J Neurol (1999) 246 [Suppl 2]: II/42–II/45

P. Limousin-Dowsey
P. Pollak
N. Van Blercom
P. Krack
A. Benazzouz
A.-L. Benabid

Thalamic, subthalamic nucleus and internal pallidum stimulation in Parkinson's disease

Abstract The limits of drug therapy in severe forms of Parkinson's disease have lead to a renewal of functional neurosurgery of the basal ganglia and the thalamus. Deep brain stimulation (DBS) of these structures was developed with the aims of reducing the morbidity of surgery and of offering an adaptative treatment. DBS was first applied to the thalamus in patients with severe tremor. Tremor of the hemibody is greatly reduced by stimulation of the contralateral electrode in 85 % of the cases. There is little change in other symptoms. However, motor fluctuations and dyskinesias are a more frequent problem than severe tremor; in attempt to treat these symptoms, DBS has recently been applied to the subthalamic nucleus (STN) and the internal pallidum (GPi). STN stimulation greatly decreases off motor symptoms and motor fluctuations, which allows a reduction of drug dosage and consequently of dyskinesias. GPi stimulation decreases dyskinesias in most patients, but the effect on off motor symptoms is more variable from one series to another, from very good to nil. The severe morbidity of DBS applied to these 3 targets is low. Comparative studies of the cost and the efficacy of DBS and lesions applied to these different targets are now required.

Key words Parkinson's disease · Deep brain stimulation · Subthalamic nucleus · Internal pallidum · Thalamus

P. Limousin-Dowsey (✉)
MRC Human Movement and Balance Unit
Institute of Neurology
23 Queen Square
London WC1N3BG
email: P.Limousin@ion.ucl.ac.uk

P. Limousin-Dowsey · P. Pollak
N. Van Blercom · P. Krack · A. Benazzouz
A.-L. Benabid
Neurosciences Department
Unité INSERM 318
CHU de Grenoble, BP 217X
38043 Grenoble, France

P. Krack
Neurology Department
University of Kiel, Germany

Introduction

Levodopa preparations are very effective in treating patients with Parkinson's disease. But after several years of treatment some patients develop motor fluctuations and dyskinesias difficult to control by adapting their drugs. As a consequence there has been a renewal of functional neurosurgery in the past ten years. The surgical approach to the basal ganglia presently benefits from new technologies to locate the target like MRI, easier access to electrophysiology, and new forms of treatment like chronic deep brain stimulation (DBS). DBS can be presently applied to three different targets: the ventrointermediate nucleus of the thalamus (Vim), the subthalamic nucleus (STN) and the internal pallidum (GPi).

Surgical procedure

The main steps of the surgical procedures are common to all three targets. The target is located using different methods which can be combined: imaging (ventriculography, MRI and CT) and electrophysiology (micro or semi-microrecordings and electrical stimulation). The electrode is implanted in stereotaxic conditions, under local anaesthesia, so the effect of electrical stimulation on parkinsonian features and adverse effects can be assessed. Subsequently the electrode is connected to a pulse generator implanted in the subclavicular area, usually under general anaesthesia. The electrode for chronic stimulation (Medtronic 3387, or 3389, Minneapolis, USA) includes 4 contacts at its' tip. One or several contacts can

be selected as a cathode. The voltage, the frequency and the pulse width delivered by the pulse generator can be adjusted.

Ventrointermediate nucleus of the thalamus stimulation

Vim stimulation is proposed as an alternative to thalamotomy since 1987 [5]. Initially it was implanted contralaterally to a thalamotomy to reduce the risk of the bilateral procedure. Subsequently bilateral stimulations were implanted with the aim to reduce morbidity. No comparative study between thalamic stimulation and thalamotomy is available yet, but one is in progress in the Netherlands [30].

Many reports show a good effect and a low rate of severe morbidity of thalamic stimulation [1, 6, 11–13, 16–18, 25]. A multicenter study published recently including 73 parkinsonian patients, 16 implanted bilaterally, shows that the stimulation of 85 % of the electrodes allows a good reduction of tremor at 12 months follow-up [25]. Both upper and lower limb tremor were reduced. Limb akinesia and rigidity were slightly reduced, but there was no effect on speech, postural stability and gait. Activities of daily living were as a consequence improved. Out of 110 patients implanted (including patients with essential tremor), side effects related to surgery included 3 subdural hematomas and 1 thalamic hematoma which resolved, 2 infections of the system which required the system to be temporarily removed, 2 subcutaneous hematomas, 1 attention-cognitive deficit, 7 mild dysarthria, 3 mild disequilibrium and 1 dystonia. The electrode was replaced in 5 patients because of loss of efficacy probably related to displacement. At 12 months follow-up the average voltage was 2.5 V, pulse width 81.9 ms and rate 162.9 Hz. There were only slight changes in medications.

Subthalamic nucleus stimulation

STN stimulation is based on studies done in the monkey model of Parkinson's disease [2, 3, 7–10, 15, 26, 34]. In these monkeys, an overactivity of the STN is found and lesions or electrical stimulation improve parkinsonian features [2, 3, 7–10, 15, 26, 34]. Therefore, STN stimulation was applied to patients with idiopathic Parkinson's disease [27]. Different studies have confirmed its efficacy [22–24, 28]. A study of 20 patients with at least one-year follow-up shows an average improvement of 60 % of off motor symptoms [24]. Akinesia, rigidity, tremor, dystonia, gait, freezing and postural stability can be improved. As a consequence motor fluctuations disappeared and activities of daily living were greatly improved. Levodopa induced dyskinesias are reduced over time, probably because levodopa dosage is reduced by 50 % in average. In the short term, STN stimulation can induce dyskinesias if electrical parameters are increased over a threshold. In the total group of 24 patients the following adverse effects were encountered: one severe bleeding, 1 extracerebral infection, 1 cognitive deficit, 8 transient confusion and 5 eyelid opening apraxia.

The average voltage at 12 months was 2.5 V, the frequency was 130 Hz and the pulse width 60 µs, patients were stimulated continuously. Patients with a good response to levodopa before surgery respond better to surgery [19].

Internal pallidum stimulation

GPi stimulation is proposed as an alternative to pallidotomy, with the aim to reduce the morbidity. There is no comparative study available between the two procedures. GPi stimulation greatly decreases levodopa induced dyskinesias in most studies [4, 14, 20, 29, 31–33]. The effect on off-symptoms varies between studies from none to important [4, 14, 20, 29, 31–33]. This discrepancy is probably related to the complexity of the connections within GPi. Two studies show very different effects of GPi stimulation according to the topography of the stimulated contact [4, 20]. Dyskinesias and akinesia can be improved or worsened, depending on whether the dorsal or the ventral GPi is stimulated. There is no proper comparative study between GPi and STN stimulation. A retrospective study in two small groups of patient is more in favor of STN because it allows a better effect on off-phase and a decrease in levodopa dosage [21].

Conclusions

DBS of Vim, GPi and STN can improve various aspects of idiopathic Parkinson's disease. However, patients with other parkinsonian syndromes, or with cognitive deficits or general disease should not be operated. Vim stimulation is effective only against tremor and should be proposed to patients disabled only by tremor. The question of an alternative target, like STN, should be raised, particularly in young patients, who might develop other symptoms. STN stimulation is very effective for patients with fluctuations and allows indirect reduction of dyskinesias. The main effect of GPi stimulation is against dyskinesias; other symptoms are variably improved. We now need comparative studies of the cost and benefit of these different surgical procedures.

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