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

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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.

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, 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

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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 & Ciccarelli, 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 & Ciccarelli, 2007b), cerebellar lesions (Fiez, Petersen, Cheney, & Raichle, 1992) or with HIV encephalopathy (Woods, Careya, Trösterc, 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, Adolphsa, & 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 & Ciccarelli, 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 and 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 constrains 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