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Short communication

Longitudinal study of speech and dual-task performance in Parkinson's disease patients treated with subthalamic nucleus deep brain stimulation

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ABSTRACT

Introduction: Impairments in speech and executive functions are both observed in Parkinson's disease (PD) and might be influenced by subthalamic nucleus deep brain stimulation (STN-DBS). We investigated the effects of STN-DBS on speech and executive functions and their mutual interference in PD.
Methods: 14 PD patients eligible for bilateral STN-DBS (PD-DBS), and 16 PD patients with best medical treatment (PD-BMT) were included. Global cognition, executive functions (inhibition and verbal fluency), speech tasks with acoustic measures, and a dual-task (DT) combining a speech task with a Go or Go/NoGo task were performed at baseline and 12 months follow-up. A normative group of matched healthy participants was included at baseline for the evaluation of speech and DT performance.
Results: In both patient groups, global cognition mildly decreased after 12 months ($p < .001$). PD-DBS showed decreased inhibition ($p = .016$) whereas PD-BMT deteriorated in vowel articulation ($p = .011$). Using the DT paradigm, PD-DBS showed a slowing of speech rate after 12 months ($p = .009$) in contrast to PD-BMT ($p = .203$).
Conclusion: STN-DBS does not seem to impair speech and global cognition but might affect certain executive functions (notably inhibition). Speech-cognition interference is relatively preserved in PD patients, even though PD-DBS present larger DT cost on speech rate at 12 months post-DBS compared to PD-BMT. An evaluation with a longer follow-up using a larger sample is needed to confirm long-term effects.

1. Introduction

Impaired speech and executive functions - both frequently observed in Parkinson's disease (PD) - may occur in early stages and deteriorate with disease progression [1,2]. STN-DBS considerably improves cardinal motor symptoms in PD but its effects on speech (hypokinetic dysarthria) are controversial [3]. Positive effects have been reported for features of dysarthria specific to PD (e.g. voice loudness and glottal tremor variations) while negative effects have been described for features of dysarthria non-specific to PD (e.g. intelligibility and articulation) [4]. Similarly, controversial effects of STN-DBS have been reported on cognition with deterioration of executive functions (e.g. phonemic verbal fluency and inhibition) [5,6] whereas global cognition seems to be unaffected.

The co-occurrence of speech and executive impairments in PD and their modulation by STN-DBS suggest a neuroanatomical link through frontostriatal circuits. Thus, a dual-task (DT) paradigm might offer a propitious method to investigate speech, executive functions, and their mutual interference after STN-DBS. Indeed, the existence of a DT cost indicates a sharing of common resources between the tested tasks [7].

The impact of cognitive load on motor function such as gait has been investigated for STN-DBS previously using a DT design [8]. In this study, we focused on a DT paradigm combining speech and executive functions in PD as multitasking in everyday life frequently involves both functions. Acoustic measures of speech were performed for a more fine-grained and objective investigation relative to the commonly used perceptual assessments [4,8]. In order to differentiate stimulation effects from disease progression a control patient group with best medical treatment was included.

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2. Methods

2.1. Participants

14 PD patients scheduled for bilateral STN-DBS (PD-DBS) in the Geneva University Hospitals were compared to 16 aged-matched PD patients with best medical treatment (PD-BMT). A control group of 16 healthy subjects (HC) allowed for the experimental tasks (speech and DT) comparisons. Inclusion criteria and demographic variables are presented in the supplementary materials (S1).

The groups were matched on age, gender and education (see S1). At baseline (t0), PD-DBS had higher levodopa equivalent daily dose (LEDD) and disease severity (Hoehn & Yahr [10]) than PD-BMT. At t1, PD-DBS ON-Med ON-stimulation had lower LEDD and less motor symptoms (UPDRS III score [11]) than PD-BMT ON-Med (see Table 1). The patient groups showed similar performance on cognitive and speech variables (see results section 3.1).

2.2. Procedures

The study was approved by the local ethical committee (CCER: n° 2015-00028-(15.258)) and participants provided written informed consent. Standard clinical treatment was not impacted by the study. For patients, speech and cognitive tests (including global cognition and certain executive functions assessed using inhibition and verbal fluency tests), DT experiment, and motor examination (UPDRS part III [11]) were performed at t0 (<4 months before surgery for PD-DBS) and t1 (12 ± 4 months after t0). HC were tested only at baseline in order to obtain normative values for speech and DT assessment (see S2 for a procedure overview).

A detailed description of cognitive, speech and DT measures is available in S3. *Speech* was assessed using several acoustic measures of MonPaGe computerized battery [9]: voice quality composite score, articulation quality index (aperture index), and speech rate composite score (syllable/sec).

Global cognition was assessed using the total score of Mattis dementia rating scale (DRS) [12]. Specific aspects of *executive functions* were evaluated with the Stroop test [13] (inhibition index), and verbal fluency as number of correct words per 1 min for semantic (animals) and phonemic (words beginning with the letter P) conditions [14].

The computerized *DT experiment* comprised a speech task (reciting continuously weekdays at comfortable speed) and two visuo-motor tasks (processing speed: Go, and inhibition: Go/NoGo) in single and DT condition. During the visuo-motor tasks, reaction time in response to a shape was assessed: a circle (Go task) and an "x" while no response was required for the "+" distractor (Go/NoGo task). For the DT, syllable rate (number of syllables per second), speech accuracy (ratio of correct words, i.e. no lexical or phonemic errors and correct sequences of weekdays), mean correct reaction time in milliseconds (RT), and manual accuracy (ratio of correct responses) were measured. To control for interindividual variations in single condition, measures were converted into a dual-task cost (DTC) index: (dual-single task)/single task performance. The index was reversed so that negative scores indicate a decreased performance. A detailed description of the DT can be found in Fournet et al. [15].

Table 1
Demographic and clinical characteristics of the two patients' groups.

	PD-DBS group	PD-BMT group	Group comparison
N	14	16	
Age at t0 in years[a]	58.79 (7.89)	64.31 (7.70)	$F(1, 28) = 3.76$, $p = .063$
Gender	F = 5; M = 9	F = 8; M = 8	$\chi^2(1) = 0.62$, $p = .431$
Level of education[b]	1 = 2; 2 = 6; 3 = 6	1 = 1; 2 = 5; 3 = 10	$\chi^2(2) = 1.31$, $p = .520$
Disease duration at t0 in years	8.21 (3.89)	6.88 (4.90)	$F(1, 28) = 0.67$, $p = .418$
Hoehn & Yahr score at t0	2.71 (0.73)	2.06 (0.85)	Z adj. = 2.12, **p = .034**
LEDD[c] at t0 in mg	1348.50 (511.97)	724.56 (442.47)	$F(1, 28) = 12.83$, **p = .001**
LEDD at t1 in mg	534.86 (308.72)	863.91 (365.71)	$F(1,28) = 6.98$, **p = .013**
UPDRS part III score at t0	16.071 (9.76)	18.19 (10.60)	$F(1, 28) = 0.32$, $p = .576$
UPDRS part III score at t1	11.21 (6.93)	20.50 (9.55)	$F(1,28) = 9.05$, **p = .006**
Side of body with more severe motor symptoms at t0	Left = 4/ Right = 10	Left = 8/ Right = 8	$\chi^2(1) = 1.43$, $p = .232$

[a] Mean and Standard deviation.
[b] 1: less than secondary school; 2: secondary school accomplished; 3: university degree.
[c] Levodopa Equivalent Daily Dose.

2.3. Analyses

2.3.1. T0 comparisons

One-way analyses of variances (ANOVA) were used with group as between factor. For the DT, a mixed ANOVA was performed adding visuo-motor task as within factor. Post-hoc comparisons were performed with Tukey Honestly Significant Difference (HSD). Critical p-value was set at .05. The analyses were performed using Statistica 14.0.14 software [16].

2.3.2. Patients' follow-up assessment from t0 to t1

Linear mixed models with likelyhood ratio tests were used for speech and cognitive measures with time as within factor, group as between factor, and their interaction. LEED and Hoehn & Yahr score at t0 were entered as covariates. Critical p-value was set at 0.05 except for interactions post-hoc tests for which it was adjusted at 0.025 (two comparisons). The same analysis was performed for DTC indexes adding the visuo-motor task and its interactions. Statistical analysis is detailed in the supplementary materials (S5).

Abnormally skewed distributions were log-transformed (voice composite score, Mattis-DRS, Stroop, semantic verbal fluency, manual RT DTC). Similarly, a non-parametrical Friedman ANOVA was used for manual accuracy.

3. Results

One PD-DBS patient was excluded from the DT analysis due to technical problems and two other patients (one PD-DBS, one PD-BMT) could not perform the Stroop task (developmental dyschromatopsia).

Performance of patients in speech, cognitive tests, and DT at t0 and t1 are presented in Table 2. Descriptive statistics are reported untransformed and only significant effects are presented in the text below.

3.1. T0 comparisons

The voice composite score was significantly different between groups ($F(2,43) = 45.56$, $p < .001$, $\eta^2p = .68$) with post-hoc comparisons showing a higher performance in HC relative to PD-BMT ($p < .001$) and to PD-DBS ($p < .001$), without significant difference between the two patients groups ($p = .410$). No other results were significant for speech and cognition. In DT, a significant task effect was found on RT of the visuo-motor task ($F(2,42) = 70.83$, $p < .001$, $\eta^2p = .63$) indicating more severe DTC for RT in Go compared to Go/NoGo task ($M_{Go} = -0.29$, $SD_{Go} = 0.19$; $M_{Go/NoGo} = -0.08$, $SD_{Go/NoGo} = 0.15$). For complete statistical results see S4.

Table 2
Descriptive results on speech, cognition, and dual-task.

	PD-DBS		PD-BMT	
	t0	t1	t0	t1
	M (SD)	M (SD)	M (SD)	M (SD)
Speech				
Voice composite score	5.79 (0.93)	5.32 (0.58)	5.35 (0.79)	5.06 (0.66)
Aperture ratio	**1.05 (0.22)**	**1.10 (0.18)**	**1.09 (0.14)**	**0.99 (0.17)**
Speech rate (syll./sec.)	4.72 (0.56)	4.77 (0.55)	4.46 (0.51)	4.50 (0.59)
Cognition				
VF semantic (words/min.)	17.79 (5.34)	18.50 (5.11)	18.63 (5.77)	21.06 (6.98)
VF phonemic (words/min.)	**12.93 (5.85)**	**11.43 (4.75)**	**14.31 (4.73)**	**16.00 (4.27)**
Stroop inhibition index	**1.87 (0.57)**	**2.15 (0.57)**	**2.08 (0.60)**	**1.89 (0.34)**
Mattis DRS total score	140.64 (3.41)	137.93 (5.33)	140.19 (2.64)	137.63 (4.01)
Dual-task				
Syllablerate DTC Go	**0.04 (0.09)**	**−0.01 (0.08)**	**0.01 (0.09)**	**0.01 (0.08)**
Syllablerate DTC Go/NoGo	**−0.01 (0.10)**	**−0.02 (0.08)**	**−0.05 (0.10)**	**0.01 (0.11)**
Speech Accuracy DTC Go	0 (0.03)	0 (0.02)	−0.01 (0.04)	−0.01 (0.02)
Speech Accuracy DTC Go/NoGo	0.01 (0.04)	0 (0.01)	−0.01 (0.04)	−0.01 (0.02)
Manual RTs DTC Go	−0.34 (0.23)	−0.27 (0.12)	−0.30 (0.24)	−0.27 (0.23)
Manual RTs DTC Go/NoGo	−0.09 (0.22)	−0.13 (0.18)	−0.12 (0.16)	−0.05 (0.11)
Manual accuracy DTC Go	−0.06 (0.11)	−0.03 (0.04)	−0.03 (0.08)	−0.01 (0.04)
Manual accuracy DTC Go/NoGo	−0.01 (0.12)	−0.01 (0.05)	−0.04 (0.07)	0.01 (0.07)

VF: Verbal Fluency.
In bold: variables showing a different evolution between groups (significant time by group interaction). To be noted, for Syllablerate the interaction did not vary upon the secondary task.

3.2. Follow-up assessment: speech and cognition

A significant effect of time was found on voice composite score, ($F(1, 29.18) = 23.70$, $p < .001$), showing that voice quality improved from t0 to t1 ($M_{T0} = 5.56$; $SD_{T0} = 0.87$; $M_{T1} = 5.19$; $SD_{T1} = 0.63$). For vowel aperture ratio, a significant effect of time by group interaction was observed ($F(1, 29.22) = 4.22$, $p = .049$). Post-hoc testing showed no effect of time for PD-DBS ($p = .821$) but a deterioration over time for PD-BMT ($p = .011$).

For Mattis-DRS, time effect was significant ($F(1, 29.18) = 23.70$, $p < .001$) with a decrease of performance at t1 ($M_{T0} = 140.40$; $SD_{T0} = 2.98$; $M_{T1} = 137.77$; $SD_{T1} = 4.59$). For Stroop index, a significant interaction between time and group was found ($F(1, 27.56) = 8.22$, $p = .008$). Post-hoc testing showed that inhibition performance significantly deteriorated at t1 for PD-DBS ($p = .016$) but not for PD-BMT ($p = .200$). For phonemic verbal fluency, a significant interaction between time and group was found ($F(1, 30) = 6.01$, $p = .020$), and performance showed a trend of improvement at t1 in PD-BMT ($p = .076$) while no significant difference was observed for the PD-DBS group ($p = .137$).

3.3. Follow-up assessment: dual-task

On *syllablerate* DTC, task effect was significant ($F(1, 84.58) = 5.34$, $p = .023$) as well as time by group interaction ($F(1, 83.76) = 8.57$, $p = .004$). Overall, a stronger negative DTC was found on syllablerate when the secondary task was Go/NoGo ($M = −0.02$; $SD = 0.09$) compared to Go ($M = 0.01$; $SD = 0.08$). Post-hoc test indicated that the DTC was significantly deteriorated after 12 months for PD-DBS ($M_{T0} = 0.01$; $SD_{T0} = 0.10$; $M_{T1} = −0.03$; $SD_{T1} = 0.06$; $p = .009$) but not for PD-BMT ($M_{T0} = −0.02$; $SD_{T0} = 0.10$; $M_{T1} = 0.01$; $SD_{T1} = 0.09$; $p = .203$). For visuo-motor RT, task effect was significant ($F(1, 84.07) = 67.33$; $p < .001$) indicating a stronger DTC for RT in Go ($M = −0.29$; $SD = 0.19$) compared to Go/NoGo ($M = −0.08$; $SD = 0.14$). Speech accuracy was not analyzed due to ceiling effect and no significant effect was found for manual accuracy.

4. Discussion

In this longitudinal study, we investigated the impact of STN-DBS in PD patients on speech, global cognition, and certain executive functions.

At baseline, no difference between PD-DBS and PD-BMT was found on speech, global cognition, inhibition, verbal fluency and motor symptoms (UPDRS III score). Compared to PD-BMT, the PD-DBS group presented a more severe disease (Hoehn & Yahr score) at t0, however this parameter did not contribute to the longitudinal analysis. In line with the well-known effects of STN-DBS, the PD-DBS group presented a remarkable improvement of motor symptoms along with a reduction of medication.

4.1. Evolution in speech and cognitive tests

At baseline, both patient groups showed poorer *voice quality* relative to HC, concordant with the initial voice disorder in PD hypokinetic dysarthria [1]. At one year follow-up, voice quality was slightly improved for both patients' groups suggesting a learning effect. A previous study [4] showed stable voice performance which is consistent with a relative preservation of voice after STN-DBS. A shorter disease duration and possibly less severe dysarthria might explain the learning effect observed in the present study.

Interestingly, speech seemed particularly preserved after STN-DBS since a deterioration was observed only in PD-BMT for *vowel articulation quality*. This finding suggests a potential protective effect of STN-DBS on the reduced amplitudes of the vocal tract movements (hypo-articulation) that characterizes hypokinetic dysarthria.

A decline of *global cognition* (Mattis-DRS) over one year was present in both groups and with similar magnitude suggesting a link with disease progression and not a direct consequence of STN-DBS - in agreement with previous findings [17].

Two results, however, suggest that *executive functions* are at risk when undergoing STN-DBS. First, PD-BMT tended to improve in phonemic verbal fluency after 12 months probably because of practice effect which was not observed in PD-DBS. Other studies showed that STN-DBS had a detrimental effect on verbal fluency [18] which might be attributed to dysfunctions of circuits involving the left frontal cortex. Worsening of semantic fluency might not have been captured due to our limited sample size. Alternatively, phonemic fluency might involve distinct executive processes [19] more sensitive to STN-DBS as compared to semantic fluency. Second, worsening of Stroop inhibition index for PD-DBS in this study is in line with previous studies suggesting a decreased inhibition after STN-DBS [5,6].

4.2. Dual-task performance

Studying speech in dual-task settings seems important as it reflects multitasking in everyday life as previously outlined in a study on speech intelligibility [20]. The dual-task paradigm is an original method to investigate speech, executive aspects, and their interferences in demanding attentional conditions. In both PD-BMT and PD-DBS groups, DTC on speech was more severe when speech and Go/NoGo tasks were simultaneously performed. In contrast, DTC on RT was more severe when speech and Go tasks were simultaneously performed. These results are similar to performance patterns presented by healthy elderly on the same DT attributed to a shift of attentional focus between speech and visuo-motor task depending on visuo-motor task complexity level [15]. Such effect appears to be consistent with the capacity limit model [7]

where a pool of attentional resources has to be shared between two parallel tasks.

A significant interaction between group and time on *syllablerate* DTC was observed indicating a negative impact of STN-DBS on speech. Indeed, DTC for articulation rate was more severe one year after surgery for PD-DBS but not for PD-BMT. Given that acoustic measures of articulation and speech rate in PD-DBS did not worsen over time (in contrast to inhibition), this DT effect could be related to a decrease of executive functions involved in speech control.

4.3. Limitations

A drop-out of 7 out of 22 patients needs to be mentioned as a limitation of our study, yet, only one patient was excluded due to severity of symptoms. More details figure in the supplementary materials (S1). Studies with larger samples and a longer follow-up are needed to better understand the impact of STN-DBS on pathophysiological mechanisms in speech and executive functions in PD.

5. Conclusion

Stable speech performance was found 12 months after STN-DBS. The global decline in cognition seems to reflect disease progression rather than a consequence of STN-DBS. Yet, some changes in executive functions - particularly verbal fluency, inhibition, and the ability to maintain speech rate under dual-task - might be precipitated by STN-DBS.

The absence of deleterious effects of STN-DBS on speech in single task and the marginal impact on executive function 12 months post-surgery is an important information for clinicians and patients who are weighing benefits and potential side-effects expected from surgery.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.parkreldis.2022.03.003.

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