EXAMINING THE EFFECTS OF DEEP BRAIN STIMULATION ON SPEECH IN PARKINSON'S DISEASE

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Introduction

- Approximately 90% of people with Parkinson's disease (PD) develop dysarthria characterized by reduced articulatory, respiratory, and phonatory precision resulting in slow, effortful, slurred speech [1, 2].
- Effects of Deep Brain Stimulation to the subthalamic nucleus (DBS-STN) on dysarthria severity are variable [3, 4].
  - Previous research shows reduced vowel space in PD relative to controls [3, 5]; however, studies do not agree on whether vowel space is higher within subjects with DBS-STN ON versus OFF [6, 7, 8, 9].
- Despite counter-balancing order of conditions [6, 8], no study showed a detailed analysis of the order of ON versus OFF conditions.

This study investigates how PD and treatment using DBS-STN affect vowel distinctness and what factors contribute to any found changes.

Q1) Do patients with PD have smaller vowel spaces than control patients?
Q2) Does DBS-STN impact vowel space in patients with PD?
Q3) Does order of DBS ON and OFF conditions influence vowel space?
Q4) What patient factors influence vowel space in different DBS conditions?

Method

- Patients with PD (n = 17) and bilateral implantation of DBS-STN produced vowels in conditions with DBS ON and OFF. Healthy control group (n = 9).
- From sustained vowels /a/, /i/, /æ/, and /u/ produced for three seconds at a habitual pitch and loudness, we calculated vowel space:
  - *vowel space area* (**VSA**) [10] & *vowel articulation index* (**VAI**) [5, 10,11]
  - VAI is more sensitive to group differences & less prone to variability [10].

	PD means (SD)	Control means (SD)
Age / Gender	62.1 (9.9), 4 female	61.7 (σ = 12.9), 6 female
Voice Handicap Index (VHI)	53.2** (23.9)	9.3 (σ = 6.6)
Multidim. Fatigue Inventory (MFI)	59.4* (18.3)	46.6 (σ = 8.4)
SIT Intelligibility[1] (OFF/ON)	59.4** (26.8) / 57.2** (30.7)	92.4 (10.7)
Years since PD diagnosis	11.1 (5.4)	
Months since last surgery	41.5 (44.3)	
Severity (MDS-UPDRS Part III)	23.8 (14.4)	
Cognition (DRS-2)[2]	138.4 (2.7)	
TEED (Estimated[3])	96.0 (57.4)	
Levodopa Equivalent Dose (LED)[4]	450.6 (500.4), 6 off meds	

p-value thresholds: **(p < 0.01 *(p < 0.05)

[1] From sentences 13-15 words in length from Speech Intelligibility Test (SIT) [12] elicited in DBS OFF/ON conditions, intelligibility is average ratings along visual analog scale from 3 raters [13, 14].

[2] For 11 patients, we derived DRS-2 scores from the MoCA [15].

[3] Total electrical energy delivered (TEED) was estimated using impedance of 1000 in the absence of values for all patients [16].

$$\text{TEED} = \frac{voltage^2 \cdot frequency \cdot pulse\ width}{impedance} * (1s) \quad [11,16]$$

[4] We used consensus across three raters to calculate LED using online calculator: https://www.parkinsonsmeasurement.org/toolBox/levodopaEquivalentDose.htm

Results

Fig. 1: Vowel spaces

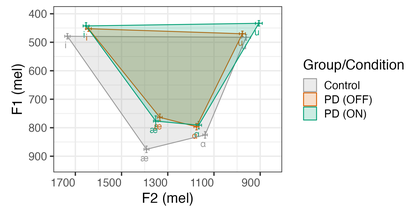
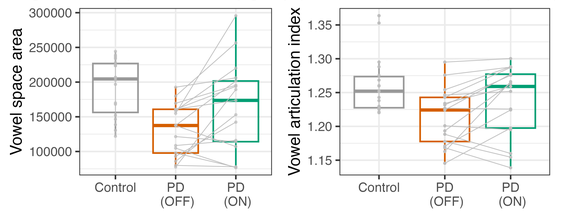


Fig. 2: Vowel space metrics by group (PD/Control) & condition (ON/OFF)



- **(Q1) Vowel spaces (VSA/VAI) are larger in controls than in patients with PD.**
  (factors: group, SIT, age, gender, VHI, MFI)
  - **VSA**: group*, *MFI*, Age*, SIT†*
  - **VAI**: group**, MFI*, *SIT†, gender†*

p-value thresholds: **(p < 0.01) *(p < 0.05) †(p < 0.10)

- **(Q2) For patients with PD, vowel spaces are larger with DBS-STN ON than OFF.**
  (factors: condition, SIT, age, gender, VHI, MFI, years PD, months since surgery, UPDRS, DRS-2, TEED, LED)
  - **VSA**: condition**, *SIT*, VHI**, TEED**, DRS-2†*
  - **VAI**: condition**, *SIT**, gender*, VHI**, years PD*, Months sx*, UPDRS*, TEED**, LED***

Fig. 3: Average vowel space by group (control/PD), condition (ON/OFF), & order (ON-first/OFF-first)

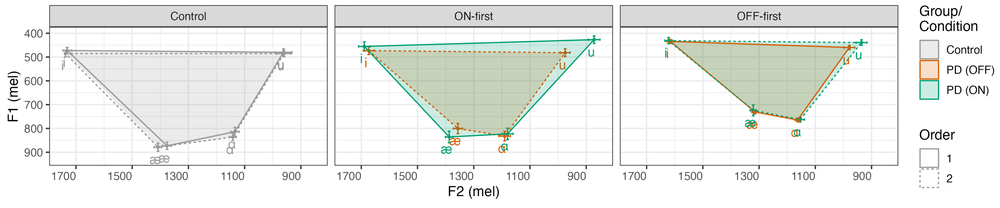
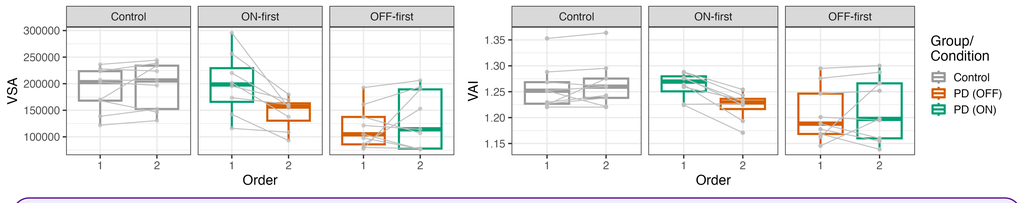


Fig. 4: Vowel space metrics separated by group (control/PD), condition (ON/OFF), & order (ON-first/OFF-first)



- **(Q3) For patients with PD, there is an interaction between condition (ON/OFF) & order (OFF-first/ON-first) when predicting VSA/VAI.**
  - **VSA**: condition**, condition x order** **VAI**: condition*, condition x order*

- **(Q4) Controlling for individual patient factors, the interaction is significant only for VSA. Robust contribution of TEED on vowel space.** (↑TEED, ↑VSA/VAI)
  (factors: condition, condition x order, SIT, age, gender, VHI, MFI, years PD, months since surgery, UPDRS, DRS-2, TEED, LED)
  - **VSA**: condition**, condition x order**, *TEED***, *Months sx†* **VAI**: *TEED***

- *For OFF-first subgroup, those who increase in VSA/VAI tend to have* ↓MFI, ↓TEED, ↑LED.

Conclusions

- **(Q1)** On average, patients with PD have smaller vowel spaces than healthy control patients.
- **(Q2)** Patients with PD have larger vowel spaces when DBS-STN is ON than OFF, as in [6, 7].
  - Stimulation increases articulatory vowel space.
  - Contribution of intelligibility, voice status, & TEED
- **(Q3)** Surprising effect of DBS order on vowel space.

ON-first: ON > OFF *(all 8 patients)*
OFF-first: ON > OFF *(only 4/9 patients)*

  - **Interpretation #1**: Fatigue cancels out benefit of stimulation when OFF precedes ON condition.
  - **Interpretation #2**: It takes more time when DBS switches back on to reach maximum benefit.
    - We waited ≥5 minutes after turning stimulation back on to perform speaking tasks.
- **(Q4)** TEED positively predicts vowel space above and beyond condition & order.
  - **VSA**: Measures total articulatory-acoustic space.
  - **VAI**: Measures ratios across extreme points within articulatory-acoustic space.

- *Impact.* This research deepens our understanding of why some patients' speech improves with DBS. This research has potential to help identify those at risk for speech decline with stimulation, thus informing personalized recommendations for surgical care and therapy addressing anticipated speech challenges.

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