

Supplementary Material

Altered Functional Connectivity of the Subthalamic Nucleus in Parkinson's Disease: Focus on Candidates for Deep Brain Stimulation

Supplementary Table 1. Cognitive and behavioral characteristics of Parkinson's disease patients and healthy controls at the study entry.

Variables	HC	Candidates for DBS	Non-candidates	p: Candidates for DBS vs. HC	p: Non-candidates vs. HC	p: Candidates for DBS vs. Non-candidates
Global cognition						
ACE-R total	96.28±3.00 (87.00-100.00)	87.42±8.22 (69.00-99.00)	89.37±7.42 (65.00-99.00)	<0.001	<0.001	0.37
Memory						
RAVLT immediate recall	45.36±10.24 (21.00-65.00)	37.89±10.50 (24.00-59.00)	38.22±11.31 (17-66.00)	0.048	0.004	1.00
RAVLT delayed recall	8.92±2.74 (4.00-13.00)	12.53±2.56 (6.00-15.00)	12.37±3.16 (0.00-15.00)	0.044	0.003	1.00
PRM [% correct]	79.69±11.46 (37.50-95.83)	74.94±11.26 (50.00-96.00)	74.48±18.24 (0.00-100.00)	1.00	0.26	1.00
SRM [% correct]	73.88±10.52 (55.00-95.00)	67.63±13.47 (40.00-90.00)	70.12±16.18 (0.00-85.00)	0.35	0.49	1.00
Language						
BNT total	58.22±1.63 (53.00-60.00)	54.26±5.08 (42.00-59.00)	55.44±8.97 (5.00-60.00)	0.048	0.08	1.00
ACE-R language	25.90±0.30 (25.00-26.00)	22.74±2.62 (18.00-27.00)	24.15±2.57 (14.00-26.00)	<0.001	<0.001	0.01
Executive functions						
Digit span backward	6.80±1.95 (3.00-11.00)	5.78±3.02 (2.00-11.00)	5.54±1.96 (0.00-11.00)	0.04	0.12	1.00
Stroop interference [total correct]	38.24±10.34 (17.00-60.00)	34.53±12.41 (14.00-55.00)	32.61±11.60 (13.00-68.00)	0.42	0.23	1.00
IED [total errors]	41.64±28.99 (7.00-146.00)	53.26±31.70 (0.00-161.00)	59.32±38.95 (11.00-225.00)	0.69	0.46	1.00
Attention						
Digit ordering [max. span]	5.77±1.24 (4.00-8.00)	5.02±1.02 (3.00-6.50)	5.23±1.13 (3.50-8.50)	0.04	0.13	1.00
Letter cancelation correct	28.44±5.53 (20.00-41.00)	23.58±6.65 (15.00-37.00)	22.43±5.70 (0.00-39.00)	0.04	<0.001	1.00
Visuospatial abilities						
Hooper	23.12±3.34 (13.00-30.00)	18.95±6.24 (9.50-29.00)	19.17±5.69 (9.00-30.00)	0.003	0.001	1.00
ACE-R visuospatial	15.80±0.40 (15.00-16.00)	15.68±0.58 (14.00-16.00)	15.22±1.12 (12.00-16.00)	1.00	0.40	0.18

Mood/behavior						
HDRS	2.30±3.63 (0.00-15.00)	6.42±5.77 (0.00-20.00)	4.88±5.05 (0.00-18.00)	0.01	0.03	1.00
HAMA	2.92±3.06 (0.00-11.00)	6.05±4.89 (0.00-16.00)	5.17±5.75 (0.00-21.00)	0.03	0.08	1.00
Apathy scale	1.74±2.90 (0.00-11.00)	11.26±9.93 (0.00-28.00)	10.15±7.68 (0.00-28.00)	<0.001	<0.001	1.00

Values are reported as mean ± standard deviation (range). Differences between Parkinson's disease patients and healthy controls and between Parkinson's disease groups at baseline were assessed using ANOVA models. p values were adjusted for multiple comparisons at $p < 0.05$. ACE-R, Addenbrooke's Cognitive Examination-Revised; BNT, Boston Naming Test; DBS, Deep Brain Stimulation; Candidates for DBS, Patients eligible for DBS; HAMA, Hamilton Anxiety Rating Scale; HC, healthy controls; HDRS, Hamilton Depression Rating Scale; IED, Intra and Extra-Dimensional shifting; Non-candidates, Patients not eligible for DBS; PD, Parkinson's disease; PRM, Pattern Recognition Memory; RAVLT, Rey Auditory Verbal Learning Test; SRM, Spatial Recognition Memory.

Neuropsychological and behavioral evaluations

Expert neuropsychologists, blinded to clinical and MRI results, performed neuropsychological and behavioral evaluations at each visit in both PD patients and healthy controls. None of patients received cholinesterase inhibitors at study entry or during the follow-up. The following tests were administered: the Addenbrooke's Cognitive Examination-revised (ACE-R) [1]; the Rey Auditory Verbal Learning Test [2], pattern and spatial recognition memory tests from the Cambridge Neuropsychological Test Automated Battery (CANTAB) [3]; executive functions with the digit span backward, Intra/Extra Dimensional Set Shift test from the CANTAB [3], and the Stroop color-word test; the digit ordering test and the letter cancellation test (attention and working memory) [4]; the Boston Naming Test [5] and the language subtest of ACE-R; semantic [5] and phonemic fluencies [6]; the Hooper Visual Organization test [7] and the visuospatial subtest of ACE-R (visuospatial abilities). Patients were defined as having severe dementia in accordance with MDS-Task Force criteria [8]. Mood was evaluated with the Hamilton Depression Rating Scale score [9], Hamilton Anxiety Rating scale score [10] and Apathy Evaluation Scale [11].

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Supplementary Figure 1. Non-candidates > candidates for DBS resting-state functional connectivity of the bilateral STN seed region. Results are overlaid on the Montreal Neurological Institute template in neurological convention, displayed at $p < 0.05$ family wise error corrected for multiple comparisons (with age, sex, LEED, UPDRS total, UPDRS II, UPDRS III, and UPDRS IV subscore variables as covariates), implementing the threshold-free cluster enhancement. Colored bar represents Z values. DBS, deep brain stimulation; LEED, Levodopa equivalent daily dose; STN, subthalamic nucleus; UPDRS, Unified Parkinson's Disease Rating Scale.

