

Surgical treatment for Parkinson's disease

Surgery shows promise for patients with severe, poorly controlled motor fluctuations

PARKINSON'S DISEASE afflicts around 78 000 Australians. Mortality is almost twice that of age-matched controls¹ and the mean disease duration is only 13 years.² No treatment has yet been shown to slow disease progression.

Fortunately, motor disability can be markedly improved with levodopa therapy. However, after 3–5 years, the duration for which each dose of levodopa is effective shortens and many patients begin to experience fluctuations in their motor function throughout the day. Involuntary movements appear, in particular painful posturing of the legs or arms, as the beneficial effect of levodopa wears off (“end of dose dystonia”) and writhing choreoathetoid movements that accompany part or even all of the period when levodopa is working (“peak dose dyskinesia”). These problems can be ameliorated to some extent by the addition of dopamine agonists or catechol-*O*-methyltransferase (COMT) inhibitors. Unfortunately, problems that are not reversed by levodopa, such as worsening of balance and speech, cognitive decline and depression, can also supervene. Patients who never experience sustained benefit from levodopa are

likely to have a different underlying pathology from idiopathic Parkinson's disease, such as vascular parkinsonism, progressive supranuclear palsy or multiple system atrophy.

It is in patients with severe, poorly controlled motor fluctuations that surgical therapy has re-emerged as a treatment option. In this issue of the Journal (*page 142*), Iansek and colleagues report the results from 14 patients at their centre who underwent bilateral deep brain stimulation of the subthalamic nucleus for the treatment of Parkinson's disease.³ Motor function was improved with subthalamic nucleus stimulation for at least six months when patients were assessed both with and without levodopa treatment. Dyskinesias were also apparently reduced, and mean levodopa dose was reduced by 30% after surgery. The procedure was not without risk (one patient had a disabling intracerebral haemorrhage, another required relocation of the stimulators to the thalamus), but overall this is an exciting and encouraging development.

Data were also collected from the first six patients in the reported series as part of an international multicentre trial,

which included another Australian centre, St Vincent's Hospital, Sydney.⁴ Results from 96 patients who underwent bilateral subthalamic nucleus stimulation showed a median reduction of 49% in motor disability without medication using blinded videotape analysis, a mean increase from 27% to 74% of the day spent with good mobility without involuntary movements, a 58% improvement in dyskinesia scores, and a 37% reduction in mean daily levodopa dose. Similar, but less marked, improvement was seen in 38 patients treated with bilateral pallidal stimulation, although the dose of levodopa was not reduced after surgery in these patients. The incidence of intracranial haemorrhage was 2.5%, and infections requiring electrode removal occurred in less than 1%. These are benchmark figures by which the results of Australian centres offering these procedures can be compared.

Surgical therapy for Parkinson's disease is not new, but there have been advances in our understanding of why it works. Loss of dopaminergic projections from the substantia nigra to the basal ganglia results in pathological overactivity of the subthalamic nucleus and globus pallidus. Patients undergoing deep brain stimulation have a wire implanted into the brain that is attached to a programmable battery implanted subcutaneously in the chest wall, much like a pacemaker. Deep brain stimulation mimics the effects of stereotactic lesioning, but has the added advantages of being reversible and allowing postoperative programming to optimise the site of stimulation. However, it is expensive and programming is time-consuming, sometimes requiring months before the optimal stimulating parameters can be established. Economic and geographical constraints limit access to therapy for many patients in whom surgery would otherwise be appropriate; such issues need to be addressed by healthcare providers.

At present, there are a number of Australian centres performing subthalamic nucleus stimulation and pallidotomy (lesioning of the globus pallidus); experience in pallidal stimulation is as yet limited. The indications and choice of operation are still evolving. Nevertheless, some general guidelines may be suggested.

Who should be offered surgery? Surgically fit patients with severe motor fluctuations or dopa-induced dyskinesia, or both, are the main candidates. Surgery does not significantly improve the patient's best response to levodopa (except by reducing dyskinesias). A good or excellent response to levodopa predicts the response to surgery, and is essential.^{5,6} The procedure, particularly subthalamic nucleus stimulation, may take hours, during which time the patient remains fully conscious, so a degree of stoicism on the part of the patient is required. For the rare patient with disabling parkinsonian tremor that is poorly suppressed by levodopa, without accompanying akinesia, thalamic surgery can be contemplated.

Who should not be offered surgery? Patients who have never responded well to levodopa will not benefit from surgery. The presence of cognitive or psychiatric complications of Parkinson's disease (frequent hallucinations, psychosis, parkinsonian dementia, uncontrolled depression) is

an absolute contraindication to surgery; significant cerebral atrophy on computed tomography or magnetic resonance imaging is also a contraindication. Levodopa-resistant symptoms such as impairment of balance or speech can worsen after surgery.⁷

Which procedure? Overall, subthalamic nucleus stimulation appears more promising than pallidal surgery. However, a randomised trial comparing the two has not been performed, and excellent and sustained improvement following both bilateral subthalamic nucleus stimulation and bilateral pallidotomy is seen.⁸ Physicians should be guided not only by theoretical considerations, but also by local experience and expertise. Objective evaluation of the results of surgery by a neurology team not involved in patient selection or the surgical procedure is an advantage, and this information should be available to patients and their treating neurologists to aid decisions about therapy.⁹

Where to refer? The process of optimising therapy for advanced Parkinson's disease, differentiating between idiopathic Parkinson's disease and related disorders, and choosing the appropriate operation, is not always straightforward. For this reason, we recommend that patients considering surgical treatment be referred to a unit with specialist expertise in movement disorders, and that surgery be offered in the setting of a multidisciplinary assessment by teams including a neurologist, neurosurgeon, neuropsychologist and Parkinson's disease nurse specialist.

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