Surgical management of Parkinson’s disease: a critical review

Parkinson’s disease is a progressive disabling movement disorder that is characterised by three cardinal symptoms: resting tremor, rigidity, and bradykinesia. Before the availability of effective medical treatment with levodopa and stereotactic neurosurgery, the objective of surgical management was to alleviate symptoms such as tremor at the expense of motor deficits. Levodopa was the first effective medical treatment for Parkinson’s disease, and surgical treatment such as thalamotomy became obsolete. After one decade of levodopa therapy, however, drug-induced dyskinesia had become a source of additional disability not amenable to medical treatment. Renewed interest in stereotactic functional neurosurgery to manage Parkinson’s disease has been seen since the 1980s. Local experience of deep-brain stimulation is presented and discussed in this paper. Deep-brain stimulation of the subthalamic nucleus is an effective treatment for advanced Parkinson’s disease, although evidence from randomised control trials is lacking.

Introduction

Parkinson’s disease (PD) is a progressive disabling movement disorder that is characterised by three cardinal symptoms: resting tremor, rigidity, and bradykinesia. The prevalence of PD in the general population is reported as being 0.2% to 0.3%. The highest prevalence has been noted in white Caucasians and the lowest in black Africans. Although PD is a neurodegenerative disease of the elderly, 5% to 10% of patients have symptoms before the age of 40 years. It is estimated that 3.4% of the elderly in nursing homes in Hong Kong have the disease. Further increases in the elderly population worldwide will likely result in a steady increase in the prevalence of this disease. Parkinson’s disease is associated with an increase in mortality and a reduction of life expectancy in comparison with age-matched controls.

Before the availability of effective medical treatment with levodopa and stereotactic neurosurgery, the objective of surgical management was...
to alleviate symptoms such as tremor at the expense of motor deficits. This approach involved performing open craniotomy and sectioning of the cerebral cortex, pyramidal tract, and cerebral peduncle. Once the concept of the extrapyramidal system (the basal ganglia, including the striatum, pallidum, subthalamic nucleus, substantia nigra, red nucleus, and dentate nucleus) was described by Spatz in 1927, a more rational experimental approach could be developed. Open craniotomy using an intraventricular approach to resect the basal ganglia (caudate nucleus and putamen) was developed in the 1940s and 1950s with reasonably good results (45% to 62%) in terms of tremor control; however, surgical mortality remained high at 12% to 41%.

In 1953, Cooper described a postencephalitic patient who underwent pedunculotomy in which the anterior choroidal artery was ligated owing to surgical injury. The resulting ischaemic infarct of the pallidum gave rise to a marked improvement of the tremor. This surgical approach of open craniotomy and pallidotomy subsequently failed to achieve a predictable and favourable outcome, while carrying a high mortality and morbidity risk. Stereotactic thermopallidotomy was then favoured because of its minimal invasiveness, but its tremor control remained unpredictable and its effects on akinesia and rigidity were poor. Stereotactic thalamotomy had gradually replaced pallidal surgery by the 1960s for tremor control.

The impact of the availability of levodopa in the 1960s was enormous. Levodopa was the first effective medical treatment for PD, and it alleviated all three cardinal symptoms—tremor, bradykinesia, and rigidity. Giving levodopa also served as a diagnostic test for the disease, and surgical treatment such as stereotactic thalamotomy became obsolete. After one decade of levodopa therapy, however, drug-induced dyskinesia had become a source of additional disability not amenable to medical treatment. Paradoxically, levodopa-induced dyskinesia had been shown to be effectively controlled by stereotactic pallidotomy of the globus pallidus interna, although its effects on tremor, bradykinesia, and rigidity are variable. Renewed interest in stereotactic functional neurosurgery to manage PD has been seen since the 1980s. In this paper, surgical procedures in the post-levodopa era are critically reviewed and local experience of various techniques presented.

Pathophysiology relevant to surgical management of Parkinson’s disease

The primary pathology of PD is a progressive cell loss of selected but heterogeneous groups of neurons. Notably, this process occurs in the melanin-laden dopaminergic neurons of the pars compacta (substantia nigra), selected nuclei in the brain stem, the hypothalamus, cingulate gyrus, olfactory bulb, and sympathetic ganglia and parasympathetic neurons in the intestines. It is believed that the dopamine-deficient state of the substantia nigra results in an increased activity of the internal segment of the globus pallidus and subthalamic nucleus. This popular model of basal ganglia circuitry explains akinesia well, but not tremor and rigidity. The model predicts that the inactivation of thalamic nuclei would worsen tremor and that pallidotomy of the globus pallidus interna would produce hemiballism. Thalamotomy has been acknowledged as an effective treatment for PD, as well as essential and other types of tremor, whereas pallidotomy of the globus pallidus interna specifically alleviates levodopa-induced dyskinesia. A surgical lesioning of the globus pallidus interna does not cause hemiballism; however, subthalamic nucleus inactivation commonly does.

Surgical management of Parkinson’s disease

There has been a resurgence in functional stereotactic neurosurgery during the 1990s, which reflects the fact that after 5 to 10 years of effective medical therapy with levodopa, patients with advanced PD are accumulating. Furthermore, a greater understanding of the pathophysiology of PD has led to the availability of effective and low-risk surgical procedures. Given that the primary problem in PD is striatal dopamine deficiency, a logical restorative therapy would involve transplantation of dopaminergic cells into the basal ganglia, thus encouraging regeneration of striatal dopaminergic innervation. Transplantation of autologous adrenal medulla to the caudate nucleus has been shown to lack efficacy, however, and it is associated with high mortality and morbidity rates. The transplantation of foetal mesencephalon has shown more promising results, although a recent randomised controlled study that used a sham control did not show a clear benefit. Other experimental strategies that have been described recently include porcine xenograft transplantation, intraventricular delivery of dopaminergic neurotrophic factor, implantation of foreign cells in semipermeable polymeric capsules (obviating the need for immunosuppression), and enhancement of tyrosine hydroxylase expression to increase endogenous synthesis of dopamine.

The most common functional stereotactic neurosurgical procedures that are currently performed worldwide for PD are surgical lesioning and deep-brain...
stimulation of the three overactive nuclei. This region includes the thalamus (nucleus ventralis intermedius or ‘Vim’) for contralateral tremor; the globus pallidus interna for contralateral rigidity, akinesia and specifically levodopa-induced dyskinesia; and the subthalamic nucleus for all three cardinal symptoms.

Magnetic resonance imaging (MRI) stereotaxy is preferred by the majority of surgeons because of its superior resolution and ease, although spatial distortion can be a problem. Systematic comparison of MRI, computed tomography, and conventional stereotaxy has demonstrated acceptable accuracy. Patients selected should be alert and cooperative, not taking antiparkinsonian drugs, and preferably have florid signs of tremor, akinesia, and rigidity. Confirmation of the surgical target by macrostimulation and assessment of the alleviation of symptoms are key to the success of the procedure.

Whether microelectrode recording (MER) will increase the functional accuracy of target selection is controversial. There is evidence to suggest that MER may increase the risk of the procedure (such as intracerebral haemorrhage) without enhancing accuracy. Generally, if there is concordance between macrostimulation and MER findings, a good result is guaranteed. The risks of intracerebral haemorrhage with this approach is small: 3.3% for each target.

Selecting the target

Thalamic nucleus ablation or stimulation results in consistent contralateral tremor control, but other symptoms of PD will not be affected. Pallidotomy (of the globus pallidus interna) has been shown to relieve contralateral akinesia and rigidity by one third, and levodopa-induced dyskinesia by 92%. The subthalamic nucleus is a small target; suppression of its overactivity leads to alleviation of all three cardinal symptoms of PD. The complication of contralateral hemiballism in subthalamotomy, however, can be significant and has been reported to be as high as one in five. Nevertheless, good results from creating lesions in the bilateral subthalamic nucleus have been reported in the UK and the view that subthalamotomy causes hemiballism has been called into question recently by Guridi and Obeso.

Lesioning or deep-brain stimulation?

Although the risk of major complications such as intracerebral haemorrhage and death occurring from unilateral pallidotomy (lesioning by thermocoagulation) is low (4% to 10%), the incidence of permanent adverse effects is reported to be 4% to 46%. Left-sided pallidotomy is associated with reduced verbal fluency, whereas bilateral procedures are associated with dysarthria, dysphonia, and gait disturbance. Deep-brain stimulation has thus become the treatment of choice (Table 1), particularly when left-sided or bilateral targeting is required, because it is not an irreversible procedure. Although there is inadequate data to suggest that deep-brain stimulation of the subthalamic nucleus is superior, the initial experience reported by Limousin favours this strategy.

Gamma-knife radiosurgery

The use of gamma-knife radiosurgery to create a lesion relies on an image without guidance from electrophysiological recordings or macrostimulation assessment. The outcome cannot be determined initially: the median time to clinical response is 2 months, with only half the patients achieving good results. A dose-response relationship has also been noted, as has the balance between response and morbidity. Gamma-knife radiosurgery is an option, however, for the patient who is not suitable to undergo standard functional stereotactic procedures.

Local experience

Stereotactic thermocoagulation thalamotomy has been reported in seven cases in Hong Kong. The rarity of the procedure reflects the effectiveness of levodopa in the 1980s. In 1997, deep-brain stimulation—specifically of the nucleus ventralis intermedius—was trialled in two patients with tremor-dominant PD at the Prince of Wales Hospital. The tremor was controlled with improvement in the tremor score in two patients (Table 2). Since 1998, nine rigid-akinetic
patients have received deep-brain stimulation of the subthalamic nucleus: seven unilaterally and two bilaterally. Preoperative and 6-month postoperative United Parkinson’s Disease Rating Scale scores were recorded for three patients (Table 3). There was no mortality or morbidity noted for the nine patients. One targeting failure occurred in the second patient, who required a subsequent operation approximately 7 months later. In another patient, the extension electrode broke in the neck region after 3 months of satisfactory results; the quadri-electrode was thus replaced.

Microelectrode recording has been performed in the two most recent procedures involving the subthalamic nucleus. A higher degree of confidence in the accuracy of targeting was experienced, at the expense of 2 hours of operating time. There was a significant reduction in levodopa dosage after the stimulation (16% to 60%; Table 4), which is consistent with the results reported in the literature. The cost difference with the reduction of levodopa and the discontinuation of second-line drug treatment can result in an annual saving of approximately US$ 2000 (Table 5).

**Conclusion**

Although bilateral deep-brain stimulation of the subthalamic nucleus has been described as the treatment of choice, there is so far no randomised controlled trial that confirms its superiority over other treatments. Considering factors such as clinical efficacy and morbidity, as well as the costs associated with a pulse generator, the use of deep-brain stimulation may be favoured for left-sided procedures and lesioning of the right side.

### References

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