Declines in Memory and Processing Speed after Deep Brain Stimulation Surgery for Parkinson Disease

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BACKGROUND

- **Deep Brain Stimulation (DBS)**
  - An effective surgical treatment for medication refractory Parkinson's disease.
  - Electrodes are implanted subcortically and deliver modifiable high frequency stimulation.
  - Surgical targets for PD include the subthalamic nucleus (STN) and globus pallidus internal segment (GPi).

- **Group-level cognitive outcomes following DBS**
  - Performance decrements following DBS surgery have been documented on a variety of tasks, including verbal fluency, memory, attention, executive functioning, and language (Parsons et al, 2006; Voon et al, 2006).
  - Group comparison studies have been limited by small sample sizes and absence of control groups.

- **Individual-level cognitive outcomes following DBS**
  - Reliable Change Index (RCI) used to control for imprecision of a measurement instrument and for expected practice effects.
  - Studies applying RCI analyses to bilateral STN DBS have documented individual-level declines on tests of memory, verbal fluency, and executive function (York et al, 2007; Higginson et al, 2008).

AIMS of Study

AIM 1: To investigate whether *unilateral* DBS leads to cognitive declines on measures of memory, processing speed, executive function, and visuospatial function.

AIM 2: To use reliable change indexes to determine the presence of individual-level changes in performance following DBS.

AIM 3: To identify risk factors (i.e., age, side of surgery, baseline cognitive and depression status) for the development of post-operative cognitive dysfunction.

METHODS

Participants

N = 43 pts from IRB-approved MDC database

	Controls N = 19	DBS N = 24
Age	64.6 (6.6)	61.7 (4.9)
Education	15.4 (3.0)	14.1 (2.6)
Male / Female	12/7	20/4
Motor		
Months with symptoms	76.5 (69.1)	141.2 (60.2)*
Hoehn & Yahr Stage	2.4 (0.4)	2.2 (0.4)
UPDRS "on"	25.3 (8.5)	22.1 (8.1)
UPDRS "off"	30.8 (8.3)	42.8 (11.3)*
Mood		
BDI-II	9.2 (8.6)	9.8 (7.6)
Cognition		
MMSE	28.3 (1.9)	28.9 (1.2)
DRS-2 (raw)	138.6 (3.5)	137.6 (4.6)
Months b/t evaluations	16.1 (7.0)	20.1 (6.3)

*Indicates significant difference between groups, p<0.05.

Measures

Administered as part of a 4-hour battery at UF Psychology Clinic at Time 1 and Time 2

Memory
- Hopkins Verbal Learning Test (HVLT-R)
- Logical Memory Stories (LM)

Processing Speed
- Trail Making Test Part A
- Stroop Word Reading Test

Executive Function
- Trail Making Test Part B
- Stroop Color-Word Interference Test

Visuospatial Function
- Judgment of Line Orientation Test (JLO)
- Benton Facial Recognition Test (FRT)

Electrode Placement

Target	N	X	Y	Z
Left STN	8	-13.2 (0.94)	-3.4 (1.7)	-3.1 (1.2)
Right STN	3	12.5 (0.75)	-3.4 (4.0)	-3.6 (-0.8)
Left GPi	8	-22.5 (1.8)	2.4 (1.7)	-0.24 (1.5)
Right GPi	5	20.6 (0.71)	4.5 (1.0)	-0.16 (1.9)

RESULTS

AIM 1: Group Differences in Cognitive Performance Over Time

- Multivariate Repeated-Measures Analyses of Variance for each cognitive domain.
  - Within-subjects factor (Time 1 v. Time 2)
  - Between-subjects factor (DBS v. control)

- Significant **Group X Time interactions** ONLY for processing speed domain ($p = 0.024$).

- Suggests significant slowing following DBS.

Processing Speed
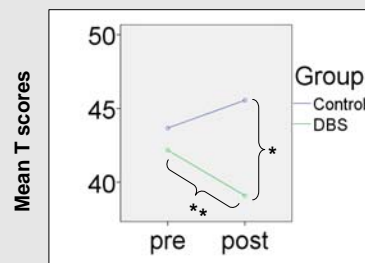
*p<0.05, Bonferroni-adjusted

RESULTS cont.

AIM 2: Reliable Change Results

- Calculated 90% RCI confidence intervals based on control group
- Patients classified as "**decliners**" or "**improvers**" if the difference between their *obtained* and *expected* scores exceeded RCI

Tests on which DBS patients had a greater proportion of decliners/improvers than controls:

Test	PD Control Decline	PD Control Improve	DBS Decline	DBS Improve
HVLT-R Immediate	0.0%	5.3%	20.8%*	8.3%
HVLT-R Delay	0.0%	10.5%	25.0%*	4.2%
Trail Making A	0.0%	5.3%	8.7%*	0.0%
Stroop Word	0.0%	5.6%	9.5%*	0.0%
Trail Making B	5.3%	5.3%	9.1%*	0.0%
Stroop Color-Word	0.0%	0.0%	19.0%*	9.5%*
JLO	5.3%	5.3%	17.4%*	26.1%*

*p<0.01, based on binomial tests

AIM 3: Predictors of Cognitive Change in DBS group

1. Age, side of surgery, baseline DRS-2 & baseline BDI-II regressed on change for processing speed and HVLT-R immediate and delayed recall.
- Models *not significant*

2. Independent samples t-tests between "decliners" and "non-decliners" on the HVLT-R:

	"Decliners" (N=6)	"Non-decliners" (N=18)	p
Baseline characteristics			
UPDRS "on"	23.0 (5.6)	21.8 (8.9)	0.76
UPDRS "off"	43.9 (12.0)	39.8 (9.4)	0.46
Months with symptoms	105.0 (22.0)	153.2 (66.9)	0.10
DRS-2	141.0 (1.6)	136.7 (4.7)	**0.004**
Change Variables	*(Time 2-Time 1)*		
UPDRS "on"	-5.8 (7.6)	0.5 (9.2)	0.143
UPDRS "off"	-13.7 (14.9)	-10.5 (7.8)	0.518

CONCLUSIONS

- Inferential analyses revealed declines only in processing speed in the unilateral DBS group compared to controls.
- RCI analysis revealed individual declines on word list recall in the DBS group.
  - These declines may be related to higher pre-surgical cognitive status on a cognitive screening measure.
  - These declines do not reflect a global memory impairment, as performance on story memory tasks was unaffected.
- Use of Reliable Change highlights the impact of individual variability and indicates that both declines and improvements can be detected even in samples that demonstrated minimal group differences upon inferential statistical comparison.