A Reliable Change Analysis of Cognitive Declines One Year after Unilateral Deep Brain Stimulation Surgery in Parkinson Disease

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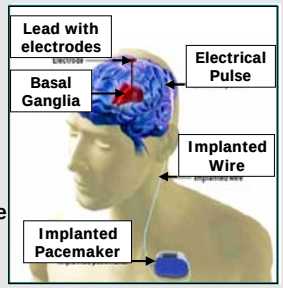
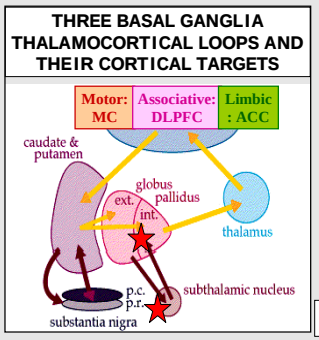
BACKGROUND

• **Deep Brain Stimulation (DBS)** is an effective surgical treatment for medication refractory PD that involves implanting electrodes subcortically and delivering modifiable high frequency stimulation.





• However, conflicting research suggests that it may result in **selective cognitive declines**, perhaps due to current spread beyond sensorimotor subregions

★ DBS targets

METHODS

Participants

N = 41

Data from IRB-approved MDC database

	Controls *N* = 19	DBS *N* = 22
Age	64.6 (6.6)	61.4 (5.0)
Education	15.4 (3.0)	14.0 (2.3)
Male / Female	12/7	18/4
Motor		
Months with symptoms	76.5 (69.1)	138.5 (63.9)
Hoehn & Yahr Stage	2.4 (0.4)	2.2 (0.3)
UPDRS "*on*"	25.3 (8.5)	22.9 (8.0)
UPDRS "*off*"	30.8 (8.3)	43.4 (11.5)
Mood		
BDI-II	9.2 (8.6)	10.1 (8.2)
Cognition		
MMSE	28.3 (1.9)	29.0 (1.1)
DRS-2 (raw)	138.6 (3.5)	138.0 (4.4)
Months b/t evaluations	16.1 (7.0)	19.3 (5.7)

Locations of DBS pts' active electrode contacts

	X	Y	Z
Right STN (N=3)	13.4 (0.8)	-0.5 (3.7)	-1.8 (1.5)
Left STN (N=7)	-11.6 (0.7)	-1.5 (1.5)	-1.2 (1.3)
Right GPi (N=5)	20.6 (0.7)	4.5 (1.1)	-0.2 (1.9)
Left GPi (N=7)	-22.1 (1.5)	2.1 (1.6)	-0.3 (1.6)

Measures

Part of a 4-hour battery at UF Psychology Clinic at Time 1 and Time 2 (Mean inter-evaluation interval:17.8 mos)

Tasks involving DLPFC	
Letter Fluency (COWAT)	Patients are given 60s generate words beginning with each letter: F, A, & S
Semantic Fluency (Animals)	Patients are given 60s to generate the names of animals
Digit Span Backward (WAIS)	Patients listen to increasingly long strings of numbers and repeat them in reverse order
Control Tasks NOT involving DLPFC	
Vocabulary (WASI)	Patients provide definitions of words increasing in difficulty
Boston Naming Test	Patients name images of common objects

AIMS of Study

AIM 1: To test the hypothesis that cognitive declines associated with deep brain stimulation surgery manifest in diminished performance on neuropsychological tasks shown to involve the dorsolateral prefrontal cortex (DLPFC)

AIM 2: To determine the significance of changes in performance on tasks shown to decline in the DBS group using reliable change indexes

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

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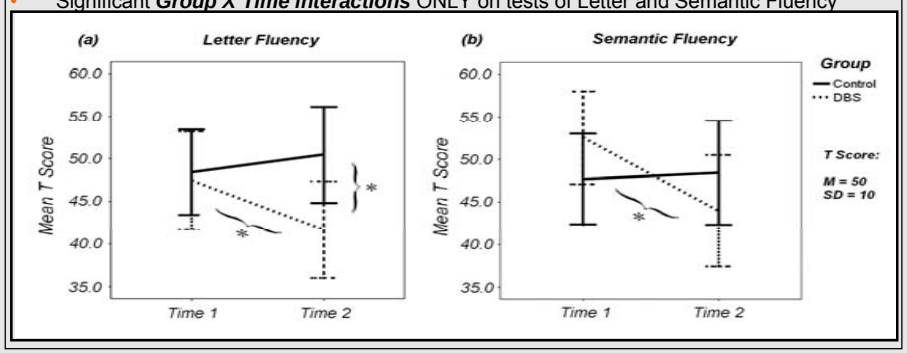
RESULTS

AIM 1: Group Differences in Cognitive Performance Over Time

(Repeated-Measures Analyses of Variance for each test)

- ***No Main Effects*** of Group of Time on ANY of the 5 cognitive tests
- Significant ***Group X Time interactions*** ONLY on tests of Letter and Semantic Fluency



RESULTS cont'd

AIM 2: Reliable Change Results

- Standard Error of the Measure (SE_M) calculated for Time 1 and Time 2
- Stand Error of the Difference (SE_{DIFF}) calculated from Time 1 and Time 2 SE_M
- Reliable Change Index defined by 90% confidence interval around SE_{DIFF}

$SE_M = SD * \sqrt{(1-r_{xx})}$

$SE_{DIFF} = \sqrt{([SE_M(Time\ 1)]^2 + [SE_M(Time\ 2)]^2)}$

$RCI = \pm 1.645 * SE_{DIFF}$

- Patients classified as "***decliners***" if the difference between their *obtained* and *expected* (baseline + mean practice effect) scores exceeded RCI

	Controls	DBS	Odds ratio	Pearson chi-square	*p*	*Phi*
Letter Fluency	1	7	8.4	4.58	.032	.33
Semantic Fluency	1	8	10.3	5.76	.019	.38
Either	2 (11%)	11 (50%)	8.3	7.34	.007	.42

AIM 3: Predictors of Cognitive Change

1. Age, side of surgery, baseline DRS-2 & baseline BDI-II regressed on change for each fluency measure

- Model ***not significant*** for Letter Fluency change (R^2=.097, p=.81)
- Only side of surgery independently predicted Semantic Fluency change (model: R^2 = .38, p = .11; surgery side: β=-.57, p=.01) such that ***LEFT-sided surgery*** was associated with cognitive decline ($\chi^2(1) = 4.20$, p = .04, Phi = .44)

2. Independent samples t-tests between "decliners" and "non-decliners"

	"Decliners" *N* = 11	"Non-decliners" *N* = 11	*p*
Baseline characteristics			
UPDRS "*on*"	22.6 (6.9)	23.2 (9.2)	.87
UPDRS "*off*"	40.4 (10.9)	46.4 (11.8)	.25
Months with symptoms	139.5 (70.1)	137.5 (60.5)	.95
Change Variables *(Time 2 – Time 1)*			
Hoehn & Yahr Stage	+ 0.4 (0.6)	+ 0.1 (0.3)	.12
UPDRS "*on*"	+ 3.1 (6.0)	- 6.5 (8.9)	**.01 ***
UPDRS "*off*"	- 5.7 (11.0)	- 15.1 (7.6)	**.04 ***

CONCLUSIONS

- Our findings provide further support for verbal fluency declines after DBS and suggests that semantic fluency declines are more common after left-sided surgery
- Reliable Change analyses suggest that fluency declines likely reflect significant changes in a *subset* patients who experience poorer surgical outcome in general