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Pre-operative obesity may influence subthalamic stimulation outcome in Parkinson's disease☆

Audrey Rouillé [a], Stéphane Derrey [b], Romain Lefaucheur [a,*], Alaina Borden [a], Damien Fetter [a], Maryvonne Jan [a], David Maltête [a,c]

[a] Department of Neurology, Rouen University Hospital, University of Rouen, France
[b] Department of Neurosurgery, Rouen University Hospital, University of Rouen, France
[c] INSERM Unit, 1073 Rouen, France

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ABSTRACT

Background: Pre-operative predictive factors for optimal post-operative effect of subthalamic nucleus (STN) stimulation in Parkinson's disease (PD) have been previously reported. No study has explicitly assessed the link between excess pre-operative body weight and STN stimulation outcome.
Methods: We retrospectively compared STN stimulation outcomes of 36 PD patients with excess pre-operative body weight (group 1) and 36 matched normal-weight pre-operative (group 2) PD patients. We focused on the post-operative outcomes in the sub-group of 12 obese (group 3) PD patients.
Results: The post-operative motor improvement and the reduction of severity of levodopa-related complications were not statistically different between groups 1 and 2 ($P > 0.05$). In the obese group (group 3), the axial subscore significantly improved by 29.8% in the *on*-drug/*on*-stimulation conditions whereas the improvement was not significant in the *off*-drug/*on*-stimulation condition (22.4%, $P = 0.20$). The post-operative Mattis Dementia Rating Score was significantly reduced in group 1 and group 3.
Discussion: We considered that the post-operative axial impairment observed in the obese PD patients might be essentially consecutive to disease progression and/or post-operative DBS consequences, i.e. surgical procedure or electrical stimulation itself. Moreover, it could be argued that musculoskeletal disorders associated with obesity were responsible for the incomplete efficacy of STN stimulation on axial sub-scores, by increasing gait and balance impairment.
Conclusion: Pre-operative obesity may be regarded as a predictive clinical factor of axial and cognitive impairment after STN-DBS.

1. Introduction

Body mass index (BMI) is often lower in patients with Parkinson's disease (PD) compared to healthy age-matched controls, especially in PD patients with advanced disease [1,2]. A variety of components, related both to motor and non-motor symptoms, involving increased energy expenditure due to muscular rigidity and increased involuntary movements, dysphagia, intestinal hypomotility, and depression, may contribute to weight loss in PD [3–7]. Underweightness is well documented in PD, but overweightness has been less reported. A recent epidemiological study suggested that 65% of PD patients might be overweight or obese [8]. The negative impact of obesity on the health and functioning of older adults is widely acknowledged.

Subthalamic nucleus deep brain stimulation (STN-DBS) is one of the most effective treatments for advanced levodopa-responsive forms of PD that rapidly improves motor disability and reduces levodopa-related complications [9]. Many studies have found that this technique is accompanied by a rapid, non-negligible weight gain that can adverselyaffect patients' metabolic status [10–12]. The weight gain after surgery in STN-stimulated PD patients is closely correlated to the dyskinesia improvement [13]. Conversely, the improvement in UPDRS motor score after STN-DBS seems to be a protective factor for weight gain [12].

Abbreviations: BMI, body mass index; PD, Parkinson's disease; STN-DBS, subthalamic nucleus deep brain stimulation; UPDRS, Unified Parkinson's disease Rating Scale; CAPIT, core assessment program for intracerebral transplantation; MDRS, Mattis Dementia Rating Scale score; WR, Stroop test word reading; CW, Stroop test color word; MADRS, Montgomery–Asberg Depression Rating Scale; LEDD, L-dopa equivalents daily dose.

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* Corresponding author at: Department of Neurology, Rouen University Hospital, 76031 Rouen Cedex, France.
E-mail address: romain.lefaucheur@chu-rouen.fr (R. Lefaucheur).

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To our knowledge, no study has explicitly assessed the link between excess pre-operative body weight and STN-DBS outcome in PD. Here, we retrospectively compared 36 normal-weight patients with 36 matched patients with pre-operative excess body weight. Moreover, since obesity is associated with significant barriers to mobility-dependent activity and participation in other activities of daily living, we focused on the post-operative outcome in an obese sub-group.

2. Patients and methods

2.1. Subjects

The selection criteria were clinically diagnosed PD, severe levodopa-related complications despite optimal adjustment of antiparkinsonian medication, no surgical contraindications, and no dementia or major ongoing psychiatric illness. The surgical procedure has been previously described [14]. Post-operative management was made according to the recommendations [15].

Data regarding weight and height were recorded, and BMI were calculated (weight in kg/height^2 in m^2). Of the 106 consecutive PD patients who underwent STN high frequency stimulation in our center between January 2004 and May 2013, 36 patients (21 men, 15 women, mean age 60.3 ± 6.8 years, mean disease duration 12.6 ± 4.1 years) were categorized in the pre-operative excess body weight group (group 1, body mass index > 25 kg/m^2). These patients were compared with 36 normal weight (group 2, body mass index 18–25 kg/m^2) PD patients matched for sex, age, disease duration, and parkinsonian motor disability (Unified Parkinson's Disease Rating Scale (UPDRS) part III in the *off*-drug condition) and levodopa responsiveness (21 men, 15 women, mean age 62 ± 6.6 years, mean disease duration 12.3 ± 4 years) who underwent the same procedure (Table 1).

Twelve patients of the group 1 (4 men, 8 women, mean age 60 ± 7.3 years, mean disease duration 12.2 ± 3.5 years) were then categorized into the obese sub-group (group 3, body mass index ≥30 kg/m^2) [16].

2.2. Clinical assessment

A baseline clinical evaluation was performed 1 month before surgery based on the CAPIT protocol [17]. The motor state was assessed by the UPDRS part III. Axial motor features were assessed separately using the corresponding UPDRS III sub-scores (items 18, 28, 29 and 30). Motor performance assessments were performed 6 months after surgery, under two conditions (*off*-drug/*on*-stimulation, *on*-drug/*on*-stimulation) as previously described [18]. Percentage improvement in motor disability was determined with respect to the pre-operative *off*-drug condition. Complications of levodopa therapy, i.e. dyskinesias (UPDRS part IVA score) and clinical fluctuations (UPDRS part IVB score), were also assessed pre and postoperatively.

All patients underwent standardized cognitive and psychiatric evaluation: Mattis Dementia Rating Scale score (MDRS), Stroop test word reading (WR) and color word (CW), phonemic and semantic verbal fluency examination, and Montgomery–Asberg Depression Rating Scale (MADRS).

Dopaminergic drugs, expressed in L-dopa equivalents daily dose (LEDD) were recorded before and 6 months after surgery. BMI was calculated at the same time.

The main cardiovascular risk factors, i.e. tobacco exposure, high blood pressure, high cholesterol, and diabetes were collected before surgery. Post-operative complications such as infection, deep vein thrombosis or pulmonary embolism, and hemorrhage were recorded. The stimulation parameters were assessed at the 6 months evaluation.

The study design was approved by the local ethics committee.

2.3. Statistics

Statistical analysis was performed with NCSS version 6.0. The different score changes were expressed as mean value ± standard deviation. The effects of STN stimulation in each group were evaluated by comparison of the different scores obtained before surgery (baseline) and six months after surgery using a Wilcoxon signed-rank test. We used a non-parametric Mann–Whitney test to compare post-operative outcomes between normal BMI group (group 2) and excess body weight group (group 1). We compared the post-operative outcomes between normal BMI group (group 2) and obese group (group 3) by using a Kruskal–Wallis test (level of significance was set at 0.05).

3. Results

3.1. Normal (group 2) versus excess pre-operative body weight (group 1)

There were no significant differences between groups (normal versus excess pre-operative body weight) with respect to pre-operative age, disease duration, LEDD, total score of UPDRS part III and axial sub-score in the *off*-drug condition, levodopa responsiveness or cognitive performances ($P > 0.05$).

Six months after surgery, the total UPDRS part III score significantly improved from baseline value (*off*-drug condition) by 56.2% in the *off*-drug/*on*-stimulation and 77.4% in the *on*-drug/*on*-stimulation conditions in group 1; and 59.3% in the *off*-drug/*on*-stimulation and 78.3% in the *on*-drug/*on*-stimulation conditions in group 2 ($P < 0.05$). The axial sub-score significantly improved from baseline by 34.1% in the *off*-drug/*on*-stimulation and 56.2% in the *on*-drug/*on*-stimulation in group 1, and 33.7% in the *off*-drug/*on*-stimulation and 65.3% in the *on*-drug/*on*-stimulation in group 2 ($P < 0.05$). The severity of levodopa-related complications (UPDRS IV) was significantly reduced by 70.2% in group 1 and 62.4% in group 2 ($P < 0.05$). Post-operative motor improvement (UPDRS III total and axial sub-score) and reduction of severity of levodopa-related complications (UPDRS IV) were not statistically different between groups ($P > 0.05$).

LEDD was significantly reduced by 38% in group 1 and 56.6% in group 2 with a significant difference between groups ($P < 0.05$). The mean BMI increased by 5.5% in group 1 and 10.5% in group 2 and differences were significant between groups ($P < 0.05$). Post-operative CT-scan revealed no intracranial complication. The clinical characteristics of PD patients are summarized in Table 1.

The mean stimulation parameters were: 150 and 150 Hz, 3.1 and 3.1 V, and 62.5 and 61.1 microseconds, respectively for the right and the left sides in group 1; 141 and 141 Hz, 2.9 and 3 V, and 63.3 and 65 microseconds, respectively for the right and the left sides in group 2. There was no difference between groups.

Pre- and post-surgical values of cognitive performances are shown in Table 1. Six months after surgery, the MDRS score decreased significantly in group 1 while it remained stable in group 2. This difference between groups was statistically significant ($P = 0.007$). Both times to read of the Stroop test WR and CW significantly increased whereas the number of total words in both semantic and phonemic fluency tests were significantly reduced in the both groups. MADRS scores did not differ significantly when comparing baseline and post-operative assessment in both groups.

3.2. Normal (group 2) versus obese (group 3)

There were no significant differences between groups (group 2 versus group 3) with respect to pre-operative age, disease duration, LEDD, total score of UPDRS part III and axial sub-score in the off-drug condition, levodopa responsiveness or cognitive performances ($P > 0.05$).

Six months after surgery, the UPDRS III total score significantly improved from baseline values (*off*-state) by 61.9% in the *off*-drug/*on*-stimulation and 76.3% in the *on*-drug/*on*-stimulation conditions in