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Pallidal stimulation in Parkinson's patients with contraindications to subthalamic target: A 3 years follow-up☆

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ABSTRACT

Introduction: Over a 3-year period, we monitored the efficacy and safety of deep-brain stimulation of the globus pallidus pars interna in patients with advanced Parkinson's disease whose cognitive, psychiatric impairment and/or dopa-resistant axial motor signs made them ineligible for surgery targeting the subthalamic nucleus.
Methods: A total of 25 patients were assessed before surgery, 1 year and 3 years after surgery, on the UPDRS and a neuropsychological battery.
Results: We noted a significant improvement of 65.9% in the Clinical global self-perceived Improvement by Visual Analog Scale and an improvement of 20.6% in the total UPDRS-III motor score at 3 years in the off-dopa condition compared to before surgery. There was an improvement in the treatment's motor complications, as measured by the UPDRS-IV, with a particularly marked reduction of 50% in the Dyskinesia subscore. Cognitive performances remained stable at 1 year but had fallen by the third year. We interpreted this deterioration as due to disease progression.
Conclusion: Bilateral pallidal stimulation in patients with contraindications to subthalamic surgery therefore seems to be effective over the long term in treating motor symptoms, especially dyskinesias, with good neuropsychological safety.

1. Introduction

Functional neurosurgery for deep-brain stimulation (DBS) has been validated as an effective treatment of choice in patients with Parkinson's disease (PD) refractory to medical treatment [1–4]. The optimal target is still debated, some studies seems to show a superiority of the subthalamic nucleus (STN) over the globus pallidus pars interna (GPi) [5–7], but some don't [8–10]. However, STN DBS has been shown to carry a risk of disabling side effects, including cognitive decline [11,12], limbic effect [13] and the worsening of dopa-resistant axial motor signs [14]. In the light of these side effects, we can now identify patients who should not undergo subthalamic surgery [15]. As GPi DBS appears to entail less cognitive deterioration and fewer axial signs [16], several centers have started offering this treatment to patients contraindicated to STN DBS. Its efficacy and safety have already been studied at 6 months post-surgery [17] in one such group of patients, with a motor benefit, no worsening of axial symptoms and no cognitive impairment. In the present study, we monitored its efficacy and safety in patients receiving bilateral pallidal stimulation over a 3-year period. All these patients had advanced PD refractory to all the usual medical treatments, with contraindications to STN DBS.

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2. Material and methods

2.1. Patients

During the 2004–2011 periods, 87 patients were selected for DBS surgery with idiopathic PD at Rennes University Hospital. The decision to operate had been taken because all the usual medical treatments had failed to adequately control the symptoms of the disease, and patients had a levodopa (L-dopa) responsiveness of ≥50%, as measured by the motor score of the United Parkinson's Disease Rating Scale (UPDRS).

Along those 87 patients, 2 refused the surgical procedure, 60 underwent STN-DBS and we studied the 25 patients who had undergone GPi DBS surgery, corresponding to the patients who had been rejected for STN surgery (Fig. 1).

The contraindication for STN surgery was, general cognitive impairment (Mattis Dementia Rating Scale (MDRS) score < 130) [18], impaired executive functions (impaired scores at almost three tests among the battery of tests assessing executive functions, according to the normal values expected in regard of age and educational level) before surgery and/or dopa-resistant axial signs (preoperative UPDRS III axial score ≥ 3 in the on-dopa condition) [19,20]. Table 1 set out the patients' characteristics immediately prior to surgery.

At 3 years, one patient could not be assessed at all, owing to an advanced dementia syndrome, and two patients did not undergo the neuropsychological tests due to cognitive impairment.

2.2. Surgical procedure

Quadripolar DBS electrodes (Medtronic, Minneapolis, MN) were implanted bilaterally in the posteroventral part of the GPi under general anesthesia in a single operating session. All dopaminergic medication had been withdrawn the day before, and patients were briefly woken during the procedure to test the clinical effect of stimulation on rigidity. The ventral contact was kept above the optical tract, as evidenced by the induction of visual flashes by stimulation. There was no Intraoperative microelectrode recording during the procedure.

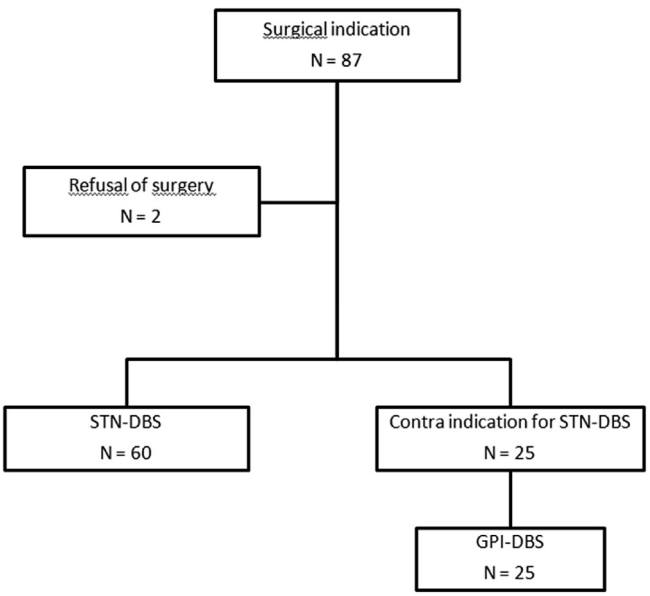

Fig. 1. Flow chart representing all patients with PD selected for DBS during the 2004–2011 periods at Rennes University Hospital.

The pulse generators (Soletra, Medtronic) were implanted 2–3 days later. The exact location of the two selected electrode contacts (one on the left and one on the right) was determined using stereotactic coordinates derived from a 3D CT scan performed a few days after surgery (Fig. 2). The stimulation parameters were set and adjusted during appointments with the consultant and regular follow-up hospitalizations, based solely on clinical efficacy criteria.

2.3. Assessments

The patients were assessed before surgery (baseline), 1 year (M12) and 3 years (Y3) after surgery. The clinical assessment included the UPDRS parts I (mental, behavior and mood), II (activities of daily living), III (motor performance) and IV

Table 1
Characteristics of the 25 patients prior to surgery.

	Value
Male	13 (52%)
Mean age at surgery (years)	60 ± 7.5
Mean disease duration at surgery (years)	12.5 ± 6.25
Mean levodopa dose (mg/d)	1263 ± 513

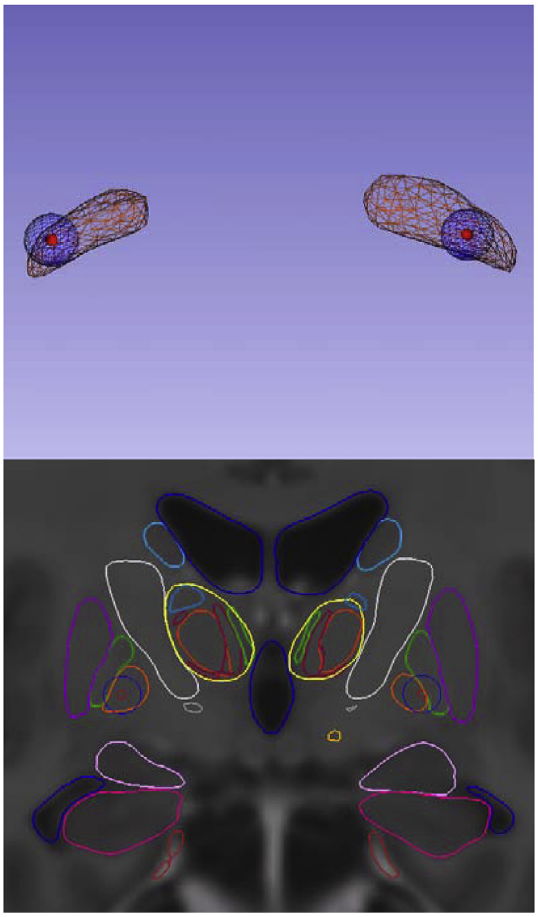

Fig. 2. Three D (top row) and coronal (bottom row) views of the Parkinson template in the 25 patients with the basal ganglia segmentation. The red circles indicate the mean contacts stimulated in the postero-inferior part of the internal pallidum (in orange on the 3D view). The blue spheres represent the standard deviation of the stimulated contacts around the mean contact Caudate nucleus (light blue), putamen (violet), lateral pallidum (green), internal pallidum (orange), internal capsule (white), thalamus (yellow), amygdala (light pink), hippocampus (dark pink). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

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