuum of progression as noted in longitudinal studies^[8,11] and typically refractory to stimulation if refractory to levodopa.^[11,24] Effective stimulation requires activation of a well-positioned cathode(s)^[25] while applying adequate stimulation intensity by adjusting polarity, pulse width, frequency, and amplitude (amps or volts).^[12,14,22] Stimulation intensity too high can cause

reversible stimulation side effects.^[2,9,12] Detection of stimulation side effects relies on patient reporting and clinical examination.^[5] Stimulation of areas adjacent to the STN can cause motor side effects that include

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increased bradykinesia and worsening gait and speech function that can mimic symptoms associated with disease progression.^[2,20] Stimulation effects can be washed out to assess efficacy^[4,10] and optimize stimulation at any time point after DBS surgery,^[7,13,15,16] however, the minimum washout period for gait or speech stimulation side effects is unknown. We describe a process to rapidly evaluate declines in speech and/or gait and the corresponding stimulation parameter changes to optimize efficacy and avoid side effects.

METHODS

After retrospective review of 50 self-referred patients who underwent our DBS troubleshooting protocol in our movement disorders outpatient clinic, we identified 29 patients that had obvious speech and/or gait improvement on examination 30 min after turning off stimulation while in the medication off state. These patients are included in our analysis. Table 1 provides an algorithm of our protocol. Our systematic approach to investigating DBS outcomes and problems was completed over 3–4 days of consecutive appointments that include the following steps:

- Unified PD rating scale motor (mUPDRS) examination off medicine/on stimulation (NOM/ONS). Medication

Table 1: Deep brain stimulation troubleshooting algorithm

Day 1

Motor testing off medication on stimulation
 Turn off stimulation for 30 min
 Motor testing off medication off stimulation 30 min
 Note whether speech, gait, or balance improve off stimulation
 If yes, proceed with electrode testing
 Record maximal improvement in either rigidity, tremor, or bradykinesia for each electrode (efficacy threshold)
 Record amplitude associated with the onset of side effect (side effect threshold)
 Set amplitude 10% below side effect threshold using most effective cathode
 Wait 30 min
 Reduce amplitude or use bipolar polarity if dyskinesia bothersome
 Motor testing off medication on new stimulation settings
 Administer medication
 Motor testing on medication on new stimulation settings
 Modify medication or reduce amplitude as indicated for dyskinesia

Day 2 and 3

Review symptom diary for motor fluctuations, motor symptoms, medication dosing
 Motor testing on medication on stimulation
 Assess for stimulation side effects
 Modify medication or reduce amplitude as indicated for dyskinesia or side effects

Day 4 reserved for out of state patients

off state was defined as at least 10 h since the last dose of dopaminergic medicine

- Stimulation is turned off for 30 min and the NOM/NOS mUPDRS is performed
- Impedance and battery analysis of the hardware system
- Our programming strategy mirrors recommendations provided by Krack *et al.*^[12] Each electrode is tested using monopolar polarity, pulse width 60 microseconds (μ s), and frequency 130 hertz (Hz). Rigidity is the primary measure for efficacy^[12] followed by hand opening bradykinesia and/or tremor. Voltage associated with maximal efficacy and onset of side effects is noted for each electrode and defined as the therapeutic window
- Stimulation parameters are further modified:
 - Electrode: The electrode providing the best motor response is selected
 - Polarity: Monopolar^[22] is chosen over bipolar unless side effects occur below 2.0 V
 - Pulse width: 60 μ s is the preferred pulse width (to maximize battery life and maximize the therapeutic window);^[12,18,21] pulse width is increased if maximal efficacy requires more than 3.5 V in monopolar polarity. If more than 3.5 V is required to reach maximal efficacy, an increase in pulse width allows for less amplitude to reach efficacy by compensating to increase stimulation intensity^[18]
 - Amplitude: The voltage associated with the onset of stimulation-induced side effect is noted, and the therapeutic voltage is calculated as 90% of the side effect threshold (i.e., side effects onset at 3.0 V therefore final voltage was 2.7)^[12]
 - Frequency: Clinical efficacy is fine-tuned by testing a hertz range between 130 and 185 and selecting the lowest effective Hz^[12,14,21]
 - Final stimulation settings are set, and an NOM/ONS mUPDRS is performed after 30 min
 - Patients take their first-morning dose of PD medication
 - A final ONM/ONS mUPDRS is completed, and voltage titrated down if dyskinesia is bothersome
 - Patient home diaries are used to monitor dyskinesia, efficacy, and medication dosing between appointments. The rainbow passage,^[6] (a clinical and research speech tool), mUPDRS examination item #18 (speech) and item #29 (gait) are used to assess for stimulation side effects and self-assessment of balance confidence after walking 30 m (queried to report worse, unchanged, or improved) is monitored daily. All patients are seen in clinic over the next 2 days
 - Medication is adjusted per change in off time or dyskinesia. Pre- and post-evaluation levodopa equivalent daily dose is calculated.^[19]

RESULTS

Group characteristics are shown in Table 2 and detailed results in Table 3. Adjusting stimulation eliminated stimulation-induced speech and gait side effects in all patients without compromising motor outcomes. At baseline, the group had a mean 29.0% motor response to stimulation and reprogramming resulted in a 54.3% response to stimulation which more closely approximated the response to medication plus stimulation (63.1%) regardless of age, duration of IPD, or months with DBS. Fourteen subjects self-reported improvement in balance confidence and two improvement in swallowing function. Improvement sustained over the 3–4 days assessment period. Levodopa dose equivalence was reduced a mean of 15.4%. All leads were reprogrammed ($n = 58$). Cathode was the primary stimulation parameter changed in 43 leads (cathode selections noted in Table 3 and visually depicted in Chart 1) and the number of active cathodes was reduced 11.6%. Pulse width decreased in 32 leads by 13.6%. The mean amplitude was decreased 8.3%, frequency reduced 5.2%, and polarity was changed in 32 leads. One patient required lead revision due to unavoidable stimulation side effects. Table 4 notes the detailed change in stimulation parameters and mUPDRS scores from a sample of five patients in the series.

DISCUSSION

Our analysis finds gait and speech declines after STN DBS may be attributed to stimulation side effects and can be identified by clinical observation and examination within 30 min of turning off stimulation. Many of the referred patients reported a history of acute decline in gait and speech after a change in stimulation. Despite the history of an acute change, the patients' dissatisfaction is what led to a second opinion. For each patient, we prioritized our time to investigate six factors that directly impact patient well-being with DBS.

First, we differentiated disease progression from stimulation-induced side effect by turning off stimulation. If gait, speech, or balance improves off stimulation, the

time invested in adjusting stimulation can offer the patient a chance to be restored to their true disease stage. Even when disease progression is present, overstimulation can contribute to disease burden by worsening speech, swallowing, balance, and gait and is a modifiable factor impacting patient health and safety.

Second, each individual's levodopa response is their benchmark for optimal stimulation. Useful to set expectations before DBS surgery, levodopa-responsive symptoms remain responsive to stimulation and a reliable measure of DBS outcome. Motor examinations in the medication off and on state offer a greater understanding about speech and gait symptoms to establish clinical expectations for stimulation. This is illustrated in Table 3 where off medication mUPDRS scores improved to more closely approximate the on medication mUPDRS scores after stimulation is optimized.

Third, systematically mapping efficacy and side effects is a simple and proven method of testing stimulation parameters to find optimal therapy settings and essential to monitor for stimulation side effects at any time postsurgery.^[7,13] The most effective electrode provides the framework for all other stimulation settings. As important is the determination of stimulation side effects. Side effects provide useful information about the general location of the electrodes in or near the STN. For instance, when eye deviation is observed, there is high probability the stimulating electrode is located in the ventral-medial area of the STN. Stimulating the medial lemniscal tract and corresponding paresthesia provides high confidence the electrode is stimulating the area posterior and medial to the STN. Ataxic gait and hypotonia can occur when stimulating medial and posterior to the STN due to the red nucleus and predominance of cerebellar tracts. The internal capsule (IC) is a prominent structure that lies lateral and anterior to the STN and rests adjacent to the desired sensorimotor area of the STN. The IC has closely associated and topographically organized tracts (corticospinal and corticobulbar)^[1] largely dedicated to voluntary motor function including gait, speech, and speed of movement. Stimulating the IC can cause muscle fiber contraction that can override normal motor control of muscles that are used when talking, walking, and swallowing. Gait, balance, and speech examination characteristics are sensitive measures of motor control. Hand opening task also provides immediate feedback when adjusting stimulation as optimal stimulation improves hand opening speed and IC stimulation causes slower hand movements. Other signs of IC stimulation include very brief paresthesia and muscle fiber contraction that is proportional to stimulation power. The lip, chin, face, eye, hand, and forearm are readily visible to monitor for the onset of muscle fiber contraction and can be enhanced by concomitant hand

Table 2: Demographics

Characteristic	Number
Sex (number of patients)	
Female	8
Male	21
Patients receiving care from movement disorders specialist	18
Age, mean (range) SD	65 (49-80) 7.5
Age IPD onset, mean (range) SD	51 (33-72) 8.5
Years IPD, mean (range) SD	15 (4-27) 5.5
Months DBS, mean (range) SD	27 (5-63) 17.0

SD: Standard deviation, IPD: Idiopathic Parkinson's disease, DBS: Deep brain stimulation

Table 3: Comprehensive data and results

Assessment data	Mean (range) SD		Percentage change
	Old stimulation settings	New stimulation settings	
NOM/NOS mUPDRS	44.52 (14-72) 13.5		
NOM/ONS mUPDRS	31.44 (12-53) 11.6	20.42 (7-37) 6.9	-35.7
ONM/ONS mUPDRS		16.4 (7-33) 7.1	
Motor change from stimulation	29.0%	54.3%	
Levodopa equivalent dose (mg)	985 (0-2500) 643.8	833 (150-2200) 425.4	-15.4
Stimulation parameters			
Mean voltage (V)	3.24 (7.4-1.0) 1.2	2.97 (4.0-1.7) 0.6	-8.3
Mean pulse width (μs)	76.6 (60-120) 17.0	65.7 (60-90) 11.9	-13.6
Mean frequency (Hz)	168.4 (95-185) 22.8	159.7 (130-185) 25.6	-5.2
	<i>n</i>	<i>n</i>	
Active cathode electrodes	69	61	-11.6
Monopolar polarity	29	27	
Bipolar polarity	29	31	
Cathode electrode 0	7	10	
Cathode electrode 1	30	19	
Cathode electrode 2	22	25	
Cathode electrode 3	9	7	

SD: Standard deviation, NOM: Off medication, ONM: On medication, NOS: Off stimulation, ONS: On stimulation, mUPDRS: Unified Parkinson's disease rating scale motor subsection score

Table 4: Sample of five subjects change in stimulation settings*

Preevaluation stimulation parameters	Postevaluation stimulation parameters	mUPDRS		
		Pre-NOM-ONS	Post-NOM-ONS	Post-ONM-ONS
Left bipolar - 3.5 V/60 μs/185 Hz/0-1-3+	Left monopolar - 3.4 V/60 μs/130 Hz/2-	29	15	9
Right monopolar - 2.9 V/90 μs/185 Hz/5-	Right monopolar - 3.0 V/60 μs/130 Hz/6-			
Left bipolar - 3.6 V/90 μs/185 Hz/1-2-3+	Left monopolar - 3.0 V/60 μs/185 Hz/3-	29	17	17
Right monopolar - 3.5 V/60 μs/185 Hz/1-	Right monopolar - 3.5 V/90 μs/185 Hz/3-2-			
Left monopolar - 3.7 V/90 μs/160 Hz/2-	Left bipolar - 3.5 V/60 μs/135 Hz/2-1+	25	14	11
Right bipolar - 2.4 V/60 μs/135 Hz/3-1+	Right bipolar - 2.5 V/60 μs/135 Hz/2-1+			
Left bipolar - 4.5 V/120 μs/185 Hz/1-2-3+	Left bipolar - 2.2 V/60 μs/145 Hz/2-3+	50	23	19
Right bipolar - 4.0 V/90 μs/185 Hz/0-2-3+	Right monopolar - 3.5 V/60 μs/130 Hz/2-			
Left bipolar - 3.5 V/90 μs/145 Hz/5-4+	Left bipolar - 3.0 V/60 μs/135 Hz/6-5+	14	8	7
Right bipolar - 3.3 V/90 μs/145 Hz/0-1+	Right bipolar - 2.5 V/60 μs/135 Hz/0-1+			

*This sample is comprised of five patients from the series. mUPDRS: Unified Parkinson's disease rating scale motor subsection score, NOM: Off medication, ONM: On medication, ONS: On stimulation

opening or finger tapping tasks. Subtle stimulation of the IC includes change in facial expression such as frowns and lip licking. The authors also noted the onset of a coarse tremor when stimulating the IC. Speech can be monitored during electrode testing to monitor for the onset of IC stimulation.

Fifth, stimulation outcome can be improved at any time postsurgery if the best stimulation settings have not been found. We chose the electrode that offered the most reduction in rigidity or bradykinesia and then adjusted the power using polarity, amplitude, and pulse width while being mindful of battery life. We used polarity and pulse width to make gross adjustments, whereas amplitude was used for fine adjustment. The amplitude that produced a very minor side effect was declared as the upper threshold

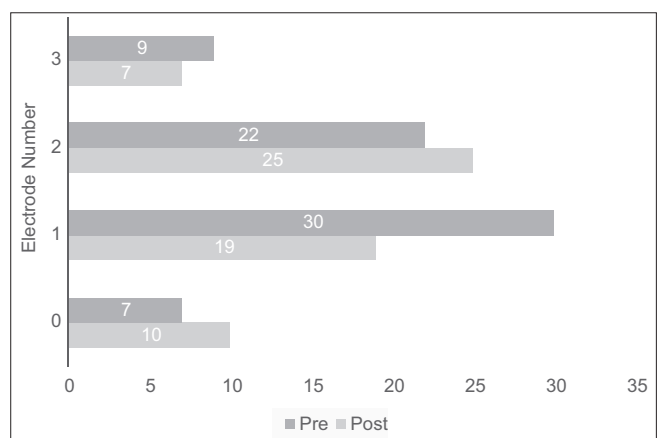


Chart 1: Pre- and Post-evaluation active cathode (negative electrode)

of the therapeutic window (using 60 μ s and 130 Hz) and provided guidance for polarity and pulse width. Our clinical protocol prioritizes amplitude to produce efficacy and pulse width, and polarity is minimized to avoid side effects. Our preference to conserve battery life is to increase pulse width >60 μ s only if the maximal tolerated amplitude is >3.5 V. When pulse width is increased, less voltage is required to activate similar volumes of tissue but can coincide with an increase in stimulation side effects as described by Butson *et al.*^[2] Pulse width reduction was a primary parameter change regardless of whether a cathode was changed. Setting maximal amplitude at 90% side effect threshold optimized motor improvement and avoided acute or delayed side effects. Our clinical protocol extends over at least 3 days to monitor for delayed side effects.

The sixth factor we include is a focus on battery longevity to reduce the number of pulse generator replacements. Pulse generator longevity is influenced by power usage and programing attributes (interleaving can reduce longevity by 50%) and replacements carry a risk of morbidity.^[17] Our use of simplified stimulation strategies led to improved motor function with less battery power by selecting the best cathode and maintaining low pulse width.

CONCLUSIONS

Our analysis focused on 29 patients with stimulation-induced gait and speech deficits that were rapidly detected and served to support the clinical time to conduct an in-depth review of factors that are known to directly impact clinical outcomes. Our findings suggest that disease progression may not be the only cause for a decline in speech and or gait after STN DBS and detection of stimulation side effects requires up to 30 min of time off stimulation. The minimal time to wash out gait and speech stimulation side effects remains unknown. Basic programing strategies continue to perform well in improving motor function and avoiding stimulation side effects. Although the electrode testing is easy to perform, the interpretation of efficacy and presence of stimulation side effects may pose a challenge as noted by the significant change in the stimulating electrode in our series. Our retrospective review is limited by an acute analysis of disease progression and change in stimulation parameters. Our assessment is further limited due to the absence of a formal gait or speech analysis which would enhance the mUPDRS and may offer additional clues to stimulation side effects.

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Conflicts of interest

There are no conflicts of interest.

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