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Subthalamic nucleus deep brain stimulation changes velopharyngeal control in Parkinson's disease

Michael J. Hammer[a,*], **Steven M. Barlow**[b], **Kelly E. Lyons**[c], and **Rajesh Pahwa**[c]

[a]Department of Surgery, Division of Otolaryngology, University of Wisconsin, Madison, WI, USA

[b]Speech-Language-Hearing, Neurosciences, Human Biology, and Bioengineering, University of Kansas, Lawrence, KS, USA

[c]Parkinson Disease and Movement Disorder Center, Department of Neurology, University of Kansas Medical Center, Kansas City, KS, USA

Abstract

Purpose—Adequate velopharyngeal control is essential for speech, but may be impaired in Parkinson's disease (PD). Bilateral subthalamic nucleus deep brain stimulation (STN DBS) improves limb function in PD, but the effects on velopharyngeal control remain unknown. We tested whether STN DBS would change aerodynamic measures of velopharyngeal control, and whether these changes were correlated with limb function and stimulation settings.

Methods—Seventeen PD participants with bilateral STN DBS were tested within a morning session after a minimum of 12 h since their most recent dose of anti-PD medication. Testing occurred when STN DBS was on, and again 1 h after STN DBS was turned off, and included aerodynamic measures during syllable production, and standard neurological ratings of limb function.

Results—We found that PD participants exhibited changes with STN DBS, primarily consistent with increased intraoral pressure (n = 7) and increased velopharyngeal closure (n = 5). These changes were modestly correlated with measures of limb function, and were correlated with stimulation frequency.

Conclusion—Our findings suggest that STN DBS may change velopharyngeal control during syllable production in PD, with greater benefit associated with low frequency stimulation. However, DBS demonstrates a more subtle influence on speech-related velopharyngeal control than limb motor control. This distinction and its underlying mechanisms are important to consider when assessing the impact of STN DBS on PD.

Keywords

Aerodynamic; Air flow; Air pressure; Frequency; Speech; Velopharyngeal area

*Corresponding author at: Room K4/769 Clinical Sciences Center, 600 Highland Avenue, Madison, WI 53792, USA. Tel.: +1 608 262 6018. hammer@surgery.wisc.edu (M.J. Hammer).

Learning outcomes: As a result of this activity, the participant will be able to (1) describe the effects of deep brain stimulation on limb and speech function; (2) describe the effects of deep brain stimulation on velopharyngeal control; and (3) discuss the possible reasons for differences in limb outcomes compared with speech function with deep brain stimulation of the subthalamic nucleus.

1. Background

Parkinson's disease (PD) affects more than 1 million individuals in the United States, resulting in impairment of limb motor control, including deficits in force recruitment, velocity, and acceleration of limb movements (DeLong, 1990, 2000; Desmurget et al., 2004; Pfann, Buchman, Comella, & Corcos, 2001; Pfann et al., 2004; Robichaud, Pfann, Vaillancourt, Comella, & Corcos, 2005). Most individuals with PD will develop impairment of speech motor control, including abnormal respiratory, laryngeal, and supralaryngeal control for breathing and speech (Baker, Ramig, Luschei, & Smith, 1998; Barlow, Iacono, Paseman, Biswas, & D'Antonio, 1998; Gallena, Smith, Zeffiro, & Ludlow, 2001; Hunker, Abbs, & Barlow, 1982; Luschei, Ramig, Baker, & Smith, 1999). The Unified Parkinson's Disease Rating Scale (UPDRS, Fahn & Elton, 1987) is a commonly employed assessment tool for PD that correlates well with more specific measures of limb motor function (Robichaud et al., 2005; Vaillancourt et al., 2006). However, the UPDRS is primarily a measure of limb-related function and only includes two speech-related items that correlate weakly with specific measures of speech function (Richards, Marder, Cote, & Mayeaux, 1994). Therefore, in assessing disease severity and the potential influence of intervention on PD, it would be valuable to efficiently sample and index specific speech-related physiology.

Adequate intraoral air pressure is essential for speech, and is often substantially decreased in PD (Bunton, 2005; Solomon & Hixon, 1993; Tamaki, Matsuo, Yanagihara, & Abe, 2000; Tzelepis, McCool, Friedman, & Hoppin, 1988). Velopharyngeal function may be less commonly recognized as a problem in PD. However, several reports described significant velopharyngeal impairment in PD including decreased velopharyngeal closure and increased transnasal air flow (Darley, Aronson, & Brown, 1975; Hirose, Kiritani, Ushijima, Yoshioka, & Sawashima, 1981; Hoodin & Gilbert, 1989a, 1989b; Logemann, Fisher, Boshes, & Blonsky, 1978; Robbins, Logemann, & Kirschner, 1986). Intraoral air pressure deficits and velopharyngeal impairments in PD may contribute to reduced speech audibility, linguistic confusion, and communicative impairment. Because these cranial systems are negatively impacted by PD, it is important to examine their response to interventions such as deep brain stimulation (DBS). However, the effects of DBS on intraoral pressure and velopharyngeal control are unknown.

In order to achieve appropriate intraoral pressure and oral resonance during production of a simple syllable such as [pa], air flow should be directed through the mouth, and air flow through the nasal cavity should be negligible. Conservative estimates suggest that adequate approximation of the soft palate (velum) with the lateral and posterior pharyngeal wall should result in a velopharyngeal orifice area of less than 5 mm^2, and nasal air flow of less than 125 cc/s (Baken & Orlikoff, 2000; Dalston & Warren, 1986; Dalston, Warren & Smith, 1990; Thompson & Hixon, 1979;Warren, 1964, 1967a, 1967b;Warren & DuBois, 1964; Zajac & Mayo, 1996). Air pressure during speech may be assessed directly through a polyethylene tube in the oral cavity during simple speech production such as in the syllable [pa] (Smitheran & Hixon, 1981). Air flow during speech may be measured directly through a nasal mask placed over the nose during syllable production. The nasal air flow signal provides information regarding velopharyngeal closure. Intraoral pressure and nasal air flow can be used together to estimate velopharyngeal area (Lotz, Shaughnessy, & Netsell, 1981; Netsell, Lotz, & Shaughnessy, 1982;Warren & DuBois, 1964). Therefore, measuring air pressure and air flow during syllable production provides a simple, non-invasive assessment to examine changes in velopharyngeal control with DBS. However, the degree to which these aerodynamic measures of velopharyngeal function are affected by STN DBS in PD is unknown.

During the past decade, deep brain stimulation (DBS) of the subthalamic nucleus (STN) has rapidly emerged as a treatment for advanced idiopathic Parkinson's disease (PD) (Breit, Schulz, & Benabid, 2004; Volkmann, 2004;Weaver et al., 2009). STN DBS involves stereotactic neurosurgical placement (typically bilateral) of a quadripolar stimulating electrode into the sensorimotor region of the subthalamic nucleus, and surgical placement of an implantable pulse generator (IPG) subcutaneously in the pectoral region of the chest. Following surgery, the clinician may program the IPG to select the stimulation frequency, pulse width, and voltage, and the combination of active contacts on the quadripolar electrode. The primary goal of STN DBS is to achieve optimal clinical benefit for limb-related function, as typically evaluated using the UPDRS. DBS has been associated with marked improvements in limb motor function and overall quality of life (Vaillancourt et al., 2006; Vaillancourt, Prodoehl, Metman, Bakay, & Crocos, 2004). However, earlier speech-related studies of STN DBS revealed different outcomes (D'Alatri et al., 2008; Dromey, Kumar, Lang, & Lozano, 2000; Farrell, Theodoros, Ward, Hall, & Silburn, 2005; Gentil, Chauvin, Pinto, Pollak, & Benabid, 2001; Gentil, Garcia-Ruiz, Pollak, & Benabid, 1999; Hoffman-Ruddy, Schulz, Vitek, & Evatt, 2001; Klostermann et al., 2008; Pinto, Gentil, Fraix, Benabid, & Pollak, 2003; Pinto et al., 2004, 2005;Rousseaux et al., 2004; Santens, De Letter, Van Borsel, De Reuck, & Caemaert, 2003; Wang, Metman, Bakay, Arzbaecher, & Bernard, 2003; Wang et al., 2006) (see reviews: Barlow & Hammer, 2009; Jones, Kendall, Sudhyadhom, & Rosenbek, 2007; Schulz & Grant, 2000;Trail et al., 2005). For example, some groups reported significant improvements in speech following bilateral STN DBS (Gentil et al., 2001), some reported modest improvements that did not reach functional significance (Dromey et al., 2000; Farrell et al., 2005), and others reported significant degradation of speech function (Klostermann et al., 2008). Non-speech studies demonstrated improvements in force recruitment and precision of upper lip, lower lip, and tongue movement in PD participants with STN DBS(Gentil et al., 1999; Pinto et al., 2003, 2004). Extended improvements up to 5 years following the initiation of STN DBS were described for isometric lip and tongue force control, but were also accompanied by increasingly severe dysarthria (Pinto et al., 2003).

The reasons for the different responses of speech, non-speech, and limb function to STN DBS may be due to the different functional requirements. High frequency STN DBS is optimized for limb-related function, as typically determined by the UPDRS, and the localization and programming of the DBS electrodes are optimized for limb-related somatotopy. However, improving the ability to generate larger magnitudes of force, as reported in the limb and orofacial force studies, may be of less benefit for the complex, low-level forces that are required for speech and voice (Barlow & Muller, 1991; Bunton & Weismer, 1994; Montgomery, 2007; Tornqvist, Schalen, & Rehncrona, 2005). Moreover, these differences are further reflected by the observation that speech may benefit more from low frequency stimulation than high frequency stimulation (Montgomery, 2007; Tornqvist et al., 2005). However, no studies known to these authors have examined changes in aerodynamic measures of speech-related velopharyngeal control in PD with STN DBS, or whether these changes may be associated with stimulation parameters (e.g., frequency, pulse width, voltage) or measures of limb function (e.g., UPDRS).

The first objective of this study was to examine the effects of bilateral STN DBS on aerodynamic measures of velopharyngeal control in PD participants. Based on the heterogeneity of participant responses reported in previous studies, we expected to observe individual increases and decreases for each of the three aerodynamic measures with DBS. However, we also wanted to examine if the heterogeneity of responses might be related to DBS simulation parameters, as suggested by earlier reports (Montgomery, 2007; Tornqvist et al., 2005), and if speech-related velopharyngeal control was related to limb function. Accordingly, our second objective was to test whether there was a significant association

between stimulation parameters (e.g., frequency, pulse width, voltage) and standard neurological ratings of limb function (e.g., UPDRS) with changes in the aerodynamic measures of velopharyngeal function.

2. Methods

2.1. Participants

This investigation was conducted in accordance with NIH regulations for the ethical treatment of human subjects. The protocol in this investigation was approved by the local institutional ethics committee for the safety of human subjects. Participants were informed of the general purposes of the study and written informed consent was obtained prior to enrolling any participants in the study. Data were collected from 17 individuals (14 men and 3 women) with advanced idiopathic PD, an average of 12 years since diagnosis, a minimum of 3 months since bilateral STN DBS surgery (Table 1), with a mean age of 59 years. Each individual also participated in a separate experiment focused on respiratory and laryngeal control (Hammer, Barlow, Lyons, & Pahwa, 2010).

2.2. Background testing

Testing was coordinated with the participant's scheduled neurological evaluation. Each participant was tested during a single morning session a minimum of 12 h since their most recent dose of anti-PD medication. During the scheduled evaluation, each participant underwent post-operative neurological assessment (DBS ON only) by a movement disorder specialist (R.P.) including the motor scale of the UPDRS, Hoehn and Yahr (H&Y) staging, and the Schwab and England Activities of Daily Living Scale (S&E) (Fahn & Elton, 1987; Hoehn & Yahr, 1967; Schwab & England, 1968). This post-operative neurological assessment (DBS ON, no medication) was compared with the most recent pre-operative assessment (no medication). Participants exhibited significant pre- vs. post-operative improvement in standard neurological ratings of limb function with STN DBS (UPDRS, $t = -5.05$, $p < .001$; H&Y, $t = -2.38$, $p < .04$; S&E, $t = 4.93$, $p < .001$). Individual neurological assessment scores are in Table 1. DBS stimulation parameters (e.g., frequency, pulse width, voltage) are provided in Table 2

After carefully considering our participants and the limited availability for testing during their scheduled post-operative neurological evaluations, we chose to assess velopharyngeal function by sampling intraoral pressure and transnasal airflow with DBS on, and again 1 h after DBS was turned off. We examined whether changes in the standard neurological ratings of limb function (e.g., UPDRS, pre- vs. post-operative) were associated with changes in measures of velopharyngeal function (DBS ON vs. DBS OFF), and whether changes in velopharyngeal function were associated with DBS stimulation parameters (e.g., frequency).

2.3. Air pressure and air flow

Participants were comfortably seated in an exam chair and instructed to repeat the syllable [pa] at a rate of 2 syllables per second at a comfortable pitch and loudness. Intraoral air pressure was measured directly using a polyethylene catheter (Intramedic PE 260, 1.77 mm ID, 7 cm length) placed in the mouth near the oral angle and oriented perpendicular to the breath stream during speech (Smitheran & Hixon, 1981). The catheter was coupled to a pressure transducer (Honeywell model 164PC01D37). A 10 cm H_2O pressure source (U-tube manometer) was used to calibrate the air pressure transducer. Air flow was measured using a Hans Rudolph nasal respiratory mask (model CR1650) and pneumotachometer (model R4719) instrumented with a pressure transducer (model 163PC01D36). A 500 cc/s air flow source (Glottal Enterprises model MCU-2) was used to calibrate the air flow transducer. Both air pressure and air flow signals were conditioned by bridge amplifiers

(Biocommunications Electronics, model 201, LP −3 dB @ 50 Hz, Butterworth 3-pole). Lip closure was carefully monitored for each participant. Only syllables with complete seal of the lips during consonant production were included in analysis. Signals were digitized at 3.3 kHz using a custom designed data acquisition and analysis program to compute intraoral pressure (P_O) and nasal air flow (Barlow, Suing, & Andreatta, 1999). We used the pressure and air flow values to compute velopharyngeal (VP) area (Baken & Orlikoff, 2000; Lotz et al., 1981; Netsell et al., 1982; Warren & DuBois, 1964).

2.4. Statistical analyses

Based on the heterogeneity of participant responses reported in previous studies, we expected to observe individual increases and decreases for each of the three aerodynamic measures with DBS such that traditional group analysis (paired *t*-tests DBS ON vs. DBS OFF, α = .05/3 measures = .017) would not reflect significant changes. We expected that *individual* PD participants would exhibit significant absolute changes in each measure, and used the individual change data (Table 3) to compute the group mean magnitude of change and the group standard error for each measure. We then examined whether individuals exhibited an absolute magnitude of change that exceeded 2 times the group standard error, and used this as our criterion for significance (Fig. 1).

Next, we compared our data with typical operating ranges reported in the literature for each of the three aerodynamic measures (Baken & Orlikoff, 2000; Dalston & Warren, 1986; Dalston et al., 1990; Netsell & Hixon, 1978; Smitheran & Hixon, 1981; Thompson & Hixon, 1979; Warren, 1964, 1967a, 1967b; Warren & DuBois, 1964; Zajac & Mayo, 1996). We examined the individual baselines, responses to DBS, and examined whether individual values approached, departed from, or stayed within the typical operating range with DBS (Table 4, Fig. 1).

To test whether the heterogeneity of speech-related responses was related to DBS simulation parameters (e.g., frequency) and standard neurological ratings of limb function (e.g., UPDRS), we calculated Pearson product moment correlation coefficients (α = .05).

3. Results

Individual values and corresponding change for each aerodynamic measure of velopharyngeal control are shown in Fig. 1, and are summarized in Table 3. As expected, we observed individual increases and decreases for each of the three aerodynamic measures with DBS such that traditional group analysis (paired *t*-tests DBS ON vs. DBS OFF, all *p*-values >.05) did not reflect significant changes. However, *individual* PD participants exhibited changes in each measure (Table 4 and Fig. 1): P_O (*n* = 10), nasal air flow (*n* = 8), and VP area (*n* = 6). Of these participants, most exhibited beneficial increases in P_O (*n* = 7), with decreases in nasal airflow (*n* = 5) and VP area (*n* = 5) (Table 4). These changes, though relatively modest, were primarily consistent with increased intraoral pressure and increased velopharyngeal closure. In addition, PD participants exhibited distinct individual responses to STN DBS. For example, of the 10 PD participants who exhibited changes in P_O with STN DBS, 7 manifested increased P_O while 3 exhibited decreased P_O.

Next, we compared our data with typical operating ranges reported in the literature for each of the three aerodynamic measures (Fig. 1) (Baken & Orlikoff, 2000;Dalston & Warren, 1986;Dalston et al., 1990;Netsell & Hixon, 1978;Smitheran & Hixon, 1981;Thompson & Hixon, 1979;Warren, 1964,1967a,1967b;Warren & DuBois, 1964;Zajac & Mayo, 1996) to examine the individual baselines, responses to DBS, and whether individual values approached, departed from, or stayed within a typical operating range with DBS (Table 4). For example, one PD participant (1) that exhibited P_O below the typical range (OFF)

approached but overshot the typical range with DBS. Very few PD participants exhibited values beyond the typical range with DBS OFF, and most exhibited values within the typical range for each measure with DBS on. Therefore, most PD participants exhibited modest changes and most exhibited measures within the typical range with STN DBS.

Finally, we examined the degree to which changes in each aerodynamic measure was associated with stimulation parameters (e.g., frequency) and changes in standard neurological ratings of limb function (e.g., UPDRS, H&Y). We found moderate correlations (all *p*-values <.05) between stimulation frequency of the right STN with P_O ($r = -.50$) and between stimulation frequency of the left STN with VP area ($r = .49$). We also found that P_O was moderately correlated with the UPDRS ($r = .60$) and H&Y ($r = .50$), and VP area was moderately correlated with the H&Y ($r = -.50$) (Pearson product–moment correlation coefficients, all *p*-values <.05). Therefore, changes in aerodynamic measures of P_O and VP area were related to DBS stimulation frequency and modestly paralleled standard neurological ratings of limb function.

4. Discussion

This study presents the first data examining the effects of bilateral STN DBS on velopharyngeal control in PD, and how these effects relate to changes in ratings of limb function (e.g., UPDRS) and DBS stimulation parameters (e.g., frequency). We observed relatively subtle changes in aerodynamic measures of speech velopharyngeal control with STN DBS. As expected, we observed individual increases and decreases for each of the three aerodynamic measures with DBS, consistent with the heterogeneity of speech-related responses described previously. However, most of the changes we observed in these PD participants were generally consistent with increased P_O and increased velopharyngeal closure.

We also examined if the heterogeneity of changes in speech-related velopharyngeal control might be related to DBS simulation parameters, as suggested by earlier reports (Montgomery, 2007; Tornqvist et al., 2005) and found that the speech-related responses were related to DBS simulation frequency. We observed a moderate negative correlation between stimulation frequency of the right STN with change in P_O and a moderate positive correlation between stimulation frequency of the left STN with change in VP area, indicating that lower frequency stimulation may be associated with greater P_O and smaller VP area. These correlations are consistent with previous observations that the complex, fine forces employed during speech may benefit more from low frequency stimulation than high frequency stimulation (Barlow & Muller, 1991; Bunton & Weismer, 1994; Montgomery, 2007; Tornqvist et al., 2005), and further suggest a differential effect of STN DBS for speech-related velopharyngeal control and limb-related control. The oscillatory patterns of the basal ganglia-thalamocortical network that influence speech, including velopharyngeal control, may operate at lower resonant frequencies, and therefore respond more positively to low frequency DBS (Montgomery, 2007). An earlier report also noted a differential effect for pulse width and voltage (Tripoliti et al., 2008). We did not observe this effect in the present study. Finally, the correlations observed in the present study may also confirm previously reported hemispheric effects (Santens et al., 2003;Wang et al., 2003, 2006). It is possible that stimulation of the right STN may have more influence on P_O and stimulation of the left STN may exert more influence on VP closure.

Changes in speech-related aerodynamic measures of velopharyngeal function with STN DBS may reflect changes in central scaling of speech-related regulation of intraoral pressure and velopharyngeal control. When we observed improvements, it may be that abnormally altered patterns of neural firing presumed to occur throughout the basal ganglia-

thalamocortical network may approximate a more normal pattern of oscillation with DBS. It is also possible that these abnormal patterns may be more amenable to beneficial compensation by remaining healthy brain tissue in the presence of DBS. However, the changes we observed were relatively subtle. In fact, most of the aerodynamic changes were within normal limits. These relatively modest changes may relate to the fact that these participants received high frequency DBS over a fairly narrow range of stimulation frequencies (145–185 Hz). In addition to stimulation frequency, several other factors may account for the modest changes and correlations we observed including variability in localization of the active DBS electrodes, stimulation fields and potential current spread beyond the STN target (e.g., internal capsule), individual variability in somatotopic organization of STN, hemispheric interactions (Santens et al., 2003;Wang et al., 2003, 2006), and differences in pre-treatment speech severity (Dromey et al., 2000; Farrell et al., 2005).

We observed that changes in the speech-related measures modestly paralleled limb-related changes (e.g., UPDRS), indicating that lower levels of PD limb severity may be associated with increased P_O and decreased VP area. The modest strength of these correlations is not surprising given that, for example, the UPDRS is weighted almost entirely for limb function, and lacks the detail to accurately and reliably assess the speech-related subsystems (Miller et al., 2007; Miller, Noble, Jones, Allcock, & Burn, 2008; Richards et al., 1994). Because of the limitations of standard neurological ratings of limb-related function to identify change in speech-related function, we would suggest a need to further integrate speech physiology measures within neurological assessments to accurately assess even subtle speech related changes in participants with neurological diseases such as PD. Aerodynamic measures of velopharyngeal control may be useful within a more comprehensive battery of speech-related measures to index potential changes in motor control associated with STN DBS in PD. Clinical neurological assessment scales focus almost exclusively on limb motor function and do not offer specific indices to detect subtle changes in speech-related motor control that may signal the onset and progression of a disease, and its potential response to treatment. Therefore, the development, refinement, and employment of clinically relevant measures of speech-related physiology, including aerodynamic assessment of velopharyngeal control, may be useful during neurological assessment of individuals with PD.

One limitation of the present study was that we only included post-operative speech testing (DBS ON vs. DBS OFF) using syllables, and correlated these speech changes with pre- vs. post-operative changes in limb function. Using these different time points for comparison may be misleading. Therefore, we would suggest inclusion of pre- and postoperative testing for comparison, to examine the potential influence of pre-treatment speech severity, and inclusion of assessments of phrases and sentences. We would also suggest that future studies consider repeating the standard neurological ratings of limb function with STN DBS turned off, to directly compare limb function DBS ON vs. DBS OFF, and include electrode coordinates with stimulation parameters to correlate with speech and limb function. A second limitation of this study was that we did not include other instrumental or perceptual measures of resonance or intelligibility. Therefore, future study designs should consider integration of speech aerodynamics within a more comprehensive instrumental assessment (e.g., laryngoscopy, nasometry, and perceptual ratings).

5. Conclusion

The effects of STN DBS on speech-related velopharyngeal control in PD were previously unknown. In our study, we applied non-invasive aerodynamic techniques to examine speech-related velopharyngeal function. We found that bilateral STN DBS may influence

velopharyngeal control during syllable production in PD. However, bilateral STN DBS demonstrates a more subtle effect on speech-related velopharyngeal control than for limb motor control. The effects on velopharyngeal control are not uniform across participants and only modestly correlate with changes in limb-related function. Our findings suggest that speech-related velopharyngeal control may benefit more from low frequency stimulation than high frequency stimulation. The distinctions between speech and limb-related function, and between high vs. low frequency stimulation, are important to consider when assessing the impact of STN DBS on PD, and may be valuable to guide clinicians in the optimization of DBS stimulation parameters for individuals with PD.

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Appendix A. Continuing education

1. The Unified Parkinson's Disease Rating Scale (UPDRS) is
    - **a.** A commonly employed assessment tool for Parkinson's disease
    - **b.** Correlates well with specific measures of limb motor function
    - **c.** Includes only two speech-related items
    - **d.** Correlates weakly with specific measures of speech function
    - **e.** All of the above
2. Deep brain stimulation has been associated with
    - **a.** Marked improvements in limb function
    - **b.** Consistent improvements in speech and voice
    - **c.** Improved quality of life
    - **d.** All of the above
    - **e.** a and c
3. The article demonstrated
    - **a.** A significant group effect of deep brain stimulation on velopharyngeal control
    - **b.** No significant group effect of deep brain stimulation on velopharyngeal control
    - **c.** Significant individual effects of deep brain stimulation on velopharyngeal control
    - **d.** The relatively subtle effects of deep brain stimulation on velopharyngeal control
    - **e.** The influence of heterogeneity of outcomes on group design
    - **f.** a, c, d, and e
    - **g.** b, c, d, and e

4. The article demonstrated that intraoral air pressure and velopharyngeal area correlated with
    a. Stimulation frequency
    b. Stimulation inter-stimulus interval
    c. Stimulation pulse width
    d. Stimulation rise time
    e. Stimulation voltage
5. Possible reasons for reported differences in limb outcomes compared with speech function with deep brain stimulation of the subthalamic nucleus include
    a. Variability in localization of the active electrodes
    b. Potential current spread beyond the subthalamic nucleus
    c. Individual variability in somatotopic organization of the subthalamic nucleus
    d. Differences in stimulation effects on each hemisphere
    e. Differences in pre-treatment speech severity
    f. Optimization of DBS settings and localization for limb rather than speech function
    g. All of the above

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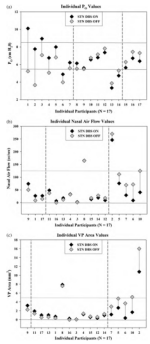

Fig. 1.

Individual values for each participant with DBS ON (black symbols) and DBS OFF (gray symbols). (a) Intraoral pressure (*P*O), (b) nasal air flow, and (c) velopharyngeal (VP) area. In each graph, dashed vertical reference lines demarcate boundaries between significant increases (left), non-significant changes (middle), and significant decreases (right). Solid horizontal reference lines demarcate a reasonably conservative typical operating range.

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Table 1

Individual neurological measures organized by participant. Unified Parkinson's Disease Rating Scale (UPDRS) UPDRSMOTOR: 0 = no symptoms; 108 = maximum score. Hoehn and Yahr (H&Y) Staging: 1 = mild; 5 = maximum score. Schwab and England (S&E) Activities of Daily Living Scale: 100 = completely independent.

Participant	Sex	Age	Months	Speech item only				PD motor measures					
			Post Surgery	UPDRS ADL		UPDRS MOTOR		UPDRS MOTOR		H&Y		S&E	
				Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
1	M	76	4	2	2	2	2	25	24	2	2	80	80
2	F	38	32	2	1	2	2	39	48	3	4	60	60
3	M	64	6	2	1	2	1	42	13	3	3	60	90
4	M	55	24	2	2	2	2	44	35	4	3	60	90
5	F	73	9	2	3	2	3	49	38	3	4	80	80
6	M	55	3	1	1	2	1	30	14	2	2	70	70
7	M	68	4	2	2	2	2	42	22	3	2	60	90
8	M	48	25	2	3	2	2	38	32	3	2	80	90
9	M	74	13	2	3	2	2	34	24	3	2	70	70
10	M	44	27	3	2	2	1	28	28	3	2	60	90
11	M	75	3	3	2	2	2	43	27	3	2	70	80
12	F	68	22	2	2	2	1	49	19	3	2	80	90
13	M	36	3	3	2	2	2	46	30	3	2	70	90
14	M	72	3	2	2	2	1	49	7	2	2	70	100
15	M	65	6	2	2	2	2	45	15	3	3	70	80
16	M	42	6	4	3	4	3	36	20	2	2	70	90
17	M	53	12	2	1	2	1	43	17	3	2	70	90

ADL SPEECH ITEM: 0 = normal; 1 = mildly affected, no difficulty being understood; 2 = moderately affected, sometimes asked to repeat statements; 3 = severely affected, frequently asked to repeat statements; 4 = Unintelligible most of the time. UPDRS MOTOR SPEECH ITEM: 0 = normal; 1 = slight loss of expression, diction and/or volume; 2 = monotone, slurred but understandable, moderately impaired; 3 = marked impairment, difficult to understand; 4 = unintelligible. Scores are provided prior to surgical placement (Pre) and following activation of the bilateral STN DBS (post). Individuals were tested a minimum of 12 h since their last dose of anti-PD medication.

Table 2

Individual deep brain stimulation (DBS) parameters and settings for each participant including stimulation frequency (Hz), voltage (V), and pulse width (μs) for left and right internalized pulse generator (IPG), and electrode configuration used for DBS.

Participant	Frequency (Hz)		Voltage (V)		Pulse width (μs)		Electrode configuration ("0" = off, "+" = anode, "−" = cathode)									
							Left active contacts					Right active contacts				
	Left IPG	Right IPG	Left IPG	Right IPG	Left IPG	Right IPG	0	1	2	3	IPG case	0	1	2	3	IPG case
1	145	145	2.8	2.9	60	60	0	−	−	0	+	0	0	−	−	+
2	145	145	1.5	1.8	60	60	0	0	0	−	+	0	0	0	−	+
3	145	145	2.4	2.3	60	60	0	−	0	0	+	0	0	−	0	+
4	170	160	3.7	3.9	90	90	+	0	0	−	0	0	+	0	−	0
5	170	170	3	3.6	90	90	0	0	−	−	+	0	0	−	−	+
6	145	145	3.2	1.6	60	60	0	−	0	0	+	0	−	0	0	+
7	145	160	2.3	2.9	60	90	0	0	−	−	+	0	+	0	0	+
8	160	185	3.2	4.1	90	90	0	0	−	−	+	−	−	+	0	0
9	160	160	3.6	2.8	60	60	−	+	−	0	0	0	0	−	0	+
10	185	185	2.8	2.4	90	60	0	−	0	0	+	0	0	−	0	+
11	185	170	2.9	2.3	60	90	0	−	−	0	+	0	−	0	0	+
12	145	145	2.5	1.8	90	90	0	+	−	0	0	0	+	−	0	0
13	145	145	3.5	1.5	90	60	+	0	−	0	0	0	0	−	0	+
14	160	185	3	4	60	60	0	0	−	0	+	0	0	−	0	+
15	145	160	2.1	3	60	60	0	0	−	0	+	0	0	−	0	+
16	145	185	2.4	3.8	60	90	0	0	−	0	+	+	0	0	−	0
17	170	170	3.8	4.5	60	90	0	0	−	0	+	0	−	0	0	+

Table 3

Individual mean value, standard error (se), and Δ (ON–OFF) for each speech measure with deep brain stimulation (DBS ON vs. DBS OFF) including intraoral air pressure (P_O), nasal air flow, and velopharyngeal (VP) area.

Participant	P_0 (cm H_20)			Nasal air flow (cc/s)			VP area (mm^2)		
	MEAN (se)		Δ	Mean (se)		Δ	Mean (se)		Δ
	DBS ON	DBS OFF		DBS ON	DBS OFF		DBS ON	DBS OFF	
1	10.10 (0.39)	5.23 (0.26)	4.87	26.50 (9.80)	8.69 (2.00)	17.81	0.70 (0.26)	0.36 (0.09)	0.34
2	7.76 (0.57)	3.65 (0.83)	4.11	246.00 (40.00)	270.00 (47.00)	−24.00	10.80 (2.60)	16.00 (3.70)	−5.20
3	8.94 (0.46)	7.06 (0.39)	1.88	2.13 (0.80)	1.22 (0.46)	0.91	0.07 (0.03)	0.05 (0.02)	0.02
4	6.75 (0.32)	5.06 (0.26)	1.69	33.00 (7.80)	31.90 (18.00)	1.10	1.20 (0.27)	1.36 (0.78)	−0.16
5	7.99 (0.37)	6.81 (0.43)	1.18	75.50 (8.90)	111.30 (15.00)	−35.80	2.67 (0.34)	4.76 (0.94)	−2.09
6	4.88 (0.12)	3.98 (0.15)	0.91	8.53 (1.70)	71.30 (8.50)	−62.77	0.39 (0.08)	3.68 (0.50)	−3.30
7	6.21 (0.12)	5.57 (0.22)	0.65	29.00 (5.00)	68.90 (5.60)	−39.90	1.17 (0.21)	2.96 (0.29)	−1.79
8	6.13 (0.47)	5.51 (0.36)	0.62	165.00 (29.00)	164.40 (16.00)	0.60	7.89 (1.80)	7.60 (1.20)	0.29
9	5.59 (0.24)	5.48 (0.29)	0.11	73.90 (5.80)	50.40 (4.30)	23.50	3.20 (0.29)	2.27 (0.22)	0.93
10	6.55 (0.37)	6.75 (0.36)	−0.20	40.40 (3.90)	124.60 (12.00)	−84.20	1.69 (0.18)	5.10 (0.59)	−3.41
11	6.79 (0.31)	7.14 (0.24)	−0.35	48.20 (7.00)	37.40 (11.00)	10.80	1.92 (0.31)	1.39 (0.40)	0.53
12	7.36 (0.56)	7.82 (0.33)	−0.46	9.19 (1.10)	17.60 (7.30)	−8.41	0.35 (0.06)	0.61 (0.26)	−0.26
13	3.33 (0.20)	3.86 (0.19)	−0.53	17.70 (2.80)	11.65 (2.30)	6.05	1.04 (0.19)	0.60 (0.12)	0.44
14	4.73 (0.27)	5.30 (0.13)	−0.58	19.10 (7.30)	27.50 (4.80)	−8.40	0.99 (0.41)	1.27 (0.25)	−0.28
15	5.63 (0.18)	6.28 (0.12)	−0.65	13.15 (1.80)	17.80 (2.80)	−4.65	0.56 (0.08)	0.72 (0.12)	−0.16
16	6.71 (0.32)	7.44 (0.42)	−0.73	6.29 (1.6)	0.00 (0.00)	6.29	0.25 (0.07)	0.00 (0.00)	0.25
17	6.38 (0.33)	7.31 (0.26)	−0.93	26.70 (4.70)	14.40 (2.00)	12.30	1.03 (0.18)	0.52 (0.07)	0.51
Group mean, standard error (se), minimum (MIN), and maximum (MAX) magnitude of change for each measure.									
MEAN (se)	1.20 (0.32)			20.44 (5.67)			1.17 (0.36)		
MIN	0.11			0.60			0.02		
MAX	4.87			84.20			5.20		

Table 4

Direction of change for each speech measure with deep brain stimulation (on minus off) including intraoral air pressure, nasal air flow, and velopharyngeal (VP) area. *Total* indicates the number and percentage of participants who exhibited a significant change (increase or decrease) with deep brain stimulation. *Approach* indicates changes toward a typical operating range. *Depart* indicates changes away from a typical operating range. *Stay* indicates a change in which the measure was within a typical operating range during both test conditions (on and off).

Variable	Number of increases				Number of decreases			
	Approach	Depart	Stay	Total	Approach	Depart	Stay	Total
Intraoral pressure (cm H_20)	4*	1	2	7 (41%)	0	0	3	3 (18%)
Nasal air flow (cc/s)	–	0	3	3 (18%)	1	–	4	5 (29%)
VP area (mm^2)	–	0	1	1 (6%)	2	–	3	5 (29%)

* Includes approaches that overshot typical range.