Deep Brain Stimulation for Parkinson’s Disease
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Deep Brain Stimulation for Parkinson's Disease with Early Motor Complications

Deep brain stimulation is FDA-approved and has been used for years to treat patients with advanced Parkinson's disease (PD) who have severe levodopa-induced motor complications. New evidence from a controlled trial suggests that it may also be effective for patients with PD and early motor complications.

SURGICAL TREATMENT — Medical therapy is effective for initial treatment of PD. Surgical ablation or deep brain stimulation has generally been recommended only for patients with intolerable dyskinesias or motor fluctuations while on levodopa. Appropriate candidates for surgery are those whose cognition is relatively intact, who are not depressed, and who have no medical contraindications.

DEEP BRAIN STIMULATION — High-frequency electrical stimulation of the subthalamic nucleus or globus pallidus from implanted electrodes has largely supplanted ablative procedures and is now the surgical treatment of choice for PD.

The device has 3 components: a neurostimulator implanted subcutaneously below the clavicle or over the abdomen, a wire implanted in the brain (the lead), and an extension that connects the neurostimulator to the lead. After implantation, initial programming of the device can take several weeks, and fine tuning may require several months of frequent visits. Additional adjustments may be needed every few months. Batteries usually need to be replaced every 3-5 years, but rechargeable batteries may last for up to 10 years.

A trial comparing bilateral subthalamic to bilateral pallidal deep brain stimulation in 299 patients with advanced PD found that both procedures resulted in similar improvements in motor function at 24 months. The levodopa-equivalent daily dose was reduced by 408 mg in patients receiving subthalamic stimulation and by 243 mg in those receiving pallidal stimulation.

Serious adverse events were similar in both groups, but the level of depression improved after pallidal stimulation and worsened after subthalamic stimulation.

THE NEW STUDY — A 2-year randomized trial (EARLYSTIM) in 251 patients 18-60 years old with PD for >4 years and fluctuations or dyskinesias for <3 years found that bilateral subthalamic neurostimulation plus medical therapy was significantly superior to medical therapy alone in improving quality of life (the primary endpoint) and motor function. Mean scores on a Parkinson's disease questionnaire (PDQ-39), which measures quality of life on a scale of 0 to 100, improved by 7.8 points in patients who received neurostimulation and worsened by 0.2 points in those who received medical therapy alone. The maximum effect was reached at 5 months and remained stable for up to 24 months. The levodopa-equivalent daily dose was reduced by 39% in patients who received neurostimulation and increased by 21% in those who received medical therapy alone.

LONG-TERM RESULTS — After deep brain stimulation, reductions in levodopa dosage may be maintained for several years. In general, treated patients have marked improvement in off-medication motor function and improvement in dyskinesias when taking medication. Some symptoms, such as speech disturbances, postural instability, freezing of gait, and cognitive problems do not improve with the procedure and may continue to become worse.

ADVERSE EFFECTS — Adverse effects of deep brain stimulation have included intracranial hemorrhage, hemiparesis, infection, depression, confusion, attention/cognitive deficits, dysarthria, and death. Even with successful surgery, decreased verbal fluency and a variety of psychosocial problems have occurred. Hardware problems, including lead migration, fracture, or malfunction, can occur.
Cognitive decline is common after deep brain stimulation in patients with pre-existing intellectual impairment and in patients ≥70 years old. In addition, deep brain stimulation can increase the incidence of falls and may increase impulsivity, which can lead to pathological gambling.

In the new clinical trial, impaired wound healing, intra-cerebral abscess or edema, dislocation of the device, or reoperation occurred in about 10% of patients who received neurostimulation. Depression was more common with neurostimulation than with medical therapy alone (4.8% vs. 0.8%).

CONCLUSION — Bilateral deep brain stimulation can improve motor symptoms and quality of life in patients <60 years old with early motor complications of Parkinson's disease, but other symptoms of the disease may continue to worsen and serious adverse effects can occur. Its long-term efficacy and safety in these patients and its effectiveness in older patients with early motor complications remain to be determined. 