

Serge Pinto
Michèle Gentil
Valérie Fraix
Alim-Louis Benabid
Pierre Pollak

Bilateral subthalamic stimulation effects on oral force control in Parkinson's disease

Abstract Dysarthria in Parkinson's disease (PD) consists of articulatory, phonatory and respiratory impairment. Bilateral subthalamic nucleus (STN) stimulation greatly improves motor disability, but its long-term effect on speech within a large group of patients has not been precisely evaluated. The aim of this study was to determine the

effect of bilateral STN stimulation on oral force control in PD. We measured forces of the upper lip, lower lip and tongue in twenty-six PD patients treated with bilateral STN stimulation. Measurements of the articulatory organ force, as well as a motor evaluation using the Unified Parkinson's Disease Rating Scale (UPDRS), were made with and without STN stimulation. Maximal voluntary force (MVF), reaction time (RT), movement time (MT), imprecision of the peak force (PF) and the hold phase (HP) were all improved with STN stimulation during the articulatory force task, as well as the motor examination scores of the UPDRS. It seems that the beneficial STN stimulation-induced effect on articulatory forces persisted whatever the duration of post-surgical follow-up. However,

dysarthria evaluated by the UPDRS was worse in two subgroups of patients with a one to two year and three to five year post-surgical follow-up, in comparison with a subgroup of patients with a three month follow-up. STN stimulation has a beneficial long-term effect on the articulatory organs involved in speech production, and this indicates that parkinsonian dysarthria is associated, at least in part, with an alteration in STN neuronal activity. Nevertheless, to confirm the persistence of the beneficial effect of STN stimulation on parkinsonian dysarthria, a longitudinal evaluation is still needed.

Key words Parkinson's disease · speech · dysarthria · STN stimulation · articulatory forces

Received: 2 January 2002
Received in revised form: 27 August 2002
Accepted: 3 September 2002

S. Pinto (✉) · M. Gentil · V. Fraix ·
A.-L. Benabid · P. Pollak
Service de Neurologie
CHU de Grenoble, BP 217
38043 Grenoble cedex 09, France
Tel.: +33 4 76 76 58 52
Fax: +33 4 76 76 56 31
E-Mail: serge.pinto@ujf-grenoble.fr

Introduction

Patients with idiopathic Parkinson's disease (PD) have a favourable response to levodopa therapy at the beginning of treatment. However, this response tends to decrease after some years [22, 30]. Motor fluctuations appear with an alternate state of severe parkinsonism ("off period", referred to "off medication") and a state of improved mobility ("on period", referred to "on medication"), often impaired by dyskinesias [43]. Neurosurgical procedures, such as thalamotomy [44] and pallidotomy [40], offer other therapeutic possibilities. Recent advances in the knowledge of basal ganglia

pathophysiology [2, 12, 45] and neurosurgical procedures [6, 46, 47] have led to a great interest in deep brain stimulation, and in particular the use of subthalamic nucleus (STN) high frequency stimulation, for the treatment of PD [38, 39].

Parkinsonian dysarthria is usually characterised by a monotony of pitch and loudness, reduced stress, variable rate, short rushes of speech and imprecise consonants [11]. These characteristics have been attributed to a weakness (hypokinesia) and slowness (bradykinesia) of movement, rigidity and rest tremor. Any or all components of speech production, including respiration [29], phonation [25] and articulation [27] may be affected. Since 1987, high frequency stimulation of diffe-

rent targets has been carried out to treat the different symptoms of PD [7]. Initial results in a group of ten patients with bilateral STN stimulation suggest that parkinsonian speech impairment can be improved by this therapy [20]. This evaluation was carried out by means of force transducers for evaluating impairments in control of the lips and tongue [3, 4, 15]. Force has been considered as one of the likely variables controlled by the nervous system in producing motor behaviour and the evaluation of non-speech oral strength has been recognised as a worthwhile tool to assess the effects of therapies on speech [41, 53].

Studies carried out on limb motor function show patients' difficulties in performing several movements simultaneously [42]. Articulatory organ activity is also dependent on the basal ganglia loop function [57], and moreover, articulatory dysfunction in PD may be related to the alteration of other non-dopaminergic structures affected by neuronal degeneration [1]. Since the STN is a key structure within the basal ganglia loop and is also connected to other neuronal structures [46], it appeared interesting to assess the effect of bilateral STN stimulation in parkinsonian dysarthria. Thus, our objectives were to estimate the STN stimulation effect on articulatory force dysfunction in a large group of PD patients and the persistence of this effect in the long-term.

Patients and methods

■ Patients

Twenty-six PD patients (10 females and 16 males) with an akinetic-rigid symptomatology participated in this study. They were distinct from patients included in previous studies from our group [20]. The mean age of the patients was 51.3 ± 7.2 years, and the mean duration of PD was 14.8 ± 6.1 years. They were bilaterally implanted into the STN for chronic high frequency stimulation because of severe levodopa-induced complications. The indication for surgery was independent of the severity of dysarthria. The electrical parameters were optimal with regard to musculo-skeletal PD symptoms for all the patients, with an adequate monopolar stimulated contact, a pulse width at 60 microseconds (μ s), a range of voltage from 1.8 volts (V) to 3.6 V and a range of frequency from 130 hertz (Hz) to 185 Hz. The selection criteria for implantation were idiopathic PD [23], disabling motor fluctuations despite all drug therapies, age under 70 years, normal cerebral magnetic resonance imaging and no other neurological impairment. PD patients eligible for articulatory organ examination were able to generate forces (excluding those with the most severe dysarthria, no speech production or unintelligible speech), had no severe cervical and orofacial tremor or dyskinesias, no ill-fitting dental apparatus and co-operated well. The study was carried out during 12 months and all consecutive patients fulfilling the latter criteria (26 among 51) entered the study. Evaluations were carried out post-operatively without levodopa administration to focus on the STN stimulation effect. This study was approved by the Grenoble University Hospital ethics committee and carried out with the consent of all the patients, in accordance with the Declaration of Helsinki.

To compare the subjective speech score with articulatory organ variables at the time of surgery, patients were separated into two subgroups (Table 1). Subgroup A ($n = 12$) had no or mild dysarthria (score 0 or 1 for item 18 of the Unified Parkinson's Disease Rating

Scale, UPDRS [16]) and subgroup B ($n = 14$) had moderate or marked dysarthria, score 2 or 3; speech was evaluated without levodopa and without STN stimulation. This subdivision, which concerns the articulatory organ variables, aims at estimating the trends of clinical subdivision. So, the subgroup A with a minor dysarthria should perform a force evaluation greater than the subgroup B, with a more severe dysarthria.

To study the effects of STN stimulation at different post-surgical follow-up, we divided the patients into three subgroups (Table 1). During the time of the study (12 months), each patient came to the Neurology service in order to perform a follow-up control evaluation. Their follow-up was different: subgroup 1 ($n = 10$) was studied three months after surgery, subgroup 2 ($n = 10$) one or two years later and subgroup 3 ($n = 6$) three, four or five years after surgery. The mean age of the three subgroups was 51.0 ± 6.4 , 54.8 ± 7.9 and 52.2 ± 8.8 years respectively; the mean duration of PD symptoms before surgery were respectively 16.1 ± 6.9 , 15.6 ± 6.1 and 11.5 ± 4.2 years for each subgroup. The aim of this classification was a preliminary investigation concerning the long-term effect of STN stimulation on orofacial impairment.

■ Clinical assessment

The patients' motor disability was assessed by the same neurologist, with (ON) and without (OFF) STN stimulation, by means of the UPDRS, part III, items 18–31. On this scale, the perceptual estimation of speech corresponded to item 18 with the following scoring: 0 for normal; 1 for slight loss of expression, diction and/or volume; 2 for monotone speech, slurred but understandable, moderately impaired; 3 for a marked impairment and difficulty in understanding the patient; and 4 for unintelligible. We also calculated an akinesia score corresponding to the addition of items 23 to 26 of both sides of the body, and an axial score corresponding to the addition of the items 18, 22 (neck) and 27 to 30 [5].

■ Force examination procedure

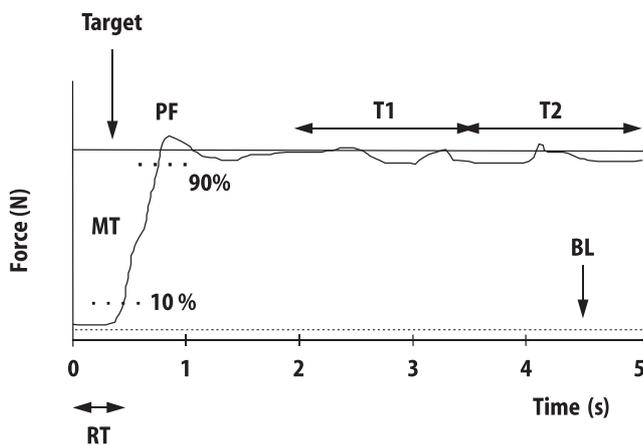
After an overnight fast, the patients were evaluated without medication in the morning under two conditions, a) during bilateral STN stimulation (ON stimulation) and b) thirty minutes after switching off STN stimulation (OFF stimulation). Force transducers (Neuro Logic Inc, Bloomington, Indiana, USA) have been described by Barlow et al. [3]. They were used to measure compression forces generated by the upper lip, lower lip and tongue. The transducer slid along a jaw yoke that was encapsulated in a mouldable dental impression block and placed between the molars. The patients were comfortably seated on a dental chair in a Faraday cage, in front of an oscilloscope screen which allowed a visual feedback. The reference condition (the baseline, BL) corresponded to the device placed in the mouth without any movement of articulatory organs. The patients were then asked to generate forces from baseline as rapidly and as accurately as possible to the different force targets, which appeared as a line on the oscilloscope screen, within two seconds of a verbal warning signal. According to our experience, we selected two levels of force (0.25 and 2 newtons, N) corresponding to the range of forces usually involved in speech. The rapid phase of force increase to reach the target (ramp phase) was followed by a stabilisation to the target level for three seconds (hold phase). Six contractions at each force target level were measured, as well as two maximal voluntary forces (MVF).

■ Force measurements

Our group has previously used and defined with details this methodology [20]. For each articulatory organ, two maximal voluntary forces (MVF) were measured, as well as dynamic and static variables concerning the ramp and hold phases of the contractions (Fig. 1). These

Table 1 Patients and subgroups in this study

Patient	Sex	Age	Interval between surgery and force evaluation	Subgroup 1, 2 or 3	UPDRS, Item 18, post-operative, without levodopa and STN stimulation	Subgroup A or B
1	M	47	3 months	1	1	A
2	F	52	3 months	1	0	A
3	M	48	3 months	1	1	A
4	M	52	3 months	1	1	A
5	F	55	3 months	1	3	B
6	M	52	3 months	1	1	A
7	F	41	3 months	1	1	A
8	M	61	3 months	1	1	A
9	F	42	3 months	1	1	A
10	M	59	3 months	1	0	A
11	F	59	1 year	2	2	B
12	M	45	1 year	2	2	B
13	F	47	1 year	2	1	A
14	M	48	1 year	2	3	B
15	M	53	1 year	2	3	B
16	F	54	2 years	2	2	B
17	F	65	2 years	2	2	B
18	M	47	2 years	2	3	B
19	M	66	2 years	2	3	B
20	M	61	2 years	2	1	A
21	M	46	3 years	3	2	B
22	M	52	3 years	3	3	B
23	F	41	3 years	3	2	B
24	M	53	4 years	3	2	B
25	M	54	4 years	3	1	A
26	F	67	5 years	3	3	B

**Fig. 1** Schematic diagram of the force parametric variables. *BL* baseline; *RT* reaction time; *MT* movement time; *PF* peak force; *T1* and *T2* mean force during the last 3 seconds of the hold phase

variables were the following: a) reaction time (RT), defined as the time interval between the appearance of the force target on the oscilloscope screen and 10% of the peak force; b) movement time (MT), corresponding to the time of the ramp phase (10%–90% of the PF); c) peak force (PF) during the ramp phase, which means the highest force level occurring in the first second after the beginning of movement; and d) mean force during the hold phase (HP), which means

during the last three seconds of the contraction divided into two intervals of 1.5 seconds, T1 and T2. Analyses of all variables were made for each articulatory organ (upper lip, lower lip and tongue), and at the two levels of force (0.25 and 2 N). To estimate the imprecision of the mean amplitude of the PF and the HP in relation to the target, we calculated the differences between the target and the mean amplitude of the actual variable.

■ Statistical analysis

To compare the clinical scores (total motor UPDRS, akinesia, axial and speech scores) and the force evaluation variables (RT, MT, MVE, imprecision of PF and HP) between the ON and the OFF stimulation conditions, we used the paired Student's *t* test (Minitab Inc, State College, Pennsylvania, USA), given all the variables followed normal probability. To correct for the probability in relation to the number of analyses and to avoid a type I error, a *p* value of 0.001 was considered to indicate statistical significance. We used the linear regression Pearson's test to correlate force variables (MVE, RT, MT at 0.25 N and at 2 N) and clinical scores. We used the non-parametric Mann-Whitney's test to compare MVE, RT and MT at 2 N between the two subgroups of patients A and B. Results of the STN stimulation-induced effect between subgroups 1 and 2, and subgroups 2 and 3, were compared using a non-parametric Mann-Whitney's test. Clinical scores and force variables were also compared for both ON and OFF stimulation conditions.

Results

Clinical assessment of patients' motor disability

For all the patients, STN stimulation decreased by 84 % the equivalent levodopa daily dose, estimated by means of the classical conversions used by Krack et al. [33]. It improved the Hoehn and Yahr stage and Schwab and England score without levodopa. With levodopa, these scores did not significantly change (Table 2). The off-medication total motor UPDRS, akinesia, axial and speech scores were also significantly improved (Table 3).

Force evaluation

Maximal voluntary forces (MVF) of the three articulatory organs were significantly improved by STN stimulation (Fig. 2). Percentages of improvement were 52 % for the upper lip, 84 % for the lower lip and 68 % for the tongue. Table 4 shows the results obtained in the ON and OFF stimulation conditions for the other variables of the force evaluation. STN stimulation significantly improved most of them. However, the comparison between the two conditions for MT at 0.25 N of the lower lip was non-significant ($p = 0.11$). In addition, the imprecision of the PF at 0.25 N was unchanged by STN stimulation for the tongue ($p = 0.92$) and significantly worsened for the upper and lower lips.

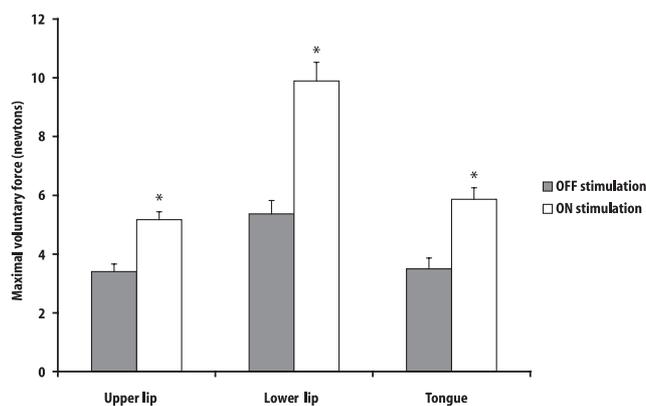


Fig. 2 Maximal voluntary forces (\pm SEM) of the articulatory organs in ON and OFF subthalamic stimulation conditions for all the patients (* $p < 0.001$; Student t test).

Relationship between clinical assessment and force measurements

The two subgroups A and B showed significant improvement of the clinical scores and force parameters with stimulation of the STN. For example, the total motor UPDRS for the subgroup A was 16.5 ± 11.1 in the ON stimulation condition, whereas it was 43.7 ± 16.6 without stimulation; concerning the subgroup B, the same values were 19.9 ± 10.6 and 49.5 ± 12.2 respectively. Subgroup A, with no or mild dysarthria, had significantly higher MVF and shorter RT and MT at 2 N (Fig. 3) than subgroup B, with moderate or marked dysarthria, for all the articulatory organs in the OFF stimulation condi-

Table 2 Clinical characteristics of the 26 patients

Mean age (years)	Mean duration of PD (years)	Mean Hoehn and Yahr stage		Mean Schwab and England score		Mean levodopa dose (mg/day of levodopa equivalent)
		ON	OFF	ON	OFF	
<i>Before surgery</i>						
51.3 ± 7.2	14.8 ± 6.1	2.2 ± 0.8	4.0 ± 0.8	85.8 ± 10.6	41.1 ± 20.5	1108 ± 439
<i>After surgery, at the time of force evaluation, with STN stimulation</i>						
52.7 ± 7.4	16.2 ± 5.9	2.2 ± 0.4	$2.4 \pm 0.5^*$	90.4 ± 8.8	$87.7 \pm 7.6^*$	$179 \pm 206^*$

All data are mean \pm SD; ON and OFF: with and without levodopa; * $p < 0.001$ (Student t test), after surgery with STN stimulation vs before surgery

Table 3 Clinical motor and speech assessments for all the patients

Clinical assessment	Total motor score, items 18–31 (maximal score, 108)	Akinesia, items 23–26 (maximal score, 32)	Axial score, items 18, 22 (neck), 27–30 (maximal score, 24)	Speech, item 18 (maximal score, 4)
Before surgery	51.7 ± 16.2	18.2 ± 6.3	12.5 ± 4.9	1.6 ± 0.6
After surgery, OFF stimulation	47.6 ± 14.5	20.8 ± 6.0	9.9 ± 3.2	1.7 ± 1.0
After surgery, ON stimulation	$18.3 \pm 10.5^*$	$7.5 \pm 4.9^*$	$4.4 \pm 2.2^*$	$1.1 \pm 1.0^*$
Improvement between OFF and ON stimulation conditions	61.5 %	63.9 %	55.5 %	35.3 %

All data are off-medication UPDRS scores, mean \pm SD; * $p < 0.001$ (Student t test), OFF vs ON stimulation conditions

Table 4 Articulatory organ forces in ON and OFF subthalamic stimulation conditions for all the patients

	RT (ms)		MT (ms)		Imprecision of the PF (N)		Imprecision of the HP (N)	
	0.25 N	2 N	0.25 N	2 N	0.25 N	2 N	0.25 N	2 N
	T1	T2	T1	T2	T1	T2	T1	T2
Upper Lip								
OFF stimulation	580 ± 340	781 ± 360	900 ± 446	0.015 ± 0.069	-0.496 ± 0.578	-0.041 ± 0.055	-0.042 ± 0.062	-0.600 ± 0.493
ON stimulation	478 ± 201*	553 ± 253*	662 ± 348*	0.070 ± 0.057*	0.065 ± 0.312*	0.007 ± 0.035*	0.010 ± 0.036*	-0.168 ± 0.224*
Lower Lip								
OFF stimulation	610 ± 371	932 ± 435	759 ± 457	0.049 ± 0.107	-0.395 ± 0.615	-0.037 ± 0.075	-0.037 ± 0.079	-0.580 ± 0.487
ON stimulation	530 ± 225*	683 ± 311*	669 ± 382	0.093 ± 0.076*	0.214 ± 0.434*	0.017 ± 0.046*	0.022 ± 0.052*	-0.147 ± 0.184*
Tongue								
OFF stimulation	623 ± 380	744 ± 386	882 ± 499	0.083 ± 0.007	-0.471 ± 0.611	-0.028 ± 0.068	-0.041 ± 0.068	-0.690 ± 0.546
ON stimulation	536 ± 214*	537 ± 386*	624 ± 327*	0.082 ± 0.099	0.116 ± 0.319*	-0.002 ± 0.056*	0.004 ± 0.060*	-0.117 ± 0.154*

* $p < 0.001$ (Student *t* test), OFF vs ON stimulation conditions

HP hold phase; MT movement time; N newtons; RT reaction time; T1 and T2 first and second period of the HP. The underlined values correspond to a worsening effect of stimulation.

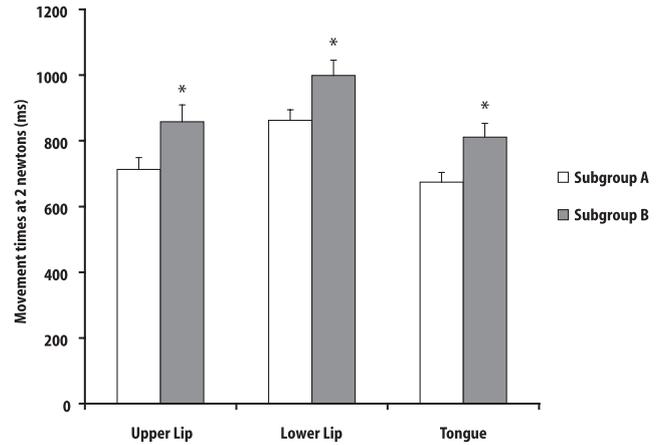


Fig. 3 Movement times at 2 newtons (\pm SEM) in OFF subthalamic stimulation condition for subgroups A and B (**subgroup A** with no or mild dysarthria scored 0 or 1 according to the UPDRS speech score, item 18; **subgroup B** with moderate or marked dysarthria scored 2 or 3; * $p < 0.05$, Mann-Whitney U test)

tion, except for the MVF and the MT at 2 N of the lower lip. For both subgroups, no correlation was found between the force variables (RT, MT at 0.25 N, MT at 2 N, MVF) and the clinical scores (total motor UPDRS, akinesia, axial and speech scores) in both ON and OFF stimulation conditions, except for the MT at 2 N and the akinesia score ($r = 0.391$, $p < 0.05$).

Long-term evaluation of the clinical scores and force variables

The beneficial STN stimulation-induced effect for the clinical scores (total motor UPDRS, akinesia, axial and speech scores) and the force evaluation (RT, MVF, MT at 0.25 N and 2 N) was not significantly different between subgroups 1 and 2 ($p = 0.13$ for total motor UPDRS; $p = 0.43$ for RT of the upper lip), and subgroups 2 and 3 ($p = 0.91$ for akinesia; $p = 1.00$ for MVF of the lower lip). We also compared the clinical and articulatory force scores with and without stimulation among the three subgroups. In both ON and OFF stimulation conditions, the speech score of the UPDRS was significantly higher in subgroups 2 and 3, in comparison with subgroup 1 (Fig. 4). We found a non-significant trend to a progressive worsening of the other clinical scores and force variables from subgroup 1 to subgroups 2 and 3.

Discussion

In agreement with previous studies, bilateral STN stimulation greatly improved the off-medication total motor UPDRS, akinesia and axial scores in 26 patients with PD [5, 17, 26, 32, 38, 39]. These patients were particularly

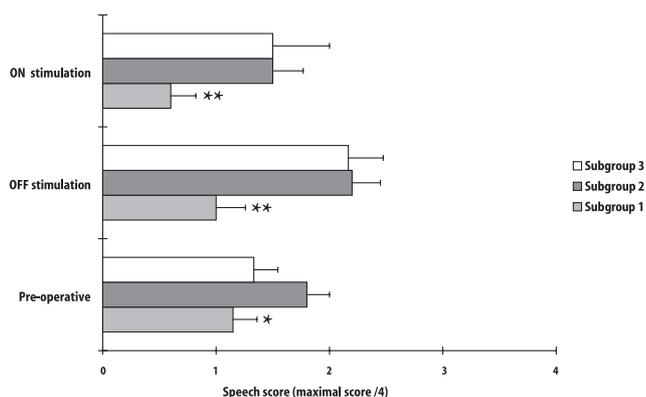


Fig. 4 Speech score (\pm SEM) in the off-medication pre-operative and post-operative ON and OFF subthalamic stimulation conditions for subgroups 1, 2, and 3 (time interval between surgery and force examination: three months for subgroup 1; one to two years for subgroup 2; three, four or five years for subgroup 3; * subgroup 1 vs subgroup 2; ** subgroup 1 vs subgroup 2 and subgroup 1 vs subgroup 3; $p < 0.05$, Mann-Whitney U test)

young; their symptoms were highly levodopa-responsive, which was one of the selection criteria for the surgery. The speech score of the UPDRS was also improved, but to a lesser degree. One reason for this moderate improvement induced by STN stimulation on speech, in comparison with the major improvements in other parkinsonian features, could be the apparent and relative independence between the parkinsonian dysarthria and the alteration of STN activity. It has been suggested that parkinsonian dysarthria is consecutive to the degeneration of multiple neuronal structures, in addition to the nigrostriatal dopaminergic defect [9, 37]. This defect is mainly at the origin of STN overactivity [8, 56]. Therefore, it is logical that alleviating STN overactivity only has a partial impact on parkinsonian dysarthria. Another reason could be the use of the UPDRS subjective five point scale, that seems to be insufficient to estimate speech disorders accurately. For example, the major change from understandable speech to that which is difficult to understand corresponds to only one point, from 2 to 3. Nevertheless, the evaluation of all the patients was made by the same neurologist in order to ensure the reliability of the clinical examination [18, 50]. It appears that a more standardised dysarthria assessment procedure would certainly be more accurate and relevant in order to provide a more informative profile of speech production characteristics. Finally, dysarthria does not have the same levodopa-response as the motor impairment of limbs; if we consider that stimulation of the STN improves only the symptoms sensitive to levodopa therapy, it is perhaps the reason why the improvement in speech is not so important as in the other dysfunctions.

Electrophysiological measurements of the articulatory organs turned out to be necessary, because speech

disorder in parkinsonian dysarthria, as qualified by Darley [11], is a motor-based disorder. Thus, articulatory organ forces were measured by means of force transducers, as reported previously [4, 5, 15]. Alteration of force variables can give an account of the akinetic-rigid symptomatology of PD. By analogy to limb movements, impairment of the RT can be related to akinesia, MT to bradykinesia and MVF to hypokinesia [42]. Bilateral STN stimulation improved these variables for all the articulatory organs, which indicates an improvement in the initiation, slowness and strength of orofacial movements. The assessment of muscle rigidity is difficult for the articulatory organs and our protocol did not focus on this symptom. However, parkinsonian rigidity may play a role in the motor control of the articulatory organs [27]. STN could be only partially involved in the articulatory movements especially with great force and amplitude, since we observed that the motor control of this latter type of movement (2 N) was better improved by STN stimulation than low-level forces (0.25 N). We also observed worsening of the MT at 0.25 N for the upper and lower lips, which would be associated with STN electrical parameter setting or global medication reduction optimally obtained for global motor function, and not for dysarthria. It must be noted that the group of patients fulfilled various selection criteria to perform the experiment, and the results obtained in this study would probably differ with a group of older patients with a later stage of PD.

Even if we found a beneficial effect of bilateral STN stimulation on both objective and subjective assessments of dysarthria, an important issue to be addressed concerns the correlation between articulatory organ forces and the global motor dysfunction, especially akinesia, and between the two types of objective and subjective measurements. On the one hand, we observed a correlation between the MVF of the tongue in the OFF stimulation condition and the akinesia score. On the other hand, no correlation was found between the force variables of the lips and the clinical scores, reflecting a possible lesser importance of lip akinesia and rigidity in articulatory dysfunction. The lack of correlation may also be due to the fact that clinical assessment does not separate akinesia from bradykinesia and hypokinesia, whereas our protocol gives an account of these different aspects of motor dysfunction. The comparison between the two subgroups of patients separated according to the perceptual speech evaluation (item 18 of the UPDRS) showed that the MVF, RT and MT at 2 N were significantly worse in the subgroup of patients with the most severe dysarthria. However, this difference was only noted in the OFF stimulation condition. This indicates that a relation between the perceptual evaluation of speech and force evaluation exists for parkinsonian dysarthria, but the effect of STN stimulation induces changes in precise force parameters which are not cor-

related with subjective speech estimation. Speech scores reflect overall speech production; the item does not discriminate dysfunctions between respiration, phonation and articulation. Speech production is the result of simultaneous parameters observed more precisely with acoustical data, which should be more relevant for a comparison with the subjective assessment of speech. Actually, in accordance with the study of Dromey et al. [14], our group noticed an improvement in dysarthria using an acoustical method which allowed for favourable changes in some parameters of phonation, such as fundamental frequency variability, by bilateral STN stimulation [19].

The beneficial effects of bilateral STN stimulation on clinical assessments and force variables were similar among the three subgroups of patients, separated according to the time interval between this study and surgery. However, in both ON and OFF stimulation conditions, we observed that the speech scores were higher in subgroups 2 and 3 than in subgroup 1. However, these observations were not obtained with a longitudinal experiment and give only a preliminary approach concerning the long-term persistence of the STN stimulation effect on dysarthria, which will be better assessed by a prospective study. Despite STN stimulation induced improvement in speech, this worsening with time may be related to the progressive degeneration of neuronal structures unrelated to dopaminergic structures and STN activity [9, 37]. In fact, with the evolution of PD, speech is known to worsen along with other axial symptoms, independently of the restoration of dopamine activity and the bilateral STN stimulation effect. STN overactivity in PD is found in relation with the striatal dopamine defect. Therefore, this suggests that STN stimulation, supposed to inhibit STN neuronal activity, can mainly improve levodopa-responsive motor symptoms. However, if the effect of bilateral STN stimulation is similar to that of levodopa for the limbs [10, 48], the effects of STN stimulation and levodopa therapy for the articu-

latory organs are different and variable: levodopa is known to improve speech [31], worsen articulatory organ activity [22], whereas STN stimulation seems to improve the articulatory organ forces [20]. In the middle and late stages of PD, axial motor impairment such as dysarthria may be the result of a combined effect of the nigral dopaminergic cell loss and the progressive degeneration of non-dopaminergic structures in the brainstem [37]. This may explain the declining levodopa-responsiveness over the course of the disease [1].

Other antiparkinsonian treatments have variable impact on dysarthria. Dopaminergic treatments have a less beneficial effect on speech than on the other motor disabilities [35, 49], particularly after ten or more years of levodopa therapy [30]. Surgical ablative therapies, such as thalamotomy and pallidotomy, variably alter speech [28, 34, 36, 51, 52, 54]. Posterolateral pallidotomy may even worsen speech, and this risk is greater when the procedure is bilateral [55]. So far, precise studies have not been published after VIM and GPi stimulation, and preliminary results showed some improvement for the GPi target, and a worsening for the VIM target [21, 24].

Conclusions

In comparison with other antiparkinsonian medical and surgical treatments, STN stimulation might appear to be an advantage for the treatment of PD to improve the motor function of both the limbs and the articulatory organs. Bejjani et al. suggested that bilateral STN stimulation can improve not only limb motor function but also axial symptoms, including speech impairment, and our present results confirm these findings [5].

■ **Acknowledgements** The authors thank V. Laing for English revision of the manuscript. S. P. received a grant from the Ministry of Research and Technology (MRT). This study was supported by the Rhône-Alpes Government and the INSERM (Institut National de la Santé et de la Recherche Médicale).

References

1. Agid Y, Cervera P, Hirsch E, Javoy-Agid F, Lehericy S, Raisman R, Ruberg M (1989) Biochemistry of Parkinson's disease 28 years later: a critical review. *Mov Disord* 4:126–144
2. Alexander GE, Crutcher MD (1990) Functional architecture of basal ganglia circuits: neural substrates of parallel processing. *Trends Neurosci* 13:266–271
3. Barlow SM, Abbs JH (1983) Force transducers for the evaluation of labial, lingual and mandibular motor impairments. *J Speech Hear Res* 26:616–621
4. Barlow SM, Cole KJ, Abbs JH (1983) A new head-mounted lip jaw movement transduction system for the study of motor speech disorders. *J Speech Hear Res* 26:283–288
5. Bejjani BP, Gervais D, Arnulf I, Papadopoulou S, Demeret S, Bonnet AM, Cornu P, Damier P, Agid Y (2000) Axial parkinsonian symptoms can be improved: the role of levodopa and bilateral subthalamic stimulation. *J Neurol Neurosurg Psychiatry* 68:595–600
6. Benabid AL, Pollak P, Gao D, Hoffmann D, Limousin P, Gay E, Payen I, Benazzouz A (1996) Chronic electrical stimulation of the ventralis intermedialis nucleus of the thalamus as a treatment of movement disorders. *J Neurosurg* 84:203–214
7. Benabid AL, Pollak P, Louveau A, Henry S, de Rougemont J (1987) Combined (thalamotomy and stimulation) stereotactic surgery of the VIM thalamic nucleus for bilateral Parkinson's disease. *Appl Neurophysiol* 50:344–346

8. Bergman H, Wichmann T, Karmon B, DeLong MR (1994) The primate subthalamic nucleus. II. Neuronal activity in the MPTP model of parkinsonism. *J Neurophysiol* 72:507–520
9. Bonnet AM, Loria Y, Saint-Hilaire MH, Lhermitte F, Agid Y (1987) Does long-term aggravation of Parkinson's disease result from non-dopaminergic lesions? *Neurology* 37:1539–1542
10. Brown RG, Dowsey PL, Brown P, Jahanshahi M, Pollak P, Benabid AL, Rodriguez-Oroz MC, Obeso J, Rothwell JC (1999) Impact of deep brain stimulation on upper limb akinesia in Parkinson's disease. *Ann Neurol* 45:473–488
11. Darley FL, Aronson AE, Brown JR (1969) Motor speech disorders. In: Saunders WB (ed) Philadelphia, pp 171–197
12. DeLong MR (1990) Primate models of movement disorders of basal ganglia origin. *Trends Neurosci* 13:281–285
13. DeLong MR, Crutcher MD, Georgopoulos AP (1985) Primate globus pallidus and subthalamic nucleus functional organization. *J Neurophysiol* 53:530–543
14. Dromey C, Kumar R, Lang AE, Lozano AM (2000) An investigation of the effects of subthalamic nucleus stimulation on acoustic measures of voice. *Mov Disord* 15:1132–1138
15. Dworkin JP, Aronson AE, Muller DW (1980) Tongue force in normal and in dysarthric patients with amyotrophic lateral sclerosis. *J Speech Hear Res* 23:828–837
16. Fahn S, Elton RL, members of the UPDRS development committee (1987) Unified Parkinson's Disease Rating Scale. In: Fahn S, Marsden CD, Calne DB, Goldstein M (ed) Recent developments in Parkinson's disease. MacMillan Health Care Information, New Jersey, pp 153–163
17. Fraix V, Pollak P, Van Blercom N, Xie J, Krack P, Koudsie A, Benabid AL (2000) Effect of subthalamic nucleus stimulation on levodopa-induced dyskinesia in Parkinson's disease. *Neurology* 55:1921–1923
18. Geminiani G, Cesana B, Tamma F, Contri P, Pacchetti C, Carella F, Piolti Martignoni R, Giovannini F, Caraceni T (1991) Interobserver reliability between neurologists in training of the Parkinson's disease Rating Scales. A multicenter study. *J Mov Dis* 6:330–335
19. Gentil M, Chauvin P, Pinto S, Pollak P (2001) Effect of bilateral stimulation of the subthalamic nucleus on parkinsonian voice. *Brain Lang* 78:233–240
20. Gentil M, Garcia-Ruiz P, Pollak P, Benabid AL (1999) Effect of stimulation of subthalamic nucleus on oral control of patients with parkinsonism. *J Neurol Neurosurg Psychiatry* 67:329–333
21. Gentil M, Garcia-Ruiz P, Pollak P, Benabid AL (2000) Effect of bilateral deep-brain stimulation on oral control of patients with parkinsonism. *Eur Neurol* 44:147–152
22. Gentil M, Tournier CL, Perrin S, Pollak P (1998) Effects of levodopa on finger and orofacial movements in Parkinson's disease. *Prog Neuro-Psychopharmacol & Biol Psychiatry* 22:1261–1274
23. Gibb WRG, Lees AJ (1988) The relevance of the Lewy body to the pathogenesis of idiopathic Parkinson's disease. *J Neurol Neurosurg Psychiatry* 51:745–752
24. Gross C, Rougier A, Guehl D, Boraud T, Julien J, Bioulac B (1997) High-frequency stimulation of the globus pallidus internalis in Parkinson's disease: a study of seven cases. *J Neurosurg* 87:491–498
25. Hanson DG, Geratt BR, Ward PH (1984) Cinegraphic observations of laryngeal dysfunctions in Parkinson's disease. *Laryngoscope* 94:348–353
26. Houeto JL, Bejjani PB, Damier P, Staedler C, Bonnet AM, Pidoux B, Dormont D, Cornu P, Agid Y (2000) Failure of long-term pallidal stimulation corrected by subthalamic stimulation in PD. *Neurology* 55:728–730
27. Hunker CJ, Abbs JH, Barlow SM (1982) The relationship between parkinsonian rigidity and hypokinesia in the orofacial system: a quantitative analysis. *Neurology* 32:749–754
28. Iacono RP, Lonser RR, Kuniyoshi S (1995) Unilateral versus bilateral simultaneous posteroventral pallidotomy in subgroups of patients with disease. *Stereotact Funct Neurosurg* 65:6–9
29. Jankovic J, Nour F (1986) Respiratory dyskinesia in Parkinson's disease. *Neurology* 36:303–304
30. Klawans HL (1986) Individual manifestations of Parkinson's disease after ten or more years of levodopa. *Mov Disord* 3:187–192
31. Kompoliti K, Wang QE, Goetz CG, Leurgans S, Raman R (2000) Effects of central dopaminergic stimulation by apomorphine on speech in Parkinson's disease. *Neurology* 54:458–462
32. Kumar R, Lozano AM, Kim YJ, Hutchinson WD, Sime E, Halket E, Lang AE (1998) Double-blind evaluation of subthalamic nucleus deep brain stimulation in advanced Parkinson's disease. *Neurology* 51:850–855
33. Krack P, Pollak P, Limousin P, Hoffmann D, Xie J, Benazzouz A, Benabid AL (1998) Subthalamic nucleus or internal pallidal stimulation in young onset Parkinson's disease. *Brain* 122:1133–1146
34. Laitinen LV, Bergenheim AT, Hariz MI (1992) Ventroposterolateral pallidotomy can abolish all parkinsonian symptoms. *Stereotact Funct Neurosurg* 58:14–21
35. Lakke JP (1985) Axial apraxia in Parkinson's disease. *J Neurol Sci* 69:34–39
36. Lebrun Y, Leleux C (1993) The effects of electrostimulation and of resective and stereotactic surgery on language and speech. *Acta Neurochir (Wien)* 56:40–51
37. Levy G, Tang MX, Cote LJ, Louis ED, Alfaro B, Mejia H, Stern Y, Marder K (2000) Motor impairment in PD: relationship to incident dementia and age. *Neurology* 55:539–544
38. Limousin P, Krack P, Pollak P, Benazzouz A, Ardouin C, Hoffmann D, Benabid AL (1998) Electrical stimulation of the subthalamic nucleus in advanced Parkinson's disease. *N Engl J Med* 339:1105–1111
39. Limousin P, Pollak P, Benazzouz A, Hoffmann D, Le Bas JF, Broussolle E, Perret JE, Benabid AL (1995) Effect on parkinsonian signs and symptoms of bilateral subthalamic nucleus stimulation. *Lancet* 345:91–95
40. Lozano AM, Lang AE, Galvez-Jimenez N, Miyasaki J, Duff J, Hutchinson WD, Dostrovsky JO (1995) Effect of GPi pallidotomy on motor function in Parkinson's disease. *Lancet* 25:1383–1387
41. Luschei E (1991) Development of objective standards of non-speech oral strength and performance. In: Moore CA, Yorkston KM, Beukelman DR (ed) Dysarthria and apraxia of speech: perspectives on management. Paul H Brookes, Baltimore, pp 3–14
42. Marsden CD (1989) Slowness of movement in Parkinson's disease. *Mov Disord* 4:26–37
43. Marsden CD, Parkes JD (1976) On-off effects on patients with Parkinson's disease on chronic levodopa therapy. *Lancet* 1:292–296
44. Nagaseki Y, Shibasaki T, Hirai T, Kawashima Y, Hirato M, Wada H, Miyazaki M, Ohye C (1986) Long-term follow-up results of selective VIM thalamotomy. *J Neurosurg* 65:296–302
45. Parent A, Cicchetti F (1998) The current model of basal ganglia under scrutiny. *Mov Disord* 13:199–202
46. Parent A, Sato F, Wu Y, Gauthier J, Lévesque M, Parent M (2000) Organization of the basal ganglia: the importance of axonal collateralization. *Trends Neurosci* 23 (S3):20–27
47. Pollak P, Benabid AL, Limousin P, Benazzouz A (1997) Chronic intracerebral stimulation in Parkinson's disease. *Adv Neurol* 74:213–220

-
48. Pullman SL, Watts RL, Juncos JL, Chase TN, Sanes JN (1988) Dopaminergic effects on simple and choice reaction time performance in Parkinson's disease. *Neurology* 38:249–254
 49. Quagliari CE, Celesia GC (1977) Effect of thalamectomy and levodopa therapy on the speech of Parkinson patients. *Eur Neurol* 15:34–39
 50. Richards M, Marder K, Cote L, Mayeux R (1994) Inter-rater reliability of the Unified Parkinson's Disease Rating Scales Motor Examination. *J Mov Dis* 9:89–91
 51. Schulz GM, Peterson T, Sapienza CM, Greer M, Friedman W (1999) Voice and speech characteristics of persons with Parkinson's disease pre- and post-pallidotomy surgery: preliminary findings. *J Speech Lang Hear Res* 42:1176–1194
 52. Schulz GM, Greer M, Friedman W (2000) Changes in vocal intensity in Parkinson's disease following pallidotomy surgery. *J Voice* 14:589–606
 53. Stein RB (1982) What muscle variables does the central nervous system control? *Behav Brain Sci* 5:535–578
 54. Stracciari A, Guarino M, Cirignotta F, Pazzacia P (1993) Development of palilalia after stereotaxic thalamotomy in Parkinson's disease. *Eur Neurol* 33:275–276
 55. Uitti RJ, Wharen RE, Duffy JR, Lucas JA, Schneider SL, Rippeth JD, Wszolek ZK, Obwegeser AA, Turk MF, Atkinson EJ (2000) Unilateral pallidotomy for Parkinson's disease: speech, motor, and neuropsychological outcome measurements. *Parkinsonism Relat Disord* 6:133–143
 56. Wichmann T, Bergman H, DeLong MR (1994) The primate subthalamic nucleus. III. Changes in motor behavior and neuronal activity in the internal pallidum induced by subthalamic inactivation in the MPTP model of parkinsonism. *J Neurophysiol* 72:521–530
 57. Wise RJS, Greene J, Büchel C, Scott SK (1999) Brain regions involved in articulation. *Lancet* 353:1057–1061