Treatment of Freezing of Gait in Parkinson's Disease with Deep Brain Stimulation of the Pedunculopontine Nucleus

Muhammad M. Nashatizadeh, M.D. and Joseph Jankovic, M.D.

Parkinson's Disease Center and Movement Disorders Clinic

Department of Neurology, Baylor College of Medicine, Houston, Texas

OBJECTIVE

To describe the response in freezing of gait (FoG) in three patients with Parkinson's disease (PD) who underwent deep brain stimulation (DBS) of the pedunculopontine nucleus (PPN).

BACKGROUND

Among the axial features of advanced parkinsonism, FoG is one of the most disabling symptoms that is often resistant to medical and surgical treatments. The role of FoG on mobility and quality of life (QoL) is well-established although there is no consensus regarding effective surgical interventions. The PPN is a potential target for DBS due to its close association with the mesencephalic locomotor region and extensive connections with the basal ganglia and descending spinal pathways. Based on limited animal and human data, low-voltage PPN stimulation has been suggested to improve gait and balance, but its effects on FoG have not been studied in PD patients.

DESIGN / METHODS

Using the Unified Parkinson's Disease Rating Scale (UPDRS), Gait and Balance Scale (GABS), and/or video reviews, we studied three patients with advanced PD and disabling FoG resistant to levodopa before and after PPN DBS.

RESULTS

Patient 1 is a 59-year-old man who underwent bilateral PPN DBS with noticeable improvement in his FoG recorded 2 and 6 weeks postoperatively. Patient 2 is a 76-year-old man who had previously received unsuccessful bilateral DBS of the globus pallidus interna (GP_i) and had transient improvement in FoG after right PPN DBS. Patient 3 is a 66-year-old man who underwent isolated right PPN but developed a worse GABS score without noticeable improvement in FoG. Sustained improvement was not seen in any of the three patients despite adjustment of DBS parameters. Furthermore, vision changes and balance problems limited these setting adjustments.

CONCLUSIONS

This is the first report of PPN DBS for severe FoG associated with PD. Further studies are needed to determine whether further adjustments in stimulating parameters will optimize and prolong the improvement in FoG, noted in two of our three patients.

TABLE 1: Characteristics and Settings of Patients with PPN DBS

Patient	Age/Gender	DBS Placement	Freezing	Volts	Rate	Pulse Width
1	59/M	bilateral PPN	2 years	4.0	25	60
2	76/M	right PPN + bilateral GP_i	4-5 years	3.6	25	60
3	66/M	right PPN	4 years	3.0	25	60

TABLE 2: Summary of FoG Details

Patient	UPDRS Freezing (question 14)	Adverse Effects	Description of Postoperative Issues
1	4 – before 4 – after	worsening balance and lightheadedness	mild subjective improvement in FoG at 2 weeks lasted 2-4 days; improved again after voltage increase (2.2 → 2.4); additional improvement after voltage increase at 6 weeks (2.4 → 2.6); ineffective at 10 weeks follow-up despite voltage increase to 4.0
2	4 – before 4 – after	occasional diplopia	mild subjective improvement in FoG for 1-2 days after turning on right PPN stimulator; improved again for two weeks after voltage increase (2.0 → 2.5); ineffective at 8 weeks
3	4 – before 4 – after	diplopia	GABS History: 25 (off), 22 (on) GABS Physical Exam: 60 (off), 50 (on) mild subjective improvement in gait initiation and in open spaces; no change in tight spaces; usually wore off after 1-2 days

REFERENCES

1. Pahapill PA, Lozano AM. The pedunculopontine nucleus and Parkinson's disease. *Brain* 2000; 123:1767-1783.
2. Mena-Segovia J, Bolam JP, Magill PJ. Pedunculopontine nucleus and basal ganglia: distant relatives or part of the same family? *Trends Neurosci* 2004; 27:585-588.
3. Jellinger K. The pedunculopontine nucleus in Parkinson's disease, progressive supranuclear palsy and Alzheimer's disease. *J Neurol Neurosurg Psychiatry* 1988; 51:540-543.
4. Kuo SH, Kenney CJ, Jankovic J. Bilateral pedunculopontine nuclei strokes presenting as freezing of gait. *Mov Disord* 2008; 23:616-619.
5. Mazzone P, Lozano A, Stanzione P, et al. Implantation of human pedunculopontine nucleus: a safe and clinically relevant target in Parkinson's disease. *Neuroreport* 2005; 16:1877-1881.
6. Plaha P, Gill SS. Bilateral deep brain stimulation of the pedunculopontine nucleus for Parkinson's disease. *Neuroreport* 2005; 16:1883-1887.
7. Stefani A, Lozano AM, Peppe A, et al. Bilateral deep brain stimulation of the pedunculopontine and subthalamic nuclei in severe Parkinson's disease. *Brain* 2007; 130:1596-1607.
8. Kenney C, Fernandez HH, Okun MS. The role of deep brain stimulation targeted to the pedunculopontine nucleus in Parkinson's disease. *Exp Rev Neurother* 2007; 7:585-589.
9. Aziz TZ, Davies L, Stein J, France S. The role of descending basal ganglia connections to the brain stem in parkinsonian akinesia. *Br J Neurosurg* 1998; 12:245-249.
10. Nandi D, Liu X, Winter JL, et al. Deep brain stimulation of the pedunculopontine region in the normal non-human primate. *J Clin Neurosci* 2002; 9:170-174.
11. Nandi D, Aziz TZ, Giladi N et al. Reversal of akinesia in experimental parkinsonism by GABA antagonist microinjections in the pedunculopontine nucleus. *Brain* 2002; 125:2418-2430.
12. Jenkinson N, Nandi D, Miall RC et al. Pedunculopontine nucleus stimulation improves akinesia in a Parkinsonian monkey. *Neuroreport* 2004; 15:2621-2624.