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Short Communication

Deep Brain Stimulation in Parkinson's Disease: Past, Current and Future

Dhanunjaya Rao Ginjupally[1,2] and Zain Guduru[3]*

[1]*Functional Neurosurgery, University of Kentucky, USA.*

[2]*Aster Prime Hospital, India*

[3]*Movement Disorders Neurologist, University of Kentucky, USA*

***Corresponding Author:** Zain Guduru, Movement Disorders Neurologist, University of Kentucky, USA.

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Deep brain stimulation is an established surgical treatment for patients with Parkinson's disease, essential tremor and dystonia. The common brain regions targeted are Subthalamic nucleus (STN), Globus pallidum (GPi) and ventro-intermediary nucleus (ViM) of thalamus. Electrical stimulation as a therapeutic intervention possibly dates back to the Ancient Egyptians, where electric eels, capable of generating powerful shocks of up to 600 volts, were used to treat neurologic and to also address pain disorders [1]. Surgical lesions in the above-mentioned brain regions were the surgical options prior to the DBS therapy. Placement of "chronic" DBS electrode by the French Neurosurgeon Alim Benabid in 1987 opened the doors for DBS in treatment of movement disorders [2]. DBS was FDA approved for essential tremor in 1999 and for Parkinson's disease in 2002. Different DBS systems includes constant voltage stimulation (Medtronic) and constant current stimulation (Abbott and Boston Scientific). A complete interdisciplinary preoperative DBS assessment should be performed prior to consideration of DBS surgery.

In Parkinson's disease, DBS helps with motor signs and fluctuations [3] but there is no data which shows that it slows down the disease progression. Appropriate patient selection is the most critical factor for successful DBS. In general, a patient with at least 3 years of motor symptoms, absence of severe psychiatric symptoms, absence of significant dementia, at least 30% improvement in Unified Parkinson's disease Rating Scale (UPDRS) motor score (Part III) following administration of a supra-threshold dose of levodopa. Patient counselling and expectations have to be clear prior to the surgery and it is also important to note that symptoms unresponsive to levodopa (gait, postural instability, speech and posture) are unlikely to improve with DBS and could even worsen [4]. The common target locations for PD patients include STN and GPi. Bilateral STN DBS has the greatest potential for lessening medications [5]. Different target locations includes zona increta, pedunculopontine nuclei are still area of research.

At University of Kentucky, we have identified a new approach to investigate the ability to alter disease progression. We use a cell-based graft that consists of peripheral nerve tissue as a source of growth factors and growth-promoting proteins for delivery into the parenchymal region with dopaminergic cell loss. We deploy the tissue grafts in the substantia nigra immediately following stimulating electrode placement into the STN in patients with PD undergoing DBS surgery [6]. It is a phase-1, open-label, single center clinical trial and over the last 6 years, we have enrolled 65 patients and we have termed it as "DBS plus." A major ethical advantage is that participants do not have to forego therapeutic benefit of the DBS to be involved in the study. The source of our cell therapy material is autologous peripheral nerve tissue obtained from the sural nerve. Schwann cells are abundant in peripheral nerve tissue and transdifferentiate after injury into "repair cells." Early phase I results at 2 years after surgery support that DBS plus is a safe and feasible platform to trial cell therapies. Meanwhile, clinical efficacy results appear to support moving to a Phase II trial to begin testing efficacy of this investigational therapy.

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