

PAPER

MRI directed bilateral stimulation of the subthalamic nucleus in patients with Parkinson's disease

N K Patel, P Plaha, K O'Sullivan, R McCarter, P Heywood, S S Gill

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Objective: Bilateral chronic high frequency deep brain stimulation (DBS) of the subthalamic nucleus (STN) has emerged as an appropriate therapy for patients with advanced Parkinson's disease refractory to medical therapy. Advances in neuroimaging and neurophysiology have led to the development of varied targeting methods for the delivery of this treatment. Intraoperative neurophysiological and clinical monitoring is regarded by many to be mandatory for accurate STN localisation. We have examined efficacy of bilateral STN stimulation using a predominantly magnetic resonance imaging (MRI)-directed technique.

Methods: DBS leads were stereotactically implanted into the STN using an MRI directed method, with intraoperative macrostimulation used purely for adjustment. The effects of DBS were evaluated in 16 patients followed up to 12 months, and compared with baseline assessments. Assessments were performed in both off and on medication states, and were based on the Unified Parkinson's Disease Rating Scale (UPDRS) and timed motor tests. Functional status outcomes were examined using the PDQ-39 quality of life questionnaire. A battery of psychometric tests was used to assess cognition.

Results: After 12 months, stimulation in the off medication state resulted in significant improvements in Activities of Daily Living and Motor scores (UPDRS parts II and III) by 62% and 61% respectively. Timed motor tests were significantly improved in the off medication state. Motor scores (UPDRS part III) were significantly improved by 40% in the on medication state. Dyskinesias and off duration were significantly reduced and the mean dose of L-dopa equivalents was reduced by half. Psychometric test scores were mostly unchanged or improved. Adverse events were few.

Conclusions: An MRI directed targeting method for implantation of DBS leads into the STN can be used safely and effectively, and results are comparable with studies using intraoperative microelectrode neurophysiological targeting. In addition, our method was associated with an efficient use of operating time, and without the necessary costs of microelectrode recording.

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During the past decade, there has been resurgence in the neurosurgical treatment of selected patients with advanced Parkinson's disease (PD) who become poorly controlled despite optimised medical therapy, and in particular suffer from motor fluctuations and drug-induced dyskinesias.

Deep brain stimulation (DBS) has become an accepted technique for the treatment of several movement disorders and in particular for PD.¹⁻³ It was first applied to the ventral intermediate nucleus of the thalamus^{4,5} to treat tremor, but more recently, the surgical target of interest has moved to the subthalamic nucleus (STN) and the internal globus pallidus, because stimulation in these structures is additionally able to improve bradykinesia and akinesia in PD.⁶⁻⁸ Although there are few comparative data between these two targets, most groups consider that STN is the optimal target for patients with PD requiring surgery.

The most appropriate targeting method to place DBS leads accurately and effectively in STN remains a subject of controversy. Typically, a combination of anatomical and physiological methods is used in the localisation of the STN. Anatomical methods include both direct and indirect techniques.⁹ Using imaging acquired in stereotactic conditions, the coordinates of the STN may be obtained directly from the image if the nucleus can be adequately visualised; alternatively, an indirect method is used, employing atlas-based coordinates generated in proportion to recognised internal landmarks, such as the anterior-posterior commissural distance or third ventricular dimensions. Physiological methods include intraoperative macrostimulation and

micro-electrode recording. Many groups continue to use an indirect method with atlas-based coordinates, but "fine tune" localisation with intraoperative clinical and electrophysiological monitoring procedures.^{6,9,10} The main points of dispute concern the need, benefit, and morbidity of intraoperative microelectrode recording for target localisation and the need for direct v indirect anatomical methods of target localisation. In this paper, we report an interim 12 month analysis of 16 patients with idiopathic PD who underwent bilateral DBS of the STN using a direct anatomical magnetic resonance imaging (MRI) directed method with intraoperative macrostimulation used for confirmation of target localisation, but without intraoperative microelectrode recording.

CLINICAL MATERIALS AND METHODS

Patient population

The study population comprises the first 16 consecutive patients (10 men, six women) to have undergone bilateral STN DBS at our centre and who have now completed a 12 month follow up evaluation. The mean age (SD) of the patients at the time of surgery was 56 (11) years, and mean (SD) disease duration was 10 (3.5) years. The selection criteria were that the patient should have L-dopa responsive idiopathic PD with severely disabling symptoms despite best medical therapy. In addition, the patients had to be able to

Abbreviations: DBS, deep brain stimulation; MRI, magnetic resonance imaging; PD, Parkinson's disease; PDQ-39, 39-item Parkinson's disease quality of life questionnaire; STN, subthalamic nucleus

function at a reasonable level of independence for at least some part of the average day. Patients with a significant history of depression, evident cognitive impairment based on neuropsychological testing (operationally defined as scores on tests of two or more cognitive domains (McCarter *et al*) being greater than 1.5 standard deviations below the population mean) and those deemed medically unfit were excluded from the study. Typically our patients had periods of severe immobility for about 50% of the day, and suffered from on dyskinesia for 30–40% of the remaining day (fig 6).

Surgery

All patients gave informed consent. The STN was localised with high-resolution MRI T2 scan sequences (1.5 Tesla TR 2500, TE 150, TSE 11, NSA 12) and per-operative macrostimulation was used to refine accuracy of targeting. Under general anaesthesia, a modified Leksell stereotactic frame was affixed parallel to the orbitomeatal plane. The anterior (AC) and posterior (PC) commissures were identified in a mid-sagittal planning scan. Axial images (fig 1), 2 mm thick, were acquired parallel to the AC–PC plane, and coronal images orthogonal to these were then obtained. We have found that these sequences give optimum delineation of the STN and related structures. We used magnified hard copies of the MRI scans and overlaid the T2 scans with inverted T2 images (fig 1) to enhance the definition of STN boundaries further. The Schaltenbrand atlas¹¹ was used as a visual guide in defining the boundaries of STN and its surrounding structures. We selected the dorsolateral STN as our target, which is functionally implicated in sensorimotor circuits.¹² The target was centred in the posterior third of the STN. The coordinates of the target were defined, and a trajectory was planned in the coronal plane, avoiding superficial blood vessels, and running through the caudate nucleus and lateral thalamus, aiming for the centre of the dorsal half of the posterior STN (fig 2).

The Leksell frame with its in-house modifications is relocatable, and in the initial number of cases in this cohort, the frame was usually removed after the MRI scan and relocated the following day under general anaesthesia, using CT to confirm accuracy of relocation, prior to waking the patient up for the first part of the surgical procedure. It was subsequently found that patients could tolerate the frame overnight, avoiding the need for relocation and its anaesthetic, and this has now become our routine practice.

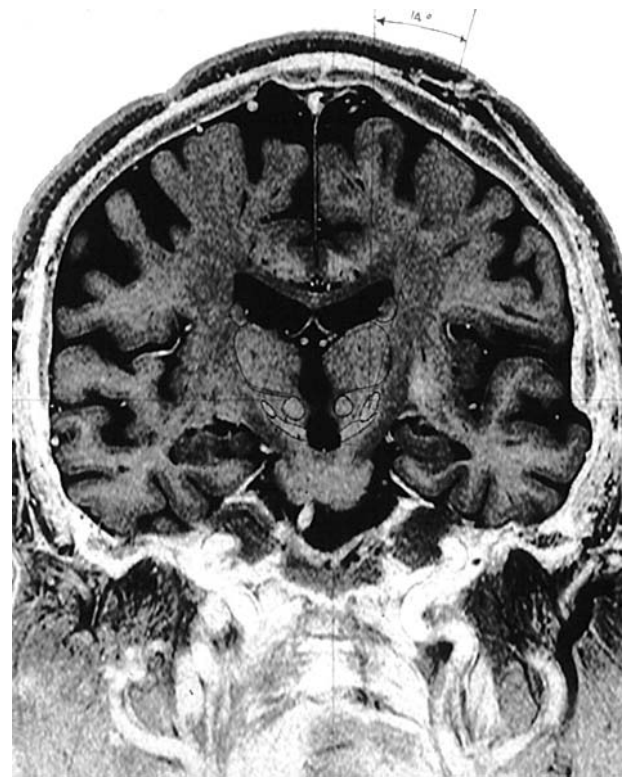


Figure 2 High resolution coronal inverted T2 weighted MR images with trajectory planned down STN axis and avoiding superficial blood vessels.

At surgery, the following day, simultaneous bilateral DBS leads were implanted with patients awake and in an 'off' state, antiparkinsonian medications having been stopped 12 h previously. Surgery was performed with the patients in a sitting position, and with constant saline irrigation of the burrhole to avoid air entering the cranium and therefore minimizing brain shift. A 1.24 mm diameter electrode with a 2 mm exposed tip (Radionics Inc., Burlington, MA, USA) was guided to the dorsolateral STN. The target was stimulated at 100 Hz, 0.75–2 V, with 1 ms pulse width, during which changes in tremor, rigidity, and bradykinesia were monitored.

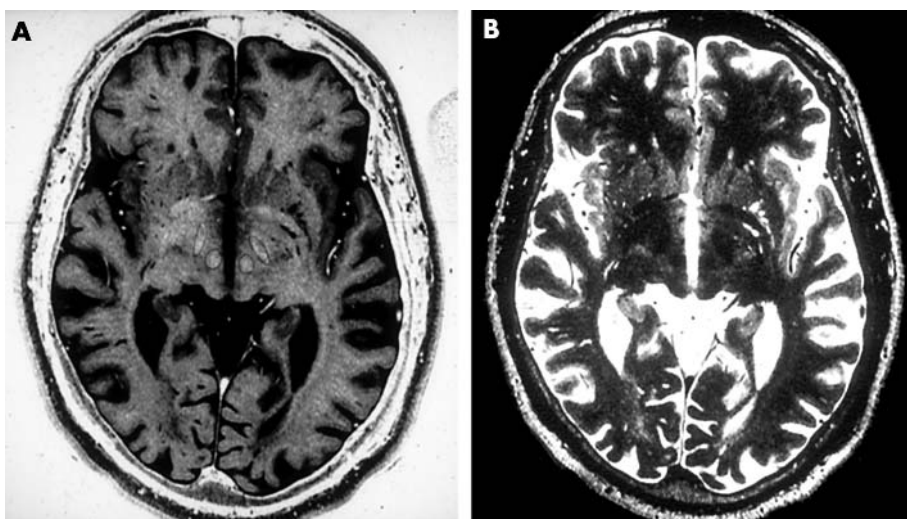


Figure 1 High resolution axial T2 weighted and inverted T2 weighted MR images with bilateral STN and red nuclei delineated on inverted image, with evident individual variability.

The depth of the probe was adjusted to gain maximum clinical improvement without the development of side effects. The optimal position for stimulation was recorded, and the stimulating electrode removed and replaced with a DBS lead (model DBS 3389; Medtronic Inc., MN, USA), which was advanced so that at least one contact was positioned below the desired target. The lead was secured to the skull with a mini-plate and screws and the ¼ inch burrhole sealed with acrylic cement.

When both DBS leads had been implanted, the patient was anaesthetised and the DBS pulse generator (Kinetra; Medtronic Inc.) implanted in a subcutaneous pocket below the clavicle. Extension leads were tunneled between the infraclavicular and scalp openings, and connected the DBS leads to the pulse generator.

Implantation of the DBS leads typically took on average between 30–45 min per side, and implantation of the Kinetra generator and connection leads a further 60–90 mins (total time for all the implants about 3 h).

Electrical stimulation setting and medical therapy

The Kinetra generator was switched on immediately or within days of surgery, with antiparkinsonian medications reduced by 50% and then re-adjusted as required. In the days following surgery, the effects of stimulation were assessed for each of the four lead contacts, and the optimal settings were programmed. Initially, a monopolar electrode setting was used, and subsequently a bipolar setting if a more focal stimulation, maintaining effect without side effects, was required. Patients were discharged generally between days 4–7 postoperatively, with preset stimulation parameters at the optimal lead contacts, and were advised to increase the stimulation amplitude and reduce medication as required, titrating to optimise effect and avoid side effects. Patients were able to contact a specialist PD nurse for advice over the phone, and were reviewed in the clinic at 6 weeks and 6 months thereafter.

Clinical evaluation

Evaluations were performed preoperatively and at 12 months postoperatively. Clinical evaluations were based on the Core Assessment Program for Intracerebral Transplantations, a validated protocol for evaluating surgical treatments of idiopathic PD,¹³ and included the Unified Parkinson's Disease Rating Scale (UPDRS), the Hoehn and Yahr scale, and timed motor tests. Patients were assessed in two conditions before surgery (off and on medication) and in four conditions after surgery (off medication, off stimulation; off medication, on stimulation; on medication, off stimulation; and on medication, on stimulation). Patients were assessed in the off state, having stopped their medication at least 12 h beforehand, and had their stimulation switched off overnight. The same assessments were then repeated on medication after administration of 200 mg L-dopa (plus 50 mg of peripheral dopa-decarboxylase inhibitor), with all patients having had a protein-free breakfast on the morning of the assessment.

In addition, pre- and post-operative neuropsychological assessments of attention, memory, executive function, language, and verbal intellect were undertaken with a battery of tests designed to minimise potential contamination of cognitive effects by motor symptoms.¹⁴ One patient did not complete both pre- and post-operative testing, and is excluded from the cognitive analysis.

Statistical analysis

The primary outcome measures were the scores on parts II (Activities of Daily Living) and III (Motor examination) of the UPDRS. The secondary measures were as follows: the

subscores on part III of the UPDRS; subscores on part IV (complications of therapy) of the UPDRS; the Hoehn and Yahr global stage; timed motor tests, L-dopa equivalent requirements; patient diaries; and quality of life as measured by the PDQ-39.

The data were analyzed using the paired Wilcoxon signed-rank and paired Student's *t* test.

The psychometric data were analysed using the Reliable Change Index.¹⁵ This robust test is increasingly used as it often provides a more clinically meaningful method of analysing change in neuropsychological performance than traditional measures of statistical significance or group differences. The latter may mask significant individual change in groups of patients who may show heterogeneous outcomes, as described after surgery for PD.^{16 17}

RESULTS

All 16 patients, who have been followed for at least 12 months, have received sustained benefit from the procedure. The effect of stimulation on the patients' motor performance (UPDRS part III) was significant in both the off and on medication states, resulting in a 61% ($p < 0.001$) and 40% ($p = 0.007$) reduction respectively (fig 3). Long-term stimulation resulted in improved scores for akinesia, rigidity, tremor, impairment of arising from chair, gait and postural instability, when patients were evaluated off medication. In the on medication state, stimulation significantly improved tremor scores (table 1).

The effect of stimulation on bradykinesia was also assessed based on changes shown in standardised timed motor tests. All the timed motor tests showed significant improvements with stimulation in the off medication state (table 2). Five patients were unable to complete the stand/walk test while in the off medication state preoperatively, but were able to accomplish the task postoperatively with stimulation on.

There was significant improvement in the patients' functional performance with stimulation on, as demonstrated by improvements in the activities of daily living scores (UPDRS part II), which were improved by 62% ($p = 0.001$) (fig 4). With stimulation on, Hoehn and Yahr scores (for global stage of disease) were significantly improved in both off ($p < 0.001$) and on ($p = 0.006$) medication states (table 1).

Stimulation significantly reduced dyskinesias and motor fluctuations based on complications of therapy scores (UPDRS part IV) (fig 5). The mean (SD) score for the duration of the off period was reduced from 2.2 (1.3) before surgery to 1.0 (1.2) at 12 months ($p = 0.007$) (UPDRS part IV,

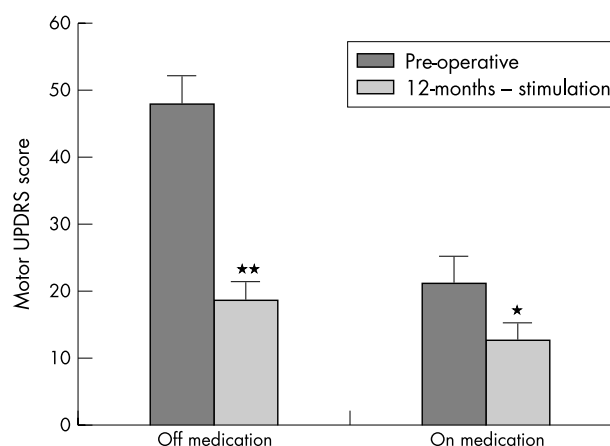


Figure 3 Mean (SD) off and on-medication scores for motor performance (UPDRS part III) at baseline and at 12 months after surgery with stimulation on. * $p = 0.007$; ** $p < 0.001$, for comparison with the same condition before surgery.

Table 1 Unified Parkinson's Disease Rating Scale motor scores and L-dopa equivalent medication requirement in patients following bilateral deep brain stimulation of the subthalamic nucleus

	Pre-operation		12 months post-operation	
	Med off	Med on	Med off	Med on
UPDRS III	47.8 (4.0)	21.1 (3.9)	18.6 (2.7)***	12.8 (2.3)***
Rigidity	10.9 (1.4)	3.9 (1.1)	3.1 (0.7)	1.9 (0.6)
Bradykinesia	18.9 (1.8)	8.0 (1.6)	9.8 (1.2)	6.9 (1.2)
Tremor	6.7 (1.3)	2.6 (1.0)	0.6 (0.4)***	0.3 (0.2)*
Arising from chair	2.1 (0.4)	0.4 (0.2)	0.6 (0.2)**	0.3 (0.2)
Gait disturbance	2.1 (0.3)	0.6 (0.2)	0.7 (0.2)**	0.4 (0.2)
Postural instability	2.1 (0.4)	0.8 (0.2)	0.8 (0.3)**	0.5 (0.2)
Speech	1.7 (0.2)	1.3 (0.2)	1.3 (0.2)**	1.2 (0.2)
Global stage of disease (Hoehn and Yahr)	4.1 (0.3)	2.7 (0.3)	2.5 (0.2)***	2.1 (0.2)**
Levodopa (mg)	856.4 (158.2)		443.9 (82.5)**	

Values are means (SEM).

For all scores, a reduction indicates an improvement in function.

UPDRS III denotes motor scores, items 18–31, maximal points = 108; tremor subscores, items 20 and 21, maximal points = 28; rigidity subscores, item 22, maximal points = 20; bradykinesia subscores, items 23–26, maximal points = 32

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, compared with the condition before surgery.

item 39; range 0–4). The mean score for the duration of dyskinesias decreased from 1.3 (1.1) to 0.7 (0.5) ($p < 0.02$) (UPDRS part IV, item 32; range 0–4). The mean disability related to dyskinesias decreased from 1.6 (1.4) to 0.2 (0.5) ($p < 0.01$) (UPDRS part IV, item 33; range 0–4). The duration of the on period increased correspondingly (fig 6). An attempt to use patient diaries to record the durations of on and off periods was unsuccessful because of poor compliance and data entry.

Medications and electrical treatment

At 12 months, the mean daily dose of L-dopa equivalents based on a formula as designated by Pahwa *et al*¹⁸ decreased significantly by 48% ($p = 0.002$) (table 1). All patients were being stimulated continuously throughout the whole day. Seven patients were receiving bilateral monopolar stimulation, six were receiving bipolar stimulation, and three were receiving bipolar stimulation on one side and monopolar stimulation on the other. The frequency was between 130 and 180 Hz and the pulse width was between 60 and 90 μ s. The middle two contacts on the quadripolar electrode were shown to be most effective in 90% of cases.

Functional status (PDQ-39)

Completed questionnaires were received for 14 out of the 16 patients (results shown in table 3). The Activities of Daily Living and Stigma dimensions were significantly lower at 12 months ($p < 0.02$ and $p < 0.03$ respectively), as was the PDQ-39 summary index ($p < 0.01$). The six other domains of the PDQ-39 were not significantly modified by the procedure; however, non-significant reductions were evident for the

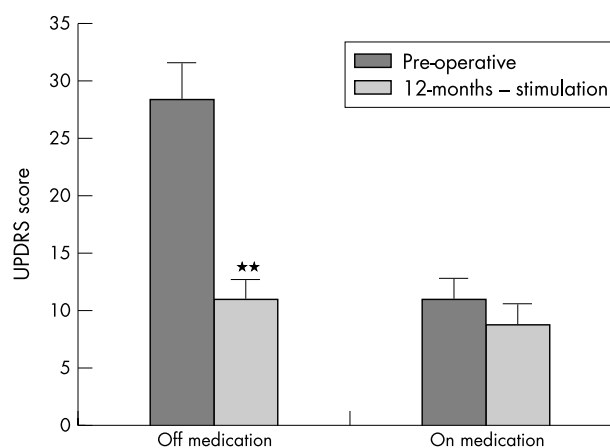


Figure 4 Mean (SD) off and on medication scores for Activities of Daily Living (UPDRS part II) at baseline and at 12 months after surgery with stimulation on. ** $p < 0.001$, compared with the same condition before surgery.

Mobility, Emotional Well-being, Communication and Bodily Discomfort dimensions. Globally, bilateral STN DBS significantly improved quality of life by 14% as measured by the PDQ-39SI.

Neuropsychometry

Cognitive testing post operatively on 15 patients revealed few clinically relevant changes and did not suggest that the

Table 2 Timed motor tests in patients with bilateral deep brain stimulation of the subthalamic nucleus

	Pre-operation		12 months post-operation	
	Med off	Med on	Off	On
Pronation-supination	44.9 (8.4)	16.4 (1.2)	21.2 (2.9)*v	17.3 (2.0)
Hand/arm movements	20.1 (2.6)	8.5 (0.7)	10.3 (0.8)**	7.6 (0.5)
Finger dexterity	55.1 (6.0)	32.8 (4.1)	41.8 (5.7)**	32.6 (3.2)
Leg movements	21.6 (3.0)	9.6 (1.2)	10.8 (1.2)**	8.3 (0.8)
Stand/walk	34.2 (8.2)	16.2 (7.6)	13.3 (2.3)*	13.0 (4.0)

Values are expressed as means (SEM). The post-operative times shown above were with stimulation switched on.

* $p < 0.05$; ** $p < 0.01$ compared with the condition before surgery.

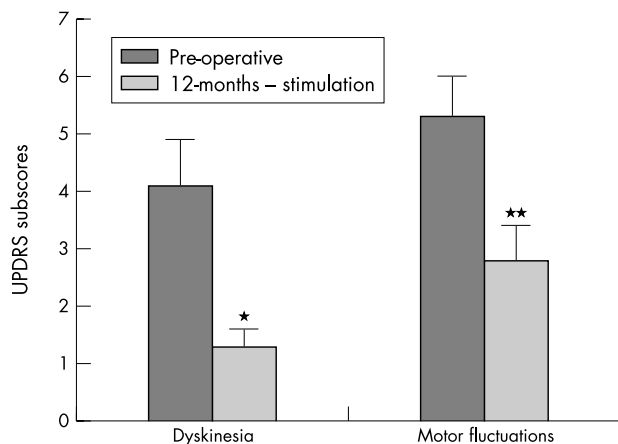


Figure 5 Mean (SD) scores for drug-induced dyskinesias and motor fluctuations before and 12 months after surgery with stimulation on. The subscores are for parts IVa and IVb of the Unified Parkinson’s Disease Rating Scale respectively. *p=0.006; **p=0.003, compared with the same condition before surgery.

procedure has significant adverse effects on cognition. A total of 204 individual test scores were available for analysis. According to the Reliable Change Index, 86% of the scores were either unchanged or improved at the 12 month post-operative follow up. Of the small number of scores that were “deteriorated”, there was no systematic pattern of deterioration. There were relatively high rates of deteriorated scores on measures of verbal IQ, verbal memory retrieval, verbal and focused attention, and perseverance on a design fluency task. Between 20% and 29% of the scores on tests related to these cognitive functions were lower at the follow up assessment. However, these lowered scores were matched by an equivalent number of improved scores on the same measures for the remaining patients, suggesting no systematic effect of DBS on these neuropsychological domains. Certainly some of the changed scores will have reflected a chance occurrence. There remains the possibility that an idiosyncratic or iatrogenic negative effect of DBS may have occurred for individual

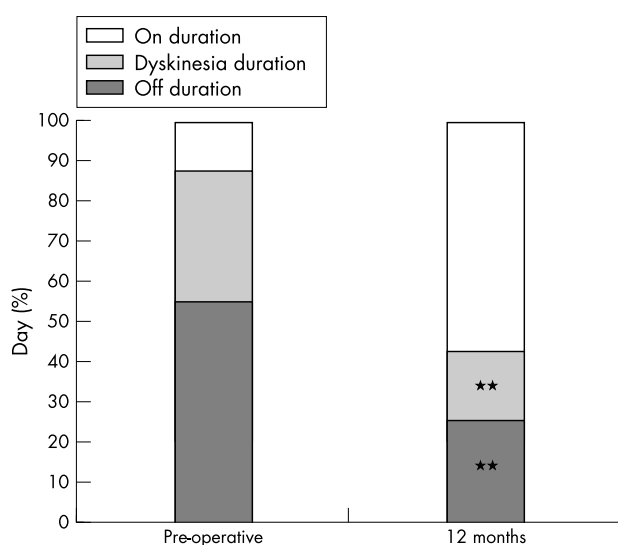


Figure 6 Mean on and off medication motor fluctuation durations before and 12 months after surgery. The dyskinesia and off period durations correspond to items 32 and 39 of part IV of the Unified Parkinson’s Disease Rating Scale respectively. **p=0.01, compared with the same condition before surgery.

Table 3 Effects of the bilateral STN DBS on QOL measured with PDQ-39 (n = 14)

	Baseline	12 months
Mobility	78.8	51.3 (–19%)
Activities of daily living	71.4	42.0 (–30%)*
Emotional wellbeing	40.8	25.6 (–15%)
Stigma	47.3	25.9 (–21%)*
Social support	21.4	22.0 (+1%)
Cognitive impairment	30.4	28.1 (–2%)
Communication	45.8	33.3 (–13%)
Bodily discomfort	57.2	42.3 (–15%)
PDQ-39 Summary Index	48.1	34.5 (–14%)**

Mean scores at baseline and at 12 months, with percentage change in brackets at 12 months.

*p<0.05 compared with the condition before surgery (paired Student’s t test, after Bonferroni correction); **p<0.01 compared with the condition before surgery (paired Student’s t test).

patients. Any such effect could only have been small as only two individuals showed deterioration across more than two tests. These individuals did not represent those with greater levels of impairment or cognitive vulnerability pre-operatively.

Surgical procedure

At surgery, perioperative macrostimulation was used for target confirmation and to optimise stimulator placement. For all cases, a single pass of the macrostimulating electrode was required for each side.

Adverse effects

In the 16 patients, there were no procedure or device related complications. Stimulation related complications included hypophonia in three patients and eyelid apraxia in two patients.

DISCUSSION

Our results are in accordance with other studies that have demonstrated that DBS of the STN is an effective treatment for patients suffering from advanced PD. Bilateral stimulation of STN greatly improved off period symptoms in these severely disabled patients. Adverse experiences were relatively few in our study cohort, and were all related to stimulation, including hypophonia in three cases and eyelid apraxia in two cases. Cognitive deterioration was detected in two of the patients, but as cognition in the remaining patients was mostly unchanged or improved, the decline in these two patients was solely progressive and presumably related to disease progression. Our results show that a predominantly anatomical MRI directed method without microelectrode recording can be used safely and effectively to deliver this treatment.

Deep brain stimulation of the STN resulted in a 61% reduction in UPDRS motor scores in the off medication state at 12 months. The cardinal parkinsonian symptoms (bradykinesia, rigidity, tremor, gait disturbances) were all significantly reduced by stimulation in the off medication state. On medication, motor scores were also significantly reduced by 40% with stimulation. The patients’ functional performance was improved with stimulation, as demonstrated by significant improvements in the Activities of Daily Living scores (UPDRS part II and PDQ-39).

The use of high resolution T2 MR images in both the axial and coronal planes greatly facilitated the targeting of the dorsolateral STN. Within the STN, the dorsolateral portion of the nucleus is functionally implicated in the sensorimotor circuits, whereas the ventral portion is connected with associative areas, and the medial tip has connections with the limbic system.¹² At surgery, perioperative macrostimulation

was used for target confirmation and to optimise stimulator placement.

There have been several reports showing that bilateral STN stimulation is a very effective treatment for advanced PD.^{8 19–23} The beneficial effects of STN stimulation are significant providing that the electrodes are placed appropriately. Most studies advocate the use of intraoperative microelectrode recording for verification of target localisation²⁴ and report an improvement in UPDRS motor scores of 58–68%.^{6 19 21 22 25} In comparison, studies relying on intraoperative macrostimulation for target verification have reported a UPDRS motor score reduction of 36–68%.^{23 26–28} Our finding of a 62% improvement is well above the median of the other studies using macrostimulation and within the range reported by studies using microelectrode recording. The mean baseline UPDRS motor score in our cohort (48) was slightly lower than that reported in the studies that used microelectrode recording (49.6–67.6). Compared with the other studies, we found a greater improvement in on period motor function; our on state improvement may in fact be an underestimate, as patients post-operatively had their on state UPDRS assessment after being given 200 mg L-dopa, and in a number of cases this made patients dyskinetic, reducing their scores.

Most investigators experienced in performing STN surgery use microelectrode recording to delineate the boundaries of the target preoperatively to ensure optimal placement of the lesion or DBS lead. Microelectrode recording usually involves 3–6 recording tracts to be made before the lesioning or DBS lead is inserted. Nevertheless, the accuracy with which the target can be defined in the coronal plane depends upon the distance between the recording trajectories, which is typically 2 mm. The maximal spatial resolution of the technique is therefore 2 mm and this may not be sufficiently precise to ensure optimal placement of a DBS lead (typically 1.3 mm in diameter) centrally within the STN (typically 3 mm in diameter). To compensate for the individual STN variations (as seen in figs 1 and 2) when using the indirect method with atlas-based coordinates, multiple microelectrode recording tracts would probably be required and the chance of accurately positioning the lead in the centre of the dorso-lateral STN would be remote.

While side effects are not uncommon for both microelectrode recording and procedures guided without microelectrode recording, the rate of severe complications, such as intracerebral haematoma, appears to be higher when microelectrodes are used.^{29 30} A review of the literature for procedures guided with and without microelectrode recording found reported side effects to be greater among groups using microelectrode recording techniques. The available literature suggests that microelectrode recording techniques neither decrease risks nor increase targeting accuracy of ablative surgery or DBS procedures, compared with macrostimulation techniques. Unfortunately, to our knowledge, no formal trial comparing outcomes from a surgical team skilled in microelectrode targeting techniques with those from a team skilled in MRI targeting has been conducted. Furthermore, microelectrode recording techniques do not result in smaller lesions or in lower electrical parameters of DBS. An additional risk of using microelectrodes is that this technique undoubtedly prolongs the operating time compared with that of macroelectrodes, and may last up to 12 h for bilateral procedures, which may increase the risk of infection. The risk of brain shift, if no special measures are taken to avoid cerebrospinal fluid leak during surgery, will also increase, making target localisation more difficult. More importantly, this technique exposes patients to many hours of surgery awake, which for parkinsonian patients in an off state can be very distressing.

We acknowledge that the data presented here will not have ended the debate between proponents and opponents of microelectrode recording, and in an ideal world a randomised study comparing clinical outcomes from surgical interventions between teams expert in microelectrode recording techniques and teams expert in MRI based techniques would perhaps provide the definitive answer; however, as at present the results of such a study are not available, we hope that our data have added to the ongoing debate.

CONCLUSIONS

DBS of the STN is an effective treatment for patients with advance PD refractory to medical therapy, and results in significant reduction in patients' UPDRS motor scores in both off and on medication states. This treatment significantly reduces dyskinesias, motor fluctuations, and the requirement for L-dopa therapy, and significantly improves their functional performance (Activities of Daily Living). A predominantly anatomical MRI directed technique with macrostimulation can be used safely and effectively without the additional need for intraoperative microelectrode recording. In addition, our method was associated with an efficient use of operating time, and obviates the necessary costs of microelectrode recording.

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MRI directed bilateral stimulation of the subthalamic nucleus in patients with Parkinson's disease

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