

Effects of stimulation of the subthalamic nucleus on naming and reading nouns and verbs in Parkinson's disease

Maria Caterina Silveri^{a,b,*}, Nicoletta Ciccarelli^a, Eleonora Baldonero^a, Carla Piano^b,
Massimiliano Zinno^b, Francesco Soleti^b, Anna Rita Bentivoglio^b, Alberto Albanese^{b,c}, Antonio Daniele^b

^a Medicine of the Ageing, Catholic University, Rome, Italy

^b Institute of Neurology, Catholic University, Rome, Italy

^c IRCCS Foundation, Neurologic Institute 'Carlo Besta', Milan, Italy

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ABSTRACT

An impairment for verbs has been described in patients with Parkinson's disease (PD), suggesting that a disruption of frontal–subcortical circuits may result in dysfunction of the neural systems involved in action–verb processing. A previous study suggested that deep brain stimulation (DBS) of the subthalamic nucleus (STN) during verb generation may affect the ability to select from many competing lexical alternatives.

In this study, 12 PD patients who had undergone bilateral STN DBS and completed an 8-year follow-up and 14 matched normal controls were administered action and object naming tasks and verb and noun reading tasks. Their responses were recorded using a microphone, resulting in a signal that marked the onset of the verbal response and allowed to measure response times (RTs). Accuracy was scored manually.

Results: Overall performance in naming (independently of stimulation): In naming task controls were faster and more accurate than PD patients. In both groups, performance (accuracy and RTs) was worse on action naming than object naming. PD patients were significantly slower than controls in naming actions. Effect of stimulation: Compared with the OFF stimulation condition, in ON stimulation condition PD patients showed improved performance on object and action naming tasks (increased accuracy, faster RTs), with a decreased number of semantic errors. Some evidence also emerged that action naming in the ON stimulation condition improved more than object naming. On noun and verb reading tasks, although accuracy was at ceiling in both groups and no significant difference was observed in RTs for nouns and verbs, PD patients were slower than controls.

Conclusions: Our findings suggest that STN DBS may improve lexical search in PD patients. We hypothesize that STN stimulation may facilitate the motor components involved in naming and reading tasks (increased speed of speech onset), resulting in shorter RTs in both naming and reading and, to some extent, in increased accuracy in naming due to fewer omissions (no response within the 7500 ms time limit). However, to account for greater accuracy in naming due to decreased number of semantic errors in the ON stimulation condition, we hypothesize that STN stimulation restores the activity of the corticostriatal circuits involved in selection processes of a target word among different alternatives.

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1. Introduction

Different classes of words can be selectively impaired in patients with different sites of cerebral damage (Martin & Chao, 2001), including words belonging to different grammatical classes such as nouns and verbs (Zingeser & Berndt, 1990; Daniele,

* Corresponding author at: Institute of Neurology, Catholic University, Rome, Italy. Tel.: +39 0630155558; fax: +39 063051911.

E-mail addresses: maria.caterina.silveri@rm.unicatt.it, silveri@rm.unicatt.it (M.C. Silveri).

Giustolisi, Silveri, Colosimo, & Gainotti, 1994; Silveri, Perri, & Cappa, 2003a). Several theoretical accounts have been proposed for noun/verb dissociations, because nouns and verbs are complex categories that can be impaired by damage to different underlying mechanisms (Matzing, Druks, Masterson, & Vigliocco, 2009).

Lesion studies suggest that deficits in noun processing are primarily associated with lesions in the left temporal lobe, whereas deficits in verb processing can be produced by a wider range of lesions not only in various cortical regions of the left hemisphere but also in subcortical structures such as the basal ganglia. An impairment for verbs has been described in patients

affected by Parkinson's disease (PD) and other parkinsonian syndromes (Daniele et al., 1994; Bertella et al., 2002; Péran et al., 2003; Péran, Démonet, Pernet, & Cardebat, 2004; Cotelli et al., 2007; Silveri & Ciccirelli, 2007a; Rodriguez-Ferreiro et al., 2009), supporting the hypothesis that disruption of frontal-subcortical circuits may result in dysfunction of the neural systems involved in action-verb processing.

An impairment of verbs has also been described in patients with the frontal-variant of frontotemporal dementia (Cappa et al., 1998; Silveri, Salvigni, Cappa, Della Vedova, & Puopolo, 2003b; Hillis, Oh, & Ken, 2004; Silveri & Ciccirelli, 2007b), cerebellar lesions (Fiez, Petersen, Cheney, & Raichle, 1992) or with HIV encephalopathy (Woods, Careya, Tröster, Granta, & the HIV Neurobehavioral Research Center (HNRC) Group2, 2005). In conclusion, lesion studies suggest that impairments of nouns are mostly associated with lateralised (left) temporal lesions (Daniele et al., 1994; Silveri & Di Betta, 1997; Damasio, Tranel, Grabowskia, Adolphs, & Damasio, 2004), whereas impairments of verbs are associated with damage primarily involving anterior regions of the brain directly or indirectly, as part of wider neural circuits that also include subcortical structures. Activation neuroimaging studies in normal subjects are another source of evidence (Perani et al., 1999; Tranel, Martin, Damasio, Grabowskia, & Hichwa, 2005; Shapiro et al., 2005; Shapiro, Moo, & Caramazza, 2006). In particular, activation of the left inferior frontal gyrus has been reported during verb processing tasks (Perani et al., 1999; Tyler, Bright, Fletcher, & Stamatakis, 2004; Shapiro et al., 2006). Since the inferior frontal lobe might play a role in decision-making and response-selection processes (Binder, Liebenthal, Possing, Medler, & Ward, 2004), it was hypothesised that activation in the left inferior frontal gyrus during verb processing tasks might be at least in part due to the greater processing demands generally required by verbs compared to nouns (Siri et al., 2008; Matzing et al., 2009).

Lesion and activation studies thus suggest that noun mostly involves lexical-semantic processes, whereas verb processing is a more complex phenomenon that also involves attentional and executive resources (Silveri & Ciccirelli, 2007b). The anatomical counterpart of the greater complexity of verb processing might be the involvement of a wide range of "anterior" brain regions.

An impairment of verbs has been consistently demonstrated in PD on different tasks and in different methodological contexts (Piatt, Fields, Paolo, Koller, & Tröster, 1999; Bertella et al., 2002; Péran et al., 2003; Signorini & Volpato, 2006; Boulenger et al., 2008), although the nature of such impairment is still unclear. According to some authors, it might reflect a grammatical disorder (Grossman, Stern, Gollomp, Vernon, & Hurtig 1994; Bertella et al., 2002; Péran et al., 2003) or a disorder of semantic/conceptual representations of actions, including motor features (Boulenger et al., 2008; Rodriguez-Ferreiro et al., 2009). More recently, however, it has been proposed that the verb deficit in PD might reflect an impairment of "executive" functioning (Colman et al., 2009), due to disruption of corticostriatal circuits (Dubois & Pillon, 1997), which frequently occurs also in non-demented patients.

A dysexecutive disorder, particularly of word selection processes, might also explain the "apparently" linguistic nature of the verb production deficit in PD. In fact, disproportionate impairment of verbs could be interpreted as a word selection deficit during language production due to the high number of competing alternatives for verbs compared with other classes of words (Péran et al., 2003; Signorini & Volpato, 2006). Crescentini, Mondolo, Biasutti, & Shallice (2008) hypothesised non-linguistic involvement of the basal ganglia and left inferior prefrontal cortex in the supervisory attentional system (Norman & Shallice, 1986), suggesting that verb production deficit in PD could be due to defective control of selection response mechanisms and inhibition of competing

alternatives. Nouns and verbs in facts are not easy to compare in this respect, as selection of a target-word and inhibition of competing alternative words might be more demanding for verb processing. For example, it has been shown that common verbs have greater breadth of meaning than common nouns (Gentner, 1981).

As the anterior neural circuits, including the frontostriatal loops, might be critical in verb processing, the ability to process verbs might be influenced by deep brain stimulation (DBS) in PD patients who underwent the permanent implantation of electrodes in the subthalamic nucleus (STN) to alleviate medically intractable motor symptoms probably by increasing the activity of the thalamocortical circuits (Timmermann et al., 2003). Although DBS improves motor symptoms it may have either beneficial or detrimental effect on cognitive performance by modifying the activity of the basal ganglia-thalamocortical circuitry (Schroeder et al., 2003). Most investigations on the "chronic" effects of STN DBS on cognitive functioning compared preoperative and postoperative performance and reported a postoperative decline of verbal fluency (Ardouin et al., 1999; Pillon et al., 2000; Daniele et al., 2003; Cilia et al., 2007; Contarino et al., 2007; Wojtecki et al., 2007; Kalbe et al., 2009; Castelli et al., 2010; Fasano et al., 2010), episodic memory (Pillon et al., 2000; Daniele et al., 2003) and response inhibition (Jahanshahi et al., 2000; Schroeder et al., 2002) while an improved postoperative performance was detected on cognitive flexibility (Jahanshahi et al., 2000; Daniele et al., 2003) and number generation (Witt et al., 2004). In a recent randomized clinical trial (Follett et al., 2010) aimed to compare postoperative 24-month outcomes in two large groups of PD patients who underwent bilateral internal globus pallidus DBS or bilateral STN DBS, no significant differences were observed in cognitive outcome between the two groups, except for a slightly greater postoperative decline of visuomotor speed in patients with STN DBS. In this latter study, however, comparisons between postoperative cognitive performances in different stimulation conditions (ON stimulation vs. OFF stimulation) have not been reported. Only a few studies have attempted to compare the "acute" effects of stimulation (by directly comparing cognitive performance ON vs. OFF stimulation) documenting an improvement of executive functions (Jahanshahi et al., 2000) and spatial working memory (Pillon et al., 2000) in ON condition. Some beneficial effects on speed of processing (assessed by reaction times) has been reported, although the beneficial effects of stimulation might decrease when the cognitive demands of the task increase (Temel et al., 2006; Alberts et al., 2008).

Castner, Chenery, and Silburn (2008) have considered the acute effects of STN DBS in a noun/verb generation task. They analysed four probe-response conditions according to a procedure proposed by Péran et al. (2003). PD patients produced more errors than controls in noun probe-verb response condition when OFF stimulation, while the performance did not differ significantly from controls ON stimulation. They also found that in verb generation errors were related to selection constraints, that is greater selection demand among competing alternative words was associated with poorer performance. Unexpectedly, in one noun generation task (noun probe-noun response), PD patients performed significantly worse than normal controls ON stimulation but not OFF stimulation. In this case no selection constraints were documented. The authors concluded that STN stimulation may affect selection from competing alternatives, which could play a critical role in the production of verbs (Péran et al., 2003; Signorini & Volpato, 2006; Crescentini et al., 2008).

In the present study, we examined PD patients treated with STN DBS who were administered action and object confrontation naming tasks and noun and verb reading tasks. Although both naming and reading tasks explore lexical production, naming a picture is supposed to be more complex than reading a word, because naming involves processes of active lexical search aimed

to select the specific word denoting the picture to be named. By contrast, at least in transparent languages, such as Italian, reading may be largely supported by grapheme-to-phoneme conversion processes, which allow oral production of the sound corresponding to a written stimulus, bypassing lexical processes (Bates, Burani, D'Amico, & Barca 2001).

We made the following predictions:

- A disadvantage of verb naming compared with noun naming was expected in PD patients, in agreement with previous studies suggesting that in PD disruption of frontal-subcortical circuits may result in the dysfunction of neural systems involved in action-verb processing.
- As it has been reported that DBS of STN might negatively interfere with item selection processes during verb production, we predicted that stimulation in PD patients would have a different impact on action and object naming and noun and verb reading tasks.

2. Materials and methods

2.1. Subjects

PD patients were recruited at the Movement Disorders Centre of the Catholic University of Rome from a group of 20 patients who had undergone bilateral simultaneous implantation of permanent electrodes in the STN (frequency = 130 Hz; mean voltage of stimulation $\pm$ SD = 2.64 ± 0.36) and had completed an 8-year follow-up after surgery (Fasano et al., 2010).

For the present study, we selected only 12 PD patients from the group of 20 who fulfilled the following inclusion criteria: (a) they were able to attend the experimental set of the present study (two patients were excluded for behavioural disorders after l-dopa assumption; one for severe hyperkinesia in OFF); (b) they showed no severe dysarthria or hypophonia, which would have interfered with acquisition of a reliable verbal response (five patients excluded). Moreover, in order to exclude PD patients with severe visual perceptual disorders, which would have prevented adequate processing of the visual stimuli in the experimental tasks, PD patients were also administered the "Background" subtest of the Visual Object and Space Perception Battery (Warrington & James, 1986) (no patient excluded).

We selected 14 healthy controls from subjects attending a fitness program at the Centre for Medicine of the Aging of the Catholic University of Rome. Only subjects without current or previous neurological, psychiatric or major internal disorders were selected as controls. All patients and healthy controls were right-handed Italian native speakers. PD patients and controls were matched for both age (PD patients: mean age $\pm$ SD = 66.58 ± 6.29 ; controls: mean age $\pm$ SD = 70.42 ± 6.35 ; Mann-Whitney U test = 1.73; p = ns) and education (PD patients: mean education $\pm$ SD = 11.50 ± 5.02 ; controls: mean education $\pm$ SD = 12.71 ± 3.77 ; Mann-Whitney U test = 0.74; p = ns). Table 1 summarises the PD patients' demographic and clinical features.

An extensive battery of neuropsychological tasks (Table e-1) was administered in both ON anti-Parkinsonian medication and ON stimulation conditions. None of the PD patients recruited in the present study was affected by dementia, although an impaired performance was detected in 5 patients on some tasks (2 patients on a set-shifting executive task, one patient on an episodic memory task, one patient on a visual attention task, one patient on both an episodic memory task and a

visual attention task). Patients were also assessed in the ON medication condition by means of the Unified Parkinson's Disease Rating Scale (UPDRS), in both ON and OFF stimulation conditions. Significant motor improvement (i.e., a significant decrease in the score of the motor examination part of the UPDRS) was observed in the ON compared to the OFF condition (Wilcoxon Matched pairs test: $z = 2.942$; $p = 0.0033$).

In the ON stimulation condition, the stimulator was switched on at least 30 min before testing; in the OFF stimulation condition, the stimulator was switched off at least 30 minutes before testing. All patients were ON medication (l-dopa) during the experimental testing. Patients 1 and 2 were not submitted to the reading tasks because of organizational problems.

All subjects gave their informed consent to participate in the study, which was approved by the Institutional Ethics Committee of our university.

2.2. Experimental tasks

2.2.1. Picture naming

2.2.1.1. Stimuli and apparatus. The object and action naming task, devised by Crepaldi et al. (2006), was adopted for this study. This task consists of 100 black-and-white line drawings, 50 representing objects (25 natural and 25 artificial) and 50 actions. Nouns and verbs denoting these stimuli were matched for many variables ("word frequency", "age of acquisition", "typicality" and "agreement of response"), except imageability (which was significantly lower for verbs) and word length (which was significantly higher for verbs because of their inflectional endings). Subjects sat in a silent room, 40 cm away from the video display. They were instructed to name aloud, as fast as possible, the pictures that appeared on the display and to avoid any other verbal production. Stimuli were presented on the video display one at time according to the following sequence: blank page (2000 ms), fixation point (500 ms), picture. Pictures disappeared either when the participant responded or after 7500 ms, if no response was given. The verbal response was recorded by means of a microphone. The output of the microphone produced a signal that marked the onset of the verbal response. Time to respond (reaction time, henceforth RT) following presentation of the picture was recorded on the PC. Accuracy was scored manually.

2.2.1.2. Procedure. All subjects were tested in both ON and OFF stimulation conditions. However, as we were not permitted (for clinical and organisational reasons) to decide "a priori" the order of the testing conditions, in the naming tasks we decided to avoid any influence of repeated presentation of the pictures that might interfere with potential effects related to the different stimulation conditions. Therefore, both objects and actions were divided into two blocks of 25 pictures each in fixed random order. Half of the PD patients started with object naming and half with action naming; and half of the PD patients started with the first block of pictures and half with the second block of pictures, in counterbalanced order. Seven PD patients started the experiment in ON and five in OFF. In this procedure, each patient was administered all of the pictures, half in ON and half in OFF stimulation conditions, and no picture was presented twice, that is, in both stimulation conditions. By contrast, controls were administered all of the pictures; half started by naming the first block and half the second block of pictures; half started with object naming and half with action naming. Each block was preceded by a three-stimulus training. In general, the naming tasks took about 20 minutes to complete.

2.2.2. Word reading

2.2.2.1. Stimuli and apparatus. In the reading tasks, the subjects had to read 20 unambiguous nouns and 20 unambiguous verbs selected from a corpus of items reported in a previous study (Colombo & Burani, 2002). Nouns and verbs were

Table 1
Demographic and clinical features of PD patients.

	Age (yrs)	Education (yrs)	Gender	UPDRS III OFF-stimulation	UPDRS III ON-stimulation	Handedness Left/Right	Body side prevalence at onset	L-dopa medication
P1	70	8	M	40	33	Right	Left	ON
P2	80	3	M	41	33	Right	Right	ON
P3	70	13	F	40	22	Right	Right	ON
P4	61	8	M	54	34	Right	Right	ON
P5	62	17	M	25	18	Right	Right	ON
P6	65	8	M	33	36	Right	Left	ON
P7	73	12	M	39	31	Right	Right	ON
P8	70	17	M	37	34	Right	Right	ON
P9	62	13	M	41	34	Right	Right	ON
P10	66	5	F	50	46	Right	Right	ON
P11	58	17	F	46	36	Right	Right	ON
P12	61	17	M	36	19	Right	Right	ON

perfectly matched for length (number of letters), concreteness, familiarity, context availability, word frequency, word-root frequency, time of reading and time of lexical decision. Nouns and verbs were presented in the same list, in fixed random order (for a total of 40 stimuli). Each stimulus word was presented on the video display preceded by a warning (a fixation point that appeared at the centre of the screen for 500 ms). The word disappeared either when the subject read the word or after 2000 ms if no response was given. Subjects were instructed to read each word aloud as fast as possible. The verbal response was recorded using a microphone; and the output from the microphone produced a signal that marked the onset of the response from the stimulus presentation (RT).

At variance with naming tasks, all stimuli were presented in the ON and OFF conditions in two consecutive sessions, in different fixed random order. Five PD patients started the experiment in the ON condition and five in the OFF condition. Accuracy was scored manually. Overall, the reading tasks took about 20 min.

2.3. Statistical analysis

Data on overall accuracy and RTs of PD patients (independently of stimulation condition) and controls on the total number of items in the object and action naming and reading tasks were analysed by means of factorial ANOVAs, with group (PD and controls) and grammatical class (noun and verb) as categorical factors and accuracy or RTs as dependent variable. For the item-analysis the mean per-item number of correct responses made by PD patients and controls was analysed by a repeated-measure ANOVA, with accuracy or RTs (within effect-two levels: objects and actions) as dependent variable and group (PD and controls) as categorical predictor.

To analyse results of DBS on naming and reading, data were submitted to factorial ANOVAs with accuracy or RTs as dependent variable and group/condition (controls¹, PD ON, PD OFF) and grammatical class (objects and actions) as grouping factors. For the item analysis repeated-measure ANOVAs with accuracy or RTs as dependent variable (within effect-two levels: objects and actions) and group/condition (controls, PD ON, PD OFF) as categorical predictor were performed. Post hoc analysis was performed by Fisher's LSD test. Between and within comparisons were carried out by Mann–Whitney *U* test and Wilcoxon pair test, respectively.

3. Results

About 10.5% of RTs were excluded for technical reasons (e.g., if they were marked by non-verbal signals or by inadequate verbal productions, such as generic verbalisations before production of the expected response). For each subject, all values that deviated from the mean (1.05%) by more than two standard deviations were excluded from the analyses. In the reading task, only RTs were analysed because the number of correct responses approached ceiling not only in controls but also in PD patients in both ON and OFF stimulation conditions.

As data were not normally distributed (Shapiro–Wilk test), before ANOVAs were carried out, raw data on correct responses (accuracy) and RTs were subjected to logarithmic transformation. Raw data are reported in the tables.

3.1. Overall performance on object and action naming

Table 2(a) reports the raw data (means and standard deviations) on accuracy (number of correct responses) and RTs obtained on the total number of items in the object and action naming tasks by PD patients (independently of stimulation condition) and controls. The same set of data, after logarithmic transformation, is reported in Fig. 1 (Fig. 1A reports the ANOVAs performed on accuracy and RTs). For accuracy, the ANOVA showed significant effects of group and grammatical class, but no significant interaction. For RTs, ANOVA again showed significant effects of group and grammatical class, but no significant interaction. In summary, preliminary analyses on the total number of items showed that PD patients performed significantly worse (they had significantly lower accuracy and longer RTs) than

Table 2
Object and action naming tasks.

a. Accuracy and RTs (mean and SD) in PD patients and controls		
	Nouns (N=50) Mean (SD)	Verbs (N=50) Mean (SD)
Accuracy		
PD	42.08 (5.32)	31.08(9.73)
C	46.23(3.13)	38.14(5.23)
RTs		
PD	1711.41 (581.61)	2337.64 (939.16)
C	950.43 (233.38)	1098.60 (322.59)
b. Accuracy and RTs (mean and SD) in PD patients ON stimulation, OFF stimulation and controls		
	Nouns (N=25) Mean (SD)	Verbs (N=25) Mean (SD)
Accuracy		
PD ON	21.58 (2.64)	16.41 (4.87)
PD OFF	20.50 (3.00)	14.67 (5.73)
C	23.21 (2.50)	18.85 (3.37)
RTs		
PD ON	1473.82 (485.82)	2341.01 (939.67)
PD OFF	1545.056 (572.64)	2355.168 (999.03)
C	909.703 (160.96)	1105.26 (353.80)

controls and that performance on action naming was significantly worse (lower accuracy and longer RTs) than performance on object naming, with no significant interactions between the group and grammatical class factors.

Non-parametric comparisons within each group (Wilcoxon matched pair test) between the raw scores (number of correct responses) obtained on object and action naming tasks showed that both PD patients and controls scored significantly better on objects than actions (PD: $z=2.90$; $p<0.0037$; C: $z=3.17$; $p<0.0014$). A similar pattern of results was observed in the two patients with left-sided predominance of Parkinsonian motor symptoms, namely with a predominant involvement of the right cerebral hemisphere.

When the difference between the number of correct responses obtained by each subject in naming objects and actions was taken into account as an indicator of disadvantage for verbs, no significant difference emerged between PD patients and controls (Mann–Whitney *U* test=77.00; $p=ns$).

Item analysis (Fig. 1B). The mean per-item number of correct responses made by PD patients and controls and the RTs were analysed by a repeated-measure ANOVA. The ANOVA showed significant effects of group and grammatical class, but no significant interaction. On the RTs, the ANOVA showed significant effects of both group and grammatical class and a significant interaction.

3.2. Effects of stimulation condition on PD patients' naming and reading task

3.2.1. Picture naming

Table 2(b) reports the raw data (mean and SD) on accuracy (correct responses) and RTs obtained on the object and action naming tasks by controls and PD patients in ON and OFF stimulation conditions. The factorial ANOVA on accuracy (Fig. 2A) showed significant effects of group/condition and grammatical class, but no interaction. In PD patients, Fisher's least significant difference (LSD) post hoc comparisons showed that accuracy on nouns or verbs did not significantly differ between ON and OFF condition. Significantly worse performance was observed in PD patients in OFF as compared with controls in naming actions ($p=0.0035$) but not objects; no significant difference was observed between PD patients

¹ In controls, the analysis was performed on 25 items (in the first block in half of the subjects and in the second block in the other half).

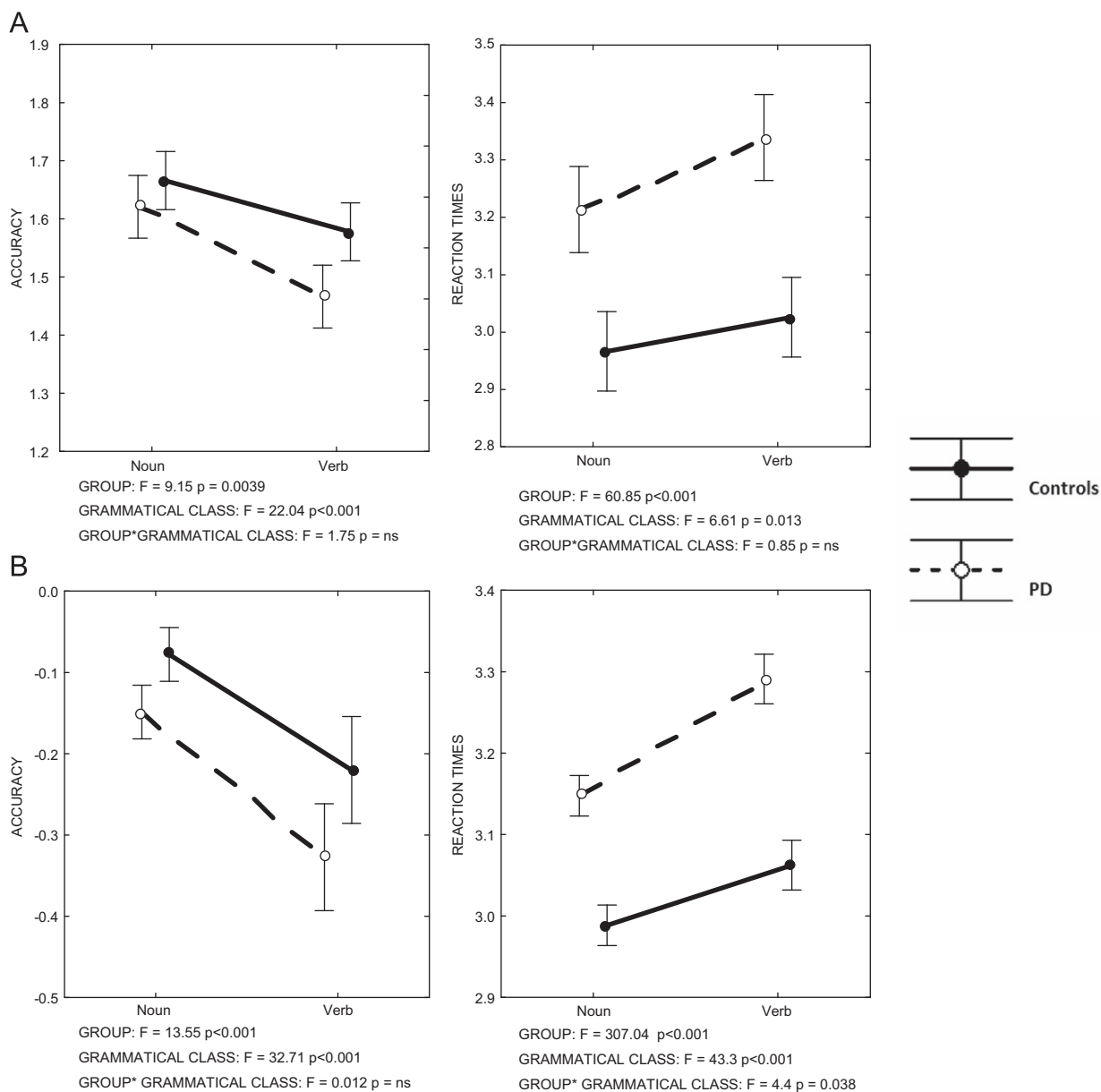


Fig. 1. Object and action naming tasks: mean (SD) accuracy and reaction times of PD patients and controls (logarithmic transformation) (A: subject analysis; B: item analysis). Results of ANOVAs are also reported.

ON stimulation and controls. Objects were named significantly more accurately than actions by controls (objects vs. actions: $p = 0.046$) and with greater statistical significance by PD patients in both stimulation conditions (ON stimulation: objects vs. actions: $p = 0.0068$; OFF stimulation: objects vs. actions: $p = 0.00046$).

Regarding RTs, the factorial ANOVA (Fig. 2A) showed significant group/condition and grammatical class effects, but no significant interaction. Fisher's LSD post-hoc showed that controls were faster than PD patients ON and OFF stimulation in naming both grammatical classes (objects: controls vs. PD ON: $p = 0.0014$; controls vs. PD OFF: $p = 0.00056$; actions: controls vs. PD ON: $p = 0.0001$; controls vs. PD OFF: $p = 0.0001$). When PD patients ON and OFF stimulation were compared, no significant difference in RTs emerged for either nouns or verbs. In PD patients, a significant difference between RTs in naming actions vs. objects was confirmed (PD ON: actions vs. objects: $p = 0.0018$; PD OFF: actions vs. objects: $p = 0.004$), whereas in controls the difference did not reach statistical significance.

Item analysis (Fig. 2B). The repeated-measure ANOVA showed a significant effect of both accuracy and grammatical class but no

interaction. Fisher's LSD test showed that actions were responded to less accurately than objects in controls and, as regards PD patients, in both conditions (PD ON: $p = 0.00021$; PD OFF: $p = 0.00046$; controls: $p = 0.00075$). Controls were more accurate than PD patients ON and OFF stimulation in naming both objects (controls vs. PD ON: $p = 0.0001$; controls vs. PD OFF: $p = 0.0001$) and actions (controls vs. PD ON: $p = 0.0001$; control vs. PD OFF: $p = 0.0001$). By contrast, no significant difference in accuracy was detected between PD ON and PD OFF in naming nouns or verbs.

Regarding RTs, the repeated-measure ANOVA showed similar results, with significant effects for both RTs and grammatical class but no significant interaction. However, Fisher's LSD test showed that RTs in controls and PD ON did not significantly differ for objects and actions, whereas in PD OFF RTs were significantly slower on actions than objects ($p = 0.00214$). In the between-group comparisons, controls were faster than PD ON stimulation ($p = 0.040$) and OFF stimulation ($p = 0.0009$) in object naming; in naming actions, controls were faster than PD OFF stimulation

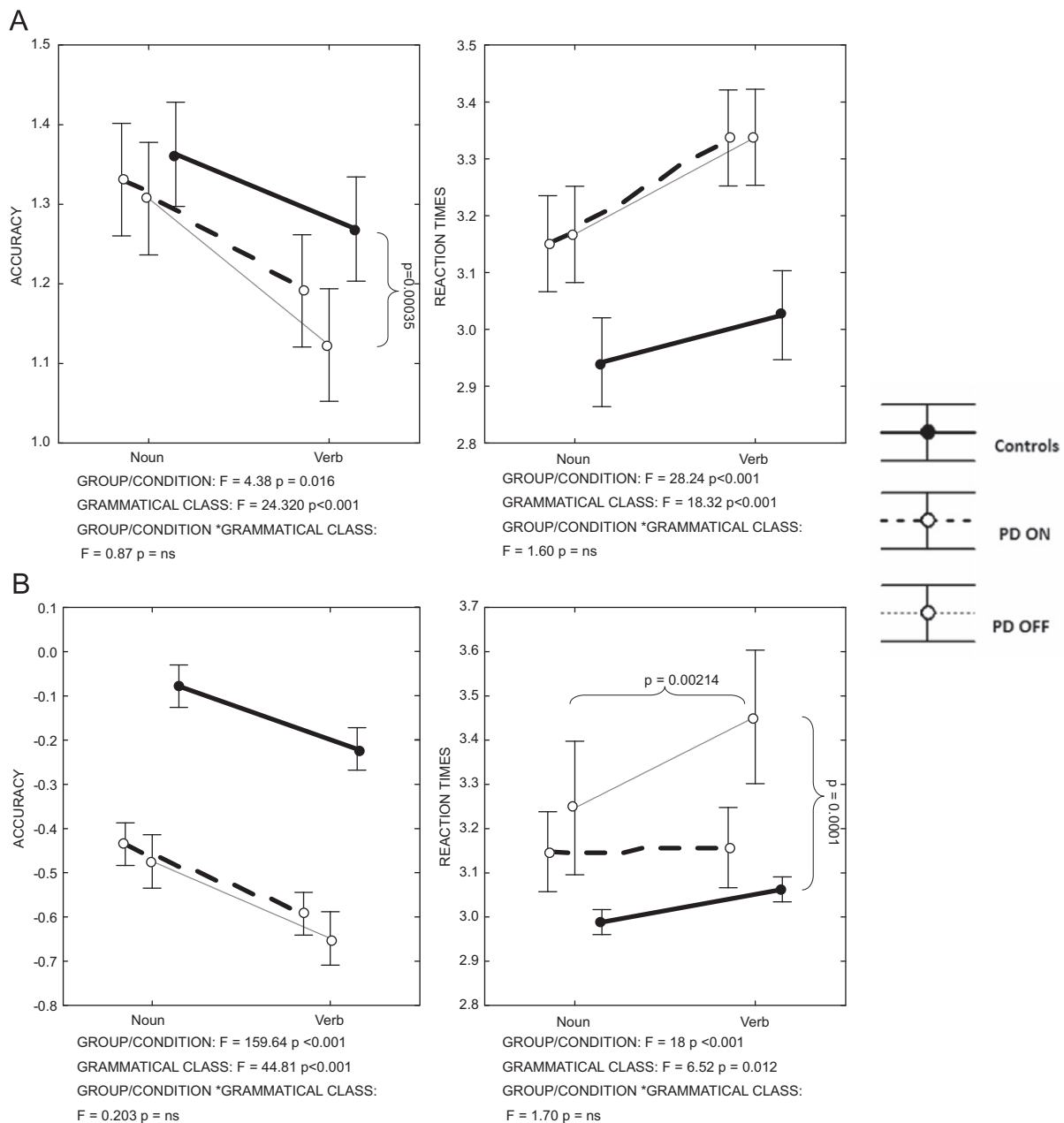


Fig. 2. Object and action naming tasks: mean (SD) accuracy and reaction times of PD patients ON stimulation, PD patients OFF stimulation and controls¹ (logarithmic transformation) (A: subject analysis; B: item analysis). ANOVAs and relevant post-hoc statistics are also reported.

($p=0.0001$) but were not faster than PD ON stimulation ($p=ns$), suggesting that actions gained more than nouns in the ON stimulation condition in terms of RTs; nevertheless, the significant effect of group in the ANOVA was due to the better performance of controls.

When accuracy in PD ON and PD OFF were directly compared by a repeated-measure ANOVA, significant effects for both condition and grammatical class (condition: $F=6.020$; $p=0.0159$; grammatical class: $F=23.87$; $p=0.000004$), but no significant interaction ($F=0.196$; $p=ns$) emerged. Similar results were obtained when the repeated measure ANOVA was performed with RTs (condition: $F=8.22$; $p=0.0059$; grammatical class: $F=3.71$; $p=0.056$; interaction: $F=2.04$; $p=ns$). Thus, direct comparisons between the ON and OFF conditions confirmed that PD patients were significantly more accurate and faster in the ON stimulation condition in both object and action naming.

3.2.2. Qualitative analysis of naming errors of PD patients in OFF and ON conditions

In the object and action naming tasks, a qualitative analysis of PD patients' errors showed that they were mainly anomias and semantic and visual errors (Table 3). In the action-naming task, many grammatical errors (nominalizations, that is, the production of a noun instead of a verb) were also produced. In PD patients, the improvement observed in ON stimulation (as compared with OFF stimulation) was mainly due to fewer anomias and semantic errors in naming actions.

3.2.3. Correlation between noun and verb naming, executive tasks and lexical variables

Probably due to the low number of subjects, no correlation between performance in naming (RTs) and executive tasks (such

Table 3

Object and action naming tasks: qualitative analysis of errors produced by PD patients in ON and OFF stimulation conditions (pool of 336 errors).

	Nouns ON	Nouns OFF	Verbs ON	Verbs OFF
Anomia	24	28	35	45
Semantic	15	16	25	33
Grammatical	0	2	35	35
Visual	5	8	16	14
Total	44	54	111	127

Table 4

Reading tasks: mean and SD (raw scores) on RTs obtained reading nouns and verbs by PD patients ON stimulation, PD patients OFF stimulation and by controls.

	N (N=20)	V (N=20)
PD ON	783.03 (194.01)	793.83 (184.04)
PD OFF	849.76 (227.86)	871.43 (238.64)
C	553.39 (80.91)	571.99 (93.70)

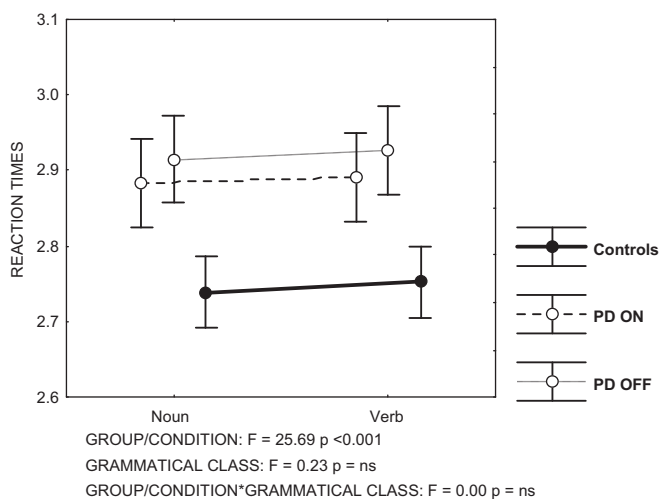


Fig. 3. Noun and verb reading tasks: mean reaction times (SD) of PD patients ON stimulation, PD patients OFF stimulation and controls (logarithmic transformation).

as MWCST) emerged. However, when correlation analysis (Spearman) was carried out between the performance on noun and verb naming (item analysis) and the lexical variables of the naming items (Crepaldi et al., 2006), no correlation emerged with verb naming in PD, while imageability (0.366; $p=0.05$), word length (0.348; $p=0.05$) and age of acquisition (0.307; $p=0.05$) were significantly correlated to the performance in controls. In naming nouns, PD performance was correlated only to imageability (0.56; $p=0.05$), while controls performance was significantly correlated to imageability (0.444; $p=0.05$) length (0.309) and age of acquisition (0.307; $p=0.05$). This suggests that naming in PD (mostly verb naming) is scarcely sensitive to lexical variables and that the performance might be influenced by other factors (for example, executive resources).

3.2.4. Word reading

As mentioned above, in reading tasks only RTs were analysed. Table 4 summarises the mean RTs obtained by PD ON, PD OFF and controls in reading nouns and verbs.

The factorial ANOVA (Fig. 3) showed a significant effect only for group/condition. We found no significant effect for grammatical

class and no significant interaction. No difference emerged in RTs between nouns and verbs (Fisher's LSD test) in either controls or PD patients. Controls were significantly faster than PD OFF and PD ON for both nouns (controls vs. PD ON: $p=0.00032$; controls vs. PD OFF: $p=0.00016$) and verbs (controls vs. PD ON: $p=0.00050$; controls vs. PD OFF: $p=0.00002$); but no significant difference was found between PD ON and PD OFF stimulation condition in reading either nouns or verbs.

However, when a repeated measure ANOVA was performed on PD patients only, a significant effect of condition emerged ($F=6.13$; $p=0.023$); there was no significant effect for grammatical class and no significant interaction.

Wilcoxon matched pairs test confirmed that PD patients ON stimulation were significantly faster in reading than PD patients OFF stimulation ($t=37.0$; $p=0.0111$). In PD patients ON stimulation and OFF stimulation, no significant difference in RTs emerged between nouns and verbs.

4. Discussion

The main results of the present study can be summarised as follows:

4.1. Picture naming

- Verbs were more difficult to name for both PD patients and controls, as accuracy and RTs were significantly better for nouns than verbs in both groups. On naming tasks, RTs of PD patients were significantly slower than those of controls, as shown by the significant group*grammatical class interaction in the ANOVA on the item analysis.
- When OFF stimulation, PD patients performed worse than controls in naming actions ($p=0.00035$) (Fig. 2A), while ON stimulation, PD patients were as accurate as controls. OFF stimulation, PD patients were significantly slower naming actions than objects ($p=0.00214$) (Fig. 2B), while PD ON and controls were as fast on actions as objects; on naming actions, PD OFF (but not PD ON) were significantly slower than controls ($p=0.0001$) (Fig. 2B).
- When ON and OFF stimulation conditions were directly compared (controls excluded), both accuracy and RTs were significantly better ON stimulation, on both grammatical classes.

4.2. Word reading

Controls were significantly faster than PD patients, and PD patients ON stimulation were faster than PD Patients OFF stimulation, without differences between grammatical classes.

4.2.1. Impairment of action naming in PD

Our PD patients were impaired on the action naming task, consistent with previous reports (Grossman et al., 1994; Piatt et al., 1999; Bertella et al., 2002; Péran et al., 2003; Signorini & Volpato, 2006; Boulenger et al., 2008). Our finding of worse performance on the verb naming task also in control subjects supports the view that verb naming is more demanding of cognitive resource than noun naming because of its intrinsic greater difficulty (Siri et al., 2008; Matzing et al., 2009).

At least two hypotheses can be advanced to account for the greater impairment in verb naming observed in PD patients than controls. First, a dysexecutive syndrome might play a critical role. Alternatively, we might hypothesize that in PD patients damage to the frontostriatal circuits might disrupt the neural systems involved in motor and conceptual representations of actions in cortical motor

areas (Hauk, Johnsrude, & Pulvermüller 2004), giving rise to the impaired verb processing (Boulenger et al., 2008; Rodriguez-Ferreiro et al., 2009) (this issue will be reconsidered later).

These two hypotheses (dysexecutive vs. representational) however, might overlap on the same core concept: unlike object representations, motor-action representations (Gentner, 1981) include dynamic aspects (i.e., more broadly, relational aspects), which must be integrated into spatial-temporal coordinates (see for example, Chatterjee, Southwood, & Basilico, 1999; Shapiro et al., 2006) and which, in turn, require executive functioning. Consistently, in our study lexical variables influenced naming performance on nouns more than verbs, suggesting that verb naming may be also sensitive to non-lexical factors (e. g., executive).

4.2.2. *Effects of STN-DBS on naming and reading tasks*

We found that PD patients showed improved performance in the ON stimulation condition (compared with the OFF stimulation condition) on both object and action naming tasks and also on noun and verb reading tasks (i.e. faster RTs with no significant differences between nouns and verbs). Thus, in the present study STN-DBS did not worsen the performance of PD patients.

The effects of STN DBS on different cognitive processes might differ and, indeed, are still controversial due to partially contrasting results reported in different studies on both the “chronic” and the “acute” effect of the stimulation (see Introduction). Methodological reasons may partly account for different findings, such as different tasks or sampling of patients; for example, in our study PD patients underwent the experimental tasks after a relatively long time interval after surgery compared to other studies, although the specific effects of such variable cannot be easily predicted at present.

Our results suggest that STN stimulation not only improves motor performance (scores on UPDRS motor subscale) but also cognitive performance on naming and reading tasks. In Follett et al.'s study (2010) naming did not improve in ON condition compared to pre implantation (whereas word fluency showed some decline), but no observation in OFF stimulation condition (after implantation) is provided, and this prevents the comparison with our results. We might hypothesise that motor improvement may have contributed to reducing RTs. In fact, RTs include a motor component (Sternberg, 1969). Although our experimental procedure was different from those requiring movement of a limb, such as pressing a key after making a decision (see for example Temel et al., 2006), we cannot exclude the possibility that the speed of speech onset, after the cognitive process of lexical search has been completed, might benefit from the facilitation of the motor component of the response produced by STN stimulation. Also increased reading speed might partially depend on this effect; and the similar increase in response speed observed in naming and reading (in spite of the different cognitive load of the two tasks) might support the hypothesis of a facilitation of the motor component of the response.

The qualitative analysis of the errors produced by PD patients in the naming tasks in the OFF and ON stimulation conditions partially support this explanation. Increased accuracy in ON condition was mainly due to the decrease in anomias, because during stimulation more responses were produced within the 7500 ms time limit. However, fewer semantic errors also contributed to increased accuracy on the naming tasks. The latter finding is difficult to explain only on the basis of a better motor response. The reduced number of semantic errors on the naming tasks in fact suggests more effective activation of the target word and greater ability to select the correct response from various alternatives.

It has been proposed (Crescentini et al., 2008) that a two-process model on the control of retrieval from semantic

memory (Badre, Poldrack, Paré-Blagoev, Insler, & Wagner 2005; Badre and Wagner, 2007) might be helpful to interpret PD patients' impaired word production (mostly on verbs). This model distinguishes between two controlled lexical-semantic processes (Badre et al., 2005; Badre & Wagner, 2007) in which different portions of the ventrolateral prefrontal cortex might play a critical role: a controlled retrieval process from long-term semantic memory, and a controlled post-retrieval selection process that resolves competition among active representations. On the basis of previous reports (Higginson, Wheelock, Carroll, & Sigvardt 2005; Longworth, Keenan, Barker, Marslen-Wilson, & Tyler 2005) and their own observations, Crescentini et al. (2008) hypothesised that the basal ganglia might modulate both controlled retrieval and post-retrieval selection through their connections to the ventrolateral prefrontal cortex; in particular, during language production the basal ganglia might modulate both active retrieval from stored semantic memory and inhibit competing alternatives to the target-word. A study based on a semantic priming paradigm confirmed that PD patients are impaired in controlled processes of semantic access (but not in automatic semantic access) and that this impairment could be restored by STN DBS (Castner et al., 2007).

The lexical retrieval required in the confrontation naming task used in the present study may not be considered an automatic process, although the demand for the control of retrieval is low compared to word generation tasks (Péran et al., 2003; Castner et al., 2008; Crescentini et al., 2008). Thus, we can hypothesise that during a naming task both controlled retrieval and post-retrieval selection among competitors associated with the target within a given semantic category are impaired in PD, and that this impairment could give rise to the production of semantic errors. Because it restores the corticobasal circuitry, STN stimulation is thought to facilitate both retrieval and post-retrieval selection, thus reducing the number of semantic errors and increasing the number of correct responses. Moreover, facilitation of these processes might result in greater speed of retrieval and selection processes, thus contributing to increase the number of responses within the time limit and response speed in general.

4.2.3. *Effects of STN-DBS on verb production*

In a previous study (Castner et al., 2008), it was hypothesised that STN stimulation interferes negatively with the ability to select from many competitive alternatives during verb production. Although STN stimulation seemed to have beneficial effects on the overall verb production as in our study, errors were mostly produced on verbs with more competing alternatives. We did not specifically consider the influence of the number of competing alternatives on naming, although verbs might have more competitors than nouns. Yet, we found that STN stimulation had beneficial effects on both accuracy and RTs in verb naming although we cannot exclude that floor effects can to some extent account for the larger improvement on verbs as compared with nouns during stimulation. If STN stimulation improves PD patients' controlled access to semantic conceptual information by restoring the functional connections between the basal ganglia and the ventrolateral prefrontal cortex, this improvement might be primarily evident for verbs, which are the class of items most sensitive to a reduction of processing resources. Moreover, verbs might be less sensitive to the bottom-up activation component of the retrieval processes than nouns (Silveri & Colosimo, 1995), thus increasing the demand for controlled activation by corticostriatal circuits.

Our results on the reading tasks are in line with this conclusion. Reading was significantly faster in the ON than the OFF stimulation condition, but no difference emerged between nouns and verbs. In other words, in tasks that do not necessarily require

an active lexical search (because they can be performed by applying grapheme-to-phoneme conversion rules), no word class effect emerged in either PD patients or controls, and the effect of STN stimulation was similar on nouns and verbs.

It is thus possible that partially different results with Castner et al.'s paper (2008), could be put on the account of different task-difficulty. In a relatively easy task such as naming (and reading) motor improvement could result in a general reduction of task demand, so that attentional resources still available can be principally directed on the proper cognitive components of the task, that is, item selection. This hypothesis needs specific validation. In Schubert et al.'s study (2002), the RTs improved during stimulation independently of the complexity of the cognitive processing involved. Although our data cannot be directly compared with this study, due to different locus of stimulation (globus pallidus vs. STN), this finding suggests that the cognitive performance might be influenced by motor components.

5. Conclusions

Verbs are generally more difficult to name than nouns in PD patients. Impairment of verbs was evident in naming (which requires active lexical search) but not in reading tasks (which can be performed by applying conversion rules). STN stimulation improved accuracy in naming and reduced RTs in both naming and reading tasks. A motor facilitation component might partially account for the shorter RTs and, to some extent, the increased accuracy in naming in PD patients in the ON stimulation condition. However, to fully account for PD patients' greater accuracy in naming during stimulation, we hypothesize that STN stimulation restores the activity of the corticostriatal circuits involved in the active control of the retrieval and selection processes from lexical-semantic knowledge. Although further studies are needed to confirm our findings we suggest that STN stimulation may not only improve PD patients' motor functioning but also their cognitive performance, at least in tasks such as naming and reading.

Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at <http://dx.doi.org/10.1016/j.neuropsychologia.2012.04.023>.

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