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Research paper

No differential effects of subthalamic nucleus vs. globus pallidus deep brain stimulation in Parkinson's disease: Speech acoustic and perceptual findings

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ABSTRACT

Background: Deep Brain Stimulation (DBS) in the Subthalamic Nucleus (STN) or the Globus Pallidus Interna (GPI) is well-established as a surgical technique for improving global motor function in patients with idiopathic Parkinson's Disease (PD). Previous research has indicated speech deterioration in more than 30% of patients after STN-DBS implantation, whilst speech outcomes following GPI-DBS have received far less attention. Research comparing speech outcomes for patients with PD receiving STN-DBS and GPI-DBS can inform pre-surgical counseling and assist with clinician and patient decision-making when considering the neural targets selected for DBS-implantation. The aims of this pilot study were (1) to compare perceptual and acoustic speech outcomes for a group of patients with PD receiving bilateral DBS in the STN or the GPI with DBS stimulation both ON and OFF, and (2) examine associations between acoustic and perceptual speech measures and clinical characteristics.
Methods: Ten individuals with PD receiving STN-DBS and eight individuals receiving GPI-DBS were audio-recorded reading a passage. Three listeners blinded to neural target and stimulation condition provided perceptual judgments of intelligibility and overall speech severity. Speech acoustic measures were obtained from the recordings. Acoustic and perceptual measures and clinical characteristics were compared for the two neural targets and stimulation conditions.
Results: Intelligibility and speech severity were not significantly different across neural target or stimulation conditions. Generally, acoustic measures were also not statistically different for the two neural targets or stimulation conditions. Acoustic measures reflecting more varied speech prosody were associated with improved intelligibility and lessened severity. Convergent correlations were found between UPDRS-III speech scores and perceptual measures of intelligibility and severity.
Conclusion: This study reports a systematic comparison of perceptual and acoustic speech outcomes following STN-DBS and GPI-DBS. Statistically significant differences in acoustic measures for the two neural targets were small in magnitude and did not yield group differences in perceptual measures. The absence of robust differences in speech outcomes for the two neural targets has implications for pre-surgical counseling. Results provide preliminary support for reliance on considerations other than speech when selecting the target for DBS in patients with PD.

1. Introduction

Deep Brain Stimulation (DBS) is well-established as a surgical technique for improving global motor function in patients with idiopathic Parkinson's Disease (PD) for whom medication effects are inadequate and/or who develop adverse side effects from pharmaceutical treatments. The most common neural targets for DBS in PD are the Subthalamic Nucleus (STN) and the Globus Pallidus Interna (GPI) (Moro et al., 2010). The two targets are reported to have similar efficacy for improving limb motor function in PD (Weaver et al., 2012), but the STN has generally been the preferred target in PD because of a greater reduction in Parkinson's medication dosage post-operatively (Williams

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et al., 2014). Some research opposes the preference for STN over GPI in PD patients, as there is evidence of equivalent improvements in motor symptoms and some potential benefits of GPI-DBS, such as improved dyskinesia control that allows for greater flexibility in dosing parameters without risking medication-induced dyskinesia (Vitek, 2003). In theory, the larger size and lower density of functional circuitry in the GPI may also reduce risk of unintentional current spread to non-target functional circuits (Zimpel et al., 2023). No comparison studies have shown significant differences in stimulation-induced motor side effects between the two targets, although there is evidence that GPI-DBS results in slightly better neurocognitive outcomes (Combs et al., 2015; Odekerken et al., 2013; Okun et al., 2009).

Although STN-DBS improves many of the global motor symptoms associated with PD, studies report highly variable post-surgical speech outcomes including deteriorations in more than 30% of patients that does not improve once stimulation is turned off (Alomar et al., 2017). GPI-DBS is reported to have equal efficacy to STN-DBS for improving limb motor function in PD (Weaver et al., 2012), but speech outcomes following GPI-DBS have received far less attention compared to STN-DBS (Au et al., 2021; Skodda, 2012; Williams et al., 2014). It is therefore not surprising that studies directly comparing speech outcomes for STN-DBS and GPI-DBS also are limited, although this line of inquiry is critical for optimizing patient outcomes and assisting with clinician and patient decision-making when considering the neural targets selected for DBS-implantation.

Rodriguez-Oroz et al. (2005) assessed the effects of STN (n = 49) or GPI (n = 20) stimulation on the speech sub-score from the motor examination part of the Movement Disorders Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS-III; Goetz et al., 2008) at 1 year and 3–4 years post-DBS implantation. When participants were in an on-medication state, speech scores for patients receiving STN-DBS were significantly poorer at 1-year post-surgery compared to pre-operative scores. Speech scores deteriorated even further at the 3–4 years post-surgery follow-up for patients receiving STN-DBS. In contrast, for patients receiving GPI-DBS, speech scores were unchanged across time points (Rodriguez-Oroz et al., 2005). Burchiel et al. (1999) reported no differences in MDS-UPDRS-III speech sub-scores for patients with GPI-DBS (n = 4) compared to patients with STN-DBS (n = 6) at 12 months post-DBS implantation, both off- and on-medication. Volkmann et al. (2001) compared averaged speech and swallowing MDS-UPDRS sub-scores from baseline to 6- and 12-months post-surgery in patients with GPI-DBS (n = 11) and STN-DBS (n = 16). Results indicated a significant worsening of scores for the STN-DBS group after 12 months on-medication, while scores for the GPI-DBS group were unchanged. Moro et al. (2010) evaluated self-reported unresolved adverse, not further specified, speech events 5-to-6 years post-surgery in patients receiving GPI-DBS (n = 16) and STN-DBS (n = 35). For patients with GPI-DBS, two adverse speech events were reported, and ten events were reported for patients with STN-DBS. In addition, UPDRS-III speech sub-scores obtained on-medication worsened for both neural targets at the post-surgical follow-up with DBS stimulation on, although no formal statistical comparison was undertaken. Relatedly, Weaver et al. (2012) reported worsening of speech as measured by the Parkinson's Disease Questionnaire (PDQ)− 39 (Peto et al., 1995) communication subscale scores for both patients with STN-DBS (n = 70) and GPI-DBS (n = 89) at 36 months post-surgery on-stimulation/on-medication as compared to scores obtained at baseline/on-medication, with no statistically significant differences between groups. Odekerken et al. (2016, 2013) obtained self-reported unspecified adverse events related to dysarthria prior to DBS implantation and at a 1-year follow-up in patients with GPI-DBS (n = 65) and STN-DBS (n = 25). Results indicated that 19 of 65 (29%) patients with GPI-DBS and 25 of 63 (40%) with STN-DBS reported adverse events related to dysarthria at 1-year follow-up. The proportion of patients self-reporting dysarthria post-DBS did not statistically differ between the two neural targets. Finally, Kopf et al. (2022) examined the impact of DBS neural target on Voice Handicap Index (VHI; Jacobson et al., 1997) scores in 12 patients with GPI-DBS and 12 patients with STN-DBS, of which a subset were participants in the current study. Self-reported VHI scale scores across all domains (i.e., physical, functional, emotional, and total scores) were obtained post-DBS implantation. VHI scores for the two neural targets were not statistically different, although there was a trend toward greater impairment for patients with GPI-DBS. Collectively, these studies might be interpreted to suggest more favorable speech outcomes following GPI-DBS versus STN-DBS. However, the small number of studies, substantial between-subject variability within studies, and coarseness of speech outcome metrics (i.e., subjective self-report measures, non-expert impressions of speech from MDS-UPDRS-III) suggest additional research is warranted.

Research directly comparing speech outcomes for patients with PD receiving STN-DBS and GPI-DBS can inform pre-surgical counseling and may ultimately advance understanding of the role of the basal ganglia in speech production. Studies to date directly comparing speech outcomes for STN and GPI neural targets employ self-report measures or clinical instruments not intended to provide a comprehensive characterization of speech. Comparative studies examining the effects of acute stimulation with neural target as an additional factor of influence are also lacking. For example, the implementation surgery itself may impact speech (i.e., lesion effect), which in turn might be ameliorated or worsened by acute stimulation. The current investigation compares the effects of DBS neural target (i.e., STN versus GPI) and acute stimulation (i.e., ON versus OFF) on objective perceptual and acoustic speech outcome metrics for individuals with PD. Associations between patient characteristics and perceptual speech outcome metrics also were explored to gain a broader understanding of factors related to speech outcomes in these populations. The current study is one of the first in providing a detailed comparison of post-operative speech acoustics and perceptual outcomes for patients with STN-DBS and GPI-DBS. Outcomes might suggest additional considerations in the decision-making process of neural target selection for patients with PD electing DBS procedures with respect to expectations of potential post-operative speech deteriorations.

2. METHODS

2.1. Participants

This study was approved by the University of Iowa (UI) Institutional Review Board. All participants provided written informed consent prior to participation. Table 1 displays participant summary information. Eighteen patients with idiopathic PD participated and spoke English as a primary language, had all undergone DBS implantation surgery at UI, were on stable DBS settings, and were being treated with PD medications for symptom management. Ten patients had undergone surgical implantation of DBS into the bilateral STN and eight patients had undergone surgical implantation of DBS into the bilateral GPI. All surgeries were performed by the same neurosurgeon. Table 1 also displays demographic information of participants, including total electrical energy delivered (TEED; voltage2 × pulse width × frequency/impedance) and levodopa equivalent daily dose (LEDD). Clinical metrics further characterizing participants were collected pre-operatively both on and off medication, while post-operative clinical variables and measures were obtained in the medication-on stimulation-on state. The DBS washout time from ON stimulation to OFF stimulation conditions typically exceeded one hour.

2.2. Procedure

Participants read aloud the first two sentences of the Rainbow Passage (Fairbanks, 1960) at their habitual speech rate and loudness while being audio-recorded. Speech recordings were obtained with DBS stimulation turned off and on respectively (i.e., DBS ON and DBS OFF

Table 1
Participant characteristics. HY: Hoehn & Yahr score; LEDD: Levodopa equivalent daily dose; MDS-UPDRS: Movement Disorder Society-Unified Parkinson's Disease Rating Scale; TEED: Total electrical energy delivered; * Right and Left DBS implants 8 months apart. * * TEED calculated using group mean impedance. * ** Testing completed in medication-off state.

Subject	STN/ GPI	Gender	Age (Yrs)	Time since PD Diagnosis (Yrs)	Time since Surgery (Months)	HY Score post-op, DBS on, on-med	MDS-UPDRS-III overall score pre-op, on-med	MDS-UPDRS-III overall score post-op, DBS on, on-med	MDS-UPDRS-III Speech Rating pre-op, off-med	MDS-UPDRS-III Speech Rating pre-op, on-med	MDS-UPDRS-III Speech Rating post-op, DBS on, on-med	TEED: total (μW)	Stimulation frequency (Hz)	LEDD post-op (mg/ day)
1	STN	F	59	6	1	1	49	26	1	0	0	9.5	130	1714
2	STN	M	62	14	37	2	38	19	1	1	2	349.8	150	0
3	STN	M	66	16	6	1	69	7	2	1	1	33.2 * *	135	2241
4	STN	M	76	8	19	3	14.5	24	0	0	2	12.1	120	200
5	STN	F	61	11	31	1	34	3	1	0	1	54.0 * *	135	760
6	STN	F	51	12	20	2	29	11	1	0	0	186.7	130	900
7 *	STN	M	69	16	12	2	31	2	0.5	0	0	316.7	130	656
8	STN	M	54	9	29	2	48	24	3	1	3	358.7	130	665
9	STN	M	72	10	14	2	45	8	2	1	1	176	130	700
10	STN	M	76	10	34	3	31	23	0	0	2	110	110	1750
Mean		3 F / 7 M	64.6	11.2	20.3	1.9	38.9	14.7	1.2	0.4	1.2	160.7	130	959
1	GPI	M	61	13	11	2.5	29	20	0	1	0	172.4	130	1110
2	GPI	M	68	9	11	1	48	3	2	1	0	195.8	130	1800
3	GPI	M	66	8	45	2	20	18	2	1	3	434.1	130	1040
4	GPI	M	62	16	42	2.5	50.5	34.5	2	0	2	294.2	130	720
5	GPI	F	73	10	49	2	32.5	23	1	0	0.5	113	130	1990
6	GPI	M	79	17	55	4	35	22	1	0	0	342.9	130	1075
7	GPI	M	70	19	54	3 * **	43.5	28.5 * **	2	1	1 * **	395.3	150	600
8	GPI	F	61	15	52	2	40	12.5	2	0.5	1	456.6	140	1930
Mean		2 F / 6 M	67.5	13.4	39.9	2.5	37.3	20.2	1.5	0.6	0.9	300.5	133.75	1283

stimulation conditions) while patients were on their regular PD medication schedule. Perceptual and acoustic outcome metrics were obtained offline from speech recordings.

Perceptual outcome metrics included intelligibility and speech severity. Intelligibility is the gold standard measure of functional communication in dysarthria, and is commonly defined as the degree to which an individual's acoustic signal is understood by a listener (Duffy, 2019; Weismer, 2008). Speech severity (a global measure that incorporates impressions of voice, resonance, articulatory precision, and prosody) is complementary to intelligibility, as this perceptual construct is sensitive to assessing speech impairment when intelligibility is mildly impaired (Sussman and Tjaden, 2012), as anecdotally noted for many speakers in the present study. Three certified speech-language pathologists (SLPs) judged intelligibility and speech severity for the 36 speech recordings (18 speakers x 2 stimulation conditions). SLPs heard the recording of a single speaker via headphones adjusted to a comfortable loudness and judged intelligibility and overall speech severity on computerized visual analog scales (VAS) in REDCap (Harris et al., 2009). Each VAS was a vertically oriented line with no tick marks. Responses were automatically converted to scores ranging from 0 (scale endpoints "Totally unintelligible" and "Severely impaired") to 100 (scale endpoints "Totally intelligible" and "No impairment"). A different random order of the 36 speech samples was presented to each SLP. After hearing a given speech sample, SLPs first judged intelligibility followed by speech severity. Eight speech samples were presented twice to each SLP for the purpose of obtaining intra-rater reliability.

Because speech symptoms associated with PD can be the result of impairments to multiple speech subsystems, speech acoustic outcome measures spanned those reflecting speech duration, voice quality, vocal intensity, voice fundamental frequency, and articulation (van Brenk et al., 2021). For acoustic measures other than total passage duration and speech rate, the start and end of phrases were marked manually. Using the combined waveform and broadband spectrogram, start and end points were determined using conventional acoustic criteria (i.e., stop release burst, voicing energy, and frication). Silences with a length of 200 ms or larger were considered pauses and excluded (Kuo and Tjaden, 2016). Phrases were then extracted and concatenated for further analysis in Praat (Boersma and Weenink, 2020). Custom Praat scripts were utilized to quasi-automatically obtain a number of speech acoustic outcome measures intended to assess impairment across multiple speech subsystems. Overall speech duration and speech rate were measured by total passage duration (in seconds), speaking rate (in syllables per second), and articulation rate (in syllables per second excluding pauses) (Van Nuffelen et al., 2010). Pitch variation was assessed by the standard deviation of fundamental frequency (F0, in Hz) and the 90th-10th percentile (to remove outliers) range of fundamental frequency (in Hz) (Kim et al., 2011). Loudness variation was assessed by measuring the standard deviation and 90th-10th percentile (to remove outliers) range of sound pressure level (SPL) (Kuo and Tjaden, 2016). Articulatory movement range and overall working-space was measured by means of the second formant interquartile range (F2 IQR; in Hz) (Yunusova et al., 2005). Perceived voice quality and laryngeal integrity were assessed by means of the Smoothed Cepstral Peak Prominence (CPPS, in dB) reflecting vocal roughness and breathiness; and overall voice quality was assessed by the Acoustic Voice Quality Index (AVQI; in arbitrary units).

2.3. Statistical analysis

Statistical analyses were carried out using R software (R Core Team, 2019). Participant characteristics for the neural targets of STN and GPI were compared using independent sample Student t-tests (i.e., interval measures) and Mann-Whitney U tests (i.e., ordinal measures) using the R *psych* package (Revelle and Revelle, 2023). Wilcoxon signed-rank tests

were used to compare MDS-UPDRS-III speech scores between on and off stimulation conditions within neural target groups. Effect sizes for t-tests were calculated with Cohen's d. Effect sizes for non-parametric Mann-Whitney U tests and Wilcoxon signed-rank tests were assessed using the Rank-Biserial Correlation Coefficient.

Given the exploratory nature of this pilot study, we employed an inductive approach to analyze potential differences in perceptual and acoustic outcome measures between neural targets. To this end, we fit separate linear mixed-effects models to the perceptual speech outcome measures of intelligibility and speech severity (averaged across the three listeners) using the R *lme4* package (Bates et al., 2014). Models included DBS target (i.e., STN and GPI) and stimulation setting (i.e., DBS ON and DBS OFF) as fixed factors, and listener (for the perceptual measures) and speaker as independent random intercepts. Each speech acoustic outcome measure was also fit with a separate linear mixed-effects model, with neural target and stimulation setting as fixed factors, and speaker as an independent random factor. In order to evaluate the fixed effects in detail, two-way analyses of variance were calculated based on the fitted model using the R *emmeans* package (Lenth et al., 2020). Significant post hoc differences of estimated marginal means were explored utilizing Tukey's method to correct for multiple comparisons. Given the multi-way analyses of variances, effect sizes were derived using partial eta-squared estimates using the R *lsr* package (Navarro and Navarro, 2022). Values of .02, .13 and .26 were interpreted to reflect small, medium and large effect sizes, respectively (Bakeman, 2005). Satterthwaite's method was used to estimate the degrees of freedom (Lenth et al., 2020). Intra-rater and inter-rater reliability for perceptual measures were tested by means of Cronbach's alpha, using the R *psych* package (Revelle and Revelle, 2023). The associations between perceptual and acoustic speech outcome metrics, and the association between perceptual metrics and participant demographic/clinical variables, including TEED, LEDD, time since DBS implantation, and years since PD diagnosis were examined using Spearman's Rho correlations, because a number of variables did not meet the normality assumption. Spearman's Rho correlations were also used to assess the relationship between perceptual metrics and ordinal values of participant characteristics, including Hoehn & Yahr (HY) scale score and MDS-UPDRS-III speech scores. A significance level of .05 was used for all hypothesis testing.

3. Results

3.1. Participant characteristics

Participants treated with GPI-DBS versus STN-DBS surgery (see Table 1) were not significantly different in age [t (16) = 0.79, p = .44, Cohen's d = 0.37] or years since PD diagnosis [t (16) = 1.26, p = .23, Cohen's d = 0.60]. Furthermore, no differences in participant groups were found for MDS-UPDRS-III overall scores pre-operation on-medication [t (16) = 0.25, p = .81, Cohen's d = 0.12], MDS-UPDRS-III overall scores post-operation on-medication, DBS on [t (16) = 1.22, p = .24, Cohen's d = −.58], MDS-UPDRS-III speech scores pre-operation off-medication [U = 51, p = .33, Rank-Biserial Correlation = 0.28], MDS-UPDRS-III speech scores pre-operation on-medication [U = 47, p = .52, Rank-Biserial Correlation = 0.18], and MDS-UPDRS-III speech scores post-operation on-medication stimulation [U = 33.5, p = .58, Rank-Biserial Correlation = 0.16]. In addition, LEDD [t (16) = 1.06, p = .31, Cohen's d = 0.49], stimulation frequency [t (16) = 0.87, p = .40, Cohen's d = 0.41] and HY Score post-operation, on-medication, DBS on [W = 53, p = .24, Rank-Biserial Correlation = 0.33] did not differ between neural targets.

In contrast, the two neural targets differed in months since implantation [t (16) = 2.71, p = .015, Cohen's d = 0.57] and TEED [t (16) = 2.19, p = .044, Cohen's d = 0.54], with GPI-DBS participants having a longer time since implantation and higher TEED values than STN-DBS participants. Pre-operative off-medication scores for MDS-UPDRS-III speech scores were higher (indicating poorer speech outcomes) than pre-operative on-medication scores for both groups (STN-DBS: W = 28, p = .018, Rank-Biserial Correlation = 1.0; GPI-DBS: W = 32.5, p = .040, Rank-Biserial Correlation = 0.81).

For both neural targets, pre-operative MDS-UPDRS-III speech scores in the on-medication state were not significantly different from post-operative MDS-UPDRS-III speech scores with DBS stimulation on (STN-DBS: W = 0, p = .053, Rank-Biserial Correlation = 1.0, GPI-DBS: W = 7, p = .53, Rank-Biserial Correlation = 0.33).

3.2. Perceptual measures

Table 2 reports summary descriptive statistics for perceptual and acoustic speech outcome metrics. Linear mixed-effects models fit to perceptual metrics indicated no statistically significant main effects or interactions. Intra-rater reliability for both perceptual metrics was excellent; intelligibility: Cronbach's α = 0.977 (95% confidence interval: 0.959 - 0.987), and speech severity: Cronbach's α = 0.944 (95% confidence interval: 0.902 - 0.969). Interrater reliability among the three raters was acceptable for intelligibility: Cronbach's α = 0.736 (95% confidence interval: 0.657 - 0.802), and excellent for speech severity: Cronbach's α = 0.944 (95% confidence interval: 0.902 - 0.969).

3.3. Acoustic measures

Linear mixed-effects models fit to acoustic measures indicated a significant main effect of neural target for F0 SD [F (1, 16) = 4.96, p = .041, η_p^2 = 0.24] and F0 range [F (1, 16) = 5.94, p = .027, η_p^2 = 0.27] with higher F0 values for the GPI-DBS group. However, post-hoc comparisons indicated that these results held only for the DBS ON setting. There also was a significant main effect of neural target for SPL SD [F (1, 16) = 14.2, p = .002, η_p^2 = 0.47], SPL range [F (1, 16) = 10.7, p = .005, η_p^2 = 0.40] and F2 IQR [F (1, 16) = 6.65, p = .020, η_p^2 = 0.29]. Post hoc testing revealed higher values for the STN-DBS group in both DBS ON and DBS OFF stimulation settings. For articulation rate, the interaction of neural target by stimulation setting was statistically significant [F (1, 16) = 7.69, p = .014, η_p^2 = 0.32]. Post-hoc tests indicated that articulation rate was faster for GPI-DBS participants compared to STN-DBS participants, but only in the DBS OFF stimulation setting. For speaking rate, there was a significant main effect of stimulation setting [F (1, 16) = 7.83, p =

Table 2
Means (and standard deviations) of perceptual and acoustic outcome measures, separately for stimulation condition and group (STN; n = 10) and GPI; n = 8). F0: fundamental frequency; SPL: sound pressure level; F2 IQR: second formant interquartile range; CPPS: smoothed cepstral peak prominence; AVQI: acoustic voice quality index. VAS: Visual analog scale.

Group	STN		GPI	
	DBS OFF	DBS ON	DBS OFF	DBS ON
F0 SD (Hz)[a]	27.1 (10.5)	24.9 (10.0)	34.9 (12.9)	40.8 (15.9)
F0 Range (Hz)[a]	48.9 (34.4)	43.8 (30.3)	72.2 (31.7)	86.8 (31.7)
SPL SD (dB)[a]	8.2 (1.7)	8.3 (1.7)	5.6 (1.4)	5.5 (1.6)
SPL Range (dB)[a]	20.2 (4.7)	20.1 (5.4)	13.7 (3.3)	13.3 (4.1)
F2 IQR (Hz)[a]	751 (104)	732 (103)	635 (115)	603 (99)
CPPS (dB)	9.5 (1.9)	9.8 (1.6)	9.0 (3.4)	8.6 (2.8)
AVQI (AU)	5.0 (1.4)	4.7 (1.2)	6.4 (2.5)	6.7 (2.2)
Duration (sec)	16.1 (9.4)	13.8 (2.4)	13.3 (3.6)	13.2 (3.3)
Articulation Rate (syll / sec)[b]	3.8 (0.5)	3.8 (0.3)	4.0 (1.2)	4.5 (1.5)
Speaking Rate (syll / sec)[c]	2.8 (0.8)	3.0 (0.5)	3.6 (1.5)	4.0 (1.8)
Intelligibility (VAS)	87.2 (14.5)	87.5 (15.2)	87.7 (24.4)	90.7 (12.2)
Speech Severity (VAS)	66.5 (24.2)	70.5 (24.5)	73.2 (24.5)	76.5 (23.4)

[a] Significant main effect of neural target.
[b] Significant interaction effect of neural target by stimulation condition
[c] Significant main effect of stimulation condition.

.013, $\eta_p^2 = 0.33$], with faster speaking rates in the DBS ON versus DBS OFF setting.

3.4. Correlations between perceptual and acoustic measures

Given the absence of statistically significant differences in perceptual outcome measures as a function of neural target and stimulation setting, perceptual and acoustic outcome measures were pooled across the two neural targets and DBS stimulation settings for use in the correlation analyses. Results are summarized in Table 3. There were significant positive correlations between acoustic measures of F0 Range, Articulation Rate and Speaking Rate and both perceptual outcome measures. An increase in each of these three acoustic measures was associated with increased intelligibility and less impaired speech severity (i.e., decreased speech severity).

3.5. Correlations between perceptual measures and participant characteristics

Correlation analyses for perceptual measures of intelligibility and speech severity with selected participant characteristics/clinical data are displayed in Table 4. There were significant negative correlations between TEED and both perceptual measures, as well as between LEDD and both perceptual measures. The MDS-UPDRS-III speech rating obtained post-operatively on-medication was negatively correlated with both intelligibility and speech severity. Higher MDS-UPDRS-III speech scores, indicating more severely impaired speech, were associated with poorer intelligibility and speech severity.

4. Discussion

This pilot study compared perceptual and acoustic speech outcome metrics for individuals with PD receiving STN-DBS and GPI-DBS, with DBS stimulation on and off. A number of group-related differences in acoustic metrics were found, including higher F0 variation and F0 range for the GPI-DBS group during the DBS ON stimulation setting; faster articulation rate for the GPI-DBS group during the DBS OFF stimulation setting; and higher SLP variation, SLP range and F2 IQR for the STN-DBS group in both DBS ON and OFF stimulation settings. Associations between perceptual ratings completed by SLPs, acoustic metrics, and selected participant characteristics were examined to gain a broader understanding of factors related to speech outcomes following DBS implantation. The two groups of individuals with PD were comparable in age, disease duration, pre- and post-operative speech scores on the MDS-UPDRS-III, post-operative overall disease severity, and post-operative medication dosage. Although both groups were judged by expert SLPs to have mildly reduced intelligibility and moderate speech severity impairment, there were no statistically significant differences in perceptual speech outcomes between the STN-DBS and GPI-STN groups, nor did perceptual outcome metrics differ as a function of stimulation setting. Clinically meaningful change in scaled speech intelligibility and speech severity has yet to be empirically established. However, related research suggests that at least a 7% difference in scaled intelligibility or speech severity between neural targets or stimulation conditions would be required to be clinically meaningful (c.f. Stipancic and Tjaden, 2022). One implication is that any statistically significant acoustic differences for the two neural targets or stimulation settings were sufficiently subtle so as not to impact functional communication, as indexed by SLP perceptual judgments of intelligibility and speech severity. Although comparative studies with larger participant numbers are needed, the current study suggests that, on average, similar speech outcomes may be expected for STN-DBS and GPI-DBS, when surgeries are performed at the same center by the same neurosurgeon (see also Kopf et al., 2022, where significant differences in total or subscale Vocal Handicap Index scores were absent between the two DBS groups also participating in the current study). MDS-UPDRS-III speech scores also did not differ from pre-operation to the post-operation assessment, or across neural target location, largely mirroring findings for perceptual outcome metrics of intelligibility and speech severity. Notably, pre-operative MDS-UPDRS-III speech scores were worse for both neural targets in the off-medication state as compared to the on-medication state. Although sometimes found to be dependent on severity, such levodopa-induced improvements in speech production have been reported in other studies (Im et al., 2019; Vandana et al., 2021).

Neither neural target nor stimulation condition had a systematic effect on acoustic measures. Previous studies reported mixed results for a variety of acoustic metrics. For example, for STN-DBS patients after DBS implantation, studies have reported significant increases in overall loudness (Tripoliti et al., 2011), significant increases in vowel space areas (Tanaka et al., 2016), and non-significant changes in second formant slopes (Martel-Sauvageau and Tjaden, 2017), with stimulation on compared to stimulation off. Overall, the lack of systematic stimulation or group differences in acoustic outcomes prevents wider conclusions. It is also important to note that benchmarks for clinically significant changes in any acoustic measure of speech are currently lacking. Although this area of research has recently been acknowledged as a need in the speech science literature (Stipancic et al., 2018; e.g., Stipancic and Tjaden, 2022), cut-offs for determining whether a particular magnitude of change in an acoustic measure is real or meaningful are not yet known. Critically, this limits the interpretation of the small absolute differences in acoustic outcome measures seen

Table 3
Results of correlations between acoustic and perceptual metrics. F0: fundamental frequency; SPL: sound pressure level; F2 IQR: second formant interquartile range; CPPS: smoothed cepstral peak prominence; AVQI: acoustic voice quality index. * $p < .05$, * * $p < .01$, * ** $p < .001$.

	Intelligibility		Speech Severity	
	Spearman's Rho	p	Spearman's Rho	p
F0 SD (Hz)	.203	.234	.312	.063
F0 Range (Hz)	.466 * *	.004	.499 * *	.001
SPL SD (dB)	.057	.740	-.076	.661
SPL Range (dB)	.163	.340	.029	.866
F2 IQR (Hz)	.288	.089	− .146	.397
CPPS (dB)	.046	.791	.093	.588
AVQI (AU)	.244	.151	.233	.172
Duration (sec)	-.022	.897	− .157	.361
Articulation Rate (syll / sec)	.448 * *	.006	.659 * **	< .001
Speaking Rate (syll / sec)	.423 *	.010	.652 * **	< .001

Table 4
Results of correlations between perceptual results and selected participant data. TEED: total electrical energy delivered; LEDD: levodopa equivalent daily dose. HY: Hoehn and Yahr. MDS-UPDRS: Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale.

	Intelligibility		Speech Severity	
	Spearman's Rho	p	Spearman's Rho	p
TEED[#]	-.566 *	.015	-.502 *	.034
LEDD	-.573 *	.013	-.609 * *	.007
Time since Implant (Months)	-.342	.165	-.305	.217
Years since Diagnosis	.737	.085	.163	.517
HY Score[#]	-.452	.060	-.442	.066
MDS-UPDRS-III Speech Rating Pre-op off-med[%]	-.149	.555	− .172	.494
MDS-UPDRS-III Speech Rating Pre-op on-med[%]	-.383	.117	-.248	.321
MDS-UPDRS-III Speech Rating Post-op on-med[#]	-.616 * *	.006	-.655 * *	.003

* $p < .05$, * * $p < .01$, * ** $p < .001$.
[#] Stimulation ON only.
[%] Stimulation OFF only.

between conditions in the current study and others.

Correlations between acoustic and perceptual measures indicated faster speech rates and increased intonation ranges to be associated with favorable perceptual outcomes. These findings suggest that very few speakers with PD presented with faster-than-normal speech rates – a potential marker of the hypokinetic dysarthria associated with PD. This is corroborated by our reported averaged speaking and articulation rates (see Table 2), as these rates reflect those of neurotypical speakers. Combined with the lack of differences in perceptual measures, the implication is that any acoustic differences between the two groups were subtle and were not reflected in perceived intelligibility or speech severity. Furthermore, the finding of significant and strong associations between MDS-UPDRS-III speech scores and perceptual outcomes derived from experienced SLPs provides further validation of this simple scale for broadly quantifying speech impairment (Spencer et al., 2022), notwithstanding the valid criticism in using such a broad speech outcome measure. A cautious interpretation of the relatively coarse MDS-UPDRS-III speech scores suggest that speech production may worsen after DBS implantation compared to pre-operation conditions. However, once implementation has been completed, the current perceptual and acoustic findings during post-operation conditions indicate that speech does not necessarily deteriorate further (i.e., no differences in perceptual measures between on and off stimulation). A significant negative correlation was found between perceptual measures and TEED, suggesting both measures were inversely associated with general disease severity. These findings support prior work reporting negative associations between TEED and speech performance (Grover et al., 2019; see e.g., Tripoliti et al., 2011). The similarly negative correlation between perceptual measures and LEDD is indicative of general disease progression, and is in line with previous findings (Cushnie-Sparrow et al., 2018).

As in many DBS studies investigating speech outcomes, participant numbers were limited and clinical characteristics varied to some extent within neural target groups (Table 1). Notably, the GPI-DBS group had been receiving DBS for a significantly longer period of time and had higher TEED values than the STN-DBS group. A prevalent observation following DBS surgery is that optimal stimulation settings require higher TEED for the GPI neural site compared to the STN neural site, evidenced by shorter battery longevity for pallidal DBS (Au et al., 2021; Rawal et al., 2014; Williams et al., 2014). Furthermore, to assess the effect of long-term DBS stimulation on speech symptoms, given the decline of DBS efficacy related to the progressive nature of PD (Brozova et al., 2021), longitudinal monitoring of speech performance is needed to model and predict long-term speech outcomes. Prospective studies should include larger cohorts of patients scheduled to undergo STN-DBS and GPI-DBS. In order to enhance the decision-making process regarding neural target selection in light of potential post-operative speech deteriorations, future research should also evaluate the impact of both DBS implantation and neural target on speech performance through pre-operative and post-operative comparisons. Future work with larger participant numbers should also consider sensitivity/specificity analyses to elucidate the best measures for determining speech production changes in this population as well as limiting possible variance in post-operative DBS management, which might contribute to variability in speech outcomes.

4.1. Conclusion

The current work has preliminary implications for pre-surgical counseling of patients with PD who are candidates for DBS. Although previous research indicates patients considering DBS implantation may experience deteriorations in speech production relative to their pre-operative state, acoustic and perceptual outcomes suggest that speech production does not appear to be differentially affected by DBS neural location. A provisional implication is that the choice of neural target should rely on considerations other than speech outcomes.

CRediT authorship contribution statement

Conceptualization, Methodology: JG, KT; Data collection and analysis: FvB, KS, AR, KT; Writing- Original draft preparation: FvB; Writing-Reviewing and Editing: All authors.

Declaration of Competing Interest

None. The authors declare that all experiments on human subjects were conducted in accordance with the Declaration of Helsinki https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/ and that all procedures were carried out with the adequate understanding and written consent of the subjects. The authors also certify that formal approval to conduct the experiments described has been obtained from the human subjects review board of their institution and could be provided upon request.

References

Alomar, S., King, N.K., Tam, J., Bari, A.A., Hamani, C., Lozano, A.M., 2017. Speech and language adverse effects after thalamotomy and deep brain stimulation in patients with movement disorders: a meta-analysis. Mov. Disord. 32, 53–63.

Au, K.L.K., Wong, J.K., Tsuboi, T., Eisinger, R.S., Moore, K., Lemos Melo Lobo Jofili Lopes, J., Holland, M.T., Holanda, V.M., Peng-Chen, Z., Patterson, A., 2021. Globus pallidus internus (GPi) deep brain stimulation for Parkinson's disease: expert review and commentary. Neurol. Ther. 10, 7–30.

Bakeman, R., 2005. Recommended effect size statistics for repeated measures designs. Behav. Res. Methods 37, 379–384.

Bates, D., Mächler, M., Bolker, B., Walker, S., 2014. Fitting linear mixed-effects models using lme4. arXiv preprint arXiv:1406.5823.

Boersma, P., Weenink, D., 2020. Praat: Doing Phonetics by Computer.

Brozova, H., Barnaure, I., Ruzicka, E., Stochl, J., Alterman, R., Tagliati, M., 2021. Short- and long-term effects of DBS on gait in Parkinson's disease. Front. Neurol. 1563.

Burchiel, K.J., Anderson, V.C., Favre, J., Hammerstad, J.P., 1999. Comparison of pallidal and subthalamic nucleus deep brain stimulation for advanced Parkinson's disease: results of a randomized, blinded pilot study. Neurosurgery 45, 1375–1384.

Combs, H.L., Folley, B.S., Berry, D.T., Segerstrom, S.C., Han, D.Y., Anderson-Mooney, A. J., Walls, B.D., van Horne, C., 2015. Cognition and depression following deep brain stimulation of the subthalamic nucleus and globus pallidus pars internus in Parkinson's disease: a meta-analysis. Neuropsychol. Rev. 25, 439–454.

Cushnie-Sparrow, D., Adams, S., Abeyesekera, A., Pieterman, M., Gilmore, G., Jog, M., 2018. Voice quality severity and responsiveness to levodopa in Parkinson's disease. J. Commun. Disord. 76, 1–10.

Duffy, J.R., 2019. Motor Speech Disorders: Substrates, Differential Diagnosis, and Management, Fourth ed. Elsevier, St. Louis.

Fairbanks, G., 1960. Voice and articulation drillbook, Second ed. Harper and Brothers, New York.

Goetz, C.G., Tilley, B.C., Shaftman, S.R., Stebbins, G.T., Fahn, S., Martinez-Martin, P., Poewe, W., Sampaio, C., Stern, M.B., Dodel, R., 2008. Movement Disorder Society UPDRS Revision Task Force Movement Disorder Society-sponsored revision of the unified Parkinson's disease rating scale (MDS-UPDRS): scale presentation and clinimetric testing results. Mov. Disord. 23, 2129–2170.

Grover, T., Georgiev, D., Kalliola, R., Mahlknecht, P., Zacharia, A., Candelario, J., Hyam, J., Zrinzo, L., Hariz, M., Foltynie, T., 2019. Effect of low versus high frequency subthalamic deep brain stimulation on speech intelligibility and verbal fluency in Parkinson's disease: a double-blind study. J. Parkinson's Dis. 9, 141–151.

Harris, P.A., Taylor, R., Thielke, R., Payne, J., Gonzalez, N., Conde, J.G., 2009. Research electronic data capture (REDCap) - a metadata-driven methodology and workflow process for providing translational research informatics support. J. Biomed. Inform. 42, 377–381.

Im, H., Adams, S., Abeyesekera, A., Pieterman, M., Gilmore, G., Jog, M., 2019. Effect of Levodopa on speech dysfluency in Parkinson's disease. Mov. Disord. Clin. Pract. 6, 150–154.

Jacobson, B.H., Johnson, A., Grywalski, C., Silbergleit, A., Jacobson, G., Benninger, M.S., Newman, C.W., 1997. The voice handicap index (VHI) development and validation. Am. J. Speech-Lang. Pathol. 6, 66–70.

Kim, Y., Kent, R.D., Weismer, G., 2011. An acoustic study of the relationships among neurologic disease, dysarthria type, and severity of dysarthria. J. Speech, Lang., Hear. Res. 54, 417. https://doi.org/10.1044/1092-4388(2010/10-0020).

Kopf, L.M., Rohl, A.H.G., Nagao, T., Bryant, K.N.T., Johari, K., Tjaden, K., Greenlee, J.D. W., 2022. Voice handicap index in Parkinson's patients: subthalamic versus globus pallidus deep brain stimulation. J. Clin. Neurosci. 98, 83–88. https://doi.org/10.1016/j.jocn.2022.01.029.

Kuo, C., Tjaden, K., 2016. Acoustic variation during passage reading for speakers with dysarthria and healthy controls. J. Commun. Disord. 62, 30–44. https://doi.org/10.1016/j.jcomdis.2016.05.003.

Lenth, R., Singmann, H., Love, J., Buerkner, P., Herve, M., 2020. Emmeans: Estimated marginal means, aka least-squares means.

Martel-Sauvageau, V., Tjaden, K., 2017. Vocalic transitions as markers of speech acoustic changes with STN-DBS in Parkinson's Disease. J. Commun. Disord. 70, 1–11.
Moro, E., Lozano, A.M., Pollak, P., Agid, Y., Rehncrona, S., Volkmann, J., Kulisevsky, J., Obeso, J.A., Albanese, A., Hariz, M.I., 2010. Long-term results of a multicenter study on subthalamic and pallidal stimulation in Parkinson's disease. Mov. Disord. 25, 578–586.
Navarro, D., Navarro, M.D., 2022. R Package 'lsr.' Companion to ``Learning Statistics with R''.
Odekerken, V.J., Boel, J.A., Schmand, B.A., de Haan, R.J., Figee, M., van den Munckhof, P., Schuurman, P.R., de Bie, R.M., Group, N.S., 2016. GPi vs STN deep brain stimulation for Parkinson disease: three-year follow-up. Neurology 86, 755–761.
Odekerken, V.J., van Laar, T., Staal, M.J., Mosch, A., Hoffmann, C.F., Nijssen, P.C., Beute, G.N., van Vugt, J.P., Lenders, M.W., Contarino, M.F., 2013. Subthalamic nucleus versus globus pallidus bilateral deep brain stimulation for advanced Parkinson's disease (NSTAPS study): a randomised controlled trial. Lancet Neurol. 12, 37–44.
Okun, M.S., Fernandez, H.H., Wu, S.S., Kirsch-Darrow, L., Bowers, D., Bova, F., Suelter, M., Jacobson, I.V., C.E., Wang, X., Gordon Jr, C.W., 2009. Cognition and mood in Parkinson's disease in subthalamic nucleus versus globus pallidus interna deep brain stimulation: the COMPARE trial. Ann. Neurol.: Off. J. Am. Neurol. Assoc. Child Neurol. Soc. 65, 586–595.
Peto, V., Jenkinson, C., Fitzpatrick, R., Greenhall, R., 1995. The development and validation of a short measure of functioning and well being for individuals with Parkinson's disease. Qual. Life Res. 4, 241–248.
R Core Team, 2019. R: A language and environment for statistical computing.
Rawal, P.V., Almeida, L., Smelser, L.B., Huang, H., Guthrie, B.L., Walker, H.C., 2014. Shorter pulse generator longevity and more frequent stimulator adjustments with pallidal DBS for dystonia versus other movement disorders. Brain Stimul. 7, 345–349.
Revelle, W., Revelle, M.W., 2023. R Package 'psych.'
Rodriguez-Oroz, M.C., Obeso, J., Lang, A., Houeto, J.-L., Pollak, P., Rehncrona, S., Kulisevsky, J., Albanese, A., Volkmann, J., Hariz, M., 2005. Bilateral deep brain stimulation in Parkinson's disease: a multicentre study with 4 years follow-up. Brain 128, 2240–2249.
Skodda, S., 2012. Effect of deep brain stimulation on speech performance in Parkinson's disease. Parkinson's Dis. 2012, 1–10.
Spencer, K.A., Brown, K.A., Elder, G., 2022. Does the unified Parkinson's disease rating scale adequately estimate severity of dysarthria? J. Neurol. Neurosci. 13, 1–4.
Stipancic, K.L., Tjaden, K., 2022. Minimally detectable change of speech intelligibility in speakers with multiple sclerosis and Parkinson's disease. J. Speech, Lang., Hear. Res. 65, 1858–1866.
Stipancic, K.L., Yunusova, Y., Berry, J.D., Green, J.R., 2018. Minimally detectable change and minimal clinically important difference of a decline in sentence intelligibility and speaking rate for individuals with amyotrophic lateral sclerosis. J. Speech, Lang., Hear. Res. 61, 2757–2771. https://doi.org/10.1044/2018_JSLHR-S-17-0366.
Sussman, J.E., Tjaden, K., 2012. Perceptual measures of speech from individuals with Parkinson's Disease and multiple sclerosis: intelligibility and beyond. J. Speech, Lang., Hear. Res. 55, 1208–1219. https://doi.org/10.1044/1092-4388(2011/11-0048).
Tanaka, Y., Tsuboi, T., Watanabe, H., Kajita, Y., Nakatsubo, D., Fujimoto, Y., Ohdake, R., Ito, M., Atsuta, N., Yamamoto, M., 2016. Articulation features of Parkinson's disease patients with subthalamic nucleus deep brain stimulation. J. Parkinson's Dis. 6, 811–819.
Tripoliti, E., Zrinzo, L., Martinez-Torres, I., Frost, E., Pinto, S., Foltynie, T., Holl, E., Petersen, E., Roughton, M., Hariz, M.I., et al., 2011. Effects of subthalamic stimulation on speech of consecutive patients with Parkinson disease. Neurology 76, 80–86.
van Brenk, F., Kain, A., Tjaden, K., 2021. Investigating acoustic correlates of intelligibility gains and losses during slowed speech: a hybridization approach. Am. J. Speech-Lang. Pathol. 30, 1343–1360. https://doi.org/10.1044/2021_AJSLP-20-00172.
Van Nuffelen, G., De Bodt, M., Vanderwegen, J., Van de Heyning, P., Wuyts, F., 2010. Effect of rate control on speech production and intelligibility in dysarthria. Folia Phoniatr. Et. Logop. 62, 110–119. https://doi.org/10.1159/000287209.
Vandana, V.P., Darshini, J.K., Vikram, V.H., Nitish, K., Kumar, P.P., Ravi, Y., 2021. Speech characteristics of patients with parkinson's disease - does dopaminergic medications have a role? J. Neurosci. Rural Pract. 12, 673–679.
Vitek, J.L., 2003. Deep brain stimulation for parkinson's disease - a critical re-evaluation of STN versus GPi DBS. Stereotact. Funct. Neurosurg. 78, 119–131.
Volkmann, J., Allert, N., Voges, J., Weiss, P.H., Freund, H.-J., Sturm, V., 2001. Safety and efficacy of pallidal or subthalamic nucleus stimulation in advanced PD. Neurology 56, 548–551.
Weaver, F.M., Follett, K.A., Stern, M., Luo, P., Harris, C.L., Hur, K., Marks, W.J., Rothlind, J., Sagher, O., Moy, C., 2012. Randomized trial of deep brain stimulation for Parkinson disease: thirty-six-month outcomes. Neurology 79, 55–65.
Weismer, G., 2008. Speech Intelligibility. In: Ball, M.J., Perkins, M.R., Muller, N., Howard, S. (Eds.), The Handbook of Clinical Linguistics. Blackwell, Oxford, pp. 568–582.
Williams, N.R., Foote, K.D., Okun, M.S., 2014. Subthalamic nucleus versus globus pallidus internus deep brain stimulation: translating the rematch into clinical practice. Mov. Disord. Clin. Pract. 1, 24–35.
Yunusova, Y., Weismer, G., Kent, R.D., Rusche, N.M., 2005. Breath-group intelligibility in dysarthria: characteristics and underlying correlates. J. Speech, Lang., Hear. Res. 48, 1294–1310. https://doi.org/10.1044/1092-4388(2005/090).
Zimpel, V.M.H., Middlebrooks, E., Santiago, N., 2023. Surgical Anatomy of the Basal Ganglia and Thalamus. in: Brain Anatomy and Neurosurgical Approaches: A Practical, Illustrated, Easy-to-Use Guide. Springer, pp. 349–358.