

# SURGERY FOR MOVEMENT DISORDERS

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Since Laitinen's report of pallidotomy for the treatment of advanced Parkinson's disease less than a decade ago, there has been a resurgence of interest in functional neurosurgery for movement disorders. The convergence of several paths, including the clinical problem of levodopa induced dyskinesias and motor fluctuations, increased understanding of cellular pathophysiology, improved brain imaging and microelectrode recording techniques, and the development of deep brain stimulation (DBS), have paved the way for novel therapeutic strategies and major advances in the field. The neurologist must work in partnership with the neurosurgeon in a multidisciplinary team, helping to optimise patient selection, assess patients interoperatively, and supervise drug treatment and stimulation parameters postoperatively.

## HISTORY OF MOVEMENT DISORDER SURGERY

Surgery for movement disorders is not new (fig 1). Before 1975, 75 000 thalamotomies had been performed worldwide. The breakthrough in the development of human stereotactic surgery came in 1947 when Spiegel and Wycis decided to use landmarks within the brain, rather than the skull. Their first patient had a pallidal lesion for Huntington's chorea. Parkinsonism (including many postencephalitic cases) was treated with lesions in the thalamus, ansa lenticularis, and pallidum. In 1952, Cooper inadvertently interrupted the anterior choroidal artery in a patient with Parkinson's disease, and the patient awoke with resolution of tremor and no deficit despite infarction of the globus pallidus. This led to the practice of injecting alcohol into this area. Lesions in the thalamus more reliably abolished tremor, so that by the late 1950s this had become the preferred target, and particularly the ventrointermediate (Vim) nucleus. Following the introduction of levodopa in 1968, stereotactic surgery for Parkinson's disease was hardly performed and interest in the field waned.

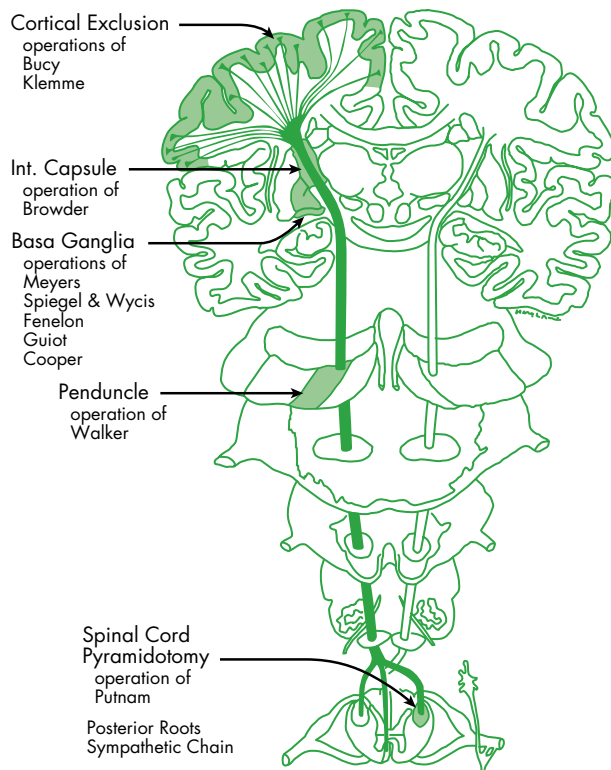
The next 15 years saw increasing numbers of Parkinson's disease patients with dyskinesias and motor fluctuations and a surgical solution was revisited. Following abortive attempts with adrenal medulla grafts, Lindvall's group in Sweden reported the transplantation of fetal dopamine cells into the striatum, but this has remained an experimental procedure. In the late 1980s pallidotomy was revisited, and by the mid 1990s many groups had confirmed its effectiveness, particularly for alleviating levodopa induced dyskinesias. Expertise and confidence in these techniques were rekindled but concern remained regarding high complication rates, particularly when bilateral lesions were required. Brice and McLellan in 1980 were the first to treat two patients with multiple sclerosis induced intention tremor by fully implantable thalamic stimulators. Experience increased and technology improved, and in 1993 Benebid reported stimulation of the subthalamic nucleus (STN), which improved almost all parkinsonian symptoms allowing substantial reduction of dopaminergic medication.

## PARKINSON'S DISEASE

### Patient selection

Patients are often referred for surgery when their disease is very advanced and the degree of disability severe. Apart from tremor response, the successful outcome of surgery for Parkinson's disease is dependent upon the presence of dopaminergic responsive symptoms to be effective. "Burned out" cases, with no useful "on" periods, will not respond to surgery; similarly non-dopa responsive parkinsonian diseases, such as multiple system atrophy, will not significantly benefit from surgery. The demographics of the ideal patient are listed in table 1. It is crucial that patients with significant cognitive or psychiatric difficulties are avoided. Drug induced hallucinosis is a poor prognostic sign, and surgery would not be recommended as a way of trying to reduce medication. Those with postural instability and dysphonia, particularly in the "on" state, do badly. The temptation is to offer surgery because nothing more can be done, but this often leads to disaster. In my view, all practical medical alternatives should have been tried. If an apomorphine service is available, then this is a preferable option in the first instance. Surgery is associated with at least a 3% risk of significant permanent morbidity even in the best hands. Some patients prefer to consider

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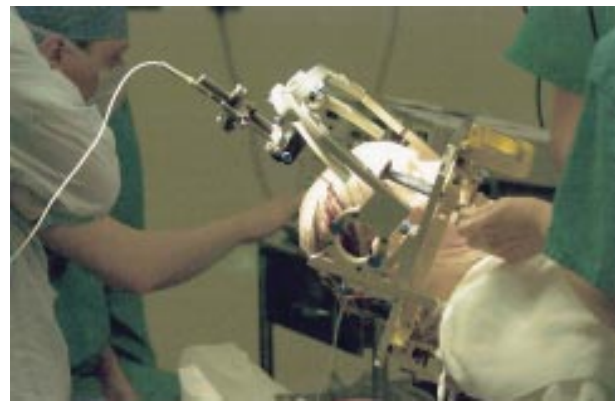


**Figure 1** Surgical targets for parkinsonism.

surgery without a trial of medication, despite thorough counselling. This may be appropriate for tremor predominant disease (particularly “benign tremulous” Parkinson’s disease), but for other types, the trade off between side effects and efficacy is not sufficiently favourable to recommend surgery early in the course of the disease.

**Surgical technique**

Target location primarily relies on imaging for initial localisation. Most groups now use magnetic resonance imaging, but some rely solely on computed tomographic scanning and occasionally ventriculography. The latter allows on table verification of anatomical localisation, but adds to patient distress. The stereotactic frame (fig 2) is usually fitted under general anaesthetic, but the patient is woken up to allow clinical confirmation of symptom effectiveness and side effects. Patients without significant tremor or rigidity in the “off” state can be difficult to assess intraoperatively. Bradykinesia does not respond rapidly to stimulation (table 2), and therefore cannot be reliably used. Many groups use microelectrode recording to



**Figure 2** Intraoperative electrode recording.

map out the various nuclei neurophysiologically. This can add considerably to the length of the surgical procedure, which in some centres with the best published outcomes often take more than 12 hours. On stimulation or lesioning of the pallidum or STN, transient dyskinesias may ensue, which are usually a predictor of successful outcome. Overall the procedure is remarkably well tolerated.

**Lesions or stimulation**

High frequency electrical DBS provides an adjustable inhibitory effect on the target site, but at increased cost (table 3). An accurately placed lesion in the thalamus or pallidum provides reliable long lasting suppression of tremor and dyskinesias respectively, with no adverse effects. Bilateral lesions are invariably associated with adverse cognitive and bulbar effects, even when well placed, and stimulation is therefore preferable in this situation. Lesioning of the STN is technically demanding because of its small size, but benefits appear to be temporary and therefore stimulation of this target is now recommended. Though effective, DBS requires careful postoperative adjustment that often takes many hours, and the replacement of equipment when hardware failure occurs. In some series up to 20% of wires move, break, or become infected. The stimulation battery unit requires replacement every five years for STN stimulation, and three years for pallidal stimulation.

**Thalamus**

The thalamus is the final common outflow pathway for all tremors. Contralateral tremor is reliably suppressed with a lesion in the Vim nucleus and rigidity in the ventralis oralis posterior (Vop) nucleus. There is no effect on bradykinesia and although dyskinesia is occasionally helped, this is not a reliable observation. Even patients with tremor predominant Parkinson’s disease will eventually develop bradykinesia in time, so it is now recommended that such patients should have STN stimulation, rather than a thalamic lesion or stimulation. Thalamic lesional surgery should therefore be reserved for non-Parkinson’s disease tremor only (see below).

**Table 1** Ideal patient for pallidal or subthalamic nucleus surgery

- ▶ Biological age less than 70 years
- ▶ UPDRS “off” motor score 40–80/108
- ▶ Suprathreshold dose levodopa improves score by 50%
- ▶ Severe drug induced dyskinesias (pallidal surgery)
- ▶ No falls when “on” (pull test)
- ▶ MMSE >24/30
- ▶ Good bulbar function (particularly in “on” state)
- ▶ No significant depression
- ▶ No drug induced hallucinosis or other significant psychotic symptoms

MMSE, mini-mental state examination; UPDRS, unified Parkinson’s disease rating scale.

**Table 2** Differing latencies\* of stimulation effects on symptoms

▶ Rigidity	Seconds
▶ Tremor	Seconds to months
▶ Bradykinesia	Seconds to days
▶ Dyskinesias	Depends on reduction of drugs and increase in stimulation

\*Same latencies apply in reverse.

**Abbreviations**

- DBS:** deep brain stimulation
- STN:** subthalamic nucleus
- Vim:** ventrointermediate
- Vop:** ventralis oralis posterior

**Pallidum**

Posteroventral pallidal lesion or stimulation will reliably abolish contralateral dyskinesias. This includes biphasic and peak dose, and “off” state dystonias. Following optimal lesioning, the benefit can persist for at least five years. The improvement in “off” state bradykinesia also persists, but any improvement in “on” state dissipates after six months. Contralateral tremor may also be improved but this is not a reliable effect. Medication remains unaltered following the procedure. Axial symptoms, including dyskinesias, do not improve, and non-dopaminergic gait and bulbar function are also not helped. “On” state postural instability and freezing may be worsened. Bilateral pallidotomy requires precise targeting, often with a smaller lesion on the less symptomatic side to minimise adverse effects. Contralateral stimulation is now preferred to lesioning to avoid frontal executive deficits. Other potential side effects include visual field defects (optic tract), hemiparesis and dysarthria (internal capsule), and haemorrhage which can be life threatening (5% mortality rate in some

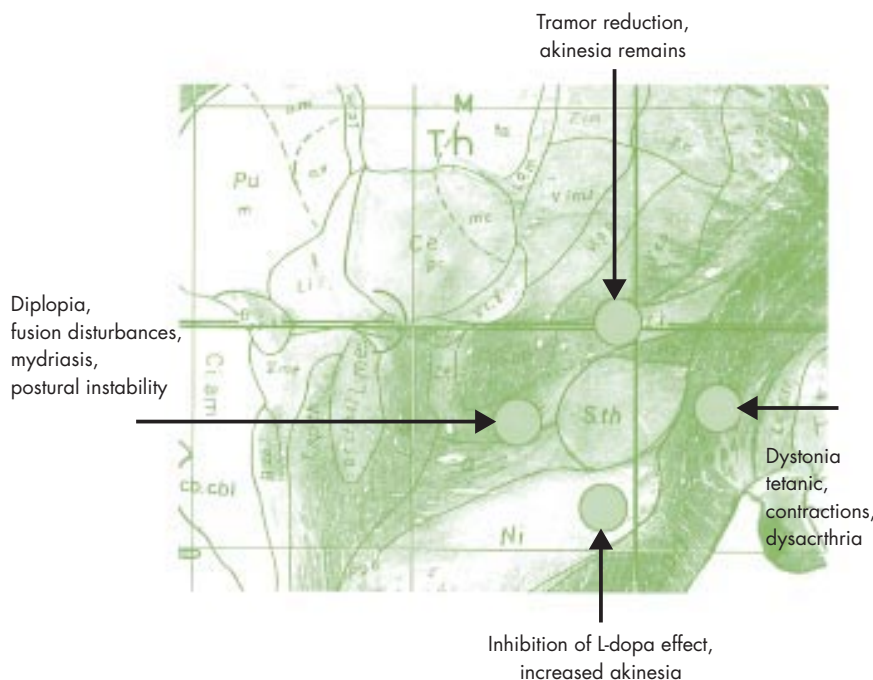
series). Delayed small vessel ipsilateral strokes (up to six months) are occasionally seen for reasons that are not clear. Weight gain, probably caused by reduction in dyskinesias, is frequently observed.

**Subthalamus**

Bilateral subthalamic stimulation alleviates all the cardinal symptoms of Parkinson’s disease and benefits are preserved for more than five years. Unlike pallidal surgery, medication can be reduced by at least half postoperatively, and this leads to a reduction in drug induced dyskinesias. Unilateral surgery can be offered to patients with very asymmetric disease, but most require bilateral surgery to avoid problems with variable medication requirements on the two sides. Complications can be transient or permanent (fig 3) and tolerance may develop to some (table 4). Dramatic rebound symptoms can be seen following acute stimulator failure, sometimes necessitating emergency admission. The recent stimulator units are less sensitive to electromagnetic interference, such as from light switches and electric motors. Patients are now usually given control devices that can be preset to alter the stimulation parameters at home. Although the results in well selected patients can be dramatic and well maintained, STN stimulation requires considerable long term commitment from the team looking after the patient. It has been estimated that each patient requires on average 40 hours of adjustment for optimum benefit and maintenance of effect. For this reason, it

**Table 3** Advantages and disadvantages of deep brain stimulation (DBS)

Advantages	Disadvantages
<ul style="list-style-type: none"> <li>▶ DBS avoids destructive brain lesion</li> <li>▶ Stimulation parameters can be adjusted to optimise benefits and adverse effects</li> <li>▶ DBS can be performed bilaterally with relative safety</li> <li>▶ DBS does not preclude the use of future “restorative” surgical techniques.</li> </ul>	<ul style="list-style-type: none"> <li>▶ Adverse events relating to procedure and implanted equipment.</li> <li>▶ Battery life restricted to 2–5 years</li> <li>▶ Cost of system and manpower</li> </ul>



**Figure 3** Adverse effects of subthalamic nucleus stimulation.

**Table 4** Habituation of stimulation induced adverse effects

▶ Dyskinesias	Days to months
▶ Ocular deviation	Days to weeks
▶ Sensory misperception	Minutes to days
▶ Flushing (ipsilateral)	Minutes to days
▶ Eyelid apraxia	Almost none
▶ Muscle contractions	None
▶ Dysarthria/dysphonia	None
▶ Worsening akinesia	None

is difficult to envisage this procedure becoming widely available, unless there is a substantial increase in the number of experienced staff in the units offering this service. There is also concern about the frequency of psychiatric side effects, particularly depression that probably arises as a result of the inhibition of STN limbic areas. The rate of suicide has been high in some series, which is rarely seen with surgery to other targets. Patients with a history of significant depression should not be offered STN surgery.

## NON-PARKINSONIAN TREMOR

### Essential tremor

A thalamic Vim lesion will reliably suppress contralateral tremor. Given the bilateral nature of the condition, bilateral thalamic stimulation is now the preferred option. Side effects are similar to those seen in pallidal surgery.

### Multiple sclerosis tremor

Careful patient selection is crucial for a successful outcome, and only a small percentage of patients will benefit long term. Titubation will not improve, and pure upper limb tremor with little or no underlying dysmetria does best. This can often be difficult to determine clinically and we use visually guided wrist tracking to identify those patients with single frequency tremor. Patients with underlying pyramidal or sensory deficits in the tremulous limb will not be functionally improved. Those with cognitive deficits are often worsened. We cover the procedure with methylprednisolone in an attempt to reduce the possibility of surgery inducing a relapse. Distal tremor responds to targeting the thalamus (Vop) and proximal tremor the zona incerta.

## DYSTONIA AND OTHER MOVEMENT DISORDERS

Improving techniques and increasing confidence in functional neurosurgery for Parkinson's disease has led to the study once more of its role in the treatment of other movement disorders, such as dystonia, chorea, and tardive dyskinesia. Thalamotomy has been the traditional target for dystonia, but the pallidum is now recognised as the preferred target. Bilateral pallidotomy has a dramatic effect on idiopathic torsion dystonia including DYT 1, but the effects wane over several years. Bilateral pallidal DBS is now the favoured technique, and benefits appear to be maintained. Even botulinum resistant spasmodic torticollis has been successfully controlled with bilateral pallidal DBS and may replace selective cervical denervation. Patients with "secondary dystonia", such as following head injury or stroke, experience more modest improvements. Intraoperative stimulation in the awake state cannot be

performed, so the procedure relies heavily on imaging and microelectrode techniques for localisation. Benefits also take several weeks and sometimes months to occur. Pallidal stimulation requires higher voltages, pulse widths, and frequencies than STN and thalamic targets, and sometimes benefits are only seen with parameters that require battery replacement every 18 months.

## SUMMARY

There can be no doubt that functional neurosurgery can produce dramatic benefits, with a relatively small risk of adverse effects in experienced hands. Most groups now favour DBS to lesion therapy, but there remains a place for "palliative" thalamotomy or pallidotomy in certain situations. The vast majority of published series have been open label, not always consecutive, and on young, highly selected patients. There must be concerns about publication bias in favour of successful outcomes. Randomised comparative trials are few and are urgently required. There needs to be an emphasis on quality of life and cost effectiveness measures to justify the high initial and long term costs of these procedures. The hope must be that "restorative surgery" will replace the need for this technique, particularly for Parkinson's disease.

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## Surfing for movement disorders

The two major problems with searching for any information on the internet on movement disorders (or indeed any other subject) are that of "data overload", and finding good quality information that is pitched at the correct level. WEMOVE is quite simply the most outstanding website on all subjects related to movement disorders. It avoids both of the above issues with high quality information that is appropriate for both a medical and lay audience (<http://www.wemove.org/>). It includes an extremely useful email alert service (EMOVE) which sends updates of recent papers on a wide spectrum of movement disorder related topics or presentations from scientific meetings (to register go to <http://www.wemove.org/emove/>). In addition there are slide sets which are very useful for teaching—I recently had to give a talk on Parkinson's disease at very short notice, and was able to put the entire talk together using their slides in less than two minutes!

WEMOVE also links to many patient support web sites on Parkinson's disease, dystonia, essential tremor, and Wilson's disease to name but a few. Unfortunately many of these other sites are not that easy to navigate around, or don't provide particularly useful information. However, two good examples are the Restless Legs Syndrome Foundation (<http://www.rls.org/>) and the "Virtual Hospital" at University of Iowa with good patient information on Tourette's (<http://www.vh.org/Patients/IHB/Psych/Tourette/TouretteSyndrome.html>).

For a more UK based approach, a good starting point is the Glaxo Neurological Centre at the Walton (<http://glaxocentre.merseyside.org/charity.html>). You will find links there to the Parkinson's Disease Society, Huntington's Disease Association, MSA (Sarah Matheson Trust), PSP Society, Tourette's Association, and many other UK based neurological charities.

It is perhaps a shame that there are not more sites which use the potential advantages of the web to illustrate movement disorders with video, such as on-off phenomena in Parkinson's disease or even some functional neurosurgery (for example, [http://medweb.bham.ac.uk/http/depts/clin\\_neuro/teaching/tutorials/parkinsons/parkinsons2.html](http://medweb.bham.ac.uk/http/depts/clin_neuro/teaching/tutorials/parkinsons/parkinsons2.html)).

Massachusetts General Hospital has a very useful site looking at functional neurosurgery for Parkinson's disease, which also has useful links including the unified Parkinson's disease (UPDRS) and Hoehn and Yahr rating scales (<http://neurosurgery.mgh.harvard.edu/PDsurgery.htm>).

In summary, if you are to visit one web site related to movement disorders it would have to be the WEMOVE site, which also has the advantage of the most easy to remember web address (<http://www.wemove.org/>)!

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