Clinical Study

Effect of deep brain stimulation on autonomic dysfunction in patients with Parkinson's disease

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ABSTRACT

Increasing attention is being paid to the non-motor symptoms of Parkinson’s disease (PD). While deep brain stimulation (DBS) of the subthalamic nucleus (STN) has been shown to clearly improve motor symptoms of PD, the effects of STN DBS on autonomic symptoms have not been well studied. We examined 11 patients undergoing STN DBS for PD. Patients were administered a questionnaire by phone to evaluate pre-operative and post-operative function. Three out of the 11 patients reported marked improvement post-DBS in one or more symptoms of autonomic dysfunction (sweating, bladder, or bowel function). All three patients had early-onset PD (EOPD), whereas the eight patients reporting no significant improvement were those with late-onset PD. Thus, we found that some patients experienced marked improvement in sweating and/or bowel and bladder function after STN DBS, with a trend towards a response in patients with EOPD. Our results suggest the utility of a larger prospective study.

1. Introduction

Subthalamic nucleus (STN) deep brain stimulation (DBS) is well established for treating the motor symptoms of patients with Parkinson's disease (PD). However, autonomic dysfunction also affects the quality of life of patients with PD. As the central dopaminergic dysfunction that leads to motor symptoms is also responsible for autonomic dysfunction, we hypothesized that STN DBS may improve autonomic function. Previous small studies have indicated that some autonomic symptoms may improve following STN DBS.1–5 In this study, we investigated whether gastrointestinal (GI), thermoregulatory, and urological symptoms of PD improve following STN DBS. We also aimed to compare patients with early-onset PD (EOPD) (symptom onset at or before the age of 45 years) to patients with late-onset PD (LOPD).

2. Case report

Under an approved protocol from the Institutional Review Board of the University of California, Irvine, School of Medicine, 19 patients who had previously undergone STN DBS were solicited for participation, and 11/19 consented. Patients served as their own control. The 11 patients had either unilateral or bilateral STN-DBS surgery between 2000 and 2008. All patients had electrodes verified in the STN by post-operative imaging and standard post-operative programming to alleviate motor symptoms. The interviews took approximately 30 minutes, and were conducted 1 hour after the patient’s last dose of PD medication.

We used two autonomic function questionnaires validated in previous studies.6,7 The first questionnaire explored components of the urinary and GI tract and the negative symptoms of PD on these autonomic systems.6 Urinary symptoms of PD were studied by assessing the patient’s frequency, urgency, nocturia, and satisfaction with their urinary function. Bowel function assessment included frequency, bowel dynamics, and satisfaction with GI function. The second questionnaire evaluated hyperhidrosis (sweating) as a symptom of thermoregulatory dysfunction in PD,7 and assessed frequency, timing, location, and association with medication.

3. Results

Three of 11 patients (patients 1, 2, 3) reported marked and significant improvement in one or more symptoms of autonomic dysfunction (sweating, urinary, or bowel function) (Table 1). All three patients had EOPD (mean age of diagnosis with PD, 39.3 years) whereas the other eight patients who did not report any marked changes had LOPD.

The three patients with post-operative improvement in autonomic function are described in the following sections (patients 1–3).
3.1. Patient 1

Patient 1 was a 56-year-old right-handed male. His age of onset of PD was 40 years of age. He underwent bilateral STN DBS at the age of 55. He reported experiencing marked improvements in sweating and bladder function. Most notably, he reported that before the surgery he experienced symmetrical sweating that worsened at night and which was associated with the timing of the PD medication. After bilateral STN DBS, he no longer experienced problems with sweating. He also expressed that he was “satisfied” with his bladder condition after STN DBS compared to pre-operatively, although urinary urgency increased post-operatively.

3.2. Patient 2

Patient 2 was a 46-year-old right-handed female. Her age of onset of PD was 37 years of age. She underwent bilateral STN DBS at 45 years of age. She reported that before surgery she was “moderately dissatisfied” with her bladder condition whereas post-operatively she was “satisfied”, experiencing no problems associated with emptying her bladder. She was also “moderately dissatisfied” with her bowel condition pre-operatively and experienced difficulty with expulsion. Post-operatively she was “satisfied” with her bowel condition of a daily bowel movement. Before the surgery she also experienced frequent, daily, symmetric sweating problems that were associated with the timing of her PD medication. She reported post-operative resolution of her sweating problem.

3.3. Patient 3

Patient 3 was a 54-year-old right-handed male. His age of onset of PD was 41 years of age. He underwent unilateral left STN-DBS surgery at the age of 51 years for motor function control of his right hand. The patient was “slightly dissatisfied” with his bladder condition before surgery and reported occasional urgency to urinate, difficulty with emptying urine, and urine leaking unwittingly while awake and asleep. Post-operatively, the patient was “satisfied” with his bladder condition. He reported having significant, symmetric sweating problems pre-operatively that worsened during the day and was worse when “off” medication. Post-operatively, he did not experience any sweating problems. Interestingly, his bilateral sweating problem resolved completely even with unilateral STN stimulation. He was the only patient who returned to replace the left STN electrode due to lead fracture. His sweating problem resumed until the electrode was replaced and the pulse generator was turned back on, at which time the sweating problem again resolved immediately.

4. Discussion

We evaluated pre-DBS and post-DBS autonomic function in a small cohort of patients with PD undergoing STN DBS using two validated questionnaires. Our results show that bladder, GI, and sweating symptoms of autonomic dysfunction associated with PD are widespread and did not improve markedly in most patients in our small sample who underwent STN-DBS surgery. However, our results show that all three patients in this limited cohort with EOPD exhibited improvement in autonomic dysfunction. Patients with EOPD benefitted from STN DBS similarly to patients with LOPD with regard to motor symptom control, but the difference observed in autonomic response has not been reported previously.

The most consistent finding was that the sweating problems experienced by the three patients with EOPD before STN-DBS resolved post-operatively. Swinn et al. found that sweating problems occurred predominantly during “off” periods but also occurred during “on” periods with dyskinesias. The variability in timing of sweating episodes and medication exhibited by our three patients with EOPD is consistent with the findings of Swinn et al. The beneficial effects of STN DBS on sweating in these three patients with EOPD was quite dramatic, and in patient 3, alleviation of bilateral sweating was accomplished even with unilateral (left) STN DBS. The significant improvement in sweating after STN DBS is also in accord with other findings.

Subjective improvement in urinary symptomatology after STN DBS exhibited by patients 2 and 3 is consistent with other studies. A study found that STN DBS increases bladder capacity and reflex volume. Another study showed that STN DBS modulated positron emission tomography activation of brain areas involved in bladder sensory processing. Clearly, a prospective study with pre-operative and post-operative urodynamics would yield more detailed information about the effect of STN DBS on bladder function.

Our study reveals little about the effect of STN DBS on GI function. Patient 2 is the only patient with EOPD who exhibited marked pre-operative GI dysfunction. She noted marked post-operative improvement in her bowel function.

Limitations of our study include small sample size and that it was conducted retrospectively. Nevertheless, our results provide insight into individual responses of patients to DBS regarding disabling autonomic dysfunction that may improve with stimulation. The most robust result was improvement in sweating after STN DBS in all patients with EOPD. Future prospective studies will be able to use these validated questionnaires evaluating subjective experience of autonomic dysfunction. Such information will be important in pre-operative counseling regarding the potential ben-
efits of STN DBS on non-motor symptoms of PD. Finally, our study suggests that further comparison of patients with EOPD and LOPD will be an important aspect of a larger prospective study.

References