Brain & Language 141 (2015) 103–109

Contents lists available at ScienceDirect

Brain & Language

journal homepage: www.elsevier.com/locate/b&l

The effects of subthalamic deep brain stimulation on metaphor comprehension and language abilities in Parkinson's disease

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ARTICLE INFO

Article history:
Accepted 15 December 2014
Available online 8 January 2015

Keywords:
Parkinson's disease
Deep brain stimulation
Language
Metaphor comprehension

ABSTRACT

The effects of subthalamic nucleus (STN) deep brain stimulation (DBS) in Parkinson's disease (PD) on different language abilities are still controversial and its impact on high-level language abilities such as metaphor comprehension has been overlooked. The aim of this study was to determine the effects of STN electrical stimulation on metaphor comprehension and language abilities such as lexical and semantic capacities. Eight PD individuals with bilateral STN-DBS were first evaluated OFF-DBS and, at least seven weeks later, ON-DBS. Performance on metaphor comprehension, lexical decision, word association and verbal fluency tasks were compared ON and OFF-DBS in addition to motor symptoms evaluation. STN stimulation had a significant beneficial effect on motor symptoms in PD. However, this stimulation did not have any effect on metaphor comprehension or any other cognitive ability evaluated in this study. These outcomes suggest that STN stimulation may have dissociable effects on motor and language functions.

1. Introduction

Parkinson's disease (PD) is traditionally characterized by motor symptoms such as bradykinesia, rigidity, tremors and postural instability. Many PD patients may also present cognitive symptoms including executive dysfunctions (e.g., working memory, mental flexibility and inhibition deficits) (Owen et al., 1992; Verbaan et al., 2007) and language impairments (e.g., verbal fluency and pragmatic deficits) (Monetta, Grindod, & Pell, 2009; Murray, 2008; Pell & Monetta, 2008; Vachon-Joannette, Tremblay, Langlois, Chantal, & Monetta, 2013). Pragmatic language such as metaphor comprehension is often impaired in PD, probably because it requires high-level language and cognitive abilities (McKinlay, Dalrymple-Alford, Grace, & Roger, 2009; Monetta & Pell, 2007). Indeed, some studies reported an association between executive deficits and metaphorical sentence comprehension impairment in PD, suggesting that metaphor processing may be dependent on intact executive functions (Monetta & Pell, 2007; Pell & Monetta, 2008; Vachon-Joannette et al., 2013). To understand a metaphor (e.g., *these spies are foxes*), in which the intended meaning does not coincide with the literal meaning of the words, people have to think beyond the literal meaning in order to understand the figurative meaning of the sentence (Bowdle & Gentner, 2005). This process requires, among other things, to recognize the words of the metaphor (lexical access), to activate the corresponding concepts (their literal and/or figurative senses) in semantic memory and then to switch between the different attributes of the concept (mental flexibility) to select the one common to the first and last words (e.g., *spies* and *foxes*) of the metaphor (Bowdle & Gentner, 2005). Language impairments, including metaphor comprehension deficits, may lead to a decrease in communicative abilities, which could affect the quality of life (Miller, Noble, Jones, & Burn, 2006).

To improve the quality of life of PD patients, treatment such as subthalamic nucleus (STN) deep brain stimulation (DBS) was implemented (Gronchi-Perrin et al., 2006). The positive effect of bilateral STN-DBS on motor symptoms in PD is well established, but the mechanisms of action of DBS are still unclear (Kleiner-Fisman et al., 2006). Several submechanisms have been suggested to be involved, including alterations in neurotransmitters and

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http://dx.doi.org/10.1016/j.bandl.2014.12.004
0093-934X/

hormonal systems, changes in neuronal firing and desynchronisation in abnormal oscillations of subcortical nucleus in addition to more global effects on neuronal networks (Benabid, Chabardes, Mitrofanis, & Pollak, 2009). STN-DBS possibly shuts down or modifies the abnormal activity in the STN, restoring neuronal networks implicated in motor functions, most likely frontostriatal pathways (Montgomery & Gale, 2008). Alexander, Crutcher, and DeLong (1990) demonstrated that basal ganglia (BG) are connected to different frontal cortex areas through five parallel frontostriatal pathways (i.e., the motor, oculomotor, prefrontal dorsolateral (PFDL), orbitofrontal and anterior cingulated circuits) (Alexander et al., 1990). The motor loop includes different parts of the frontal cortex (motor, premotor and supplementary motor area) and is known to regulate motor functions, while the PFDL loop is implicated in cognitive processes including executive functioning (Zgaljardic, Borod, Foldi, & Mattis, 2003).

Even if the beneficial effects of STN-DBS on motor symptoms are well established, their effects on cognition and language are still controversial and the mechanisms of action remain unclear. The STN facilitates the communication between the striatum and the globus pallidus internus (GPi) by the intermediary of the globus pallidus externus (GPe) (Parent & Hazrati, 1995) and may influence the frontostriatal pathways. Different regions have been identified in the STN, including a dorsolateral sensorimotor and a ventromedial associative regions, (Parent & Hazrati, 1995), suggesting that STN contributions may be related to motor control and to cognitive functions, including language abilities (Whelan, Murdoch, Theodoros, Silburn, & Hall, 2004). Moreover, ablative lesions of bilateral or left STN have been shown to deteriorate specific executive abilities (McCarter, Walton, Rowan, Gill, & Palomo, 2000). Thus, STN-DBS may also influence language abilities, and particularly metaphor comprehension most likely dependent on intact executive functions, via the frontostriatal pathways (Alexander et al., 1990). Indeed, some studies suggested the implication of a frontostriatal neuronal network, most likely the PFDL circuit, in executive and pragmatic abilities, including metaphor comprehension (Pell & Monetta, 2008; Thoma & Daum, 2006).

Some studies have reported a decrease in executive functions and memory after STN-DBS (Fasano et al., 2010; Klempířová et al., 2007; Saint-Cyr, Trépanier, Kumar, Lozano, & Lang, 2000; Smeding, Speelman, Huizenga, Schuurman, & Schmand, 2011) while others have observed an improvement in executive abilities (Daniele et al., 2003; Schoenberg, Mash, Bharucha, Francel, & Scott, 2008; Temel et al., 2006). Despite these divergent results, a meta-analysis completed by Parsons, Rogers, Braaten, Woods, and Tröster (2006) demonstrated a significant (but small) deterioration in executive functions and memory following STN-DBS. In studies exploring the effects of STN-DBS on language, verbal fluency was certainly the most investigated ability. Most of these studies reported a deterioration in verbal fluency after surgery (Schoenberg et al., 2008; Wojtecki et al., 2006). This deterioration was observed a few months after surgery, suggesting that this effect could be caused by the implantation of electrodes (Morrison et al., 2004). There are still few studies about the effects of bilateral STN stimulation on other language abilities and their results often seem contradictory: while a decline in syntactic, semantic, morphological and grammatical abilities was observed in some studies (Castner et al., 2008; Phillips et al., 2012; Schulz et al., 2012), others have demonstrated an improvement in syntactic and semantic abilities (Silveri et al., 2012; Zanini et al., 2003). More specifically, Whelan, Murdoch, Theodoros, Hall, and Silburn (2003) did not note any significant difference at 3 months post-surgery in metaphor comprehension in PD patients with bilateral STN-DBS. In a following study, Whelan, Murdoch, Theodoros, Silburn, and Hall (2005) reported an improvement in PD patients at 3 and 12 months post-surgery in high-level language abilities, including metaphor comprehension. It is still unclear if STN-DBS has an effect on this language ability. In most of DBS studies, measures of language abilities were performed before and after electrode implantation. Therefore, these measures simultaneously evaluated the effects of surgery and those of electrical stimulation. No study has investigated only the effects of electrical stimulation of the STN on pragmatic language such as metaphor comprehension. Moreover, the effects of this stimulation on other language capacities such as lexical and semantic abilities are still controversial.

Since the effects of STN-DBS on language are unclear and a majority of studies suggest a worsening in these functions after DBS, PD patients with important language impairments tend to be excluded as candidates for STN-DBS surgery (Mattis, Chaya, & Kathryn, 2013). Therefore, it is very important to better know the effects of STN-DBS on language abilities to ensure an optimal selection of the candidates. Metaphoric language is used every day and is an important means of communication that can assist in a better understanding and explanation of abstract ideas (Cardillo, Watson, Schmidt, Kranjec, & Chatterjee, 2012; Kovecses, 1988). Therefore, the impact of STN-DBS on this language ability is important to determine.

In the present study, the effects of STN-DBS on metaphor comprehension and other language capacities (verbal fluency, lexical and semantic capacities) were investigated ON and OFF-DBS. A majority of studies have shown a decline in executive functions associated with STN-DBS. A deterioration in metaphor comprehension and the other language abilities tested were thus expected when comparing participants on and off STN-DBS, since these abilities require several cognitive functions, including executive functions.

2. Methods

2.1. Participants

Eight native French speakers diagnosed with idiopathic PD (mean ± SD; age: 67 ± 7 years; education: 13 ± 5 years; 5 women and 3 men) participated in this study. The diagnosis of idiopathic PD was made by a movement disorder neurologist on the basis of accepted motor criteria (Calne, Snow, & Lee, 1992). All participants were right-handed and underwent a bilateral implantation of electrodes in the STN at the Centre Hospitalier universitaire de Québec (CHUQ) at least two years prior to their participation in this study. They were recruited in Quebec City between 2011 and 2013. They had stabilised medication and stimulator parameters at the time of assessment. Motor disability was evaluated with the Hoehn and Yahr (H&Y) staging criteria and the Unified Parkinson's Disease Rating Scale part III (UPDRS-III) ON and OFF-DBS (Fahn & Elton, 1987). One patient had tremor dominant motor symptoms, four patients had dominant rigidity and the remaining had mixed symptoms. In addition to their dopaminergic medication (L-Dopa medication (mean ± SD) = 563 ± 396 mg/day), three patients (No. 1, 7 and 8) took medication for depressive symptoms: citalopram ($n = 1$) and venlafaxine ($n = 2$). Twenty healthy elderly without neurological impairment (mean ± SD age: 67 ± 5 years; education: 14 ± 3 years; 8 women and 12 men), right-handed native French speakers, were recruited to be healthy controls (HC). No participant in the control group took drugs for depression. The Beck Depression Inventory version IA (BDI-IA) was used to assess depressive symptom severity (Beck, Steer, Ball, & Ranieri, 1996). Since these symptoms may have an impact on cognition (Tremblay, Achim, Macoir, & Monetta, 2013; Tremblay, Monchi, Hudon, Macoir, & Monetta, 2012), we ensured that the control group was similar to the PD group relative to depressive symptom severity.