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Chapter 6

Bilateral pallidotomy in Parkinson's disease: a retrospective study

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Summary

Objective To evaluate the effects of bilateral pallidotomy in patients with advanced Parkinson's disease.

Methods Thirteen patients with Parkinson's disease had a staged bilateral pallidotomy if they had severe response fluctuations, dyskinesias, painful dystonia, or bradykinesia despite optimum pharmacological treatment. Assessment scales were the unified Parkinson's disease rating scale (UPDRS), the Schwab and England scale, and a questionnaire on the effects of disability in activities of daily living and adverse effects. Postoperative magnetic resonance imaging was evaluated for lesion location and extension.

Results The median off phase UPDRS motor score was reduced from 43.5 to 29 points after the first pallidotomy and it was further reduced to 23.5 points after the second pallidotomy (n=8). The UPDRS activities of daily living off phase score improved from 28.5 to 20.5 points after the first pallidotomy and was 19 after the second pallidotomy (n=6). The Schwab and England scale off phase score showed an improvement after both procedures, first from 40 to 60, and thereafter to 90 (n=8). On phase dyskinesias were reduced substantially. Of the thirteen patients, ten had adverse effects of whom five had problems with speech. One patient became hemiplegic due to a delayed infarction. Ten patients experienced further benefit from the second procedure.

Conclusions Bilateral pallidotomy reduces dyskinesias. A second contralateral pallidotomy may reduce parkinsonism, although to a lesser degree compared to the first pallidotomy and with an increased risk for adverse effects.

Introduction

Patients with advanced Parkinson's disease often face fluctuations between immobility ('off' phase) and mobility, usually associated with dyskinesias ('on' phase), despite optimum pharmacological treatment. The results of several studies indicate that unilateral pallidotomy can improve parkinsonism in the off phase and reduce dyskinesias in the on phase,¹⁻⁴ especially on the contralateral body-side.⁵⁻¹⁰

There are a few reports on bilateral pallidotomy, most concerning a small number of patients. Some groups claim a good and sustained effect, without many adverse effects,¹¹⁻¹³ while others report a high risk for adverse effects and cognitive decline.^{2,14-17}

Between 1994 and 1999 we performed staged bilateral pallidotomies in 13 patients with Parkinson's disease. We present the follow-up of these patients to contribute in the discussion concerning the validity of this procedure.

Methods

Patients

All patients with idiopathic Parkinson's disease, who had a bilateral pallidotomy in our hospital, participated in this follow-up study. Patients were eligible for unilateral pallidotomy if they had (1) idiopathic Parkinson's disease¹⁸ and (2) severe response fluctuations, dyskinesias, painful dystonia, and/or bradykinesia, despite optimum pharmacological treatment. Patients with a successful unilateral pallidotomy, who suffered from ipsilateral severe response fluctuations, dyskinesias, painful dystonia, and/or bradykinesia — despite optimum pharmacological treatment — were offered a second contralateral pallidotomy. Exclusion criteria were: a mini mental state examination¹⁹ score of 24 or less, psychosis, or general surgical contraindications (e.g. unstable cardiac or pulmonary disease, coagulation disorder).

Surgical treatment

Bilateral pallidotomies were always done in two sessions. The first and second — contralateral — pallidotomy were done in a similar way. The technique has been described earlier.¹ For target localisation, a positive contrast ventriculography was done. The target coordinates for the posteroventral globus pallidus at the border of the medial and lateral segments were 2-3 mm anterior to the midcommisural point, 5 mm below the intercommisural line and 21-23 mm lateral to the midline of the third ventricle. Microelectrode recording was not done. Electrical monopolar test stimulation was carried out using an electrode with a 2.1 x 4.0 mm bare tip. With the same electrode, radio-frequency thermolesions were made at 80°C for 60 s at each 2 mm step. The number of lesions varied

between two and five (median five) and was equal for the first and second pallidotomy. The number of lesions depended on the effects of electrical monopolar test stimulation and the effects of lesioning.

Outcome measures

Clinical assessment In most cases, clinical assessment before the first and second pallidotomy had been performed in provoked off and on phases. Patients were assessed during a follow-up visit after the second pallidotomy. The off phase was defined as the condition of the patient after withholding antiparkinson medication for 12 h and being awake for at least 1 h. The on phase was the condition 1 h after taking the usual first morning dose.

The scales used were the motor examination and the activities of daily living section of the unified Parkinson's disease rating scale (UPDRS)²⁰ and the Schwab and England scale.²⁰

During this follow-up visit patients filled out a questionnaire with the following questions: (1) how is your impairment in activities of daily living at present compared to the level of impairment in activities of daily living before the first pallidotomy; (2) how is your impairment in activities of daily living at present compared to the level of impairment in activities of daily living before the second pallidotomy; and (3) would you choose again for a second pallidotomy. The first two questions could be answered with: clearly worse, moderately worse, slightly worse, unchanged, slightly improved, moderately improved, or clearly improved. The third question could be answered with yes or no.

Adverse effects At the follow-up visit patients filled out a questionnaire about adverse effects. Patients classified the adverse effects as transient (< 3 months) or permanent (> 3 months).

Lesion location All the postoperative magnetic resonance imaging (MRI) done in the patients were collected. Each lesion was visually evaluated (RdB and JDS) on the MRI scans for location and extension in relation to the globus pallidus pars interna (GPi), globus pallidus pars externa (GPe), putamen, and internal capsule. Additionally, we recorded possible infarctions or haemorrhages.

Statistical analysis

Changes in clinical assessment data were analysed with the non-parametric Friedman test. If the Friedman test showed a $p < 0.05$, Wilcoxon signed-rank test statistics were used to determine between which assessments differences occurred.

Results

Patient flow and follow-up In our centre 13 patients had a staged bilateral pallidotomy (table 1). Patient two and four had a thalamotomy before the first pallidotomy.

The mean interval between the two operations was 45 weeks (range 6-98). Preoperative assessments in standardised conditions were performed in nine patients. Follow-up assessments in standardised conditions were performed in nine patients 41 weeks (range 1-97) after the first pallidotomy and in 12 patients 96 weeks after the second pallidotomy (range 7 weeks - 4 years, three < 1 year, four between 1 and 2 years, and five > 2 years).

Patient four became hemiplegic two weeks after the second pallidotomy and he remained severely disabled. We did not perform an assessment after his second pallidotomy. Patient six refused off phase assessment at follow-up after the second pallidotomy. Patient one and two did not have response fluctuations after the second pallidotomy, therefore, we did only off phase assessments. The UPDRS activities of daily living score of patient eight was missing. Patient 13 lives far away from our centre, therefore we could not perform assessment in standardised conditions after the second pallidotomy, however, he did fill out the questionnaire. There were no significant changes in the use of medication; patients used a median of 725 levodopa equivalent units¹ before surgery and 687 at the follow-up visit.

Table 1. Baseline characteristics of the 13 patients

Characteristic	Value
Gender: men / women [no of patients]	7/6
Mean age in years \pm SD	53.3 \pm 7.8
Mean age of disease onset in years \pm SD	35.5 \pm 8.8
Median Hoehn and Yahr stage off / on (range)	4 (2.5-5) / 3 (2-4)
Median medication in levodopa equivalent units ¹ (range)	725 (325-5000)

Clinical assessment The UPDRS motor score was reduced from median 43.5 to 29 points after the first pallidotomy (n=8, Wilcoxon signed-rank test p=0.025, table 2) and to 23.5 after the second procedure, which was not statistically significant. The UPDRS activities of daily living off phase score improved from 28.5 to 20.5 points after the first pallidotomy and was 19 after the second pallidotomy (n=6). The Schwab and England scale showed an improvement after both pallidotomies, first from 40 to 60 (n=8, Wilcoxon signed-rank test p=0.048) and subsequently to 90 percent (Wilcoxon signed-rank test p=0.026).

For on phase assessment, the UPDRS motor, the UPDRS activities of daily living, and the Schwab and England scale did not show any significant changes (table 3).

Table 2. Scores in standardised off phase

Patient	UPDRS motor			UPDRS activities of daily living			Schwab and England scale		
	Pre	Inter	Post	Pre	Inter	Post	Pre	Inter	Post
1	70	17	27	23	-	15	50	40	80
2	60	-	34	-	-	23	50	-	90
3	98	-	33	-	25	19	40	-	80
4	-	56	-	-	-	-	-	50	-
5	41	30	18	29	14	22	30	80	90
6	46	46	-	23	40	-	30	30	-
7	33	39	23	20	21	17	40	60	90
8	25	18	24	-	20	21	70	60	60
9	46	28	26	24	11	13	60	80	90
10	69	36	22	28	24	21	40	60	90
11	49	47	44	32	28	32	30	40	40
12	33	14	14	31	20	13	20	80	90
13	13	17	-	13	12	-	60	80	-
Median score*	43.5	29	23.5	28.5	20.5	19	40	60	90

Pre=preoperative, Inter=after first and before second pallidotomy, Post=after second pallidotomy; * for the UPDRS motor and Schwab and England scale, patients 1, 5, 7, 8, 9, 10, 11, and 12 were included and for the UPDRS activities of daily living, patients 5, 7, 9, 10, 11, and 12 were included; Friedman test UPDRS motor $p=0.005$, UPDRS activities of daily living $p=0.07$, and Schwab and England scale $p=0.02$.

Table 3. Scores in standardised on phase

Patient	UPDRS motor			UPDRS activities of daily living			Schwab and England scale		
	Pre	Inter	Post	Pre	Inter	Post	Pre	Inter	Post
1	-	-	-	-	-	-	-	-	-
2	-	-	-	-	-	-	-	-	-
3	-	32	31	-	15	15	-	-	80
4	-	-	-	-	-	-	-	-	-
5	20	12	16	17	12	18	70	90	90
6	9	8	17	10	28	20	90	90	80
7	1	8	26	8	7	12	80	90	90
8	3	11	12	-	14	16	90	80	80
9	7	9	22	9	7	13	80	90	90
10	4	5	9	9	4	11	80	90	90
11	9	7	16	13	1	20	90	80	80
12	11	10	4	11	12	11	90	90	90
13	4	5	-	10	16	-	80	90	-
Median score*	8	8.5	16	10	7	13	85	90	90

Pre=preoperative, Inter=after first and before second pallidotomy, Post=after second pallidotomy; * for the UPDRS motor and Schwab and England scale, patients 5, 6, 7, 8, 9, 10, 11, and 12 were included and for the UPDRS activities of daily living, patients 5, 6, 7, 9, 10, 11, and 12 were included; Friedman test UPDRS motor $p=0.09$ and UPDRS activities of daily living $p=0.10$.

There was a trend towards worsening on the UPDRS motor scale. Almost all patients suffered from levodopa induced dyskinesias before the first pallidotomy, and although we did not use a scale to assess dyskinesias, it was obvious that the involuntary movements were reduced significantly on both sides after bilateral pallidotomy.

Patient four, who suffered a delayed infarction, did not fill out the questionnaire. The question "how is your impairment in activities of daily living at present compared to the level of impairment in activities of daily living before the first pallidotomy?" was answered as improved by all patients (table 4). The question "how is your impairment in activities of daily living at present compared to the level of impairment in activities of daily living before the second pallidotomy?" was answered as unchanged by one and as improved by 11 patients. Two of the 12 patients who filled out the questionnaire, would not choose for a second pallidotomy if they could choose again.

Table 4. Follow-up questionnaires

Patient	How is your impairment in activities of daily living compared to the level of impairment in activities of daily living before the first pallidotomy?	How is your impairment in activities of daily living compared to the level of impairment in activities of daily living before the second pallidotomy?	Choose again for second pallidotomy?
1	Clearly improved	Clearly improved	Yes
2	Slightly improved	Moderately improved	Yes
3	Clearly improved	Slightly improved	Yes
5	Clearly improved	Clearly improved	Yes
6	Moderately improved	Unchanged	No
7	Clearly improved	Moderately improved	No
8	Clearly improved	Clearly improved	Yes
9	Clearly improved	Slightly improved	Yes
10	Moderately improved	Slightly improved	Yes
11	Moderately improved	Moderately improved	Yes
12	Moderately improved	Slightly improved	Yes
13	Clearly improved	Clearly improved	Yes

Adverse effects Ten patients had adverse effects (table 5). Patient four suffered a delayed infarction two weeks after the second, right-sided pallidotomy. He remained hemiplegic with severe dysarthria. Patient two, who had a contralateral thalamotomy previously, suffered from severe dysarthria after the first pallidotomy, which did not deteriorate after the second pallidotomy. The third patient had a left-sided congruous superior homonymous quadrantanopia following the second pallidotomy. Patient five had mild dysarthria after the first pallidotomy that did not worsen after the second procedure. In addition, he noticed mild chorea of the contralateral arm en leg lasting for several hours directly following the first pallidotomy. We did not classify this as an adverse effect since it is

Table 5. Adverse effects in 13 patients

Patient	After first pallidotomy		After second pallidotomy	
	Transient	Permanent	Transient	Permanent*
2		Dysarthria		Dysarthria
3	Facial paresis		Changed personality	Visual field defect
4				Delayed infarct, hemiplegic, severe dysarthria
5			Dysarthria	Dysarthria, emotional flattening
7		Slight facial paresis, changed personality		Slight facial paresis, changed personality, severe dysarthria
8	Dysphasia			Dysarthria, drooling
9				Dysarthria
10			Hiccups, intermittent during 1 day	Mild dysarthria, emotional flattening
11				Hypophonia, emotional flattening
12			Confusion, the day after surgery	

* Permanent effects after the second pallidotomy includes permanent adverse effects after first pallidotomy.

associated with favourable surgical outcome.⁴ Following the second pallidotomy, patient seven had severe dysarthria. He would not choose for a second pallidotomy if he could choose again, because speech decline outweighed the benefits he experienced from the second pallidotomy. Patient eight, nine and ten suffered from mild, non disabling dysarthria after the second pallidotomy.

Lesion location Magnetic resonance imaging was done in all patients after the first pallidotomy and in ten patients after the second pallidotomy (table 6). For the left side (n=11), seven patients had the lesion in the posterior part of the GPi and GPe, three patients had a lesion in the GPi only, and one patient had a lesion in the GPe only. For the right side (n=12), eight patients had a lesion in the GPi and GPe, of whom in one the lesion extended into the putamen. One patient had a lesion in the GPi and a delayed infarction in the internal capsule two weeks after surgery and three patients had a lesion in the GPe only.

Discussion

A shortcoming of the present study is the range in follow-up assessments. Assessments were unblinded and included self reported efficacy and adverse effects, which are subject to biases. The results after unilateral pallidotomy of patient five, six, seven, ten, 11 and 13, and the results after bilateral surgery of patient one, two and three have been reported earlier.^{11,21} The patients' off phase UPDRS motor, UPDRS activities of daily living, and Schwab

Table 6. Lesion location

Patient	Right side		Left side	
	GPI	GPe	GPI	GPe
1	x	x	x	—
2*	x	x		
3	x	x	x	x
4†	x	—	x	x
5	—	x	x	—
6			—	x
7	—	x	x	x
8‡	x	x	x	x
9	x	x	x	x
10	—	x	x	x
11	x	x		
12	x	x	x	—
13	x	x	x	x

Magnetic resonance imaging was done in all patients after the first pallidotomy and in 10 patients after the second pallidotomy.

— No lesion visible.

* Lesion in left thalamus from earlier surgery.

† Lesion in the right internal capsule (delayed infarction) and left thalamus from earlier surgery.

‡ Lesion right putamen.

and England scale score improved after the first pallidotomy. These results are in agreement with earlier studies.^{1,5} Following the second pallidotomy there was a trend for improvement in off phase UPDRS motor and Schwab and England scale score.

In the on phase, dyskinesias were significantly decreased. The median on phase UPDRS motor scale score showed a trend for decline, which is probably related to disease progression. The UPDRS activities of daily living and the Schwab and England scale on phase scores were unchanged.

Ten of the 13 patients experienced adverse effects. Three patients had severe permanent adverse effects, of whom one suffered a delayed infarction. The two other patients had severe dysarthria. Six patients had non disabling permanent adverse effects, of whom five had a problem with speech. Four patients stated that they have experienced permanent emotional flattening or changed personality. Neuropsychological assessments were not performed and therefore it is likely that we overlooked neuropsychological adverse effects. Ghika et al.¹⁶ reported the outcome in four patients and showed that cognitive, mood, and behavioural deficits may follow bilateral contemporaneous pallidotomy. The proportion of adverse effects in our cohort is in agreement with other reports on bilateral pallidotomy and is higher compared to unilateral pallidotomy, in particular for speech problems.^{2,12,14-17} This seems analogous to the adverse effects in unilateral versus bilateral thalamotomy.²²⁻²⁴

Despite the less important effects on parkinsonism and the number of adverse effects,¹⁰ patients stated that they had made the right decision when they opted for the second contralateral pallidotomy. We feel that the balance between improvements and adverse effects should be thoroughly investigated prior to judging whether bilateral pallidotomy could be a treatment for Parkinson's

disease. A remaining question is the place of pallidotomy in advanced Parkinson's disease in view of the cohort studies that investigate the effects of deep brain stimulation in the subthalamic nucleus.²⁵ The results of studies comparing both procedures have to be awaited.

Bilateral pallidotomy reduces dyskinesias. The findings of our study suggest that a second contralateral pallidotomy may reduce off phase parkinsonism, although to a lesser degree compared to the first pallidotomy and with an increased risk for adverse effects.

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