Perceptual and Acoustic Correlates of DBS of Subthalamic Nucleus versus Globus Pallidus Interna for IPD: A Comparative Pilot Study

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INTRODUCTION

BACKGROUND

- Deep Brain Stimulation (DBS) has become a common treatment to improve gross motor function in patients with medically refractory idiopathic Parkinson's Disease (PD) and those who develop adverse side effects from drug treatments.
- The main neural target for DBS is Subthalamic Nucleus (STN). While STN-DBS improves many motor symptoms of PD, studies report a deterioration of speech that does not improve once stimulation is turned off. Globus pallidus interna (GPI)-DBS has equal efficacy to STN-DBS for improving limb motor function in PD (Weaver et al., 2012), but speech outcomes following GPI-DBS have not been rigorously defined (Skodda et al., 2012).
- Research directly comparing speech outcomes following STN-DBS versus GPI-DBS is crucial for informing clinical practice. This work also has the potential to advance mechanistic understanding of DBS.

PURPOSE

1. Compare effects of bilateral STN-DBS and bilateral GPI-DBS on perceived Speech Severity (Sussman & Tjaden, 2012; Weismer et al., 2001) in context of stimulation ON versus OFF paradigm. Speech Severity was of interest rather than intelligibility, as Speech Severity is sensitive to even very mild dysarthria.

2. Explore speech acoustic changes associated with variations in perceived Speech Severity.

METHODS: Speakers

Table 1 summarizes speaker demographics.
- STN-DBS: 12 speakers (8 M, 4 F)
- GPI-DBS: 8 speakers (6 M, 2 F)
- 6 months post-surgery, with exception of STN_01
- Single center/site surgery by same neurosurgeon

TABLE 1 Speaker	Age at recording	Gender	Years since Dx	Months post-implant	UPDRS III Score^ (Pre-op/post-op med ON)		H & Y Score*
STN_01	59	F	13	1	n/a	26	1
STN_02	63	M	13	37	n/a	19	2
STN_03	67	M	16	6	n/a	7	1
STN_04	76	M	8	19	n/a	24	3
STN_05	61	F	11	31	n/a	3	1
STN_06	52	F	12	20	n/a	11	2
STN_07	69	M	14	12	n/a	2	2
STN_08	54	M	9	29	n/a	24	2
STN_09	73	M	10	14	n/a	8	2
STN_10	59	F	13	40	n/a	16	1
STN_15	83	M	18	20	44	10.5	n/a
STN_16	77	M	10	34	n/a	23	n/a
AVG (SD)	66.1 (9.3)		12.3 (2.8)	21.9 (11.9)			
GPI_01	62	M	9	11	27	19	2
GPI_02	68	M	8	11	41	10	2
GPI_04	66	M	8	45	n/a	16	2
GPI_06	63	M	13	42	n/a	n/a	n/a
GPI_07	73	F	10	49	n/a	23	n/a
GPI_08	79	M	17	43	n/a	n/a	n/a
GPI_09	70	M	11	54	n/a	n/a	n/a
GPI_10	62	F	15	52	n/a	12.5	n/a
AVG (SD)	67.9 (5.6)		11.4 (3.1)	38.4 (16.3)			

^ Unified Parkinson's Disease Rating Scale on meds with DBS on; range 0-108
* Hoehn and Yahr scale on meds with DBS on; range 1-5

METHODS: Stimuli and Listeners

Speech Stimuli and Recording Procedures
- **Reading:** first two sentences of Rainbow Passage
- **Monologue:** spoke about travel, employment, hobbies. Lengthy samples truncated to approximately 40 seconds. Samples ranged in length from 14 to 48 seconds.
  - DBS ON: Monologue mean duration 38 sec. (SD=7)
  - DBS OFF: Monologue mean duration 35 sec. (SD=10)
- Recorded with stimulation ON and OFF while optimally medicated.
- All STN speakers first recorded with stimulation OFF. Five of the eight GPI speakers recorded with stimulation OFF first.

Listeners
- 10 native English listeners passed hearing screening and reported minimal experience with motor speech disorders
- Judged overall Speech Severity (Sussman & Tjaden, 2012; Weismer et al. 2001): "pay attention to combination of articulation, voice, resonance, respiration, and speech rate"

METHODS: Perceptual Task and Procedures

Within-speaker STIM ON vs. STIM OFF paired-comparison paradigm (Park et al., 2016)
- Pairs of reading passages or monologues presented in both DBS stimulation ON-OFF and OFF-ON orders.
- After hearing both samples in a pair, listeners indicated whether sample A or B was **LESS** severe (i.e., better), by typing **A** or **B**. If the two samples were the **same** (no difference), listeners typed **S**.
- Stimuli were pooled across speakers and neural targets, then blocked by speech task, and randomized. 10% of stimuli were judged twice for intrajudge reliability. For all listeners, intrajudge reliability was at least *r*=.6.
- Half of the listeners judged the reading passage first and half judged monologues first. The task was self-paced and took approximately 2 hours.
- Responses were pooled across listeners, and the proportion of On Best, Off Best, and Same responses were calculated for speaker and task.
- Data for each speak task were analyzed separately with Chi-square tests.

METHODS: Acoustic Measures

To investigate whether acoustic characteristics could account for the perceptual findings **across groups and tasks**, selected acoustic measures were obtained (semi-) automatically by means of customized scripts in Praat.
- Only stimuli pairs with a **minimum proportion of .55** for either On Best or Off Best conditions were included (8 pairs STN-Rainbow; 4 pairs GPI-Rainbow; 7 pairs STN-monologue; 0 pairs GPI-monologue).
- Pearson Correlations were used to evaluate the strength of the relationship between the On – Off scores and the **ratio of the acoustic measures in the On / Off condition**.
- Results were pooled across stimulation location and speaking task.

Global Timing:
- Speaking rate
- Articulation rate
- Ratio of speech (i.e., articulation) time to total time.

Respiratory-Laryngeal:
Voice measures were obtained from all concatenated voiced fragments.
- Smoothed Cepstral Peak Prominence (CPPS)
- F0 Mean, Median, SD, and Range (90th – 10th percentile)

Segmental Articulation:
- F2 Inter Quartile Range (IQR; 75th – 25th percentile)

To further explore acoustic changes associated with **individual speaker variation** in perceptual outcomes, acoustic measures from Rainbow Passage for 8 STN-DBS speakers (4 On Best, 4 Off Best) were examined in both stimulation ON and Off conditions.

RESULTS: Speech Severity

Figure 1. Monologue

Figure 1 reports the percent of Monologue trials for which DBS Stimulation OFF (red bars) or ON (green bars) was judged to be best/less severe. Black bars indicate the proportion of trials judged to have the same perceived Speech Severity for ON and OFF stimulation. Data for the Rainbow Passage are reported below in Figure 2. Chi-square tests for Monologue were not significant.

For Rainbow Passage in Figure 2, the proportions of ON best, OFF best and Same responses for GPI and STN approached significance (p=.051).

Follow-up testing further indicated that the proportion of OFF best and ON best responses was significantly different (p=.04) for the two groups. For GPI-DBS, ON stimulation was clearly perceived as less severe than OFF stimulation.

Figure 2. Rainbow Passage

Figures 1 and 2 report group data. Individual speaker outcomes are reported Figures 3 and 4. For each speaker, the proportion of trials for which Stimulation OFF (red bars) or ON (green bars) was judged to be best/less severe is reported as well as the proportion of trials for which stim ON and OFF were judged to be the same (black bars). There was substantial interspeaker variability, especially for STN-DBS. A subset of STN speakers was clearly perceived to be less severe with stim ON (bar mostly green) and others were perceived to be less severe with stim OFF (bar mostly red)

Figure 3. Monologue

Figure 4. Rainbow Passage
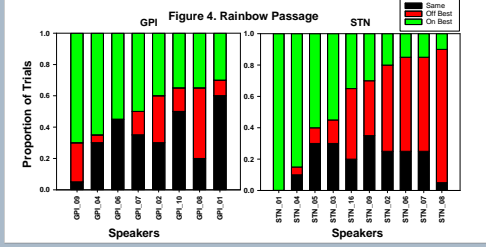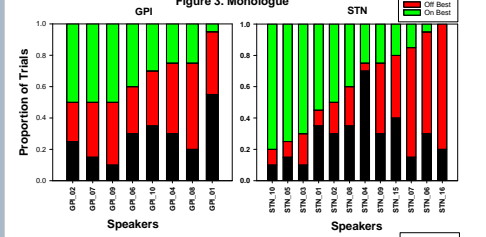
GROUP RESULTS: Acoustic Measures

Table 2 summarizes results of the correlational analyses between On – Off scores and ratios of acoustic measures.

TABLE 2 Acoustic Measure	Pearson r	p-value	Correlation
Speaking Rate	.463*	.046	Lower severity associated with higher speaking rate
Articulation Rate	-.072	.693	
Speech proportion	.482*	.036	Lower severity associated with higher ratio of speech to total time
CPPS	.174	.476	
F0 Mean	-.467*	.044	Lower severity associated with lower mean F0
F0 Median	-.562*	.012	Lower severity associated with lower median F0
F0 SD	-.322	.179	
F0 Range	-.421^	.072	Lower severity associated with smaller F0 range
F2 IQR	.380^	.109	Lower severity associated with larger F2 IQR range

**significant p < .01 *significant p < .05 ^notable trend

INDIVIDUAL RESULTS: Acoustic Measures

Figures 5-8 display acoustic results from Rainbow Passage for a subset of STN-DBS speakers for whom ON stimulation (left panel in each pair) or OFF stimulation (right panel in each pair) was judged for majority of trials to be less severe/best.

Figure 5.

Figure 6.
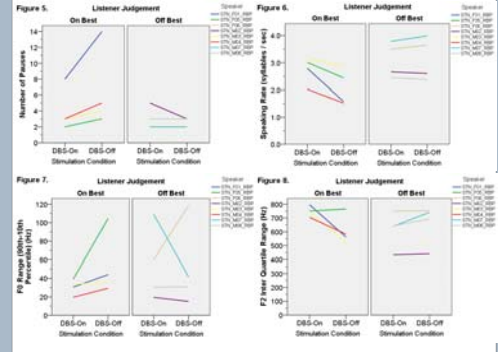
Figure 7.

Figure 8.

CONCLUSIONS

- **Neural Target**: Acute DBS stimulation did not have same impact on perceived Speech Severity for STN-DBS and GPI-DBS.
- **Speech Task**: Any perceptual benefit of active DBS stimulation was speech task specific (Figure 2 GPI-DBS).
- **Interspeaker Variability**: Variability in perceptual outcomes was notable, especially for the STN-DBS group (right panels Figures 3 and 4).
- **Acoustics**: Changes in global speech timing, articulation and F0 were associated with variations in perceived Speech Severity.

Summary: Speech outcomes following GPI-DBS vs. STN-DBS warrant further study with larger subject numbers. Delineating the source and mechanism(s) of interspeaker variability following STN-DBS is critical for improving pre-operative counseling, optimizing therapeutic effects of DBS and ultimately for developing targeted and effective speech management protocols.