A study of medial pallidotomy for Parkinson’s disease: clinical outcome, MRI location and complications

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Summary
We have studied the effects of unilateral ventral medial pallidotomy in 26 patients with medically intractable Parkinson’s disease with marked drug-induced dyskinesias. Preoperatively, all patients were assessed during one 5-day admission according to the Core Assessment Programme for Intracerebral Transplantation (CAPIT) protocol, including rating in the ‘practically defined off’ and ‘best on’ states before and during a single-dose levodopa challenge. Motor performance was assessed with subset categories of the Unified Parkinson’s Disease Rating Scale (UPDRS), timed motor tests and a standard dyskinesia rating scale. Pallidotomy was performed under stereotaxic CT guidance with intra-operative extracellular microelectrode recording made from the basal ganglia. All patients were re-assessed 3 months postoperatively and a subgroup (n = 9) have so far also been re-assessed after 1 year. Pre- and postoperative performance scores were compared in order to determine which categories of performance improved postoperatively. Significance was accepted at P < 0.005 in order to take into account the multiple number of comparisons performed. Patient medication was compared pre- and postoperatively and the morbidity associated with surgery was also recorded. The most significant improvement postoperatively was the diminution of ‘on’ dyskinesias contralaterally (67%, P = 0.0001); however, ipsilateral (45%, P = 0.0006) and axial (50%, P = 0.0008) dyskinesias also improved. Contralateral to pallidotomy, the median ‘off’ motor UPDRS score improved by 27% (P = 0.001) and a significant improvement was also observed in contralateral rigidity by 25% (P = 0.001). There were trends towards improvement in contralateral tremor (33%, P = 0.016) and bradykinesia (24%, P = 0.013) scores.

Keywords: pallidotomy; Parkinson’s disease; clinical; MRI; complications

Abbreviations: AC–PC = anterior commissure–posterior commissure (plane); CAPIT = Core Assessment Programme for Intracerebral Transplantation; DDCI = levodopa/dopa decarboxylase inhibitor; UPDRS = Unified Parkinson’s Disease Rating Scale

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Introduction

James Parkinson noted in 1817 that the tremor of paralysis agitans improved following an acute lesion of the motor system which resulted in co-incident paralysis. By the 1930s, surgical section of the motor and premotor cortex had been investigated as treatment for Parkinson’s disease but hemiparesis occurred in conjunction with alleviation of tremor (Bucy and Case, 1939). The early work of Russell Meyers, however, demonstrated that surgical resection of the head of the caudate nucleus and the anterior limb of the internal capsule (Meyers, 1942) and of pallidofugal fibres (Meyers, 1951) could improve rigidity and tremor without inducing paresis. Concurrent evolution of the stereotaxic technique (Spiegel et al., 1947) allowed human neurosurgery to be performed with improved precision and less hazard and stereotaxic chemopallidotomy using procaine oil (Narabayashi and Okuma, 1953), alcohol (Cooper and Bravo, 1958a) and electrocoagulation (Guiot and Brion, 1953; Guiot, 1958) were reported to improve parkinsonian tremor and rigidity effectively. Svendson et al. (1960) were the first to report that when the posteroverentral internal pallidum was lesioned additional benefit to general motor function (interpreted as corresponding to relief of akinesia) could be obtained. At this time, stereotaxic lesions of thalamic nuclei which directly receive pallidal efferents (i.e. of ventral anterior and lateral thalamus) were generally felt to provide more effective relief of parkinsonian tremor and rigidity than pallidotomy (Cooper and Bravo, 1958a, b) but the introduction of levodopa as effective anti-akineti therapy for Parkinson’s disease in 1967 led to a major reduction in the use of pallidotomist and thalamotomy in the treatment of parkinsonism.

However, the chronic administration of levodopa in Parkinson’s disease is associated with the development of fluctuations in motor response and with dystonic and choreic involuntary movements (dyskinesias). Early in the course of Parkinson’s disease, dyskinesia is generally associated with peak plasma levels of levodopa and can usually be controlled by decreasing the size of each dose and increasing the frequency of dosing. Eventually, with disease progression, the ‘therapeutic window’ narrows and dyskinesias may develop, either throughout any period of benefit or bifasically. At this stage, medical management consists of balancing the relief of bradykinesia against induction of dyskinesias, often with neither being managed optimally. This unsatisfactory state of affairs prompted the resurrection of surgical therapy in Parkinson’s disease and recent reports of pallidotomy (Dogali et al., 1995; Iacono et al., 1995; Laitinen, 1995; Lozano et al., 1995; Sutton et al., 1995; Baron et al., 1996) have demonstrated significant improvement of the cardinal features of Parkinson’s disease (bradykinesia, tremor, rigidity and gait disturbance) as well as a marked diminution of levodopa-induced dyskinesias. We wished to study the efficacy of medial pallidotomy in the treatment of Parkinson’s disease and over the last 2 years we have performed unilateral ventral medial pallidotomy in 26 patients with severe Parkinson’s disease. We report here the surgical method employed, lesion locations and the effect of the procedure on motor performance, levodopa-induced dyskinesias, level of dopaminergic medication required postoperatively and the associated morbidity and mortality.

Methods

Between March 1995 and July 1996, 26 patients (17 male, nine female, mean age 55.9 ± 9.1 years, mean duration of Parkinson’s disease 15.4 ± 6.3 years) with medically intractable idiopathic Parkinson’s disease underwent unilateral medial pallidotomy. All patients were selected by at least two senior neurologists (N.P.Q., A.J.L. and C.D.M.) and fulfilled the criteria for the diagnosis of idiopathic Parkinson’s disease (Gibb and Lees, 1988). Thirteen of them had young-onset Parkinson’s disease (Quinn et al., 1987). Patients with ‘parkinsonian plus’ syndromes and other neurological disorders were excluded. Patients were examined by a psychologist and underwent formal psychometric testing in order to exclude those suffering from dementia. All patients had a significant response to levodopa and other dopaminergic drugs, but in each case the response to medical therapy was accompanied by the development of severe dyskinesias, unpredictable on–off fluctuations and wearing-off phenomena. In two subjects (Patients 3 and 5) levodopa-induced dyskinesias were so disabling that they avoided taking levodopa altogether preoperatively, preferring to remain bradykinetic. The characteristics of the patients are detailed in Table 1.

Two other patients had also been selected for pallidotomy but did not undergo surgery. One of these, with severe ‘off’ period panic and anxiety declined to proceed on the morning of surgery while ‘off’ medication. The other developed respiratory embarrassment related to the flexed position of her neck when the stereotaxic frame was fixed to the operating table and the procedure was abandoned uneventfully after the burr hole had been made. These two patients are not considered elsewhere in this paper.

The study protocol was approved by the Joint Medical Ethics Committee of the National Hospital for Neurology and Neurosurgery and the Institute of Neurology. Informed consent was obtained from each patient prior to surgery.

Preoperative assessments

Patients were admitted to hospital 1–3 months preoperatively for assessment. Motor performance was assessed according to the Core Assessment Programme for Intracerebral Transplantation (CAPIT) (Langston et al., 1992). All patients were initially assessed in the ‘practically defined off’ state. From the Unified Parkinson’s Disease Rating Scale (UPDRS), ‘activity of daily living’ scores (items 5–17 of the UPDRS...
Table 1  Patient characteristics preoperatively

<table>
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Mean 55.9 15.4 53.3 22.8

SD 9.1 6.3

*Young onset Parkinson’s disease. Am = amantadine; Ap = apomorphine; Br = bromocriptine; Bz = benzhexol; Cb = carbergoline; Cl = clonazepam; D = deprenyl; L = levodopa; O = orphenadrine; P = pergolide.

scale, maximum = 52) and total motor scores (items 18–31, maximum = 108) were considered to reflect overall functional severity of Parkinson’s disease. However, as we were interested to determine the effects of pallidotomy on specific aspects of motor control, we calculated separate subset UPDRS scores for the following categories of motor performance contralaterally and ipsilaterally: hemibody motor score (items 20–26, maximum = 36); hemibody tremor (items 20–21, maximum = 12); hemibody rigidity (items 22, maximum = 8) and hemibody bradykinesia (items 23–26, maximum = 16). Subset scores were also generated for gait and postural instability (items 13–15 and 27–30, maximum = 28), speech (items 5 and 8, maximum = 8) and freezing (item 14, maximum = 4). Patients were also timed during performance of standard motor tests which included repetitive alternate pronation and supination of each forearm (20 repetitions), sequential finger to thumb opposition for each hand (10 cycles) and repetitive hand/arm movements between two points 30 cm apart (10 repetitions). To assess gait, a timed test was performed in which the patients were required to stand from sitting, walk 7 m, turn, walk a further 7 m and sit again.

Patients were also tested preoperatively with an identical battery of tests following the administration of 200 mg of dispersible levodopa (plus 50 mg benserazide) after withdrawal of anti-parkinsonian medication for 12 h. The three most severely affected subjects (Patients 1–3) were not able to tolerate 12 h without medication and required a nocturnal dose of apomorphine, but in each case this was given at least 6 h prior to the clinical evaluation. Patients were assessed repeatedly throughout the duration of action of the levodopa dose and ‘best on’ responses, as agreed by the patient and clinician, were recorded for each patient. These responses usually occurred 30–90 min after the administration of the test dose of levodopa.

All patients developed choreic and dystonic involuntary movements during the duration of action of the test dose of levodopa. Since the severity of dyskinesia varied with motor actions, we rated dyskinesias according to the protocol of Goetz et al. (1994) during rest and performance of the following motor tasks: (i) walking; (ii) raising a glass to the mouth with each hand and attempting to drink; and (iii) putting on, buttoning, unbuttoning and then taking off a jacket. For each patient, dyskinesia was assessed every 20 min for the duration of action of the test dose of levodopa. Dyskinesia was rated for neck, trunk and each limb
individually and scores were assigned from 0 to 4. A score of 0 was recorded for successful task performance without dyskinesia, while a score of 4 was given to functionally disabling dyskinesia which prevented the completion of a motor task. Scores of 1, 2 and 3 were given to intermediate levels of disability. Subset scores were calculated for (i) maximum contralateral dyskinesia (arm and leg, maximum score = 5); (ii) maximum ipsilateral dyskinesia (arm and leg, maximum score = 5); and (iii) maximum axial dyskinesia (neck and trunk, maximum score = 5).

Preoperatively, all patients had their medication recorded and overall daily ‘off’ time was scored according to part IV of the UPDRS (item 36). All patients underwent routine MRI brain scans (1.5-T GE Signa system, spoiled grass, TR = 650 ms, TE = 4.2 s, flip angle = 20°, field of view = 20 cm, 256 × 224 matrix and 1.5-mm slice thickness). Patients were also examined by a neuro-ophthalmologist and their visual fields were objectively documented by Goldmann perimetry or tangent screen examination.

**Surgery**

Twenty-one patients underwent unilateral left pallidotomy and five underwent unilateral right pallidotomy. On the morning of the operation, patients initially received a short general anaesthetic for the fitting of a Cosman–Roberts–Wells stereotaxic frame (Radionics, USA). While still anaesthetized, they were transferred to a CT scanning suite for anatomical selection of the target which was identified as the ventroposterior medial pallidum contralateral to the side which showed the worse dyskinesia. Patients were subsequently returned to the operating theatre and allowed to wake from the anaesthetic prior to proceeding.

Patients were awake throughout the procedure, which was preceded by appropriate application of local anaesthetics. A 17-mm burr hole was made in the precoronal frontal bone. A monopolar microelectrode for recording electrophysiological responses from the pallidum was introduced into the brain at an angle of 30° to the vertical, aiming posteriorly, in a sagittal plane 20–22 mm lateral to the midline. This was slowly advanced towards the anatomical target by a manually operated hydraulic micromanipulator which was pre-calibrated so that the distance of the electrode tip from the target was known at all times and displayed. The electrode consisted of a tungsten wire of diameter 0.12 mm, tapered and insulated except at the tip and fixed inside an insulated stainless steel tube of 0.6 mm diameter, so that 12 mm of the tungsten wire projected from the tube. The tube, in turn, passed through a 1.0-mm diameter steel tube whose tip was fixed at a preset distance (10 or 15 mm) above the target and which was itself supported by a 1.5-mm guide tube higher up.

As the microelectrode tip was advanced towards the target, extracellular action potentials from cells in lateral pallidum, medial pallidum and intralaminar border zones were amplified, appropriately filtered and recorded, displayed on an oscilloscope screen and heard on a loudspeaker. Cell activity was recorded with the patients at rest and, on occasion, during contralateral passive or voluntary movements of the wrist, elbow or ankle. The typical patterns and frequencies of activity obtained in these different regions have been documented elsewhere (Hutchinson et al., 1994) and were easily identifiable. The ventral border of the medial pallidum was clearly demarcated by the characteristic transition from the high frequency cell activity (>60 Hz) to the low frequency sparse activity characteristic of white matter. Below this demarcation the microelectrode was advanced further into white matter and massed neuronal activity recorded during 1-Hz stroboscopic visual stimulation in order to confirm the proximity of the upper surface of the optic tract.

The positional information obtained from these electrophysiological data was then correlated with the appropriate sagittal brain maps of the Schaltenbrand and Wahren (1977) neurosurgical atlas and, if necessary, a correction made to the anticipated position of the anatomical target. While a single track was sufficient to achieve this correction in 10 of the 26 patients, it was necessary to make at least one additional track at a different anterior–posterior or lateral coordinate in the remainder. Three tracks were made in six patients and four tracks in two patients. The target correction averaged over all 26 patients was 2.4 mm (range 0–5.0 mm).

A bipolar radio-frequency stimulating electrode (Radionics, USA; diameter 2 mm) was then introduced into one of the microelectrode tracks and advanced to the target. High frequency stimulation was applied (300 Hz, 0.2-ms pulses, intensity 0.1–1.5 mA) and thresholds for motor and visual phenomena were identified. The electrode position and thresholds were finalized when stimulation produced no detrimental motor, visual or speech effects. Pallidotomy was performed by thermocoagulation (70–72°C for 60–80 s) via the same electrode in situ at the physiological target. Clinical testing of the patients was performed repeatedly during electrode stimulation and lesioning. Each pallidotomy comprised two to four overlapping individual lesions and typically occupied the space of a cylinder 2–4 mm in diameter and 6–8 mm in length, with the distal end lying in the most ventroposterior portion of the medial pallidum. Clinical improvements in rigidity, tremor and bradykinesia were often evident as soon as the lesion was made.

Following pallidotomy, anti-parkinsonian medication was restarted on the same evening of the operation. We made particular efforts to document any possible complications of surgery. Usually, after one night in intensive care, patients were returned to the neurological ward for a further 4–6 days during which they were re-examined and questioned about any postoperative changes. Unwanted effects were classified as major if they were life-threatening or interfered with the patient’s daily routine and minor if they caused minimal or no interference with the patient’s daily routines. Complications were also classified as persisting (lasting >3
months) or transient (lasting <3 months) and as delayed if they developed only after discharge home.

Postoperative assessments
All patients underwent routine MRI 1–2 days postoperatively to document lesion locations. Eleven patients were also available for high resolution volume MRI 5–6 weeks postoperatively (1.0-T Picker HPQ system, TR = 24 ms, TE = 6 ms, voxel size 1.0 × 1.0 × 1.3 mm³ at the Hammersmith Hospital, London, UK) in order to determine the location and size of pallidotomy more accurately. Calculations were performed using Analyze version 7.0 image display software (BRU, Mayo Foundation, USA).

Three months postoperatively, patients were re-admitted for repeat neurological examination in a manner identical to their preoperative assessments. In order to reduce inter-rater variability, each patient was assessed by the same clinician who had performed the preoperative assessment. UPDRS subset scores and CAPIT performance times were calculated for the same categories as preoperatively (i.e. ‘practically defined off’ and ‘best on’ contralateral, ipsilateral and axial scores). Medication requirements and visual fields were documented as preoperatively.

To date, it has also been possible to assess nine patients 1 year postoperatively. These assessments were carried out in an identical manner to the preoperative and 3-month postoperative assessments.

Statistical comparisons
Since UPDRS and dyskinesia scores were categorical data and all of our patients had severe Parkinson’s disease, it was unlikely that the distribution of our subset scores would be normal. Therefore, we calculated median preoperative and postoperative group scores for each category and compared them using paired Wilcoxon sign rank tests. For the contralateral, ipsilateral and sit–walk–stand timed tests, we compared mean preoperative performance time with mean postoperative performance time by paired Student’s $t$ tests. Patients who were not able to complete a timed test were excluded from the analysis for that category. In order to take into account the multiple number of comparisons performed, a statistical threshold of $P < 0.005$ was considered to be sufficiently conservative. Levels of significance which did not reach this level, but in which $P < 0.05$, were considered as marginally significant. For categories which showed a significant change postoperatively, we calculated the percentage change in median score or mean performance time.

Preoperatively, patients were taking a variety of anti-parkinsonian medication including levodopa/dopa decarboxylase inhibitor (DDCI) formulations ($n = 24$), apomorphine ($n = 3$ by continuous pump infusion, $n = 5$ by regular injection), pergolide ($n = 15$) and bromocriptine ($n = 1$). Although we attempted to leave postoperative medication for each patient unchanged for at least 3 months after pallidotomy, this was not possible in 13 patients since their postoperative clinical condition necessitated a change in medication. We compared preoperative with postoperative mean daily doses of levodopa/DDCI, pergolide and apomorphine separately using Student’s $t$ tests. In order to assess changes in medication for the entire group, we calculated preoperative and postoperative total equivalent levodopa/DDCI doses (equivalents of 100 mg of levodopa were 133 mg of sustained release levodopa, 10 mg bromocriptine or 1 mg pergolide) for each patient and compared these by a Student’s $t$ test. An equivalent apomorphine conversion factor is lacking and so apomorphine doses were excluded from this conversion. Furthermore, those patients taking apomorphine were only considered for the group analysis if their total daily doses of apomorphine had remained unchanged postoperatively ($n = 5$). Since the number of comparisons relating to medication was four, we accepted a level of $P < 0.05$ for significant changes in medication doses.

For the nine patients so far re-assessed 1 year postoperatively, the UPDRS scores, dyskinesia scores, motor performance times and medications were compared with their preoperative scores in an identical manner.

Results
Three months postoperatively, we were unable to carry out a complete series of assessments on one patient and another was recovering from a major complication (see below). Additionally, two patients died unexpectedly in the immediate postoperative period. We were, therefore, only able to perform group analyses of subset scores from 22 out of the 26 patients.

Lesion location
The routine 1.5-T MRI scans which were obtained 1–2 days postoperatively confirmed that the lesion was situated in the medial pallidum in all cases. In the first patient, in whom it had been possible to record extracellular action potentials from only one track, the lesion was seen to encroach on the posterior limb of the internal capsule. In three other patients, the lesion extended more dorsally and laterally and included a portion of lateral pallidum. The preoperative MRI scan of another patient had revealed that his posterior cerebral artery was in close proximity to the ventral portion of the medial pallidum and so the most ventral point of his lesion was tailored to lie 2–3 mm more dorsally than usual, but was still confined to the medial pallidum. This was confirmed on his postoperative high-resolution volume MRI brain scan and also at autopsy (see below).

In 11 patients, high resolution volume 1.0 Tesla MRI scans were obtained 5–6 weeks postoperatively. These included nine patients in the first half of the series and two patients in the second half. Overall, the mean lesion volume was $145 \pm 49 \text{ mm}^3$. The location of the centre of the lesion was located $21 \pm 2 \text{ mm}$ lateral to the midline and $3 \pm 2 \text{ mm}$...
Fig. 1 (A) Sagittal MRI brain section showing a typical electrode path with a pallidotomy at the distal end of the track. (B) The extension of (left) pallidotomy below the axial plane of the AC–PC plane.

Anterior to the mid-commissural point, while the most ventral point of the lesion lay 4 ± 3 mm below the anterior and posterior commissure (AC–PC) plane. A typical recording track and pallidotomy lesion are shown in Fig. 1.

* Practically defined off* parkinsonism
These results are shown in Table 2. The median activity of daily living score improved significantly by 16.9% postoperatively ($P = 0.002$) and the median total motor UPDRS score improved by 17.8% ($P = 0.003$). When ipsilateral and contralateral hemibody motor scores were considered separately, we detected a significant 27.3% ($P = 0.001$) improvement in the median contralateral motor UPDRS score, but the median ipsilateral motor UPDRS score did not alter significantly.

There was a 25.0% significant improvement in contralateral rigidity ($P = 0.001$), but the improvements in contralateral tremor and bradykinesia scores were only marginally significant. Considering the ipsilateral subset scores, rigidity improved significantly by 22.2% ($P = 0.005$), but there was no significant change in median tremor or bradykinesia scores.

Figure 2A presents the pre- and postoperative ‘practically defined off’ mean performance times. Mean performance time for contralateral hand/arm movements decreased significantly from 16.5 ± 8.9 s preoperatively to 12.6 ± 6.6 s postoperatively ($n = 19, P = 0.0001$). This represented an improvement of 23.6%. For contralateral pronation/supination, mean performance time decreased from 24.9 ± 13.4 s preoperatively to 17.3 ± 6.6 s postoperatively ($n = 17, P = 0.010$), while mean contralateral finger dexterity performance time decreased from 41.0 ± 13.6 s preoperatively to 33.8 ± 12.4 s postoperatively ($n = 15, P = 0.018$). These represent marginally significant improvements of 30.6% and 17.5%, respectively.

When mean pre- and postoperative ipsilateral motor performance times were compared, no significant improvements were detected (Fig. 2A).

There was a small and marginally significant 7.1% ($P = 0.007$) improvement in the median UPDRS subset score for gait/postural instability postoperatively compared
Table 2 Pre- and 3-month post-operative median UPDRS subset scores (n = 22)

<table>
<thead>
<tr>
<th>Item</th>
<th>‘Practically defined off’ scores</th>
<th>‘Best on’ scores</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Preoperative median (range)</td>
<td>Postoperative median (range)</td>
</tr>
<tr>
<td>Activity of daily living</td>
<td>32.5 (7–45)</td>
<td>26.5 (11–42)</td>
</tr>
<tr>
<td>Total motor score</td>
<td>53.5 (26–92)</td>
<td>42.5 (22–69)</td>
</tr>
<tr>
<td>Contralateral motor score</td>
<td>16.5 (8–30)</td>
<td>12.0 (5–24)</td>
</tr>
<tr>
<td>Contralateral rigidity</td>
<td>4.0 (1–8)</td>
<td>3.0 (1–7)</td>
</tr>
<tr>
<td>Contralateral tremor</td>
<td>3.0 (0–10)</td>
<td>2.0 (0–9)</td>
</tr>
<tr>
<td>Contralateral bradykinesia</td>
<td>8.5 (4–15)</td>
<td>7.0 (4–13)</td>
</tr>
<tr>
<td>Ipsilateral motor score</td>
<td>15.5 (3–32)</td>
<td>14.5 (4–27)</td>
</tr>
<tr>
<td>Ipsilateral rigidity</td>
<td>4.5 (1–8)</td>
<td>3.5 (0–7)</td>
</tr>
<tr>
<td>Ipsilateral tremor</td>
<td>3.0 (0–9)</td>
<td>4.0 (0–9)</td>
</tr>
<tr>
<td>Ipsilateral bradykinesia</td>
<td>7.0 (1–16)</td>
<td>7.0 (3–14)</td>
</tr>
<tr>
<td>Gait/postural instability</td>
<td>14.0 (2–28)</td>
<td>13.0 (3–27)</td>
</tr>
<tr>
<td>Freezing</td>
<td>3.0 (0–4)</td>
<td>2.5 (0–4)</td>
</tr>
<tr>
<td>Speech</td>
<td>4.0 (2–8)</td>
<td>4.0 (2–8)</td>
</tr>
<tr>
<td>Contralateral dyskinesia</td>
<td>6.0 (3–8)</td>
<td>2.0 (0–8)</td>
</tr>
<tr>
<td>Ipsilateral dyskinesia</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

**Significant changes (P < 0.005) and *marginally significant changes (P < 0.05).
Fig. 2 Mean preoperative and postoperative motor performance times for (A) ‘practically defined off’ and (B) ‘best on’ states. PS = pronation/supination, FD = finger dexterity, HAM = hand/arm movements between two points, SSW = sit–stand–walk test. Filled bars = preoperative times, hatched bars = 3-month postoperative times. **P < 0.005 and *P < 0.05, categories which showed significant differences postoperatively versus preoperatively.

with preoperatively (Table 2). Additionally, the mean performance time for the sit–walk–stand test decreased from 25.6 ± 10.9 s preoperatively to 18.1 ± 5.3 s postoperatively (n = 12, P = 0.014), a marginally significant improvement of 29.3% (Fig. 2A).

‘Best on’ motor parkinsonism
These results are presented in Table 2 and Fig. 2B. No ‘best on’ category showed a significant change postoperatively compared with preoperatively. Although we detected a 28.6% improvement in median ‘best on’ gait/postural instability subset UPDRS score and a 15.9% improvement in performance time of the sit–stand–walk test (n = 19), neither of these differences was significant.

Levodopa-induced dyskinesias were of smaller magnitude, but also highly significant (Table 2).

Medication
The mean daily levodopa/DDCI dose increased significantly by 13.4% (P = 0.02, n = 22), from 1032 ± 658 mg preoperatively to 1170 ± 715 mg 3 months postoperatively. Eight patients increased while two decreased their daily levodopa/DDCI doses. Two patients increased and one patient decreased their daily dose of pergolide 3 months postoperatively, but there was no significant difference between pre- and postoperative mean daily pergolide doses (preoperatively 2359 ± 1648 µg, postoperatively 2390 ± 1653 µg, n = 15). Of the three patients using apomorphine by pump, one patient increased and two decreased the total daily dose 3 months postoperatively. None of the five patients who took apomorphine by regular injection changed their 3-month postoperative doses. Overall mean daily apomorphine doses did not change significantly (preoperatively 27 ± 22 mg, postoperatively 22 ± 25 mg, n = 8); only one patient was taking bromocriptine preoperatively but this dose was unchanged 3 months postoperatively and discontinued 6 months postoperatively.

When mean pre- and 3-month postoperative total levodopa/DDCI equivalent doses were compared, a significant 10.6% (P = 0.04, n = 20) increase was detected (preoperatively 1218 ± 638 mg, postoperatively 1347 ± 698 mg). Nine patients increased, while only two decreased, their mean total daily levodopa/DDCI equivalent doses.

The preoperative median daily ‘off’ time score was 2.0 (range 1–4) while the postoperative median daily ‘off’ time score was 1.0 (range 1–4). This represented a marginally significant reduction (P = 0.007) from 25–50% daily preoperatively to 1–25% daily postoperatively.

Postoperative assessments at 1 year
We have so far assessed nine patients 1 year postoperatively, but two of these patients had not been available for assessment 3 months postoperatively. Therefore, in total, seven patients underwent complete assessment (preoperatively, 3 months postoperatively and 1 year postoperatively). We confined the analyses of the 1-year scores to those categories which had shown a significant improvement 3 months postoperatively. These results are presented in Fig. 3A. One year postoperatively, median UPDRS subset scores were still improved when compared with preoperative median scores, but were marginally higher than these patients’ 3-month postoperative median scores. We were, however, not able to detect significant differences (P < 0.005) when we compared median 1-year postoperative UPDRS subset scores with median preoperative scores. Similarly, we were unable to demonstrate significant differences (P < 0.005) in ‘practically defined off’ performance times for the four timed tests employed. This may have been due to the small number of
patients available for assessment at this time \( n = 7 \) for UPDRS scores, \( n = 5 \) for pronation/supination timed test, \( n = 4 \) for finger dexterity timed test, \( n = 5 \) for hand/arm movements timed test, \( n = 4 \) for sit–stand–walk test).

Reductions of contralateral and ipsilateral dyskinesia scores at 3 months were maintained at 1 year (Fig. 3B). However, perhaps due to the small numbers, the scores at 1 year compared with preoperative scores were only marginally significantly improved; contralateral dyskinesia was reduced by 33% \( (P = 0.017) \) and ipsilateral dyskinesia was reduced by 17% \( (P = 0.040) \). The reduction of axial dyskinesia among these patients 1 year postoperatively was not significant.

Of the nine patients whose medication was also assessed 1 year postoperatively, we were unable to calculate levodopa/DDCI equivalent doses for two patients who had increased their apomorphine doses. For the remaining seven patients, mean levodopa/DDCI equivalent doses postoperatively (1008 ± 584 mg) were greater than those preoperatively (716 ± 516 mg, \( P = 0.05 \)).

**Correlation between lesion locations and clinical outcome**

For the 11 subjects who underwent high resolution volume MRI, we found that distance of the most ventral point of the lesion below the AC–PC plane was significantly correlated with improvement in contralateral UPDRS bradykinesia scores (Spearman’s rank correlation statistic \( \rho = 0.64, P = 0.03 \)) (Fig. 4). In only one case (Patient 10) did the most ventral point of the lesion lie above the AC–PC plane. We found no correlation between lesion volume and improvement in bradykinesia \( (\rho = 0.17, P = 0.58) \), between distance of the most ventral point of the lesion and resolution of dyskinesia \( (\rho = 0.32, P = 0.24) \) or between lesion volume and resolution of dyskinesia \( (\rho = 0.50, P = 0.11) \).

**Complications**

Two patients (8%) experienced fatal complications. One, a 69-year-old woman (Patient 12) suffered a deep haemorrhage at the site of the lesion and she died several days later. Another younger woman (Patient 16) sustained a massive haemorrhagic middle cerebral artery territory infarction with oedema and midline shift to which she succumbed several days later. Post-mortem examination revealed an appropriately placed non-haemorrhagic operative lesion in the medial pallidum (Fig. 5A) and there was no obvious association between the needle track and the infarct. The clinical deterioration in these two patients was first evident subsequent to surgery in the intensive care unit.

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**Correlation between magnitude of preoperative levodopa response and clinical outcome**

For each patient, we calculated the improvement in total motor UPDRS score after the preoperatively levodopa challenge and found a significant correlation between the magnitude of preoperative response to levodopa with the improvement in total motor ‘off’ UPDRS following pallidotomy (Spearman’s rank correlation statistic \( \rho = 0.7, P = 0.001 \)).
Among the other 24 patients, four (15%) experienced major complications; these were persisting in two and transient in two cases. One of these four patients, the first operated in this series and in whom it had only been possible to make microelectrode recordings from a single track, developed contralateral facial weakness, contralateral motor hemineglect, and severe dysarthria and dysphagia which necessitated a gastrostomy. The onset of these symptoms occurred in the intensive care unit postoperatively. Six weeks postoperatively, her gastrostomy was closed and 5 months postoperatively, balancing her complications against the reduction of disabling chorea and ballism, she considered herself to have crossed the ‘gain line’. Her complications have, however, not fully resolved 1 year postoperatively. A second subject (Patient 7) developed an impaired level of consciousness with focal seizures on the day of surgery, followed by disinhibition, hallucinations and worsening of his parkinsonism and balance. MRI revealed a small deep haemorrhage at the operative lesion site and a second small superficial mesial frontal haematoma associated with infarction of mesial frontal cortex. One year postoperatively, he has made a steady improvement and his sole persisting deficit is a superior homonymous quadrantanopia. A third subject (Patient 22) developed transient facial weakness and dysphagia 2 days postoperatively together with dysarthria and worsened balance, which have now both improved. The fourth subject to experience major complications (Patient 26) developed transient confusion lasting 2 days, accompanied by dysphagia requiring temporary placement of a nasogastric tube for several weeks; MRI revealed a 1-cm³ haemorrhage close to the lesion site.

Minor transient (<3 months) and persisting (>3 months) complications were more common. Overall, including the four patients above, there were two (8%) instances of persisting quadranct field defects and another patient developed transient coloured lights in his central visual field. Additionally, seven patients (27%) noted increased dysarthria, five (19%) increased dysphagia, four (15%) increased hypophonia, four (15%) sialorrhea, three (12%) contralateral facial weakness, two (8%) motor hemineglect and one patient developed a mild transient hemiparesis. One patient developed a delayed deep venous thrombosis and a depressive episode. Two patients described a reduction in motivation; in one it was transient and in the other it resolved 5 months postoperatively. Another patient, a heavy smoker, experienced two transient ischaemic attacks 4.5 weeks postoperatively comprising weakness, dysarthria and dysphagia, with each lasting <5 h. Repeat postoperative MRI suggested the new development of a small posterior internal capsular infarct on the operated side.

Finally, one of the patients who had experienced an excellent result developed a hemiplegia ipsilateral to the operative side 4.5 months postoperatively. This was due to an aggressive malignant glioblastoma. His clinical condition deteriorated rapidly after diagnosis of the tumour and he died 6 weeks later. His preoperative and 5-week postoperative MRI brain scans showed no evidence of tumour. He was the individual in whom the lowest of the three planned coagulations was omitted because of the proximity of the posterior cerebral artery. Post-mortem examination of the brain (Fig. 5B) revealed that the lesion had been placed superior to the artery but within the confines of the medial pallidum, as planned.

Ten patients (39%) had experienced no adverse effects, with the exception of increased salivation in one. Overall, 20 (77%) of the 26 patients operated considered unilateral pallidotomy to have improved their quality of life.

Other assessments
The patients of this series were additionally examined on a range of cognitive measures sensitive to dysfunction of prefrontal cortical regions. Although generally impaired on these tasks preoperatively, preliminary results suggest little in the way of consistent or sensitive change following surgery (Jahanshahi et al., 1997). There is a preliminary indication, however, that there may be some deterioration on tasks which load strongly on verbal working memory. These data are to be the subject of a future full and independent report.

Discussion
Effects of pallidotomy on motor performance
Currently, selective characteristics to determine which Parkinson’s disease patients are likely to experience benefit in both ‘on’ dyskinesias and ‘off’ motor disability following
Fig. 5 (A) Post-mortem photograph of the lesion of Patient 16 who died as a result of a middle cerebral artery haemorrhagic infarction. The pallidal lesion is non-haemorrhagic and lies in the ventral medial pallidum. (B) Post-mortem photograph of the lesion of Patient 8 who died 6 months postoperatively from an incidental malignant glioma in the hemisphere opposite to the pallidotomy. The pallidal lesion lies more dorsally to avoid the posterior cerebral artery which was immediately ventral to the medial pallidum (not shown). (C) Five-week postoperative T1-weighted MRI brain axial sections of Patient 8 showing the pallidotomy extending below the AC–PC plane. The signal void of the posterior cerebral artery is clearly visible immediately below the lesion, 4 mm below the AC–PC plane. (D) Magnified coronal MRI section of Patient 8 corresponding to B.
medial pallidotomy are unclear. The results of our preliminary study show that, at 3 months postoperatively, the most significant improvement was reduction of dyskinesias, especially contralateral to pallidotomy, and this was maintained for 1 year in those available for follow-up. We also detected smaller but significant reductions in axial and ipsilateral dyskinesias. The improvement in underlying contralateral rigidity in the ‘off’ state was also significant at 3 months, but improvements in tremor and bradykinesia scores were more variable. We were, however, unable to demonstrate the maintenance of these responses for 1 year but this may reflect the small number of subjects who were available for assessment at that time.

These results are in agreement with reports from other centres (Dogali et al., 1995; Iacono et al., 1995; Lozano et al., 1995; Sutton et al., 1995; Baron et al., 1996) suggesting that alleviation of dyskinesia is the most marked improvement observed after medial pallidotomy. By reducing the potential for levodopa to induce involuntary movements, medial pallidotomy permitted us to prescribe higher doses of dopaminergic medication to nine subjects and to increase the dose of apomorphine in one subject. One patient who was intolerant of all dopaminergic medication preoperatively was successfully restarted on a small dose of levodopa 3 months postoperatively. The observed reduction in overall daily ‘off’ time postoperatively may be attributable to the increase in postoperative medication. We also found a significant correlation between the magnitude of response to levodopa preoperatively with improvement in total motor ‘off’ UPDRS after pallidotomy, supporting the notion that a good anti-parkinsonian response to levodopa preoperatively may predict a good outcome after surgery. Therefore, pallidotomy may be viewed as an adjunct to medical therapy in some Parkinson’s disease patients whose parkinsonism is levodopa-responsive but accompanied by disabling involuntary movements. This is in contrast to other studies where pallidotomy was associated with an overall reduction in dopaminergic medication postoperatively (Iacono et al., 1995; Lozano et al., 1995; Baron et al., 1996). The reasons for this difference may include the variable responses of bradykinesia scores to pallidotomy among different centres, differences in patient selection and the performance of bilateral pallidotomy in some institutions.

Our results show that medial pallidotomy significantly improved ‘off’ contralateral UPDRS motor performance by 27%. Although the magnitude of improvements for contralateral parkinsonism was similar, the improvement in UPDRS score for rigidity was much more significant than the scores for tremor and bradykinesia. There are difficulties in interpreting changes in UPDRS bradykinesia scores. The bradykinesia tests which were employed tap the combined effects of rigidity and bradykinesia, and possibly tremor. An improvement in UPDRS score for bradykinesia may, therefore, reflect simultaneous changes in rigidity, without necessarily any true change in the initiation, speed and sequencing of movement. Nevertheless, ‘off’ motor performance, as assessed by the repetitive hand/arm timed motor test, improved by 24%. Our other two timed motor tests (sequential finger/thumb opposition and pronation/supination) may rely more on distal motor function and were more variably improved among our patients. Additionally, the reduced number of subjects who were able to complete the timed motor tests reflects the generally demanding nature of these tests in patients with severe Parkinson’s disease.

Interestingly, we found a significant correlation between the ventrality of medial pallidotomy and degree of improvement in contralateral UPDRS bradykinesia scores. The caudal medial pallidum has been shown to contain cells which directly respond to passive manipulation and limb movements (Hutchinson et al., 1994; Beric et al., 1996) and is thought to represent the motor portion of the medial pallidum. It is likely that ventral pallidotomy interrupts axons of the ansa lenticularis as well as cell bodies of neurons of the ventral pallidum. The ansa lenticularis is one of the major pallidofugal pathways which traverses the internal capsule to project to the ventral lateral and ventral anterior nuclei of the thalamus (Carpenter, 1976) and it is interesting to note that ansotomy was previously one of the earliest successfully employed surgical interventions in the treatment of parkinsonism (Fénelon, 1950; Spiegel and Wycis, 1954).

We found a significant improvement in ipsilateral ‘off’ rigidity (22%) postoperatively but no significant changes in tremor or bradykinesia scores ipsilaterally. Postoperatively, gait was marginally significantly improved ‘off’ medication. One explanation for the effect of medial pallidotomy on ipsilateral and axial motor function, and dyskinesia is that each medial pallidum sends extensive projections, via the ventral anterior and lateral thalamus, to the mesial frontal cortex (Alexander et al., 1990) which contain bilateral limb representations. Direct projections from the medial pallidum to the pedunculopontine nucleus of the spinal cord may also contribute to the effect of pallidotomy on posture and control of axial muscles (Flaherty and Graybiel, 1994). Despite significant improvements in ipsilateral ‘on’ dyskinesia, the residual ipsilateral symptoms remained disabling to our patients since the magnitude of the ipsilateral improvements was less than the contralateral improvements. Many of our patients, having experienced dramatic relief of dyskinesias contralaterally, wished to proceed to a staged bilateral pallidotomy, but the efficacy and morbidity of bilateral pallidotomy currently remains variable and uncertain.

Recent results from other centres also indicate that the response of bradykinesia scores following pallidotomy is variable. While Lozano et al. (1995) and Dogali et al. (1995) found that medial pallidotomy significantly improved bradykinesia both contralaterally and ipsilaterally, a more recent study (Baron et al., 1996) detected an improvement in contralateral but variable responses of ipsilateral bradykinesia scores. Sutton et al. (1995) in a smaller study (n = 5), did not detect a significant improvement in either contralateral or ipsilateral bradykinesia scores. Iacono et al. (1995) only studied their medial pallidotomy patients in the ‘on’ state
and reported a surprising 61% improvement in overall bradykinesia scores. In a large series of pallidotomy operations, Laitinen (1995) reported significant improvements in contralateral bradykinesia scores, rigidity and tremor, but the location of these lesions was moved after his earlier report (Laitinen et al., 1992), to lie more laterally in the pallidum. The pathways lesioned in these series may, therefore, be distinct from those lesioned by medial pallidotomy. Additionally, the standard assessment scales, employed in this study and others, were primarily compiled for the assessment of Parkinson’s disease patients undergoing mesencephalic transplantation (unilateral and bilateral) in whom the responses to surgery may not be so localized. It is, therefore, possible that the standard assessment scales may become imprecise when they are applied to patients with severe Parkinson’s disease and regional dyskinesias undergoing pallidotomy and, indeed, Obeso et al. (1996) have recently used more complex neurophysiological assessments to show that the effects of medial pallidotomy on bradykinesia and rigidity may be localized to motor function around only one joint of one limb. The development of a more unified approach of patient selection, surgical technique and method of assessment, coupled with improved anatomical imaging to record lesion location precisely, may help to resolve these issues in future and enable pallidotomy to be ‘prescribed’ for individual patterns of symptoms.

Complications

In any unit embarking on pallidotomy, there is an inevitable ‘learning curve’. Our subjects with major persisting complications were Patients 1 and 7, and the two with operation-related deaths were Patients 12 and 16. Twelve of the first 14 patients operated, but only four of the next 12, experienced adverse effects.

The effects of pallidotomy over time may be due to a range of mechanisms. Acutely, the lesion itself causes a central core of neuronal death surrounded by an area of damaged cells. Additionally, perilesional oedema may become evident from 36 h onwards, and may last up to 3–4 weeks postoperatively. The early effects of the procedure (both beneficial and detrimental) may be the result of sub-lethal neuronal damage or perilesional oedema. In contrast, long-term effects assessed at 3 months and 1 year are related to the balance between the necrotic lesion and the medium/long term recovery of the penumbra. For example, two of our patients experienced dramatic relief of both parkinsonism and dyskinesias during the first 2 postoperative weeks, but subsequently lost the anti-parkinsonian benefit while maintaining the anti-dyskinetic benefit. This transient relief of parkinsonism may have resulted from perilesional oedema extending the effects of a suboptimally placed lesion into the optimal lesion site. Similarly, transient unwanted effects may be due to the converse process; one of our patients only experienced adverse effects temporarily (beginning 2 days postoperatively and resolving by 3 months). Assessments carried out on the first postoperative day, with subsequent patient discharge to remote or foreign parts, can, therefore, be a poor guide to longer term results, so that most units now carefully assessing pallidotomy have chosen 3- and 12-month postoperative time points, with some incorporating intervening times.

As with beneficial effects, negative effects following pallidotomy have varied widely between different series. Initial reports were characterized by remarkably low morbidity. Only recently was mortality reported (Obeso et al., 1997). In our first 26 patients unilaterally operated, there was an 8% mortality rate and a 15% rate of major complications. The overall risk of severe permanent complications from pallidotomy would, therefore, appear to be similar to other forms of deep brain stereotaxis surgery (Krauss et al., 1994; Jankovic et al., 1995).

The most serious complication in our series was haemorrhage which occurred superficially (4%) and at the target (12%). Superficial haemorrhage may be postulated to occur as a result of trauma to superficial bridging veins during manipulation of the recording and lesioning electrodes and would be more likely to occur in elderly patients in whom cortical atrophy is present. One of our haemorrhagic fatalities had been taking diclofenac preoperatively. Similarly, one patient from the Emory series, who suffered a severe non-fatal haemorrhage, had been taking a large amount of aspirin (Obeso et al., 1997) and we now stipulate that any candidate for stereotaxis surgery should be specifically instructed to discontinue non-steroidal anti-inflammatory drugs at least 6 weeks prior to surgery. In two cases, haemorrhage was associated with infarction. We hypothesize that these patients may have experienced superficial bleeding in the subarachnoid space resulting in vasospasm with secondary infarction.

There is also the question of whether the multiple passes associated with intraoperative recordings might increase the risk of complications. While the notion of such an increase may appear instinctive, there is no conclusive evidence that this is indeed the case. The potential risk of haemorrhage from multiple needle passes must be balanced against the risk of injury to the vital structures which surround the ventral medial pallidum which, if damaged by an inaccurately placed lesion, may fail to relieve symptoms and lead to severe motor, visual or psychiatric disturbance. The mean number of tracks for the first 14 patients was 2.4 ± 0.9, while the mean number of tracks for the subsequent 12 patients was 1.5 ± 0.8. This might give the impression that a greater number of tracks may be associated with increased morbidity. However, this is not supported when one correlates the relationship between the number of needle tracks and complications in individual patients. To date, no formal trial has compared pallidotomy with and without electrophysiological microelectrode recording and so the advantage of one method over the other is currently based on empirical data. Such an important trial would now be timely and welcome. However, it is possible that improved imaging
techniques will, in future, be sufficiently accurate to pinpoint the target without the need for invasive electrophysiological recording. We speculate that the haemorrhages which occurred in our patients were more likely to have occurred during lesioning rather than during recording, since the associated deterioration in clinical condition occurred postoperatively in the intensive care unit rather than intraoperatively at the time of electrophysiological recording. Moreover, experience with deep brain stimulation, including initial microelectrode recording in many cases, and also cases in which no deliberate lesion is performed, has revealed a very low rate of intracerebral complications.

Minor and transient complications which did not interfere with the patients’ quality of life were common (39%) but these patients considered that the improvement in motor function, particularly dyskinesias, outweighed the disability associated with their complications. In our series, as in others (Baron et al., 1996; Johansson et al., 1997; Lang et al., 1997), transient worsening of speech was noted, and no patients noted improvement in speech. Patients should, therefore, be warned that this feature is unlikely to improve and may worsen postoperatively. However, severe pre-existing dysarthria is not necessarily a bar to unilateral pallidotomy since Patient 2, with severe pre-existing parkinsonian speech impediment, had an excellent motor response with no adverse effects. Only one patient experienced a transient hemiparesis but we witnessed postoperative motor hemineglect in two subjects. Neither of our two patients with quadrantanopia were troubled by their visual deficit, although this precluded them from driving. Only one patient had early focal seizures postoperatively, but no patient should drive for 6 months postoperatively because of the general risk of seizures after an intracranial procedure.

It is intriguing, but sad, that one patient subsequently died from a malignant glioma in the hemisphere opposite to the lesion. One of 22 Parkinson’s disease patients who had undergone unilateral pallidotomy recently reported by Johansson et al. (1997), developed a malignant glioma 8 months postoperatively ipsilateral to the operative lesion. Also, one of four patients who received adrenal medullary grafts at Columbia University (Fazzini et al., 1991) subsequently died 1 year postoperatively from a glioblastoma multiforme (two separate foci in right frontal lobe and one in left thalamus; the graft was in left caudate). We have never encountered another patient with Parkinson’s disease who has developed a malignant glioma, but are unable to determine whether these three instances are coincidental or are in some way related to basal ganglia surgery.

Five of our patients complained of worsened gait postoperatively, although this was not evident on examination. We encountered similar problems in the interpretation of the outcome to pallidotomy in several patients who reported that motor performance had deteriorated on the non-operated side. While it is possible that ipsilateral symptomatic deteriorations were a true consequence of medial pallidotomy, these phenomena are perhaps more likely explained by disease progression. In this respect, the impact of pallidotomy on clinical outcome could, in future, be more meaningfully assessed by including quality of life scales incorporating measurements of functional improvement, e.g. the ability to walk unassisted, live independently or return to employment postoperatively, as originally discussed by Svnnilson et al. (1960).

### The roles of pallidotomy in motor control remain unclear

Current theories of basal ganglia connectivity (Alexander et al., 1990; Flaherty and Graybiel, 1994; Marsden and Obeso, 1994) suggest that dopamine depletion in the striatum results in increased subthalamic and medial pallidal neuronal activity (Filion and Tremblay, 1991; Hutchinson et al., 1994). The medial pallidal output projections are inhibitory to the thalamus and so the inappropriately increased medial pallidal output is postulated to inhibit neuronal activity in the motor thalamus, and consequently in cortical motor and association areas. Medial pallidotomy, by alleviating excessive inhibition of the thalamic nuclei, is postulated to allow the thalamus to facilitate activity of cortical areas associated with movement. This could explain the mechanism by which medial pallidotomy may improve ‘off’ bradykinesia scores. In support of this, a recent [18F]fluorodeoxyglucose PET study has confirmed that resting metabolic activity in the thalamus is reduced after medial pallidotomy, as would be predicted from a lesion which disrupts pallidothalamic efferents (Eidelberg et al., 1996). Furthermore, PET activation studies using H 15O have confirmed that medial pallidotomy increases motor, premotor and prefrontal cortical activity during motor activation tasks, as would be also predicted by this model (Grafton et al., 1995; Samuel et al., 1997). However, the difficulties in interpreting changes in UPDRS bradykinesia scores (see above) do not allow any definite statement as to which components of ‘off’ motor performance are principally changed.

This theory of basal ganglia connectivity would also predict that medial pallidotomy should lead to an increase in propensity to levodopa-induced dyskinesias (rather than the observed decrease) and that lesions of the ventral anterior and lateral thalamic nuclei would be expected to worsen parkinsonism by disconnecting the basal ganglia from the cortex (Marsden and Obeso, 1994). Thalamic infarcts (Lee and Marsden, 1994) do not lead to parkinsonism and specific stereotaxic lesions of the ventrolateral thalamic nuclei do not worsen parkinsonism (Marsden and Obeso, 1994). On the contrary, ventrolateral stereotaxic thalamotomy has been shown to alleviate parkinsonian tremor and rigidity (Hassler et al., 1979; Fox et al., 1991) as well as reducing levodopa-induced dyskinesia in MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine)-treated primates (Page et al., 1993) and patients with Parkinson’s disease (Narabayashi et al., 1984; Jankovic et al., 1995). These findings are clearly at odds...
Pallidotomy in Parkinson’s disease

with the clinical outcome observed after medial pallidotomy, for how can ventrolateral thalamotomy (directly reducing thalamic activity) and medial pallidotomy (postulated to increase ventrolateral thalamic activity) produce the same clinical consequence in Parkinson’s disease?

Several factors need consideration to explain these apparently contradictory observations. First, the functional effects of preservation of the remaining dysfunctional basal ganglia and thalamic nuclei, co-existing with pallidotomy, have yet to be addressed. Secondly, the outcome following pallidotomy may depend more on the pattern of neuronal firing within pallidothalamic pathways rather than the presence or absence of firing (Marsden and Obeso, 1994). It is possible that removal of a ‘noisy’ disturbed system is equally, if not more effective, than simply reducing overactivity. Thirdly, evidence on the physiological effects of levodopa on individual subcortical nuclei is currently lacking and, consequently, the effect of pallidotomy on parkinsonian thalamocortical circuits, with and without the influence of levodopa, remains unclear. Fourthly, any cortical adaptation occurring after medial pallidotomy will, via corticostriatal projections, influence the already perturbed function of the remaining pallidotomy-induced circuits. Clearly, further elucidation of functional, as opposed to anatomical, connectivity between pallidum, thalamus and cortex is required in order to explain the mechanism by which medial pallidotomy can improve dyskinesias ‘on’ medication and bradykinesia scores ‘off’ medication.

Conclusion

The results of this preliminary study confirm that the most significant effect following unilateral ventral medial pallidotomy in Parkinson’s disease is the diminution of contralateral dyskinesias, while ipsilateral and axial dyskinesias improved to lesser degrees. The presence of disabling dyskinesias, therefore, remains the major current clinical indication for pallidotomy. The improvement in underlying parkinsonism is less pronounced but correlates significantly with the ventrality of medial pallidotomy. Pallidotomy is, however, associated with a significant risk of morbidity and mortality, and potential adverse events should, therefore, be weighed against expected improvements in dyskinesias and bradykinesia scores. The rate of complications declined with increasing operative experience. Postoperatively, the resolution of levodopa-induced dyskinesias may enable some patients to tolerate higher doses of dopaminergic medication in order to further improve their underlying parkinsonism.

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