INTRODUCTION

The limits of drug therapy for Parkinson’s disease have led to a renewal of functional neurosurgery. The technique of deep brain stimulation has been developed to reduce the side effects of lesions and allow bilateral surgery (1). Three targets are now available: the thalamus (usually the ventrointermediate nucleus, Vim), the internal pallidum (GPI) and the subthalamic nucleus (STN).

SURGERY

In some regards, the surgical procedures for the different targets are similar. The target can be located using a combination of imaging (MRI, CT, ventriculography, depending on the centre) and electrophysiology (electrical stimulation and, in some centres, microrecordings). Implantation of the electrode is generally performed under local anaesthesia to allow the evaluation of the effect of the stimulation on parkinsonian signs and symptoms. A quadripolar electrode (model 3387 or 3389; Medtronic; Minneapolis, MN, USA) for chronic stimulation is implanted in the area giving the best effect and showing the expected pattern of neuronal activity (2,3). In a second session, or in the same one, the electrode is connected to a pulse generator implanted in the subclavicular area and equipped with subcutaneous wires (Itrell II or Kineta, Medtronic). Electrical
parameters of stimulation (voltage, pulse width, frequency) can be adapted to control parkinsonian signs and symptoms reducing side effects to as few as possible.

THALAMIC STIMULATION

Thalamic stimulation is mainly effective on tremor (4). Bradykinesia, rigidity, gait and dyskinesias are mildly or not improved (4). A randomised study comparing thalamic stimulation and thalamotomy has shown that the efficacy is comparable but side effects are more frequent with thalamotomy, and therefore the functional benefit is higher with thalamic stimulation (5). Unfortunately, 65% of patients undergoing thalamic stimulation develop motor fluctuations and dyskinesias after 4 years (6). Thus, even if the stimulation is still helping their tremor, it is not improving their main problems. Therefore, implantation in another target should be considered even in parkinsonian patients with tremor-dominant disease.

PALLIDAL STIMULATION

Pallidal stimulation is usually offered in parkinsonian patients with motor fluctuations and severe dyskinesias. The improvement of the off-periods is variable between series with improvements in motor UPDRS ranging from 0 to 56% in five recent ones (Fig. 1) (7-11). The improvement in dyskinesia scores is more constant: 77-85% in three series (Fig. 2) (9-11). Medication is not usually changed after surgery. The side effects are relatively mild, even in the case of bilateral stimulation. Worsening of on-freezing, asymptomatic haemorrhage, facial dystonia, extracerebral infection, lead dislocation, skin erosion and transient confusion have been reported. No major change in cognitive functions has been reported either in these studies or in others more oriented towards cognitive function assessment (12-15). The five series mentioned earlier (7-11) included only a small number of patients (from 5 to 9) followed up for a short period of time (from 2 to 15 months). The complexity of the GPi might explain the variability of results between individual patients and also between series. Two studies (16,17) have shown that stimulating the ventral GPi can worsen akinesia and improve dyskinesias while stimulating the dorsal GPi can improve akinesia and worsen dyskinesias. Another study (18) has shown different effects of pallidotomy depending on the location of the lesion, with antero-medial lesions leading to
a greater improvement in off-rigidity and on-
dyskinesia, central lesions improving akinesia, stability and gait, and postero-lateral lesions improving tremor.

**SUBTHALAMIC NUCLEUS STIMULATION**

Stimulation of the STN produces a very consistent improvement in off-periods: a 41-65% improvement in the motor UPDRS score reported in four series (19-22) (Fig. 3). Off-drug, akinesia, rigidity, tremor, balance, gait and dystonia are improved. Dyskinesias are also improved over time, with reduction of dyskinesia scores ranging from 64 to 86% (Fig. 4). Levodopa and other dopaminergic drugs can be reduced greatly after surgery (by 37 to 65%). This drug reduction is probably the main factor in the reduction of dyskinesias. On-drug motor scores show only mild changes. The response to levodopa before surgery is a good predictive factor of the response to STN stimulation. Severe side effects are relatively infrequent: there have been reports of symptomatic haemorrhage (approx. 1%), strokes (2%), extracerebral infection (2%) and worsening of cognitive performances (3%). Transient post-surgery confusion is relatively frequent. Worsening of depression, eyelid opening apraxia and speech problems have also been reported. It is possible to induce dyskinesias in most patients depending on the voltage selected. Apart from a few patients, usually with marked cognitive deficit before surgery, there is very little change in cognitive performances (14,15). Few comparative data on STN and GPi stimulation are available. Preliminary results on 10 patients in a blinded randomised study, show a 40% improvement in off-motor UPDRS scores in both groups; dyskinesias were also reduced in both groups, whereas levodopa was reduced only in the STN group (23). In a retrospective open study conducted on 13 patients, Krack et al. found a 71% improvement in off-motor UPDRS scores in the STN group and a 39% improvement in the

**INCLUSION CRITERIA**

Candidates for surgery are patients with idiopathic Parkinson’s disease, since none of these procedures have been shown to be effective on other parkinsonian syndromes. They are still responding to levodopa, and this response to levodopa has been shown to be a predictor of the re-
response to STN stimulation. These subjects must have tried all possible medications and, despite this, still be suffering from motor fluctuations and/or dyskinesias. They have to be in a good general state, without major cognitive impairment, or major depression. Patients with cognitive impairment are more at risk of a worsening of their cognitive functions. In the same way, depression can worsen after surgery. Brain imaging has to be considered normal.

CONCLUDING REMARKS

Thalamic, GPi and STN stimulation can be performed bilaterally in parkinsonian patients with a relatively low risk of side effects. Thalamic stimulation has very few indications and in some centres is no longer considered for Parkinson’s disease. GPi stimulation improves dyskinesias greatly, off periods less consistently and does not allow medication to be reduced. In many centres, the STN is emerging as the preferred target for stimulation in view of a very good effect against off-periods and dyskinesias, probably because it allows medication to be reduced considerably. Nevertheless, comparative studies of the targets, as well as long-term follow-ups in large groups of patients, are needed.

REFERENCES