Short- and Long-Term Outcomes of Deep Brain Stimulation in Patients 70 Years and Older with Parkinson Disease

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■ BACKGROUND: **Parkinson disease (PD) is a common neurodegenerative disease in elderly patients that may be treated with deep brain stimulation (DBS). DBS is an accepted surgical treatment in PD patients <70 years that demonstrates marked improvement in disease symptomology. Patients ≥70 years historically have been excluded from DBS therapy. Our objective is to evaluate the short- and long-term outcomes in patients with PD ≥70 years who underwent DBS at our center.**

■ METHODS: **In our single-center study, we retrospectively assessed a prospective registry of patients with PD treated with DBS who were ≥70 years old at the time of their procedure. Univariate analyses and 1-sample paired *t* test were used to evaluate data. Motor scores were evaluated with the Unified Parkinson's Disease Rating Scale III, and the effects on medication requirements were evaluated with levodopa equivalence daily doses (LEDD).**

■ RESULTS: **Thirty-seven patients were followed for an average of 42.2 months post-DBS. The average ages at diagnosis and at the time of DBS surgery were 63.05 years and 72.45 years, respectively. Significant reductions in the average Unified Parkinson's Disease Rating Scale III score were observed (preoperative 31.8; postoperative 15.6; $P < 0.0001$). Significant reductions in the average LEDD (preoperative 891.94 mg; postoperative 559.6 mg; $P = 0.0008$) and medication doses per day (preoperative 11.54; postoperative 7.97; $P = 0.0112$) also were present.**

■ CONCLUSION: **DBS is effective in treating elderly patients with PD. Patients experienced improvement in motor function, LEDD, and medication doses per day after DBS. Our results suggest that DBS is an effective treatment modality in elderly patients with PD.**

INTRODUCTION

Deep brain stimulation (DBS) is a major treatment option for patients with Parkinson disease (PD).[1] PD itself is classically divided into the phenotypic subtypes of akinetic-rigid and tremor-dominant.[2,3] Medical management, although effective, is associated with a number of adverse effects,[4] and long-term treatment ultimately may bring about "wearing off" symptoms as well as dyskinesias.[5,6] Traditionally, DBS surgeries have targeted the ventral intermediate nucleus of the thalamus in tremor-dominant PD,[7-10] whereas the subthalamic nucleus (STN) and the globus pallidus interna (GPi) are targeted in akinetic-rigid dominant disease.[1]

Treatment with DBS is aimed at reducing all the cardinal motor features of PD.[1] It is considered an adjuvant to medical therapy that allows for a reduction in daily doses and markedly decreases treatment-induced dyskinesia and motor fluctuations.[11] Specifically, stimulation of the STN and the GPi have

Key words
- Deep brain stimulation
- Elderly
- Levodopa equivalence daily doses
- Parkinson disease
- Unified Parkinson's Disease Rating Scale

Abbreviations and Acronyms
DBS: Deep brain stimulation
GPi: Globus pallidus interna
HY: Modified Hoehn and Yahr
LEDD: Levodopa equivalence daily doses
PD: Parkinson disease
STN: Subthalamic nucleus
UPDRS III: Unified Parkinson's Disease Rating Scale III

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demonstrated motor improvement, as assessed by the motor score of the Unified Parkinson's Disease Rating Scale III (UPDRS-III) reported postoperatively at 6 months,[12,13] 1 year,[14,15] and 2 or more years.[16-20]

These aforementioned outcomes have established DBS as the surgical treatment of choice for patients with PD who are refractory to medical therapy.[11,21,22] Furthermore, analyses of DBS in PD have demonstrated STN targeting to provide a greater reduction of dopaminergic medication, as measured by levodopa equivalency daily doses (LEDD), compared with GPi,[23] and the former generally is thought to be the more effective target.[24,25] Despite this advantage, increased cognitive and behavioral complications have been observed in targeting the STN,[24] and some studies suggest that Gpi-targeted DBS is the safer treatment option.[15,26]

Although DBS is a proven modality of treatment for younger patients with PD, traditionally there has been hesitance to proceed to surgical intervention in elderly patients. In the literature, "elderly" generally is acknowledged as an age greater than 68–70 years at the time of DBS surgery and has served traditionally as a strong contraindication to DBS, resulting from the increased incidence of comorbidities and surgery-related complications.[13,27-29] Despite these reports, a small number of studies have demonstrated that elderly patients with PD who underwent treatment with DBS showed similar outcomes compared with their younger counterparts,[13,27-33] with the authors of 1 study even reporting a significantly decreased rate of infection.[34] As such, several authors suggest that advanced age should not be considered an absolute contraindication to DBS and that such patients may simply require a more meticulous follow-up.[30-33]

The historical exclusion of elderly patients from DBS studies has resulted in a poor characterization of the surgical outcomes and potential health benefits of DBS in these populations.[34] Although it has been shown that elderly patients possess a lower tolerance for major procedures with greater incidences of infection, hemorrhage, pneumonia, neurologic sequelae, pulmonary embolism, and death,[34-36] these generalizable morbidities are not specific to treatment with DBS. The overall lack of data precipitated by this historic precedence is highly unfortunate, because PD remains one of the most common neurodegenerative diseases in the elderly population, with a mean age at diagnosis of 60 years and an average duration of disease before DBS of 14 years.[37]

Furthermore, the number of patients with PD is projected to double by 2030 as a result of the aging population,[38] which makes the outcome data of DBS treatment in elderly populations pertinent now more than ever before. The purpose of this study was to use existing markers of PD-associated morbidity to evaluate the short- and long-term outcomes of DBS treatment in a cohort of patients considered "elderly" by previous definitions within the literature. It should be noted that this is the first of a number of studies planned to evaluate the effects of DBS with relation to age within, and between, temporal cohorts.

METHODS

This retrospective study was approved by the Institutional Review Board at Ochsner Medical Center (New Orleans, Louisiana, USA). Retrospective patient data were collected into a password-protected encrypted database by the senior author (R.S.) for 37 patients with PD at our institution who were 70 years or older at the time of their DBS procedure. Major patient data collected included sex, PD subtypes, age at diagnosis, age at time of surgery, modified Hoehn and Yahr (HY) stage, DBS target, and medications and medication doses at baseline and postoperatively. LEDD were used to assess the effects of DBS on patient anti-PD medication requirements, as previously discussed.[39] Motor score was evaluated with the UPDRS-III at baseline and repeatedly after surgery. Paired *t* tests and Wilcoxon signed-ranked test were used to determine means, standard errors, and *P* values for statistical significance. The threshold for statistical significance was set at $P < 0.05$.

Surgical Procedure

DBS target localization and hardware installation in all 37 reported patients took place at Ochsner Medical Center during the course of 3 consecutive surgeries. During the first surgery, patients were brought to the operating room for the placement of fiducial screws for precision neuronavigational use in the subsequent procedures. In the second surgery, which occurred the following day, the DBS target was localized with the assistance of intraoperative microelectrode recording and stimulation to achieve precise DBS lead placement. In the third surgery, 1 week after DBS lead implantation, an intermittent pulse generator was placed. The first 2 procedures were performed with the patient under local anesthesia and monitored anesthesia care, whereas the third was performed with the patient under general anesthesia. At discharge, they were instructed to continue their scheduled home regimen of anti-PD medications pending a postoperative evaluation for initial programming 2 weeks after surgery at the home facility's movement disorder clinic. During the course of their follow-up, patients were encouraged to present to the neurosurgery clinic for postoperative management and wound checks as needed.

RESULTS

From 2008 to 2014, a total of 37 patients with PD were found to be 70 years or older at the time of their treatment with DBS, thus meeting our inclusion criteria. The average time of postoperative follow-up was 42.2 months with a range of 4–70 months. Of these, 6 patients (16.2%) followed up at 12 months or less postsurgery, 10 (27.0%) at 1–3 years, 13 (35.1%) at 3–5 years, and 8 (21.6%) at 5–7 years.

Patient Demographics and Diagnoses

Of the patients included in our study, 24 (64.86%) were male, and 13 (35.14%) were female. Patients had an average age at diagnosis of 63.05 years (range 50–74) and an average age at surgery of 72.45 years (range 70–81). On average, patients waited 11.97 years between the time of their diagnosis and the time of their DBS operation. The most common subset of PD was tremor dominant 29 (78.38%), with akinetic-rigid dominant accounting for 8 (21.62%). At the time of surgery, patients had an average of 1.5 comorbidities with as many as 5. Disease progress most often was categorized as HY stage 2 (17 patients; 45.9%), with HY stages 3 (9 patients; 24.3%), and stage 4 (7 patients; 18.9%, UPDRS III) being the next most common (**Table 1**).