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Research report

Unilateral subthalamotomy in Parkinson's disease: Cognitive, psychiatric and neuroimaging changes

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ABSTRACT

Unilateral subthalamotomy is an effective treatment for the cardinal motor features of Parkinson's disease (PD). However, non-motor changes possibly associated with right or left subthalamotomy remain unknown. Our aim was to assess cognitive, psychiatric and neuroimaging changes after treatment with unilateral subthalamotomy. Fourteen medicated patients with PD were evaluated before and after (mean 6 months after operation) unilateral subthalamotomy (5 right, 9 left). In addition to motor assessments, cognitive (global cognition and executive functions), psychiatric (apathy, depression, anxiety, mania, hypo- and hyperdopaminergic behaviours, impulsivity), quality of life evaluations and volume of lesions were obtained. After surgery, significant improvement of motor signs was observed. Unilateral subthalamotomy improved general cognitive status, but left subthalamotomy reduced semantic verbal fluency compared to the pre-operative state. Depression and quality of life were improved with both right and left subthalamotomy. However, hyper-emotionality was present after surgery and right subthalamotomy increased impulsivity and disinhibition (on NeuroPsychiatric Inventory and Ardouin Scale for Behaviour in PD), a result linked to larger lesion volumes. We conclude that unilateral subthalamotomy is effective for treating the cardinal motor features of PD and improves mood. Right subthalamotomy is associated with greater risk of impulsivity and disinhibition, while left subthalamotomy induces further impairment of semantic verbal fluency.

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1. Introduction

Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is a well-established treatment for Parkinson's disease (PD), whereas ablative surgery, i.e., subthalamatomy, is limited to special medical and economic circumstances. PD laterality is a critical aspect for surgery as implantation of DBS electrodes or surgical lesioning is guided by the most affected body side, determining if surgery is performed uni- or bilaterally. If the patient's motor signs are predominant on one hemibody, DBS or lesions are completed unilaterally (Alvarez et al., 2009; Krack, Fraix, Mendes, Benabid, & Pollak, 2002). A host of controlled studies and meta-analyses (Combs et al., 2015; Wang et al., 2016) have established that STN-DBS does not induce any significant decline in global cognition, but verbal fluency, some tests of executive function and inhibitory control show impairment with STN stimulation (Jahanshahi, 2013; Jahanshahi, Obeso, Rothwell, & Obeso, 2015; Jahanshahi et al., 2000; Obeso, Wilkinson, Rodríguez-Oroz, Obeso, & Jahanshahi, 2013; Witt et al., 2008). In terms of behaviour and mood, after STN-DBS, some authors report improvement in apathy (Campbell et al., 2012) and depression (Witt et al., 2008); while others have documented worsening of depression and apathy (Lhommee et al., 2012; Thobois et al., 2013) in association with medication reduction.

Unilateral subthalamotomy has also been successfully used to treat the motor features of PD (Alvarez et al., 2009, 2005; Patel et al., 2003). Although unilateral and bilateral subthalamotomy for PD are by and large efficacious and safe (Alvarez et al., 2005, 2009), the cognitive and neuropsychiatric effects of subthalamotomy have only been examined in three studies. McCarter, Walton, Rowan, Gill, and Palomo (2000) evaluated cognitive functioning before and 12 months after subthalamotomy in 12 PD patients with a variety of surgical procedures, including 3 with right subthalamotomy, 2 with left subthalamotomy, 4 with right subthalamotomy + left STN-DBS and 4 with bilateral subthalamotomy. They reported no significant change after subthalamotomy on the cognitive tests used, but it was noted that left subthalamotomy was associated with worse cognitive outcome. However, the mixed group of patients with subthalamotomy and DBS leaves the results up to verification. A similar result of no change in cognition was obtained in 6 patients who had right and 7 who had left subthalamotomy (Patel et al., 2003). In the third study (Bickel et al., 2010), on 10 PD patients who had bilateral subthalamotomy, there was no significant change in cognition but a parallel motor and neuropsychiatric (depression and apathy) improvement was reported 24 months after surgery, whereas disinhibition and euphoria increased post-operatively.

Thus, the available evidence regarding the cognitive and psychiatric effects of subthalamotomy is inconsistent and potential laterality effects are not well-defined. Clarifying laterality effects is important since the two most consistent side effects of surgery (particularly after DBS) such as verbal fluency and disinhibition have clear hemispheric effects and may mainly present as side-effects of left or right subthalamotomy respectively.

In this study, our aim was to assess whether unilateral left and right subthalamotomy in PD may impact cognition, mood and behaviour differently. With this aim, we used an extensive battery of measures of cognition, mood and behaviour combined with imaging morphometric measures after subthalamotomy.

2. Methods

2.1. Patients

Fourteen (12 males) consecutive patients with PD who were candidates for unilateral subthalamotomy were enrolled in the study from October 2009 to December 2014 in the Centro Internacional de Restauración Neurológica (CIREN) in La Habana (Cuba). The patients were diagnosed with PD according to UK Brain Bank criteria (Hughes, Daniel, Kilford, & Lees, 1992) (see Table 1). Following previous surgical protocols (Alvarez et al., 2001, 2009), unilateral subthalamotomy was indicated based on predominant asymmetric hemibody motor features (mainly tremor and bradykinesia). Patients receive ablation of the STN contralateral to hemibody motor signs performed in a single surgery session. The STN sensorimotor region was localized using microrecording and stimulation while neurologists explore the motor signs while the patient is awake. Finally, when the target is located, a thermolytic lesion was placed accordingly. Nine patients received left and 5 right subthalamotomy. Neuropsychological assessment (by IO and EC) was completed before surgery and repeated approximately 6 months after surgery. All patients were under levodopa treatment during assessments (except for the UPDRS-III OFF evaluation, see below).

Study exclusion criteria were presence of focal neurological deficits, cognitive impairment (Mini-Mental State Examination, MMSE<26), major neuropsychiatric problems refractory to medical treatment or other health condition that was a contra-indication to surgery. Ethical approval was obtained from the CIREN scientific committee and the Cuban National Ethical Committee. All participants provided informed consent.

2.2. Assessments

Change in motor signs was evaluated using the Unified Parkinson's Disease Rating Scale (UPDRS-III, motor), rated by a neurologist prior and after surgery. Patients were assessed both in the ON and OFF medication states (with OFF state defined as overnight medication withdrawal).

The neuropsychological assessment focused on global tests of cognition and also on executive function. The MMSE and the Mattis Dementia Rating Scale-2 (MDRS-2) were used for assessment of global cognition and screening for dementia. The Frontal Assessment Battery (FAB) was used to assess executive function. Other executive function measures as the Stroop test and Hayling test were included: (i) the Stroop test from the Delis-Kaplan Executive Function System (DKEFS) battery was used, consisting of 4 subtests: word reading, color naming, inhibition and inhibition/switching (for details see (Obeso et al., 2011)). (ii) The Hayling sentence completion test (Burgess & Shallice, 1997) in Spanish was included as previously used (Obeso et al., 2011). The test has two sections: