Effects of Deep Brain Stimulation in Multiple System Atrophy

Yuncheng Wu MD, PhD[1,2], Mike A. Almaguer, RN[2], Farah Atassi, MD[3], Eugene C. Lai, MD,PhD[3], Joseph Jankovic MD[2], William G. Ondo[2]

[1]Department of Neurology, Shanghai First People's Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, P.R. China

[2]Parkinson's Disease Center and Movement Disorder Clinic, Department of Neurology, Baylor College of Medicine, Houston, Texas, USA

[3]Parkinson's Disease Research, Education and Clinical Center, Department of Neurology, Michael E. DeBakey VA Medical Center, Baylor College of Medicine, Houston, Texas, USA

ABSTRACT

Objective: To analyze outcomes after one year of bilateral STN deep brain stimulation (DBS) in patients with multiple system atrophy-parkinsonism MSA-P. **Background:** The efficacy of DBS has been demonstrated in idiopathic Parkinson's disease. However, the experience with DBS in MSA-P is limited and controversial. **Methods:** Information about the demographic and clinical data (Unified Parkinson's Disease Rating Scale) from six MSA patients treated with DBS currently followed in our clinic was entered into a database and analyzed. **Results:** Six patients with MSA (mean age at onset 44.3±5.6 years, 2 women, 4 men) have been treated with bilateral STN stimulators, the mean duration between DBS surgery and disease onset is 6.5±3.4 years. All of the patients had dyskinesias and postural instability. Five of them had subjective benefit from levodopa. During the six months after surgery, the clinical status of four patients improved with a decrease of dyskinesia. However, by one year, the symptoms reappeared and progressed in all patients. Overall, the mean "off" medication UPDRS score worsened 22.1+14.1 one-year after surgery. The levodopa dosage was not reduced after surgery. One patient developed paranoia and violent behavior, three patients developed hypotension after the surgery. **Conclusions:** Our data shows that DBS can transiently improve parkinsonian signs, especially dyskinesia. However, by one year, motor signs and other co-morbidities (autonomic, cognitive, etc.) continue to worsen. This data does not support the use of STN DBS for MSA-P.

INTRODUCTION

Deep brain stimulation (DBS) for Parkinson's disease (PD) entered widespread clinical use in the late 1990s and the attractiveness of DBS is related in part to the fact that stimulation is adjustable and reversible (Follett, 2000). Subthalamic nucleus (STN) DBS has already gained wide acceptance for improving motor function and disability in advanced idiopathic Parkinson's disease (PD) (Krack et al, 2003; Deuschl et al, 2006; Weaver et al, 2009). STN DBS improves the cardinal features of PD and reduces motor fluctuations while allowing for reduction in levodopa equivalent dosing, ameliorating L-dopa induced dyskinesia (Deuschl et al, 2006; Weaver et al, 2009).

However, not all patients who received DBS improve (Deuschl et al, 2006), quality of life outcomes favored deep brain stimulation for 64% and favored medical therapy in 36% of PD pairs randomized to DBS or medical therapy. Similarly, although DBS resulted in improved motor functioning in 71% of pairs, the functioning was better in 27% of the cases for the medically treated patients (Deuschl et al, 2006). Patients with features indicative of atypical parkinsonism (AP) such as multiple system atrophy (MSA) and progressive supranuclear palsy (PSP) usually have a poorer and less sustained response to levodopa and a poorer prognosis overall when compared with patients with PD (Shih and Tarsy, 2007). The experience in the use of DBS with this group of patients is limited and evidence is lacking with regards to its efficacy and adverse effects. The results of most studies generally were unfavorable and they suggested that DBS should not be recommended for AP, especially MSA (Tarsy et al, 2003; Chou et al, 2004; Lezcano et al, 2004; Shih and Tarsy, 2007; Lambrecq et al, 2008).

METHODS / RESULTS

We retrospectively reviewed medical records of six MSA patients with STN DBS therapy at Baylor College of Medicine Movement Disorders Clinic. Demographic, clinical characteristics, UPDRS-III and other features related to DBS therapy were recorded. Six patients with MSA (mean age 44.3 ± 5.6 years, 2 women, 4 men) have been treated with bilateral STN stimulators. All of the patients had dyskinesias, postural instability, and three of them have motor fluctuations. Five of them were L-dopa responsive. The mean duration between DBS surgery and disease onset is 6.5 ± 3.4 years.

Four of them had transient, minimal improvement within six months of surgery, especially for dyskinesia. One patient developed paranoia and violent behavior, three patients developed hypotension after the surgery. The L-dopa dose was not reduced after surgery. Despite some initial motor improvement, the mean increase of "off" medication UPDRS score was 22.1+14.1 one-year after surgery.

Table 1. Demographic and clinical features of MSA patients in our clinic

No.	Gender	Age of onset	Age of surgery	Asymmetry	Initial symptoms	Signs
1	F	44	49	Yes	Migrographia, acute action tremor	Minimal rigidity, bradykinesia, mask face
2	M	43	47	Yes	Stiffness, slowness of left side, hesitating gait	Severe dysarthri and bradykinesia, rigidity
3	M	44	57	Yes	Decreased left armswing, and slowness in left	Dysarthria, marked rigidity and brady kinesia
4	F	39	46	Yes	Tremor in left hand, decreased arm swing, shoulder pain	Tremor, rigidity and brady kinesia
5	M	55	59	Yes	Hand tremor, rigidity, cannot write	Tremor, rigidity, hypotension
6	F	41	47	Yes	Hand tremor, bradykinesia	Cogwheel rigidity

Table 2. The results of STN DBS therapy in MSA patients in our clinic

No.	Motor fluctuations	L-Dopa responsive	DBS response	UPDRS-III change one year later after surgery (off medication)	Early adverse effects	Subsequent clinical course
1	Peak dose dyskinesia	Yes	Improve transiently, but worse after six months	41 to 49.5	No	Bladder incontinent, constipation, sexual dysfunction
2	Wearing off, peak dose dyskinesia	Yes	Minimal response, but worse after six months	39 to 69	Discomfort, dyskinesias in the right hand	Rigidity and slowness, slurred speech
3	Wearing off, peak dose dyskinesia	Yes	No	38 to 60	No	progressive
4	Wearing off, peak dose dyskinesia	No	Dyskinesias reduced but worsened	46 to 57	No	progressive
5	None	No	Improve transiently, but rapid progression	43 to 37	No	worsening
6	Wearing off, peak dose dyskinesia	Yes	No	23 to 69	Dyskinesia, stiffness, infection of stimulator	worsening

DISCUSSION

- Our data shows that DBS can improve cardinal parkinsonian signs and dyskinesia in MSA-P, but only transiently and minimally.
- STN DBS cannot be recommended in MSA as one year motor signs are worse than baseline.
- Alternative target selection for the treatment of midline symptoms poorly responsive to STN DBS might have an important future role to play as new targets for DBS therapy in MSA.

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