Libyan International Medical University

Faculty of Basic Medical Science

Deep Brain Stimulation in Parkinson's Disease

Submitted by: Hashim H. Almatri, 3rd Year Medical Student, Faculty of Basic Medical Science, Libyan International Medical University.

Supervisor: Dr. Sarah Almagerhi, Tutor, Faculty of Basic Medical Science, Libyan International Medical University.

Date of Submission: 30/6/2018

Abstract

Deep brain stimulation is the surgical procedure of choice for patients with advanced Parkinson's disease. Neurosurgical procedures use electrical stimulation of small targets in the brain by use of a pacemaker-like device to deliver constant stimulation. Most neurosurgery for Parkinson's disease has been done on the thalamus, globus pallidus pars interna, or subthalamic nucleus. High frequency stimulation improves all cardinal features of PD, including resting tremor. This benefit in the parkinsonian symptoms allows a drastic reduction in daily levodopa requirements. Dyskinesias become drastically attenuated, possibly as a consequence of reduced dopaminergic medication, thus avoiding the problems associated with standard levodopa replacement therapy.

Introduction

Parkinson's disease is caused in part by loss of dopaminergic neurons in the substantia nigra pars compacta; the resultant abnormal neuronal oscillatory and synchronous activity between the subthalamic nucleus, globus pallidus interna, and cerebral cortex leads to increasing problems with tremor, rigidity, bradykinesia, and postural disturbances. Levodopa and other dopaminergic drugs relieve these movement disorders, but dyskinesia and motor fluctuations develop years later.[1]

Initial observations in patients with tremor treated with deep brain stimulation (DBS) of the thalamus suggested that application of high-frequency stimulation (HFS) had a lesion-like effect. New clinical information from patients treated with DBS of the subthalamic nucleus (STN), globus pallidus internus (GPi) and pedunculopontine nucleus suggested a more complex mechanism of action. Recent experiments in the rat have shown that HFS of the STN was accompanied by increased release of glutamate and dopamine in the substantia nigra and striatum, respectively. Observations made in the GPi of parkinsonian patients during surgery suggest that stimulation may excite GABA release in axons from afferent connections. Therefore, although depolarization block may remain a major mechanism of action, generation of action potentials and release of neurotransmitters may also be involved in the therapeutic effects of DBS in Parkinson's disease.[2]

Discussion

Subthalamic Nucleus and Globus Pallidus Internus

Ten patients with idiopathic PD, L-dopa-induced dyskinesia, and response fluctuations were randomized to implantation of bilateral GPi or STN stimulators. Neurological condition was assessed preoperatively with patients on and off L-dopa and on DBS at 10 days and 3, 6, and 12 months after implantation. Patients and evaluating clinicians were blinded to stimulation site throughout the study period. Complete follow-up data were analyzed for four GPi patients and five STN patients.[3]

When off-L-dopa, both GPi and STN groups demonstrated a similar response, with approximately 40% improvement in Unified PD Rating Scale motor scores after 12 months of DBS. Rigidity, tremor, and bradykinesia improved in both groups. In combination with L-dopa, Unified PD Rating Scale motor scores were more improved by GPi stimulation than by STN stimulation. On-L-dopa axial symptoms were clinically improved in the GPi but not the STN group. L-Dopa-induced dyskinesia was reduced by DBS at either site, although medication requirement was reduced only in the STN group. There were no serious intraoperative complications among patients in either group.[3]

Pedunculopontine Nucleus

Six patients with unsatisfactory pharmacological control of axial signs such as gait and postural stability underwent bilateral implantation of DBS electrodes in the STN and PPN. Clinical effects were evaluated 2–6 months after surgery in the OFF- and ON-medication state, with both STN and PPN stimulation ON or OFF, or with only one target being stimulated. Bilateral PPN-DBS at 25 Hz in OFF-medication produced an immediate 45% amelioration of the motor Unified Parkinson's Disease Rating Scale (UPDRS) subscale score, followed by a decline to give a final improvement of 32% in the score after 3–6 months. In contrast, bilateral STN-DBS at 130–185 Hz led to about 54% improvement. PPN-DBS was particularly effective on gait and postural items. In ON-medication state, the association of STN and PPN-DBS provided a significant further improvement when compared to the specific benefit mediated by the activation of either single target. Moreover, the combined DBS of both targets promoted a substantial amelioration in the performance of daily living activities. These findings indicate that, in patients with advanced Parkinson's disease, PPN-DBS associated with standard STN-DBS may be useful in improving gait and in optimizing the dopamine-mediated ON-state, particularly in those whose response to STN only DBS has deteriorated over time.[4]

Long Term Follow Up

48 patients were studied after bilateral subthalamic nucleus deep brain stimulation (STN-DBS) who were evaluated 6 months after the surgical procedure using the Unified Parkinson's Disease Rating Scale (UPDRS) in a standardized levodopa test. Additional follow-up was available in 32 patients after 12 months and in 20 patients after 24 months. At 6 months follow-up, STN-DBS reduced the UPDRS motor score by 50.9% compared to baseline. This improvement remained constant at 12 months with 57.5% and at 24 months with 57.3%. Relevant side effects after STN-DBS included intraoperative subdural hematoma without neurological sequelae, minor intracerebral bleeding with slight transient hemiparesis, dislocation of impulse generator, transient perioperative confusional symptoms, psychotic symptoms, depression, hypomanic behaviour, and transient manic psychosis. Complications of STN-DBS comprise a wide range of psychiatric adverse events which, however, were temporary.[5]

Conclusion

Stimulation of the subthalamic nucleus, pars interna of the globus pallidus and pedunculopontine nucleus appears to be safe and efficacious for the management of advanced PD, and is associated with significant improvement in motor function in patients with Parkinson's disease whose condition cannot be further improved with medical therapy.

References

1. Adrian Williams, Steven Gill, Thelekat Varma, Crispin Jenkinson, Niall Quinn, Rosalind Mitchell, Richard Scott, Natalie Ives, Caroline Rick, Jane Daniels, Smitaa Patel, Keith Wheatley. Deep brain stimulation plus best medical therapy versus best medical therapy alone for advanced Parkinson's disease (PD SURG trial): a randomised, open-label trial, *The Lancet Neurology*, Volume 9, Issue 6, 2010, Pages 581-591, ISSN 1474-4422, https://doi.org/10.1016/S1474-4422(10)70093-4.
2. Benazzouz A, Hallett M. Mechanism of action of deep brain stimulation. *Neurology*. 2000;55(12 Suppl 6) S13-6. PMID: 11188968.
3. Kim J. Burchiel, Valerie C. Anderson, Jacques Favre, John P. Hammerstad; Comparison of Pallidal and Subthalamic Nucleus Deep Brain Stimulation for Advanced Parkinson's Disease: Results of a Randomized, Blinded Pilot Study, *Neurosurgery*, Volume 45, Issue 6, 1 December 1999, Pages 1375–1384, https://doi.org/10.1097/00006123-199912000-00024
4. Alessandro Stefani, Andres M. Lozano, Antonella Peppe, Paolo Stanzione, Salvatore Galati, Domenicantonio Tropepi, Mariangela Pierantozzi, Livia Brusa, Eugenio Scarnati, Paolo Mazzone; Bilateral deep brain stimulation of the pedunculopontine and subthalamic nuclei in severe Parkinson's disease, *Brain*, Volume 130, Issue 6, 1 June 2007, Pages 1596–1607, https://doi.org/10.1093/brain/awl346
5. Herzog, J. , Volkmann, J. , Krack, P. , Kopper, F. , Pötter, M. , Lorenz, D. , Steinbach, M. , Klebe, S. , Hamel, W. , Schrader, B. , Weinert, D. , Müller, D. , Mehdorn, H. M. and Deuschl, G. (2003), Two-year follow-up of subthalamic deep brain stimulation in Parkinson's disease. *Mov. Disord*., 18: 1332-1337. doi:10.1002/mds.10518