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ORIGINAL ARTICLE

Clinical predictors of speech changes after subthalamic neurostimulation in Parkinson's disease

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Abstract

Objective To identify preoperative clinical predictive factors of postoperative speech changes in Parkinson's disease (PD) patients with bilateral subthalamic nucleus deep brain stimulation (STN-DBS).

Methods Demographic variables, neuroimaging data, and clinical characteristics were retrospectively collected from consecutive PD patients, before, 1 and 10-years after bilateral STN-DBS at the Grenoble University Hospital (France) from 1993 to 2015. Predictors of postoperative speech changes (demographic, clinical and MRI variables) were assessed with univariate and multivariate logistic regression analyses. We considered as "event" a worsening of speech subscore (UPDRS item 18; MDS-UPDRS item 3.1) in the postoperative on-stimulation/off-medication (1-year follow-up) or under chronic treatment (10-years follow-up) conditions compared with the preoperative off-medication condition.

Results 324 PD patients (males: 196; disease duration at surgery: 11.10 [±4.13] years; age at surgery: 56.25 [±8.52] years) were included in the analysis. Overall, the speech item of the clinical rating did not change in 138 patients (42.6%), it improved in 113 patients (34.9%) and worsened in 73 patients (22.50%) 1-year after surgery. The preoperative off-medication speech item score and the degree of motor improvement after surgery in the med-off condition predicted the 1-year postoperative speech change. In the long-term subgroup (n=51) the preoperative percentage of daily time spent with fluctuations was associated with long-term speech worsening.

Interpretation Effects of STN-DBS on speech can substantially vary in PD patients. Predictors of short-term speech deterioration appears to be related to preoperative off-medication speech impairment and degree of motor improvement after surgery.

Keywords Deep brain stimulation · Dysarthria · Parkinson's disease · Subthalamic nucleus · Speech

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Introduction

In patients with advanced Parkinson disease (PD), deep brain stimulation of the subthalamic nucleus (STN-DBS) is a well- recognized effective treatment for motor symptoms in both the short- and long-term follow-up [1–4]. However, the impact of STN-DBS on speech can vary, improving, being stable or worsening, the latter possibly counterbalancing the overall benefits of STN-DBS [5, 6]. Speech worsening after surgery is not a rare occurrence, indeed the prevalence of DBS-related speech issues has reported to be around 9.3% [6, 7]. It is currently assumed that although speech loudness or voice quality can be improved after STN-DBS, a decrease in speech intelligibility in the short-term after surgery may arise [8, 9]. The induction of dysarthria is a well-known adverse effect of STN-DBS in some patients, probably as a result of the spread of current-to-adjacent pathways [6, 10–12], such as the cerebello-thalamic or corticobulbar fibers [11, 13, 14].

In particular different clusters have been identified including: stuttering type, strained voice type and spastic dysarthria type which are linked to the current diffusion to different structures including corticobulbar and cerebello-thalamo-cortical fibres [10].

As a consequence, the patient's satisfaction concerning DBS surgery, particularly with regard to dysarthria and reduced ability to communicate with their family, can be markedly reduced [9, 15]. Unfortunately, if present, DBS-induced speech issues are not always easy to manage [16].

In the past 20 years, several preoperative predictive factors of both short- and long-term motor outcome after STN-DBS have been identified [7, 17–19]. In particular, the preoperative levodopa response, the motor phenotype (tremor-dominant), the cognitive status, the presence of vascular lesions on preoperative brain MRI, and the disease severity in the off-medication condition have been identified as the main clinical predictors of short-term motor outcome after STN-DBS [7, 17–20]. However, only a few studies have assessed the presence of preoperative predictors of speech outcome in the short- and long-term after surgery. These studies have shown that the most significant predictive factors for speech deterioration after surgery were a lower pre-operative speech intelligibility in the on-medication condition, a longer disease duration, a medially placed active electrode contact in the left hemisphere, and capsular stimulation [11, 15, 21]. Nevertheless, these studies have as main limitation the analysis of small cohorts of PD patients treated with STN-DBS. To date, no study has tested the presence of predictors of speech changes in large cohorts of operated patients. This was the objective of our study, in order to confirm previous or find new predictive factors of postoperative speech modifications in a large cohort of PD patients treated with bilateral STN-DBS.

Materials and methods

Study population

All consecutive PD patients who underwent bilateral STN-DBS at the Grenoble Alpes University Hospital (Grenoble, France) from 1993 to 2015 were retrospectively evaluated. At time of surgery, all patients fulfilled the UK Brain Bank criteria for PD[18] and the following inclusion conditions: presence of disabling motor complications (i.e. motor fluctuations or levodopa-induced dyskinesia) not optimized with anti-parkinsonian medication, and age at surgery lower than 75 years [1, 17, 22]. Exclusion criteria were: presence of dementia, ongoing severe psychiatric disorders, severe atrophy or diffuse cerebral ischemic lesions on brain MRI, and systemic comorbidities interfering with surgery [1, 17, 22]. The institutional research centre authority of the Grenoble Alpes University Hospital approved the study protocol that was registered with clinicaltrials.gov (ClinicalTrials.gov Identifier: NCT03528460) on May 17, 2018.

Surgical procedure

The surgical procedure has been previously described in detail [23–25]. A post-operative brain MRI performed within the first week after surgery allowed to verify the correct leads positioning and the presence of surgical complications. Few days after the electrodes positioning, two single-channel or one double-channel implantable pulse generators (IPG) (Itrel II, Soletra, Kinetra; Medtronic, Minneapolis, MN, USA) were positioned in the subclavicular region under general anaesthesia [23–25].

Clinical assessment

Patients were evaluated before surgery (baseline), 1-year and 10-years after surgery.

At baseline, patients were assessed in both the "defined-off" and in the "defined-on" medication conditions [17, 23], using the Hoehn and Yahr scale (H&Y) [26], the Unified Parkinson's Disease Rating Scale (UPDRS, from 1993 to 2010) and, from 2011, with the Movement Disorder Society-sponsored revision of the UPDRS (MDS-UDPRS) [27]. One year after surgery, patients were re-evaluated using the UPDRS (up to 2011) or the MDS-UPDRS (from 2012) in the on-stimulation/off-medication and on-stimulation/

on-medication conditions while 10-years after surgery under chronic medication and stimulation [28].The UPDRS-III total scores at baseline and at 1-year after surgery collected before 2011 were regressed to the corresponding MDS-UPDRS scores using the available conversion formula [29].

A comprehensive neuropsychological evaluation was performed both at baseline and at 1-year follow-up, including the Mattis Dementia Rating Scale (MDRS) for global cognitive assessment, the Frontal Score for the assessment of frontal-lobe dysfunction, and the Beck Depression Inventory-II for mood evaluation (BDI-II) [22, 23].

The total amount of the dopaminergic treatment was determined using the levodopa equivalent daily dose (LEDD) [30]. Furthermore, for each patient, stimulation parameters (frequency [Hz], pulse width [µs], amplitude [V]) and type of stimulation (monopolar, bipolar, double monopolar) at 1-year follow-up were collected.

Statistical analysis

Descriptive statistics was used to describe demographical and clinical characteristics at baseline and at postoperative evaluations. Continuous variables were expressed as mean (±SD) and median (range) while frequencies and percentage were calculated for categorical variables.

The primary objective was to investigate potential predictors of speech change (improvement or worsening) after bilateral STN-DBS. For statistical purposes, we considered as "event" an improvement or a worsening of the speech item (UPDRS item 18; MDS-UPDRS item 3.1) in the on-stimulation/off-medication condition 1-year after surgery (short-term follow-up) or chronic treatment condition 10-years after surgery (long-term follow-up) both compared with the preoperative off-medication-condition.

Several variables were selected as independent covariates for regression modelling, including sex, age at surgery, PD duration at surgery, age of PD onset, history of hyperdopaminergic behavioural disorders, years of fluctuations and dyskinesia at surgery, percentage of daily time spent with dyskinesia or fluctuations (dichotomized if greater or less than cut-off score of 50%), presence of white matter hyperintensities of vascular origin (WMH) on preoperative brain MRI, preoperative scores including: MDS-UPDRS part-III score, H&Y staging and speech item (UPDRS item 18; MDS-UPDRS item 3.1) in the off- and on-medication conditions; presence of gait (UPDRS item 29; MDS-UPDRS item 3.10) and postural stability (UPDRS item 30; MDS-UPDRS item 3.12) alterations with and without medication (alteration was present if the corresponding score was equal to or more than one), levodopa responsiveness, LEDD, BDI-II score, MDRS score, Frontal Score and PD motor phenotype [i.e. dominant postural instability and gait disorder (PIGD), indeterminate and tremor-dominant (TD)] [31]; stimulation parameters (amplitude, frequency and pulse width).

In addition, the percentage change between the MDS-UPDRS part-III score in the on-stimulation/off-medication condition one year after surgery and the baseline score in the off-medication condition (motor outcome of STN-DBS) was also calculated and included among the variables. Univariate and multivariate logistic regression analyses were applied to identify independent factors associated with speech item change (worsening or improvement) at 1-year and 10-years follow-up. Only significant variables from univariate analyses were entered into the multivariate model to determine the optimal combination of variables. Correlated independent variables were excluded from the model to avoid multicollinearity. Results were reported as standardized β coefficient (standardized-β) followed by 95% confidence intervals (CI) of β coefficient (95% CI) and p value. A <0.05 p value was considered significant.

Furthermore, in order to assess the short-term cognitive and mood changes, we compared pre- and postoperative MATTIS, BDI-II and Frontal scores applying the Wilcoxon signed rank tests. Statistical analyses were performed using the IBM SPSS Statistics for Windows version 20.0 (IBM, Armonk, NY, USA).

Results

A total of 546 PD patients operated on with bilateral STN-DBS surgery from 1993 to 2015 were retrieved from the Movement Disorders Center database of the Grenoble University Hospital. From the analyses, 222 patients were excluded because of: incomplete medical records and missing data ($n=173$), surgical complications responsible for persistent neurological sequelae (i.e., symptomatic brain intracerebral or intraventricular hemorrhage, ischemic infarction, extradural hematoma) ($n=18$), other brain surgical procedures ($n=17$), and electrode misplacement ($n=14$). Finally, 324 patients were included. The main baseline clinical characteristics are described in Table 1 whereas stimulation parameters and settings are reported in Table 2. Supplementary Table 1 reports the baseline characteristics of the long-term subgroup ($n=51$).

Globally, speech score decreased significantly after surgery, by comparing the baseline off-medication condition (1.34 [±0.85]; 1.00 [0.00–4.00]) with the postoperative on-stimulation/off-medication condition (1.18 [±0.88]; 1.00 [0.00–4.00]) (p=.003) (Fig. 1).

In details, 138 patients (42.60%) did not show any change of the speech MDS/UPDRS item post-operatively, 113 patients (34.90%) presented with an improvement, and 73 patients (22.50%) had speech worsening at 1-year after

Table 1 Demographic and clinical characteristics of the PD patients at baseline

Variable	N=324 No. (%); mean [SD]; median {range}
Sex	
Male	196 (60.50%)
Female	128 (39.50%)
Missing data	0 (0.00%)
PD duration (years)	11.10 [±4.13]; 11.00 {3.00–28.00}
Age (years)	56.25 [±8.52]; 57.00 {29.00–74.00}
Age at PD onset (years)	45.27 [±8.34]; 46.00 {12.00–64.00}
MDS-UPDRS part-III in off-med condition	52.39 [±17.46]; 50.30 {16.0–105.40}
MDS-UPDRS part-III in on-med condition	17.66 [±9.47]; 16.00 {2.0–62.30}
Speech item in off-med condition	1.34 [±0.84]; 1.00 {0.0–4.00}
Speech item in on-med condition	0.80 [±0.78]; 1.00 {0.0–4.00}
Levodopa responsiveness (% of improvement)	68.42 [±14.90]; 70.24 {7.14–97.43}
Hoehn & Yahr scale off-med	3.15 [±0.98]; 3.00 {1.50–5.00}
Hoehn & Yahr scale on-med	1.89 [±0.70]; 2.00 {0.00–3.00}
PD motor subtype	
PIGD	161 (49.70%)
Indeterminate	41 (12.70%)
TD	114 (35.20%)
Missing data	8 (2.50%)
History of Hyperdopaminergic disorders	
No	202 (62.30%)
Yes	94 (29.10%)
Missing data	28 (8.60%)
Presence of gait alterations in off-med condition	
No	44 (13.60%)
Yes	271 (83.60%)
Missing data	9 (2.80%)
Presence of gait alterations in on-med condition	
No	177 (54.60%)
Yes	138 (42.60%)
Missing data	9 (2.80%)
Presence of postural stability alterations in off-med condition	
No	48 (14.80%)
Yes	265 (81.80%)
Missing data	11 (3.40%)
Presence of postural stability in on-med condition	
No	140 (43.20%)
Yes	173 (53.40%)
Missing data	11 (3.40%)
Time spent with dyskinesia	
≤50% of waking day	248 (76.50%)
>50% of waking day	62 (19.10%)
Missing data	14 (4.30%)
Time spent in the OFF state	
≤50% of waking day	240 (74.10%)
>50% of waking day	69 (21.30%)
Missing data	15 (4.60%)
BDI-II	11.46 [±7.70]; 9.00 {0.00–44.00}

Table 1 (continued)

Variable	$N=324$ No. (%); mean [SD]; median {range}
MDRS	137.06 [±5.91]; 138.00 {108.00–144.00}
Frontal score	39.34 [±7.60]; 41.00 {17.60–50.00}
LEDD	1354.17 [±574.09]; 1295.00. {265.00–4200.00}

Hyperdopaminergic disorders: impulse control disorders, punding, dopamine dysregulation syndrome.

Beck Depression Inventory-II (BDI-II); Dominant postural instability and gait disorder (PIGD); Levodopa equivalent daily dose (LEDD); Magnetic Resonance Imaging (MRI); Mattis Dementia rating scale (MDRS); Parkinson's Disease (PD); Young-onset PD (YOPD); White matter hyperintensities of vascular origin (WMH); Tremor dominant (TD).

Table 2 Stimulation parameters at postoperative evaluation

Stimulation parameters and settings	Total $n=324$ patients *N.* (%), mean, [±SD]; median {range}
Frequency setting	
High frequency	312 (96.30%)
Low frequency	1 (0.30%)
Stimulation not active	2 (0.60%)
Missing data	9 (2.80%)
Left STN	
Type of stimulation	
Single monopolar	278 (85.80%)
Bipolar	29 (9.00%)
Double monopolar	9 (2.80%)
Missing data	8 (2.50%)
Voltage (V)	2.79 [±0.65]; 2.80 {0.80−5.50}
Frequency (Hz)	137.35 [±16.83]; 130.00 {80.00–200.00}
Pulse width (usec)	61.77 [±7.16]; 60.00 {52.00–90.00}
Right STN	
Type of stimulation	
Single monopolar	288 (8.90%)
Bipolar	20 (6.20%)
Double monopolar	9 (2.80%)
Missing data	7 (2.20%)
Voltage (V)	2.77 [±0.62]; 2.80 {1.00 −4.70}
Frequency (Hz)	137.24 [±17.48]; 130.00 {60.00–200.00}
Pulse width (usec)	61.49 [±6.60]; 60.00 {52.00–90.00}

surgery. When comparing stimulation parameters and settings between the two cohorts we did not find significant differences. Besides, bilateral STN-DBS significantly reduced motor symptoms of the disease with a mean percentage reduction of 49.34% (±0.24.32; 51.76 [−41.40–93.77]) of the MDS-UPDRS part-III score by comparing the postoperative on-stimulation/off-medication condition with the preoperative off-medication condition. In addition, a reduction of the MATTIS score one year after surgery from preoperative (137.06 [±5.91]; 138.00 [108.00–144.00]) to postoperative (135.47 [±7.17]; 138.00 [103.00–144.00])) values was also found ($p=.003$) together with a significant reduction ($p=.001$) of both BDI-II (preoperative: 12.32 [±8.28], 10.00 [0.00–44.00]; postoperative: 10.33 [±7.86]; 9.00 [0.00–37.00]) and Frontal Score (preoperative: 40.33 [±7.06], 42.00 [23.30–50.00]; postoperative 38.79 [±8.32], 41.00 [15.70–50.00]). On the contrary, speech score significantly increased in the long-term follow-up by comparing the baseline off-medication condition (1.27 [±0.75]; 1.00 [0.00–3.00]) with the chronic treatment condition 10-years after surgery (1.94 [±0.94]; 2.00 [0.00–4.00]) ($p<.001$) in the long-term subgroup.

Predictors of speech worsening after STN-DBS

Direct logistic regression was performed to assess the impact of independent factors on the worsening of speech after bilateral STN-DBS, and six preoperative, off-medication, variables were retained for the multivariate analysis: the MDS-UPDRS part III score, the H&Y staging, the MDS-UPDRS speech item, the presence of postural instability, the LEDD, and the motor phenotype; a seventh variable considered was the pre- vs. post-operative percentage of variation of the MDS-UPDRS part III score, off medication (Table 3). The full model containing all predictors was significant, χ^2 (7, $N=324$) = 46.806, $p<.001$, indicating that the model was able to distinguish between PD patients who developed and did not develop speech worsening after bilateral STN-DBS. The model explained between 14.2% (Cox and Snell R square) and 21.8% (Nagelkerke R squared) of the variance in speech worsening after surgery, and correctly classified 79.1% of cases. As shown in Table 3, only two of the independent variables made a significant contribution to the model: the pre- vs. post-operative percentage of variation of the MDS-UPDRS part III score without medication, and the preoperative speech item in the off-medication condition, which was the strongest predictor of speech worsening after surgery. The odds ratio was of 0.38 (Table 3), indicating that for every additional point of speech score, PD patients were 0.38 times less likely to develop speech worsening after surgery, controlling for other factors in the model. In the long-term subgroup the preoperative percentage of daily time spent with fluctuations resulted the strongest predictor of long-term speech worsening after surgery (supplementary Table 2).

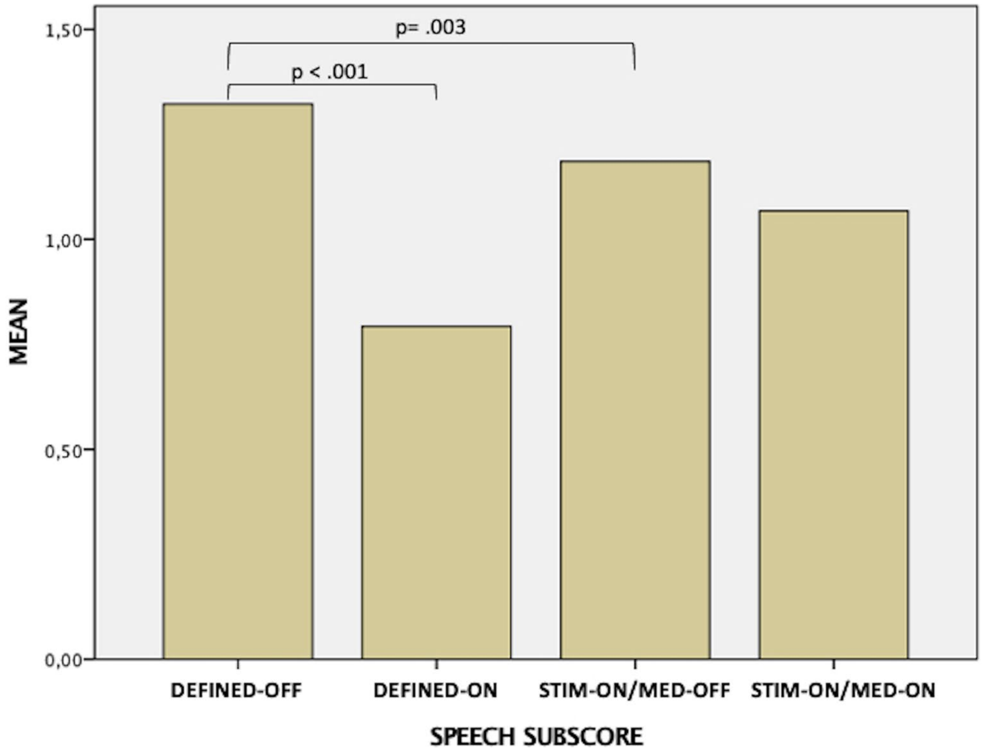

Fig. 1 Short-term changes of the MDS/UPDRS speech item score in the different preoperative and post-operative treatment conditions

Table 3 Factors influencing short-term speech worsening after STN-DBS ($n=324$)

Baseline variable	Univariate Analysis			Multivariate Analysis		
	Odds ratio	Odds ratio 95% CI	*p* Value	Odds ratio	Odds ratio 95% CI	*p* Value
Speech item in the off-medication condition	0.369	0.253 to 0.538	**<0.001**	0.380	0.240 to 0.601	**<0.001**
presence of postural instability in defined-off condition	0.435	0.223 to 0.846	**0.014**	0.825	0.357 to 1.904	0.652
MDS-UPDRS part-III off-medication	0.979	0.963 to 0.995	**0.009**	1.000	0.974 to 1.028	0.982
H&Y stage off-medication	0.714	0.533 to 0.958	**0.025**	1.162	0.741 to 1.821	0.513
LEDD	0.999	0.999 to 1.000	**0.027**	1.000	0.999 to 1.000	0.368
TD phenotype	1.934	1.096 to 3.414	**0.023**	1.772	0.848 to 3.704	0.128
% variation of the MDS-UPDRS part III score without medication*	0.981	0.971 to 0.992	.**< 0.001**	0.975	0.962 to 0.987	**<0.001**

Values are reported as standardized β coefficient, followed by 95% confidence intervals (CI) of β coefficient and p-values

* percentage variation between the MDS-UPDRS part-III score in the on-stimulation/off-medication condition at 1 year after surgery and the baseline score in the off-medication condition (motor outcome of STN-DBS)

Hoehn & Yahr scale (H&Y); Levodopa equivalent daily dose (LEDD); Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale Part-III (MDS-UPDRS III); Parkinson's Disease (PD); Tremor dominant (TD).

Predictors of short-term speech improvement after STN-DBS

Direct logistic regression was also performed to assess the impact of independent factors on the improvement of speech after surgery. The multivariate model retained seven preoperative, off medication, variables: the MDS-UPDRS part III score, the H&Y staging, the MDS-UPDRS speech item, the presence of postural instability, the LEDD, the motor phenotype and the PD duration at surgery; an eighth variable considered was the percentage of the pre- vs. post-operative percentage of variation of the MDS-UPDRS part III score (Table 4). The full model containing all predictors was statistically significant, χ^2 (8, $N=324$) = 115.505, $p<.001$, indicating that the model was able to distinguish between PD patients who developed and did not develop improvement of speech after surgery. The model explained between 31.4% (Cox and Snell R square) and 43.4% (Nagelkerke R squared) of the variance in speech improvement after surgery, and correctly classified 76.5% of cases. As shown in Table 4, the same two independent variables made a statistically significant contribution to the model: the pre- vs. post-operative percentage of variation of the MDS-UPDRS part III score and the pre-operative speech item off-medication.

Table 4 Factors influencing short-term speech improvement after STN-DBS ($n = 324$ PD patients)

Baseline variable	Univariate Analysis			Multivariate Analysis		
	Odds ratio	Odds ratio 95% CI	*p* Value	Odds ratio	Odds ratio 95% CI	*p* Value
PD duration at surgery (years)	1.061	1.004 to 1.121	**0.036**	1.008	0.921 to 1.081	0.953
Speech item in the off-medication condition	4.051	2.795 to 5.871	**0.000**	4.922	3.059 to 7.921	**<0.001**
Presence of postural instability in the defined-off condition	2.695	1.253 to 5.796	**0.011**	1.045	0.392 to 2.781	0.930
MDS-UPDRS part-III in off-medication	1.024	1.010 to 1.038	**0.001**	0.997	0.972 to 1.022	0.824
H&Y stage in off-medication	1.363	1.080 to 1.720	**0.009**	0.118	0.434 to 1.099	0.118
LEDD	1.001	1.000 to 1.001	**0.003**	1.000	1.000 to 1.001	0.130
TD phenotype	0.680	0.883 to 0.524	**0.004**	1.772	0.478 to 1.023	0.070
% variation of the MDS-UPDRS part III score without medication*	1.028	1.106 to 1.040	**<0.001**	1.047	1.030 to 1.064	**<0.001**

Values are reported as standardized β coefficient, followed by 95% confidence intervals (CI) of β coefficient and p-values

*Percentage variation between the MDS-UPDRS part-III score in the on-stimulation/off-medication condition at 1 year after surgery and the baseline score in the off-medication condition (motor outcome of STN-DBS)

Hoehn & Yahr scale (H&Y); Levodopa equivalent daily dose (LEDD); Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale Part-III (MDS-UPDRS III); Parkinson's Disease (PD); Tremor dominant (TD).

Again, in this case, the strongest predictor of speech improvement after surgery was the baseline score of the speech item in the off-medication condition, recording an odds ratio of 7.095; thus, indicating that for every additional point of speech score, PD patients were 7.095 times high likely to present with an improvement of speech after surgery, controlling for other factors in the model.

Discussion

In this large longitudinal cohort of PD patients operated on bilateral STN-DBS, the speech assessment provided by the item by the MDS-UPDRS in the preoperative off-medication condition and the degree of motor improvement after surgery, assessed by the MDS-UPDRS part III, predicted significantly the short-term postoperative speech outcome.

Using the UPDRS speech item ratings alone, a meta-analysis of 37 cohorts comprised of 921 patients reported an incidence of dysarthria of 9.30% as adverse event under STN-DBS [6, 7]. Several studies have reported that speech may improve only during the first two years after surgery, and then progressively returned to baseline by five years [8, 32, 33]. In particular, speech worsening has been reported in different cohort studies, with a prevalence of 70% three years after surgery [34], 57% at 5 years [35] and 90% at 8 years [36, 37]. Obviously, particularly for long-term studies also the disease progression should be taken into account for this worsening.

Results from our cohort confirm that speech can improve one year after bilateral STN-DBS, as demonstrated by the significant reduction of speech score after surgery in the off-medication condition. This has already been confirmed by a recent analysis from the EARLYSTIM data which showed that STN-DBS did not result in a consistent deterioration in blinded speech intelligibility assessment in PD patients with early motor complications two years after surgery, if compared with best medical treatment [8].

As mentioned above, the impact of STN-DBS on speech performance can be variable, and the available data still do not allow predicting the risk of the onset or deterioration of dysarthria at the individual patient level [6]. A previous study found a correlation of poorer speech outcome one year after surgery with higher presurgical general motor impairment in the on-medication condition, probably explained by the presence of a diffuse nondopaminergic degeneration and the possible link with axial symptoms [6, 9, 38]. On the contrary, in our cohort the severity of speech impairment in the preoperative off-medication condition emerged as the main clinical preoperative predictor of postoperative speech change as recently reported [39]. In particular, patients with a higher preoperative severity of speech impairment in the off-medication condition presented a reduced odd ratio of postoperative speech worsening, with a contemporary higher odd ratio of postoperative speech improvement. This is not surprising if considering that also for motor symptoms, the lesser preoperative severity in the off-medication condition represents a predictor of good motor outcome [7, 17]. This finding has been reported in a previous meta-analysis of 37 cohorts comprised of 921 patients [7], and subsequently confirmed in a large cohort study from our group [17].

Based on these results, we may propose that patients with a better speech before surgery could benefit from both preoperative/preparatory and early postoperative speech therapy interventions to limit the possible worsening of post STN-DBS speech. In this setting, a previous small-group study has assessed the effects of an intensive voice therapy (LSVT(®)LOUD) treatment in PD patients with or without STN-DBS confirming its usefulness particularly for voice and speech alterations [40]. However, it should be taken into account that these beneficial effects were more variable within the LSVT-DBS group highlighting the importance of an additional preoperative/preparatory intervention [40].

It should be considered that our findings may be influenced by a possible ceiling effect even if it has been reported that the ceiling effect of the MDS-UPDRS part III is comprised between 0.1–0.2% [27]. Furthermore, the degree of motor improvement after surgery also predicted postoperative speech outcome, indicating that patients with a higher motor benefit from stimulation have also a lower risk of speech worsening after surgery.

Keeping in mind that the induction or worsening of dysarthria after bilateral STN-DBS may occur as a result of the spread of current-to-adjacent pathways [6, 10, 11], we may hypothesize that patients with a more adequate leads location within the sensorimotor region of the STN may present better motor and speech outcomes. In this setting, the greater motor benefit may be directly due to the stimulation of the sensory-motor area as previously reported [41] whereas the lower risk of speech worsening may be related to the reduced risk of current spread and adverse effects. Unfortunately, this hypothesis cannot be confirmed in our study considering that it was not possible to define lead's location and the corresponding volume of tissue activated (VTA).

Concerning the long-term follow-up, we found that only the preoperative percentage of daily time spent with fluctuations predicted the long-term speech worsening after. Obviously, this is a preliminary result that has been obtained in a small subgroup of patients and need to be tested in larger cohorts in order to be confirmed. Moreover, several limitations of the study should be mentioned including: the retrospective monocentric nature of the study, the high number of patients excluded for incomplete medical records which could reduce the statistical power and potentially introducing bias; the low percentage of the variability explained by the model; the lack of specific speech scales or acoustic measures; the very broad period (1993–2015) considered for the analysis. Despite these limitations our findings come from one of the largest populations so far available, and we remain aware that future studies are still needed to better define the influence of lead location and speech worsening after surgery.

Conclusions

In our cohort, the severity of speech impairment in the preoperative off-medication condition and the percentage of motor improvement after surgery represented the main clinical preoperative predictors of speech changes one year after STN-DBS. Our results provide evidence that preoperative PD features can contribute to better address the foreseen speech outcome of STN-DBS surgery when counselling patients. Furthermore, this information should allow implementing preoperative and/or early speech interventions after surgery in patients treated with STN-DBS at higher risk of speech deterioration.

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Declarations

Ethics The work described here has been carried out in accordance with the Declaration of Helsinki. The institutional research centre authority of the Grenoble Alpes University Hospital approved the study protocol that was registered with clinicaltrials.gov (ClinicalTrials.gov Identifier: NCT03528460) on May 17, 2018.

Conflicts of interest Several authors received funds from Boston Scientific (BS), Medtronic (MT) manufacturers of DBS equipment, for work not related to this study. These include VF receiving honoraria for lecturing (BS, MT); SC receiving grants and personal fees (BS, MT); AC receiving grants from MT and reimbursement of travel expenses (BS, MT); EM receiving honoraria from MT and funds from AbelsonTaylor, Ipsen and French Association for Parkinson's Disease. FC, FB, AZ, SM, AG, ES, PP, FV, AS, SP, have nothing to report.

Data availability After a reasonable request, access to the data of this study might be granted by the authors.

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