Speech changes induced by deep brain stimulation of the subthalamic nucleus in Parkinson disease: involvement of the dentatorubrothalamic tract

Albert J. Fenoy, MD,1 Monica A. McHenry, PhD,2 and Mya C. Schiess, MD3

1Department of Neurosurgery, Mischer Neuroscience Institute, and 3Department of Neurology, Movement Disorders and Neurodegenerative Disease Program, McGovern Medical School, University of Texas–Houston Health Science Center, Houston, Texas; and 2Department of Speech-Language Pathology, New York Medical College, Valhalla, New York

OBJECTIVE Patients with Parkinson disease (PD) who undergo subthalamic nucleus (STN) deep brain stimulation (DBS) often develop a deterioration in speech performance, but there is no clear consensus on the specific effects seen or the mechanism involved and little description of the impact of DBS on conversational speech. Furthermore, there has been no fiber tract connectivity analysis to identify the structures potentially modulated by DBS to cause such deficits. The main objective of this study was to quantify spontaneous speech performance and identify potential involvement of the dentatorubrothalamic tract (DRTt) in patients who underwent STN DBS, because this tract has been implicated in speech deterioration.

METHODS Spontaneous speech samples were obtained with STN DBS in both on and off modes in 35 patients with PD and assessed across multiple domains. Diffusion tensor imaging tractography seeded from the therapeutic DBS contacts was performed to identify the fiber tracts involved and, specifically, the DRTt. The position of active electrode contacts was assessed relative to that of the STN.

RESULTS Fifteen patients with akinetic-rigid (AR) PD and 20 with tremor-dominant (TD) PD subtypes were identified. In the AR-PD subgroup of patients, in whom there was DRTt involvement, 71% demonstrated much better overall speech and largely improved or unchanged fluency in the DBS-off condition. In patients with TD PD with DRTt involvement, 50% demonstrated better overall speech in the off condition, and equivocal results regarding improved or worsened fluency were found. When there was minimal DRTt involvement, 75% of patients with AR PD had better overall speech in the DBS-on condition and better or minimal fluency changes. Similarly, 83% of patients with TD PD with minimal DRTt involvement had better or minimal overall speech and fluency changes in the on condition. More medially placed left electrode contacts were associated with more DRTt involvement in 77% of patients (10 of 13).

CONCLUSIONS To the authors’ knowledge, this is the first study to have investigated a specific fiber tract involved in STN DBS in different subtypes of PD relative to its impact on spontaneous speech. At optimal therapeutic programming of STN DBS, overall spontaneous speech and fluency were affected more negatively in patients with AR PD than in those with TD PD when there was DRTt involvement. After fiber tract analysis and modeling, it was found that medially positioned left electrode contacts more often involved fibers of the DRTt. If possible, avoidance of the DRTt by using active electrode contacts that are positioned less medially, specifically in patients with AR PD, might result in less speech deterioration.

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KEY WORDS deep brain stimulation; speech effects; Parkinson disease; tractography; dentatorubrothalamic tract; functional neurosurgery
At some point in the disease process, patients with Parkinson disease (PD) experience speech deterioration, characterized by hypokinetic dysarthria, which results from a multidimensional impairment of phonation, articulation, and prosody.\textsuperscript{22,27} Presentation varies, but often seen are reduced loudness, monotony of pitch and loudness, short rushes of speech, imprecise articulation, and reduced intelligibility.\textsuperscript{1,12,17,20}

Deep brain stimulation (DBS), most commonly targeting the subthalamic nucleus (STN), is now considered the standard surgical intervention for patients with PD who develop motor symptoms that remain inadequately treated by medical therapy alone. Although quite effective in ameliorating motor symptoms of bradykinesia, rigidity, and tremor, STN DBS has often been associated with variable effects on speech, with deterioration most common in speech production and its perception by others.

There is no clear consensus in the literature as to how exactly STN DBS affects speech, and the issue is clouded further by the variability in the measures used and the almost exclusive use of structured (read or repeated) speech samples for evaluation. Articulatory and voice characteristics are not stable across all forms of speech; spontaneous speech is typically 30\% less fluent than reading or repetition.\textsuperscript{2,25,34} In patients with PD, dysfluencies are prominent in conversational speech; therefore, those who evaluate DBS effects on speech should assess unstructured spontaneous speech to obtain a more accurate picture of changes that have occurred, and this is what we did in the present study.

The site of stimulation or the location of electrodes within the STN area and its relationship to motor control and speech effects has been the subject of a few reports,\textsuperscript{30,31,33} and there are common themes that have evolved, implicating the spread of current to certain structures as causative of dysarthria.\textsuperscript{13,29} However, there has not been an analysis of specific fiber tract modulation by the active contact or elucidation of structures that are potentially involved in mediating such speech effects. Similarly, analyses relating speech effects caused by STN DBS with PD subtypes are lacking.

In this study, we analyzed 2 STN-DBS conditions and their contrastive effects on speech in a population of patients with PD manifesting as either the akinetic-rigid (AR) or tremor-dominant (TD) PD subtype. By using diffusion tensor imaging (DTI) tractography seeded from the therapeutic DBS electrode contacts, we sought to elucidate the involvement of likely fiber tracts that potentially contribute to the specific observed speech effects. We were interested specifically in the involvement of the dentatorubrothalamic tract (DRTt), because it has been implicated in other reports of STN DBS–induced dysarthria.\textsuperscript{38} It is important to note that specific clinical characteristics of each individual, such as age, severity of disease, disease duration, and subtype of disease, are analyzed here in relation to their possible structural involvement in STN DBS–mediated effects on speech.

**Methods**

**Participants**

A total of 35 patients with PD were recruited to participate in this study, which was approved by our local institutional review board. Informed consent was obtained from each patient. Fifteen patients were classified as having AR PD and 20 were classified as having TD PD based on their overall phenotypical presentation.\textsuperscript{25} The mean (± SD) age of patients in the AR-PD group was 66 ± 8 years and of those in the TD-PD group was 60 ± 8 years (difference nonsignificant [NS]). The mean disease duration before surgery was 9.6 ± 3.1 years for patients with AR PD and 8.2 ± 3.7 years for patients with TD PD (NS). Presurgical levodopa equivalent dosage was not significantly different between groups (812 ± 444 mg [AR-PD group] vs 778 ± 474 mg [TD-PD group]) (Table 1).

**Surgical Procedure**

Each patient underwent staged DBS surgery targeting the STN using the following standard stereotactic protocol: preoperative MRI was performed; a Leksell head frame (Elekta) was used, and CT images were acquired; reference CT images were fused to MR images for target determination; and intraoperative microelectrode recording was performed (Guideline 4000; FHC) to identify nuclear boundaries and to verify STN localization. Electrode placement (Medtronic 3387 model electrode) occurred after intraoperative test stimulation brought on improvement in tremor, rigidity, and/or bradykinesia. Lead extensions and an Activa PC/RC dual-channel pulse generator were implanted at a separate stage 2 weeks later.

**Speech Analyses**

All speech samples were audio recorded in a quiet room using a head-mounted microphone (AKG C520) and preamplifier (AudioBox, PreSonus). Samples were digitized at 44,100 Hz (Praat phonetics program [see http://www.fon.hum.uva.nl/praat/]). Participants produced unstructured spontaneous speech, typically in response to picture stimuli.

All speech samples were recorded at least 3 months after the demonstration of optimal control of motor symptoms with stable DBS programming. All samples were 30–60 seconds long and were first transcribed in detail from audio recordings. An overall impression of speech production was made by the second author (M.A.M.), considering all of the following measures.

**Articulation Rate**

The number of syllables produced was determined by transcription, repeated listening, and visualization using Praat. The articulation rate was calculated as the number of syllables produced/total time without pauses. Part-word, word, and phrase repetitions were included in the total number of syllables.

**Fluency Measures**

Dysfluencies were defined as part-word, word, or phrase repetitions; revisions; hesitations; and fillers. Dysfluency measures were based on repeated listening and visualization of the speech samples in Praat. Typical dysfluency measures of percent dysfluent words/total number of words were not used because of insensitivity to dysfluen-
cies in patients with PD. Instead, the percentages of time on target and actual syllables on target were calculated. To determine the percent time on target, the duration of the sample including all dysfluencies and pauses was determined. Dysfluencies and pauses were then edited out using Praat software. Percent time on target was calculated as the duration without dysfluencies or pauses/total duration of the sample. The percentage of syllables on target was calculated as the number of target syllables produced/total number of syllables produced.

Voice, Prosody, and Cognition

A subjective impression of the predominant vocal quality and prosody was determined by the second author (M.A.M.). A subjective impression of cognition was also obtained based on the number and length of pauses needed to generate language and evidence of cognitive slowness, such as difficulty generating something to say.

Intelligibility

A subjective estimate of intelligibility was determined by the second author (M.A.M.) and 4 2nd-year graduate students in speech-language pathology. Several months after the initial data analysis, the 5 listeners, blinded to the DBS condition, heard randomized speech samples. Each listener independently estimated the percent intelligibility. If there was disagreement greater than 5%, the listeners reached a consensus after discussion.

Imaging Analyses

MRI data were acquired preoperatively using a 3-T HdxR Release 16.0 twin-speed MRI system (GE Healthcare). A T2-weighted 3D isotropic sequence was acquired in sagittal orientation (TR 3000 msec, TE 66.9 msec, field of view 24 mm, matrix 288 × 288, 190 slices, thickness 1.0 × 1.0–mm isotropic slices, 5:43-minute acquisition time). The resulting data were reconstructed to 1.00-mm3 isotropic voxels. For DTI, a spin-echo echo-planar imaging (SE-EPI) pulse sequence was applied (TR 17,000 msec, TE 86.3 msec, field of view 25 mm, matrix 128 × 128, 66 slices, 2.0-mm slice thickness, 32 gradient directions, 1000 sec/mm2 b value, 9:38-minute acquisition time). The sequence resulted in 2-mm3 isotropic reconstructed voxels, acquired in axial orientation.

The 3D inversion-prepared T1-weighted gradient echo (3D-MPRAGE) sequence was acquired in axial orientation after contrast (Gd diethylenetriamine pentaacetic acid) administration (TR 7.0 msec, TE 3.8 msec, 8° flip angle, inversion recovery preparation 900, field of view 28 mm, matrix 256 × 256, 180 slices, thickness 1.0 × 1.0–mm isotropic slices, 13:07-minute acquisition time). It resulted in 1-mm3 reconstructed voxels.

In deterministic tractography, all pathways that intersected a volume of tissue activated (VTA), which was modeled by a spherical region around the therapeutic electrode contacts, were saved for display and further analysis. The radius of the spherical VTA was estimated using therapeutic cathodal electrode contact parameters and an isotropic model, as proposed by Butson et al.3 For probabilistic tractography, the tracking algorithm was initialized...
using the modeled VTA as a single-mask-seed region. The location of the therapeutic contact in relation to presurgical anatomy was determined by localizing the contact center on a thin-slice (1-mm) CT volume after coregistration to the T2 anatomical volume.

Fiber tracking was performed on a Stealth S7 workstation using the StealthViz DTI software application (Medtronic Navigation) and the following parameters, as suggested by others: fractional anisotropy level 0.2, minimal fiber length 20 mm, and seed density 5.0; the maximal directional change of fibers was chosen to be 52°. Fibers that passed through the VTA of the therapeutic cathodal contact were then qualitatively assessed for their involvement of the DRTt. Functionally, the DRTt consists of fibers that emanate from the cerebellar output nuclei (dentate, emboliform, globose) and ascend into the superior cerebellar peduncle, where most decussate, surround, and enter the contralateral red nucleus, projecting onward to the ventral intermediate nucleus or ventralis oralis posterior nucleus of the thalamus before terminating in the primary motor cortex. Thus, the DRTt was defined as fibers that emanate from a region of interest in the cerebellar deep nuclei following the superior cerebellar peduncle through to the precentral gyrus, as visualized on T2-weighted MRI and as suggested by Coenen et al.

Each patient’s individual fiber tract involvement was drawn; after viewing each of them, qualitative assignments of DRTt involvement were given, ranging from “no” or “minimal” involvement to “more” involvement. These assignments were based on comparisons between such depictions from all patients. “Minimal DRTt involvement” by the VTA of the active contact was defined as less than 33% of the activated fibers coursing through such a tract; “DRTt involvement” was defined as anything more than minimal. The pyramidal tract was intersected by the VTA of each active contact, as expected.

Each patient’s preoperatively obtained T2-weighted MRI was merged with the postoperative CT images, and the resulting combined image for each patient was inspected to analyze the location of the active cathodal contact relative to the directly visualized borders of the STN. To account for CT artifacts, we used the center of the represented electrode volume. The cathodal electrode contact that was considered to be bordering the medial aspect of the STN border or medial to the STN was labeled “medial.” The most rostral contacts (Left 2 or 3, Right 10 or 11) were considered rostral to the STN based on the use of a Medtronic 3387 lead when targeting contact 0 to be at the ventral border of the STN using microelectrode recording and assuming the maximal STN thickness to be < 6 mm. These contacts are shown in Table 1.

Statistical Analysis

Statistical analysis was performed with SPSS-18 for Mac. The Student paired t-test was used to compare groups of data using 2 tails and assuming 2 samples of equal variance. Fisher exact tests were used in GraphPad Software (http://graphpad.com/quickcalcs/contingency2/) to assess if differences between groups were statistically significant.

Results

After stable, consistent programming of DBS for optimal symptomatic benefit, the mean postsurgical voltage and pulse width of the active electrode contacts were recorded. Pulse widths varied most commonly between 60 and 90 μsec in all patient settings; as such, according to the Butson et al. isotropic model, cathodic voltage seemed to be the most important variable affecting the size of the estimated VTA and therefore is presented herein. When we compared overall mean voltages of the left and right electrodes between the AR-PD and TD-PD groups, only right voltage was significantly higher in the overall TD-PD group than in the overall AR-PD group (2.3 V [AR PD] vs 3.1 V [TD PD], p = 0.02; AR/TD left voltage 2.8/3.0, NS).

In DRTt-subset comparisons (those patients with AR PD or TD PD who had relatively more DRTt involvement, labeled as AR-DRT or TD-DRT, respectively), the difference in the mean voltage in the AR-DRT group (2.3 V) versus that of the TD-DRT group (3.1 V) was significant for the left side (p = 0.04) but not significant for the right side. In a comparison of the AR-PD and TD-PD patients with minimal DRTt involvement (AR-minDRT or TD-minDRT), differences were not significant for the left-, right-, or same-side electrode contacts (Table 1).

Overall, of the entire sample of patients who underwent STN-DBS, 10 (29%) had improved speech, 15 (43%) had worse speech, and 10 (29%) had no change. Thus, we performed the following subgroup analyses to determine if disease type and DRTt involvement are factors involved in these various speech changes.

Patients With AR PD

Of the 15 patients with AR PD, overall speech/language/cognition was better in the DBS-off condition in 41% of patients (better in the on condition in 46%; minimal change in 13%), with improved (40%) or unchanged (27%) fluency in the off condition (Table 2).

Prominent DRTt involvement was demonstrated by deterministic fiber tracking through the active electrode contact in 7 of the 15 patients. In these patients, overall speech/language/cognition was better in the DBS-off condition than in the on condition in 71%, with improved (57%) or unchanged (43%) fluency. In this group, intelligibility was better in the off condition in 56% and better in the on condition in 14% (minimal change in 28%). See Fig. 1 for an example of VTA estimation using the active electrode contact, which resulted in fiber tract involvement that included some of the DRTt.

Minimal DRTt involvement was seen in the remaining 8 of 15 patients with AR PD. In these patients, overall speech/language/cognition was better in the DBS-on condition in 63%, with better or minimal fluency changes. In this group, intelligibility was typically affected minimally (75% of patients), with only 25% of patients having more intelligible speech in the on condition; none was better in the off condition. See Fig. 2 for an example of estimated VTAs using the active electrode contacts that incurred less DRTt involvement.

Overall, all patients with AR PD produced a faster rate of speech in the on condition (0.28 syllables/second differ-
ence) (Table 2). Most patients in either subgroup (i.e., more or minimal DRTt involvement) had either faster speech or a minimal change in their rate of speech in the on condition.

Results of comparisons of mean voltages between the left and right therapeutic electrode contacts in patients with AR PD overall and between DRT groups were not significant; in the AR-minDRT group, mean left voltage was 3.2 V and mean right voltage was 2.3 V (p = 0.038). The difference between mean left active contact voltages in the DRT

<table>
<thead>
<tr>
<th>Patient Condition</th>
<th>No.</th>
<th>Overall Speech Improved (% on/% off [% min ∆])†</th>
<th>Intelligibility Improved (% on/% off [% min ∆])†</th>
<th>Time on Target (mean % on/mean % off [% min ∆])†</th>
<th>Time on Target Improved (% on/% off [% min ∆])†</th>
<th>Mean Rate (on/off) (syl/sec)</th>
<th>Rate (syl/sec) Improved (% on/% off [% min ∆])†</th>
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</thead>
<tbody>
<tr>
<td>AR overall</td>
<td>15</td>
<td>46/41 (13)</td>
<td>20/40 (40)</td>
<td>86/90</td>
<td>33/40 (27)</td>
<td>4.7/4.4</td>
<td>40/7 (53)</td>
</tr>
<tr>
<td>AR DRT</td>
<td>7</td>
<td>29/71 (0)</td>
<td>14/58 (28)</td>
<td>87/90</td>
<td>0/57 (43)</td>
<td>4.9/4.7</td>
<td>43/14 (43)</td>
</tr>
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<td>AR minDRT</td>
<td>8</td>
<td>63/12 (25)</td>
<td>25/25 (75)</td>
<td>85/80</td>
<td>63/24 (13)</td>
<td>4.6/4.3</td>
<td>38/9 (63)</td>
</tr>
<tr>
<td>TD overall</td>
<td>20</td>
<td>15/45 (40)</td>
<td>5/10 (85)</td>
<td>88/83</td>
<td>40/20 (40)</td>
<td>4.6/4.5</td>
<td>30/10 (60)</td>
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<tr>
<td>TD DRT</td>
<td>17</td>
<td>17/41 (42)</td>
<td>6/14 (80)</td>
<td>85/80</td>
<td>35/18 (47)</td>
<td>4.7/4.7</td>
<td>29/14 (57)</td>
</tr>
<tr>
<td>TD minDRT</td>
<td>3</td>
<td>0/67 (33)</td>
<td>0/0 (100)</td>
<td>95/90</td>
<td>67/33 (0)</td>
<td>4.6/4.5</td>
<td>33/0 (67)</td>
</tr>
</tbody>
</table>

min ∆ = < 5% difference between conditions; syl = syllable.

* Stimulation condition in which speech was better, which was a consensus of speech-language pathologists of overall speech characteristics, including voice, cognition, articulation, fluency, rate, and intelligibility.

† Improved: defined as > 5% difference in the on and off conditions or > 0.5 syllables/second for rate category.

FIG. 1. Estimated VTA from therapeutic electrode contact using postoperative CT images of the DBS electrode location merged with preoperatively obtained DTI and T2 MRI sequences in coronal (A), axial (B), and sagittal (C) slices; the VTA radius was used to draw a 2D area that was used to construct the seed region represented in each plane using StealthViz software. D–F: Depiction of the fiber tracts involved (orange) using the estimated VTA at the active contact as a seed region. G–I: The corticospinal tract (yellow) and DRTt (blue) are represented relative to the electrode and estimated VTA. The corticospinal tract is drawn extending from the crus cerebri through the internal capsule to the precentral gyrus; the DRTt is drawn using a seed region in the cerebellar deep nuclei extending through the superior cerebellar peduncle to the precentral gyrus. J–L: Depiction of modulated fiber tracts relative to the corticospinal tract and DRTt. The active left electrode contact is delineated (crosshairs) in each panel. Figure is available in color online only.
(2.3 V) and minDRT groups (3.2 V) was 0.9 V (p = 0.06, NS); there was no difference for right contact voltages.

**Patients With TD PD**

Of all 20 patients with TD PD, overall speech/language/cognition was better in the DBS-off condition in 45% (better in the on condition in 50%; minimal change in 50%), with improved (20%) or unchanged (40%) fluency in the off condition (fluency was better in the on condition in 20%) (Table 2).

Prominent DRTt involvement was found in 17 of 20 patients; in this TD-DRT subset, speech/language/cognition in the off condition was nearly equal to that in the on condition, with better speech in the off condition in 45% of patients (better in the on condition in 20%; minimal change in 40%). Fluency again was varied, with minimal change in 47% or improved fluency in 47% in the on condition and improved fluency in 47% in the off condition. In the TD-minDRT subset (n = 3), overall speech/language/cognition was either better in the off condition (47%) or minimally changed (33%), with fluency better in the off condition (66%) or minimally changed (33%). See Fig. 3 for an example of VTA estimation using the active electrode contact resulting in fiber tract involvement that had prominent or “greater” DRTt involvement.

In both DRTt subgroups, most patients with TD PD had either faster speech or a minimal change in rate in the on condition. Voltage differences across the TD-PD subtypes and left-versus-right active electrode contacts were not significant.

**Comparison of Speech Effects in AR and TD Subtypes**

Comparison of the AR-PD and TD-PD groups showed no significant difference in the number of participants whose overall speech improved (or stayed the same) or worsened (p = 0.99, Fisher exact test), which suggests equivocal results regarding improved or worsened speech with DBS. For more detailed analysis, data from the subgroups of the patients with AR PD and those with TD PD were also subjected to Fisher exact tests. When we compared the patients with AR PD with and those without DRTt involvement, the difference between subgroups was significant (p = 0.04), which confirms that when the DRTt is involved, the overall speech of patients with AR PD is worse with DBS on. When we compared the patients with TD PD with and those without DRTt involvement, the difference between subgroups was not significant (p = 0.64). Although these findings are based on a relatively small number of patients, it can be inferred that the involvement of the DRTt has a greater negative impact on the speech.
of patients with AR PD than on the speech of those with TD PD.

Disease Duration

Among patients with AR PD, those who had a disease duration of 10 years before DBS surgery had worse overall speech in the DBS-on condition than those patients who had a disease duration of 8.5 years before DBS surgery, but this difference was not significant (p = 0.3). Similarly, for patients with TD PD, there was an insignificant difference between disease durations before DBS surgery for patients with better and those with worse speech with DBS on (7.5 vs 9 years, respectively; p = 0.4). See Table 1 for group differences; no group differences in disease durations were significant.

Electrode Contact Position and Tract Involvement

In other studies, analysis of which active electrode contacts produce stable optimal motor control suggested that more involvement of the DRTt occurred with more medial placement relative to the STN for each patient.31 Using the imaging-analysis method described previously, we determined active contacts located more rostral or medial to the STN (Table 1). Electrode contacts positioned lateral to the center of STN were used infrequently. Based on conclusions of other investigators that the left active contact was most implicated in increased DRTt involvement,31,32 the coordinates of each active left contact are shown transposed onto a stereotactic atlas24 in Fig. 4. The overall mean (SD) xyz coordinates relative to the anterior commissure–posterior commissure midpoint for the therapeutic electrode contact in patients with AR PD were $x = 11.2 (1.4)$, $y = -0.8 (1.4)$, and $z = -1.9 (1.8)$ (left) and $x = 10.7 (1.0)$, $y = -0.5 (1.7)$, and $z = -2.4 (1.9)$ (right); and in patients with TD PD, they were $x = 10.8 (1.2)$, $y = -1.0 (1.1)$, and $z = -1.9 (1.3)$ (left) and $x = 10.7 (1.0)$, $y = -1.1 (1.2)$, and $z = -2.3 (1.2)$ (right).

The mean (SD) xyz coordinates of the therapeutic electrode contact for patients with AR PD with speech deterioration were $x = 10.9 (1.4)$, $y = -1.3 (1.1)$, and $z = -2 (1.7)$ (left) and $x = 10.6 (1.4)$, $y = -1 (1)$, and $z = -2 (1.7)$ (right); for those with speech improvement were $x = 11.4 (1.6)$, $y = -0.9 (1.5)$, and $z = -2.1 (1.9)$ (left) and $x = 10.8 (0.8)$, $y = 0 (2.1)$, and $z = -3.1 (1.8)$ (right); and for those with a minimal change were $x = 11 (0.5)$, $y = 0.7 (1.1)$, and $z = -1 (-2.8)$ (left) and $x = 11 (0.5)$, $y = 1.0 (1.1)$, and $z = -1 (2.8)$ (right).

The mean (SD) xyz coordinates of the therapeutic electrode contact for patients with TD PD with speech deterioration were $x = 10.8 (1.5)$, $y = -0.7 (1.3)$, and $z = -1.6 (1.8)$ (left) and $x = 10.8 (1.3)$, $y = -0.8 (1.5)$, and $z = -2.3 (1.6)$ (right); for those with speech improvement were $x = 11.6 (1.2)$, $y = -1.5 (2.1)$, and $z = -2.2 (1.6)$ (left) and $x = 11.3 (0.6)$, $y = -1.5 (1.5)$, and $z = -2.7 (1.3)$ (right); and for those with a minimal change were $x = 10.4 (0.7)$, $y = -1.1 (0.7)$, and $z =$
Discussion

The effects of DBS on overall speech and fluency varied according to DRTt involvement and PD type (AR or TD). When there was DRTt involvement, 71% of patients with AR PD had much better overall speech with largely improved or unchanged fluency in the DBS-off condition and 50% of patients with TD PD demonstrated better overall speech in the DBS-off condition, with equivocal fluency changes. When there was minimal DRTt involvement, 75% of patients with AR PD had better overall speech in the DBS-on condition with better or minimal fluency changes. Similarly, 83% of patients with TD PD with minimal DRTt involvement had better or minimal overall speech and fluency changes in the on condition.

Intelligibility was impacted minimally by DBS-on or -off condition in any subgroup except for patients with the AR subtype and DRTt involvement; 58% of these patients had improved intelligibility with DBS off. This result seems to follow the trend for overall speech and fluency in this subset. In this study, intelligibility was assessed subjectively. Judgments were influenced primarily by articulatory precision, which was affected occasionally by speaking rate. In the DBS-on condition for each group, rates improved. It was typical for both speaking rate and intelligibility to increase concurrently; however, there were some patients whose speech was considered blurred, and when the rate increased in the on condition, intelligibility deteriorated. These differences, however, were not evident in the averaged data (see Table 2).

The methods described in the literature that were used to assess the effect on speech of STN DBS in patients with PD have been highly variable and do not adequately characterize conversation, the most common form of speech. Almost all of these methods have used structured speech—reading aloud standardized passages, such as the Rainbow Passage—or even more limited measures, such as Speech Item 18 of the Unified Parkinson’s Disease Rating Scale \( \text{for assessing dysarthria.} \) The assumption that articulatory and voice characteristics are stable across speaking tasks is erroneous, because production differs for spontaneous speaking, repetition, and reading aloud. In patients with PD, it is spontaneous conversational speech that is considered to be most dysfluent, possibly because of the decreased ability of these patients to generate a novel action plan, execute it, and monitor it using internal models rather than relying on external cues (reading or repeating). One goal of our study was to establish a method of objectively quantifying spontaneous speech, to show how it is affected by STN DBS, and to determine if the DRTt is involved. It should be noted, however, that depending on the elicitation strategy, spontaneous speech might not be truly equivalent to conversational speech. There is less cognitive load when performing spontaneous speech tasks, such as describing a picture. The person is not required to follow a conversation and formulate appropriate responses in a timely manner.
Nonetheless, the strategy to elicit spontaneous speech in this study yielded a sample that is closer to conversational speech than reading or repetition.

**Electrode Contact Position Relative to Speech Deterioration**

Only a few studies have investigated what could be contributing to detriments in speech production and have implicated structures likely stimulated by contact location33 or identified by metabolic imaging.17,18 Tripoliti et al.33 used a listener to assess speech intelligibility in read sentences (Computerized Assessment of Intelligibility in Dysarthric Speech [CAIDS])36 in their series of patients who underwent STN DBS, and they found deterioration in 25 patients and improvement in 7 patients. In these patients, active contacts positioned inside the left STN were associated with less detrimental effects on speech intelligibility than contacts positioned medial to it, whereas contacts located in the superior STN were associated with improved speech. Through their location analyses, the authors hypothesized that speech deterioration associated with such medial contacts, which also required higher voltage for control of movement, might be caused by spread to the DRTt.

We investigated the possibility that active electrode contacts rostral or medial to the STN could have an effect on cerebellothalamic or DRTt involvement. The subthalamic white matter contains pallidothalamic and subthalamic tracts (ansa lenticularis, lenticular fasciculus, thalamic fasciculus) connecting the globus pallidus with the ventral thalamus56 and the zona incerta, the caudal/posterior medial component of which is sometimes targeted for tremor.11 The DRTt continues from the red nucleus medial to the STN to the ventral lateral nucleus of the thalamus,16 Active contacts positioned medial or rostral to the STN, or within the STN and producing a large enough VTA, might involve fibers of the DRTt.

Because specifically left-side DBS (over the right side) has been implicated as causing more speech deterioration,23,31,36 which correlates with imaging data showing left-hemisphere dominance in speech and articulation,26,28,37 we focused on the positions of the left electrode contacts in this series (see Fig. 3).

After investigating positions of therapeutic left electrode contacts in our series, we discovered that in the AR-PD group, 2 (50%) of 4 patients with medial contacts and 5 (63%) of 8 patients with rostral contacts had more DRTt involvement. These results were different from those in the TD-PD group, in which 8 (89%) of 9 patients with medial contacts and 9 (82%) of 11 patients with rostral contacts had more DRTt involvement. Such a relative medial position incurring DRTt involvement is in line with other reports.31 It is likely that the greater use of more medial/rostral contacts in the TD-PD subset occurs because of therapeutic necessity, since involvement of the DRTt is sought for tremor control.3,6 Such was not necessary in the AR-PD subset and reflects the nearly equal findings of DRTt involvement with regard to improved or worsened speech here.

Similarly, the higher voltages needed for patients with TD PD versus those with AR PD overall (both left and right) might be a reflection of the need for tremor control, because a larger VTA incurs greater involvement of the posterior subthalamic fibers or DRTt.

It is important to note that it is very likely that all patients, especially in the TD-PD subset, did have some component of DRTt involvement because of the chosen electrode contact for therapeutic control of tremors. Our classification of “more” versus “less” involvement is quite subjective and qualitative, based on multiple models and imaging sources with inherent error. Our classification here was an effort to relate speech changes to more DRTt involvement. Errors are inherent in estimating the VTA, because we can calculate this only on the basis of the cathode, when in actuality there are often bipolar settings, or even possibly 2 cathodal points, which will change the shape of the VTA. Such errors are understood, as are other modeling limitations (non-constant charge density, individual patient differences, etc.).

**Why Does DRTt Involvement Affect Speech in Patients With AR PD More Than Those With TD PD?**

The answer to this question is unclear, but differential DRTt involvement might be a result of the fundamental pathophysiological differences between the AR and TD subtypes: AR-PD subtypes, rather than TD-PD subtypes, have been shown to have decreased functional connectivity in the medial frontal cortex/precentral gyrus9 and hypo-prefrontal connectivity of the putamen–premotor cortex network.21

As early functional disruption of the precentral gyrus and associated default mode network in patients with PD before clinical evidence of cognitive impairment occurs,26 less functional coordination of the precentral gyrus in patients with AR PD than in those with TD PD9 suggests that the AR subtype results in more rapid development of cognitive decline.14,19 It is unclear if and how this could relate to a decline in linguistic ability, but there could be greater susceptibility to stimulation-induced fiber pathway involvement with overall speech deterioration.

Based on our experience in this study, it seems that in the treatment of patients with AR PD, greater DRTt involvement results in a more significant adverse effect of STN DBS on speech than in patients with TD PD. To this end, we have devised a simple algorithm to avoid such DRTt involvement and thus potentially negative effects on speech in patients with AR PD (Fig. 5).

**Conclusions**

This is the first study, to our knowledge, that investigated individual fiber tracts involved relative to the therapeutic electrode contact in STN DBS in different subtypes of PD. Specifically, we were interested in DRTt involvement and its impact on spontaneous speech. Our findings corroboration those of other studies that reported that placement of the left electrode contact medial to the STN can negatively impact speech. Here, through fiber tract analysis, we found that this is most likely a result of DRTt involvement, which seemed to be more influential in the AR-PD subtype. If possible, avoiding the DRTt by placing leads less medially, and by using a less medial active contact, might result in less speech deterioration.
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References


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Correspondence
Albert J. Fenoy, Department of Neurosurgery, Mischer Neuroscience Institute, University of Texas–Houston Health Science Center, 6400 Fannin, Ste. 2800, Houston, TX 77030. email: albert.j.fenoy@uth.tmc.edu.