

MOTOR PERFORMANCE AFTER POSTEROVENTRAL PALLIDOTOMY AND VIM-THALAMOTOMY IN PARKINSON'S DISEASE

A 1-YEAR FOLLOW-UP STUDY

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ABSTRACT -Twenty-three patients with Parkinson's disease underwent stereotactic surgery. To study the long-term motor performance, the patients were evaluated at the pre-operative period and at the 1st, 3rd, 6th, and 12th post-operative months, with the following scales: Unified Parkinson's Disease Rating Scale (UPDRS) motor score and Larsen's Scale for Dyskinesias. The patients under levodopa therapy were assessed both in "on" and "off" periods. Fourteen unilateral ventrolateral thalamotomies (VLT), 4 unilateral posteroventral pallidotomies (PVP), 2 bilateral PVP, and 3 VLT with contralateral PVP were performed. The motor improvement was significant and long-lasting in the "off" period, except for 2 patients. The "on" period quality improved, mainly due to the control of dyskinesias. The improvement of dyskinesias was long-lasting for the majority of the patients. There was no significant decrease in the levodopa dose. Three patients showed permanent complications, but none was severe.

KEY WORDS: Parkinson's disease, thalamotomy, pallidotomy.

Desempenho motor após palidotomia póstero-ventral e talamotomia ventro-lateral na doença de Parkinson: acompanhamento de um ano

RESUMO - Vinte e três pacientes portadores de doença de Parkinson foram submetidos a cirurgia estereotáxica para tratamento da doença. Com o objetivo de estudar o desempenho motor a longo prazo, os pacientes foram avaliados clinicamente no período pré-operatório, no 1^o, 3^o, 6^o, e 12^o mês pós-operatório, com as seguintes escalas: Escala Unificada para Doença de Parkinson (Unified Parkinson's Disease Rating Scale-UPDRS), item III, escore motor e com a Escala de Larsen para Discinesias. Os pacientes que utilizavam levodopa foram avaliados nos estados "off" e "on". Foram realizadas 14 talamotomias ventro-laterais (TVL) unilaterais, 4 palidotomias póstero-ventrais (PPV) unilaterais, 2 PPV bilaterais; 3 TVL associadas à PPV contralateral. O benefício motor foi observado de forma significante no estado "off", e manteve-se a longo prazo na maioria dos pacientes, exceto em 2. Houve melhora da qualidade do período "on", devido ao controle das discinesias. A melhora das discinesias se manteve a longo prazo na maioria dos pacientes. As cirurgias não promoveram um decréscimo significante na dose de levodopa. Três pacientes tiveram complicações permanentes, mas nenhuma delas foi considerada grave e nem houve prejuízo funcional importante em decorrência das mesmas.

PALAVRAS-CHAVE: doença de Parkinson, talamotomia, palidotomia.

Levodopa remains the goldstandard treatment for patients with Parkinson's disease (PD). However, after some years, part of these patients develop complications related to the prolonged use of the drug, such as fluctuations and disabling dyskinesias¹. In the absence of satisfactory pharmacological therapy, there has been a resurgence of interest for stereotactic surgery in the last

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two decades. Although these procedures have been performed for a long time, there are some difficulties to compare the results of different reports. The reports of the pre-levodopa era²⁻⁴ used nonvalidated methods of assessment, and those patients presented a different clinical profile when compared to the patients of the levodopa era. More recent studies⁵⁻¹⁶ present different methods of assessment, leading to different conclusions.

This report presents our experience with stereotactic surgery in patients with PD, who were followed-up for one year. We evaluated their motor performance with motor scales along this period to determine the long-term effects of surgery.

METHOD

Patients - Twenty-three patients from the Movement Disorders Clinic of the Universidade Federal de São Paulo with the diagnosis of PD according to clinical criteria¹⁷ underwent stereotactic surgery between March 1996 and July 1997. The mean age of the group was 55.9 years (range, 43-70 years), the average history of PD was 8.7 years (range, 3-17 years). Hoehn & Yahr staging ranged from 2.5 and 4. All patients presented a response to levodopa, but two could not receive it due to gastric side effects. Fifteen patients presented dyskinesias. Despite an optimal regimen of antiparkinsonian drugs, these patients presented with disabilities in the activities of daily living. Exclusion criteria included moderate to marked cognitive disjunction and uncontrolled medical disorders. All patients gave informed consent, and the university's ethical committee approved this study.

Surgeries - Unilateral VIM-thalamotomy (VLT) was performed in 14 patients which showed a predominance of tremor and/or rigidity; unilateral posteroventral pallidotomy (PVP) was performed in 4 patients which showed mainly asymmetric bradykinesia and/or dyskinesia; 2 patients with very disabling, symmetric off period bradykinesia and on period dyskinesias underwent bilateral PVP; and 3 patients with mixed forms of the disease underwent unilateral VLT and contralateral PPV. All bilateral procedures were performed simultaneously. The surgical methods have been described in detail elsewhere¹⁸.

Evaluations - Patients were clinically evaluated in the practically defined "off" and in the best "on" periods before surgery and during the follow-up period at 1, 3, 6 and 12 months after the procedure (the two patients who were not under a levodopa regimen were evaluated only once in each period and the results were considered as "off" period scores for statistical analysis). According to the CAPIT Committee definition, the practically defined "off" results from a 12h withdrawal of antiparkinsonian medications and the best "on" is defined as that condition that both patient and physician agree represents the maximal therapeutic benefit from medication¹⁹. The motor performance was evaluated with the UPDRS motor score-item III (scores range from 0 to 108)²⁰ and the dyskinesias were scored according to a dyskinesia rating scale proposed by Larsen et al. (scores range from 0 to 18)²¹. The levodopa doses (not including the dopa decarboxylase inhibitors doses) were analyzed during the follow-up period.

Statistical analysis - For the UPDRS motor scores and the levodopa doses we used a Friedman's analysis of variance²². When significant, this analysis was complemented with Hollander's multiple comparisons test²³. The dyskinesias scores were analyzed with kappa statistic²⁴. A p value of ≤ 0.05 was considered to indicate statistical significance.

RESULTS

UPDRS motor scores (Fig 1) - There was a statistically significant improvement ($p < 0.001$) in the "off" period scores of the 1st (mean 36.2), 3rd (mean 38.0) and 6th (mean 41.3) postoperative months, when compared with the base line scores (mean 55.3). Although the scores of the 12th month (mean 45.1) were better than those of the base line, this difference was not statistically significant ($p > 0.05$). All the "on" period scores improved when compared to the preoperative period (mean scores: base line 34.6; 1st month 26.7; 3rd month 28.4; 6th month 28.3; 12th month 30.9), but these changes were not statistically significant ($p > 0.05$). In those patients with unilateral procedures the scores improved mainly on the contralateral side and to a lesser extent on the ipsilateral side.

Dyskinesias (Fig 2) - The dyskinesias scores improved significantly ($p < 0.001$) at the 1st (mean 3.52), 3rd (mean 3.71) and 6th month (mean 3.76), when compared to the base line scores (mean 7.24). At the 12th month there was a mild increase in the mean score (4.47), but the improvement was still significant ($p < 0.01$). In those patients with unilateral procedures, the dyskinesias improved

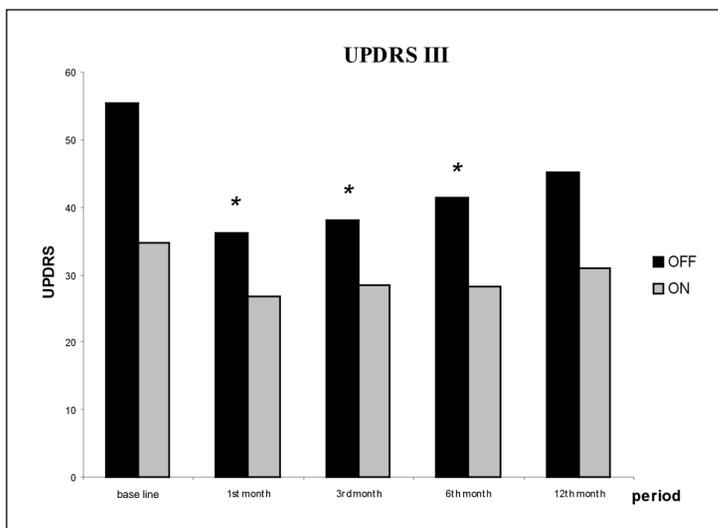


Fig 1. Mean scores for UPDRS III (motor function) during off and on periods in patients with Parkinson's disease before surgery and during follow-up. The asterisks indicate scores that differed significantly from the base line values.

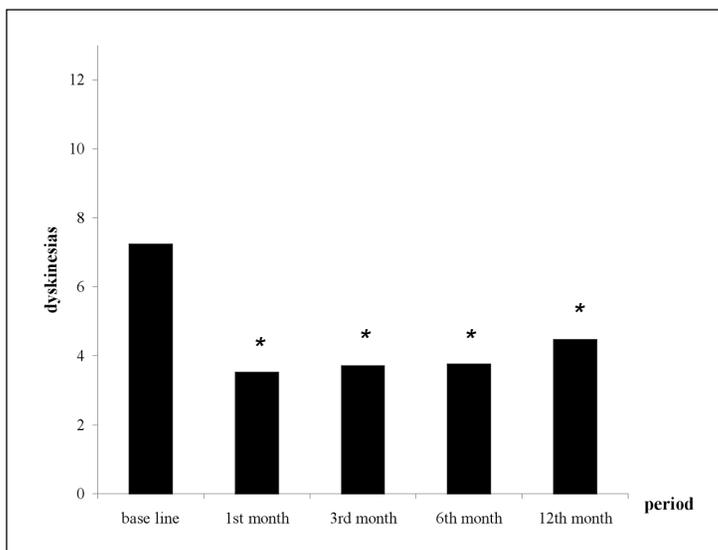


Fig 2. Mean scores for dyskinesia scale in patients with Parkinson's disease before surgery and during follow-up. The asterisks indicate scores that differed significantly from the base-line values.

mainly on the contralateral side. We also observed some improvement on the ipsilateral side, but it disappeared after the 6th month.

Levodopa doses (Table 1) - There were no statistically significant changes in doses during the follow-up period.

Table 1. Mean and median doses of levodopa (mg) of patients with Parkinson's disease at baseline and at 1, 3, 6 and 12 months after surgery.

	base line	1 month	3 months	6 months	12 months
mean	671.4	572.6	575.0	632.7	609.5
median	600.0	500.0	500.0	600.0	562.5

Table 2. Adverse effects of stereotactic surgery for the treatment of Parkinson's disease and follow-up of the complications.

Patient	Age (years)	Surgery	Complications	1-year follow-up
1	52	L THAL	contralateral facial weakness	total improvement at the 2 nd month
2	64	L THAL	temporal disorientation/ abulia	total improvement at the 1 st month
3	45	L THAL / R PAL	dysarthria/ hypophonia/ left facial weakness	total improvement at the 3 rd month
4	68	R THAL	contralateral hypotonia	partial improvement at the 3 rd month
5	62	B PAL	hypophonia/ dysarthria	total improvement at the 6 th month
6	52	L PAL	mild hypophonia/ dysarthria	total improvement at the 3 rd month
7	58	R PAL	contralateral facial weakness/hypo- phonia/ dysarthria/hallucinations	total improvement at the 1 st month
8	61	R THAL	contralateral facial weakness/contra- lateral face and hand paresthesias	partial improvement at the 3 rd month
9	50	R THAL	contralateral hypotonia	partial improvement at the 3 rd month
10	60	R PAL	hypophonia	total improvement at the 3 rd month

THAL, thalamotomy; PAL, pallidotomy; R, right; L, left; B, bilateral.

Complications (Table 2) - Ten patients had complications, most of them were mild and transitory. Three patients had mild persistent complications that did not outweigh the improvement in motor function obtained from surgery.

DISCUSSION

We present the results of the motor performance of 23 patients with PD surgically treated due to disabilities. Most studies agree that only patients with persistent disability despite an optimal drug regimen should be considered for surgery^{6,25-29}. Our results show a statistically significant improvement in the "off" period UPDRS motor scores at the 1st, 3rd, and 6th postoperative months. At the 12th month the mean motor scores showed a tendency toward a sustained improvement, but the value was not statistically significant when compared to the base line score, probably due to the correction for multiple comparisons and a not so large number of patients. The analysis of this particular period showed that 7 patients presented a worst UPDRS motor score when compared to the baseline score. In 4 of these patients, the surgical benefits were sustained, the motor score worsened due to the progression of the disease on the non-operated side. The other 3 patients lost the surgical benefits observed in the initial months and also had a progression of the symptoms on the non-operated side. The "on" period scores showed some improvement but with no statistical significance. Although the UPDRS motor scores of the "on" period did not change significantly, the quality of this period improved due to the control of the dyskinesias. The patients usually report an increase of the "on" period hours. Iacono et al.⁵ reported a one-year follow-up study of patients who underwent either

unilateral or bilateral PVP. The patients were evaluated in the "on" period and they found a significant improvement sustained until the 12th postoperative month. This result differs from ours probably due to a different statistical method of analysis and to the larger number of patients enrolled in their study. Lang et al.⁶ assessed 40 patients who underwent unilateral PVP at six months, one year and two years. They concluded that much of the "off" period disability improvement is sustained, but the "on" period symptoms that are resistant to dopaminergic therapy do not respond to pallidotomy. Samuel et al.³⁰ reported similar results. Fazzini et al.³¹ performed a different statistical analysis and observed a significant and sustained improvement of the "off" period scores until the 4th year after PVP.

The improvement of dyskinesias after PVP is well documented in the current literature^{5,6,30-34}. We observe the importance of the surgery for the "on" period when we analyze the "on" period dyskinesia scores. There was a marked improvement in the control of dyskinesias. Patients with unilateral procedures presented a sustained benefit on the contralateral side and lost it on the ipsilateral side after the 6th month. Lang et al.⁶ also reported a loss of benefit on the ipsilateral side after 1 year. Dalvi et al.³⁴ reported a sustained and statistically significant improvement of both ipsilateral and contralateral dyskinesias at the 12th month after PVP. There are no controlled studies of the effects of VLT over dyskinesias. Some authors suggest that dyskinesias can be controlled with VLT⁷. Some of the patients of our study who underwent VLT had mild dyskinesias before surgery and the improvement after VLT was sustained on the contralateral side. Those patients with disabling dyskinesias underwent PVP. Our study does not allow a comparison between the effects of the different types of surgery over the control of dyskinesias, the groups have different clinical profiles, and the small number of patients in each group does not allow a proper statistical analysis.

There was no statistically significant change in levodopa doses during the follow-up period. Other studies reported similar results^{6,34}. Laitinen et al. reported a reduction of 50 to 75% in levodopa doses³⁵. The effect of the surgery over the doses of levodopa varies according to the patient. For those patients that report a longer "on" period, there is a possibility of reducing the levodopa intake, without clinical worsening. Those patients who, due to disabling dyskinesias, were unable to take higher doses, may benefit from an increase in the dosage after surgery, with longer "on" periods and less dyskinesias. Skalabrin et al.³⁶ reported that PVP widens the levodopa therapeutic window. Some of our patients were able to reduce the levodopa intake, with no worsening of the motor symptoms.

The surgical complications (Table 2) in this group of patients were similar to those described in the literature^{5,6,8,11,12,31-35}. For TVL, the studies reported complication rates between 36 and 61%, for PVP they range from 6,3 to 66,6%. The most common ones are dysarthria, dysphagia, hypophonia, acute confusional states and contralateral limb weakness. They are usually not persistent. Weight gain, intracerebral hemorrhage and visual field loss are less common. Of our 23 patients, 10 had complications, the majority was related to speech (dysarthria/ hypophonia) and contralateral facial weakness. In most cases they were mild and did not persist. Three patients had persistent complications (2 with contralateral hypotonia, 1 with contralateral facial weakness and paresthesias), but these did not outweigh the surgical benefit. At present, except for bilateral thalamotomy, there is not enough information in the literature concerning bilateral procedures and it is not possible to conclude that they lead to a higher rate of complications. Iacono et al.⁵ performed bilateral PVP simultaneously and did not observe persistent complications. Taha et al.³⁷ published a literature review and concluded that bilateral PVP is still controversial, some authors reported a better improvement in motor function after bilateral pallidotomy than after an unilateral procedure, with an increased risk of hypophonia and cognitive deficit. In their own experience, patients with bilateral pallidotomy did not suffer from gross cognitive deficit, those patients who developed hypophonia did not consider their speech to be severely affected, and staging the procedure did not decrease the risks associated with simultaneous surgery. On the other hand, Bronstein et al.²⁹ recommend to consider bilateral pallidotomy only as a staged procedure with at least a 6-month interval between surgeries. Due to the small number of bilateral procedures in our study, we can not conclude whether they lead to a higher rate of complications or not. Of the five patients who underwent bilateral procedures, two had complications which were not persistent.

In conclusion, one year after VIM-thalamotomy or posteroventral pallidotomy, most of the patients showed sustained "off" period motor benefits and "on" period dyskinesias control, with minimal persistent complications. The impact of these findings on the quality of life must be taken into consideration in further studies.

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