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ORIGINAL ARTICLE

Different effectiveness of subthalamic deep brain stimulation in Parkinson's disease: A comparative cohort study at 1 year and 5 years

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Background/Purpose: Subthalamic nucleus deep brain stimulation (STN-DBS) has been shown to produce long-term symptom improvement in Parkinson's disease. The aim of this study was to identify the target symptoms that show the most improvement at 1 year and at 5 years after STN-DBS.

Methods: This was a 5-year cohort study of 41 consecutive patients treated with bilateral STN-DBS. Clinical evaluations were performed 1 month prior to surgery and 1 year and 5 years after surgery. The outcome measurements at 1 year and 5 years were the changes compared with the baseline in Unified Parkinson's Disease Rating Scale (UPDRS) parts I, II, III, and IV scores, the Hoehn and Yahr stage, and Schwab and England Activities of Daily Living (SEADL) scores in the conditions of off-medication/on-stimulation and off-medication/off-stimulation. Further analysis included changes in the levodopa equivalent daily dose.

Results: When compared to the preoperative baseline off-medication condition, significant improvements were observed in the UPDRS parts I, II, III, and IV and SEADL ($p < 0.001$) scores in the off-medication/on-stimulation condition 1 year after STN-DBS. Five years after STN-DBS, improvements in UPDRS scores were observed only for parts II, III, and IV ($p < 0.001$). In the

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off-medication/off-stimulation condition, no significant improvement was observed. At 5 years, significant deteriorations were observed in scores for the UPDRS part III axial subitem ($p = 0.005$), UPDRS part I ($p = 0.005$), UPDRS part II ($p < 0.001$), and SEADL ($p = 0.001$).
Conclusion: The long-term effect of STN-DBS on motor function is promising, although the magnitude of its effectiveness varied over the 5-year period.

Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disorder. It is characterized by muscle rigidity, resting tremor, bradykinesia, and postural instability. The pathologic hallmarks of the disease are the degeneration of dopaminergic neurons in the substantia nigra pars compacta of the midbrain and the presence of Lewy bodies, which are cytoplasmic aggregations of the protein α-synuclein in brain neurons. Exposure to various toxins or pesticides may be a secondary etiology. PD is likely to be a result of multiple factors, including normal aging, genetic predisposition, and environmental exposure.[1,2] Although an optimal pharmacological therapy with levodopa and other adjuvant regimes can be achieved, complications associated with the treatment of PD, such as dyskinesia and motor fluctuation, inevitably occur 5 years after the initiation of therapy.[3,4] The progressive decline in motor function and the comorbidity associated with PD negatively affect health-related quality of life.[5] Since the first application of deep brain stimulation of the subthalamic nucleus (STN-DBS) for PD[6] in 1993, high frequency stimulation of the STN has rapidly become the surgical treatment of choice. The long-term effects of STN-DBS on medically refractory PD have been well documented. According to some reports, the motor improvement induced by STN-DBS is sustained for up to 5—8 years after surgery,[3,6—13] but part of the initial improvement, mainly regarding axial signs, become progressively deteriorated. However, the effects of STN-DBS on the motor and nonmotor symptoms may vary. The aim of this study was to identify the target symptoms that show the most improvement at short-term (1 year) and long-term (5 year) follow-up in the same group of patients after STN-DBS.

Methods

Patient enrollment

From 2002 to 2007, 41 patients from a single DBS center in Taiwan who underwent bilateral STN-DBS were enrolled in this cohort study. The diagnosis of PD followed the diagnostic criteria of the United Kingdom PD Society Brain Bank.[14] The inclusion criteria were: (1) a good levodopa response on the Unified PD Rating Scale (UPDRS) part III; (2) drug-related complications (e.g., dyskinesia, *on—off* phenomenon, or psychiatric symptoms), even under optimal antiparkinsonian medication adjustments; (3) no structural lesions on the brain magnetic resonance imaging (MRI); and (4) an absence of dementia. The study was approved by the Tzu Chi General Hospital Research Ethical Board in Hualien, Taiwan. All the patients provided written informed consent for STN-DBS surgery and for the study's evaluation procedure.

Surgical procedure

All the patients were evaluated for the STN-DBS surgery by standard MRI scans (1.5-T; General Electric, Milwaukee, WI, USA), using T1-weighted axial images (0.75 mm thick) and T2-weighted axial images (2 mm thick). The quadripolar DBS electrodes (model 3389; Medtronic, Englewood, CO, USA) were implanted after the microelectrode recording and test stimulation procedures. After 1 week, the electrode cables were connected to an implantable pulse generator (Kinetra; Medtronic, Minneapolis, MN, USA). The surgical procedures have been described in detail in our previous study, and the same surgical team performed all the operations.[15] We arranged a postoperative computed tomography immediately after the operation to ensure that the correct target was used for the stimulating electrode for each patient and an MRI 3 months later (Fig. 1).[16] We

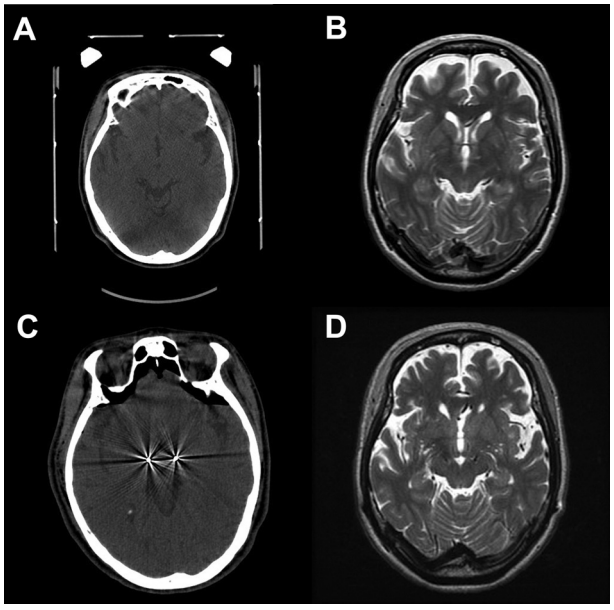

Figure 1 (A) Preoperative computed tomography and (B) magnetic resonance imaging were both performed for the stereotactic surgery and to localize the subthalamic nucleus. (C) Postoperative computed tomography and (D) magnetic resonance imaging were conducted to verify the electrode coordinates and to evaluate any neurological lesions, such as intracerebral hemorrhage.