

# ACOUSTIC VOICE ASSESSMENT IN PARKINSON'S DISEASE PATIENTS SUBMITTED TO POSTEROVENTRAL PALLIDOTOMY

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**ABSTRACT** - Long-term complications in levodopa treated Parkinson's disease (PD) patients caused a resurgence of interest in pallidotomy as an option of treatment. However, postoperative complications such as speech disorders can occur. *Purpose:* The aim of this study is to evaluate the acoustic voice in PD patients, before and after posteroventral pallidotomy. *Method:* Twelve patients with PD were submitted to neurological and voice assessments during the off and on phases, in the pre-operative, 1<sup>st</sup> and 3<sup>rd</sup> post-operative months. The patients were evaluated with the UPDRS and the vocal acoustic parameters - f<sub>0</sub>, NHR, jitter, PPQ, Shimmer, APQ (using the software MultiSpeech - Kay Elemetrics - 3700). *Results:* The off phase UPDRS scores revealed a tendency to improvement at the 1<sup>st</sup> month and the off phase worsened. The shimmer and APQ improved. *Conclusion:* This study shows that pallidotomy has little improvement on functional use of communication of PD patients.

**KEY WORDS:** Parkinson's disease, pallidotomy, voice.

## Parâmetros acústicos da voz em pacientes com doença de Parkinson submetidos a palidotomia posteroventral

**RESUMO** - O uso prolongado da levodopa na doença de Parkinson (DP) pode ocasionar alterações em seu rendimento e possibilitou o interesse no ressurgimento da palidotomia. Contudo, complicações pós-operatórias podem ocorrer. *Objetivo:* O presente estudo tem por objetivo avaliar alguns parâmetros acústicos da voz de pacientes com DP pré e pós a realização da palidotomia posteroventral. *Método:* foram avaliados 12 pacientes com DP submetidos a avaliação neurológica e da voz durante as fases off e on do uso da levodopa, nos momentos pré-operatório, no primeiro e no terceiro mês pós-operatório. Os pacientes foram avaliados com base na escala UPDRS - item motor - e por meio dos parâmetros acústicos da voz - f<sub>0</sub>, NHR, jitter, PPQ, Shimmer, APQ (usando o software MDVP - Kay Elemetrics - 3700). *Resultados:* Na fase off o escore UPDRS revelou tendência de melhora no 1º pós-operatório e na fase on piora. Os parâmetros acústicos shimmer e APQ apresentaram melhora. *Conclusão:* Este estudo mostrou que a palidotomia resulta em discreta melhora no uso funcional da comunicação dos pacientes com DP.

**PALAVRAS-CHAVE:** doença de Parkinson, palidotomia, voz.

The options of treatment in Parkinson's disease (PD) are, among other drugs, levodopa therapy, surgical treatment, such as pallidotomy and thalamotomy, fetal cell transplant and deep brain stimulation, besides physical therapy, psychotherapy, and speech therapy. Levodopa remains the mainstay treatment of PD patients but long term complications, such as motor fluctuations and dyskinesias are quite frequent<sup>1</sup>. Some authors suggest that levodopa treatment interferes in a positive way in com-

munication symptoms. Jiang et al.<sup>2</sup> and Sanabria et al.<sup>3</sup> observed improvement in the acoustic (F<sub>0</sub>, jitter, SPI e FTRI) and glottographic parameters after the administration of levodopa. In an electromyography study, Gallena et al.<sup>4</sup> observed an increase in the activity of the thyro-arytenoid muscle after the administration of levodopa.

Posteroventral pallidotomy (PVP) consists of the lesion of the internal pallidum (Gpi) with radio-frequency lesions in its sensory-motor territory. Pos-

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Received 30 June 2004. Accepted 25 September 2004.

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teroventral pallidotomy can improve the cardinal motor signals, and also reduce dyskinesias and drug-related motor fluctuations<sup>5,6</sup>. Buck and Cooper<sup>7</sup> studied the speech after chemopallidectomy or occlusion of the anterior coroid artery, and observed a reduction of the diadochokinetic rate of the vocal folds. Schulz et al<sup>8</sup> studied the effect of pallidotomy on selected voice and speech characteristics of 6 PD patients. Acoustic measurements were analyzed pre-pallidotomy and again at 3 months following surgery. Preliminary findings indicated that all participants demonstrated positive changes in at least one acoustic measure; 2 patients consistently demonstrated positive changes in phonatory and articulatory measures, whereas 3 patients did not consistently demonstrate positive changes after surgery. The results are discussed in relation to differential effects observed among the participants. In 2000, Schulz et al.<sup>9</sup> perceived that vocal intensity was greater after PVP in patients that showed mild disarthrophonia.

The aim of this study is to investigate the changes in acoustic voice parameters in patients with idiopathic PD, before and after posteroventral pallidotomy, during the off and on phases of the levodopa effect.

## METHOD

*Sample selection criteria* – Patients were selected from the Movement Disorders Clinic of the Department of Neurology of the Universidade Federal de São Paulo. They were clinically diagnosed as having the idiopathic PD, according to the criteria defined by Ward, Gibb<sup>10</sup> and

had to have indication for posteroventral pallidotomy surgery, with the following criteria: 1) physical incapacity for daily life activities (DLA), in spite of the use of adequate doses and combinations of antiparkinsonian drugs; 2) presence of fluctuation or disabling dyskinesias with antiparkinsonian therapy. The exclusion criteria were based on the presence of moderate or severe cognitive implications (evaluated by the unit's neurologists). PVP was performed contralateral to the most affected side of the body. In symmetrically affected cases, PVP was performed on the side that could bring the most benefit to the patient, taking into account whether he was right or left-handed. Based on the prior neurological evaluations, the following surgical targets were indicated: three right pallidotomies and nine left pallidotomies (Table 1).

*Patients* – Twelve patients were included in this study. Five were females and seven males. The average age of the group was 62.4 years (ranging from 50 to 71 years old) The average disease duration of disease onset was 13.5 years (ranging from 7 to 32 years). Disarthrophonia was considered as moderate in eight and mild in four (Table 1).

*Surgical procedure* – All patients were submitted to surgical procedures as described by Aguiar et al.<sup>11</sup>

*Neurological evaluation* – All individuals were rated by the Unified Parkinson's Disease Rating Scale - UPDRS<sup>12</sup>, focusing on the motor score (items 18 to 31) in the on and off phases of the levodopa effect.

Patients were submitted to neurological evaluation in a period ranging from one week to one month before the surgical procedure (pre-op), after 30 (1<sup>st</sup> po) and 90 (3<sup>rd</sup> po) days of the surgical procedure. All individuals

Table 1. Characterization of the sample according to gender, age, time of disease and side of posteroventral pallidotomy and dysarthrophonia degree pre- and post-surgery.

Patient	Gender	Age (years)	Time of disease (years)	Side of the surgery	Dysarthrophonia degree	
					Pre-surgery	Post-surgery
1	M	71	32	R	moderate	moderate
2	F	60	10	L	moderate	mild
3	M	50	15	L	moderate	moderate
4	M	61	8	L	moderate	moderate
5	F	71	17	L	mild	mild
6	M	69	10	R	moderate	severe
7	M	60	20	L	mild	mild
8	M	54	7	L	mild	moderate
9	F	58	19	L	mild	mild
10	M	55	8	L	moderate	mild
11	F	71	6	L	moderate	severe
12	F	69	10	R	moderate	moderate

M, male; F, female; R, right; L, left.

received levodopa treatment, with doses varying according to each patient's requirements. Since all the individuals received levodopa therapy, the option was made to evaluate them in the on and off phases. The definition of the on and off phases was adapted from that suggested by the Core Assessment Program for Intracerebral Transplantation<sup>13</sup>. The evaluation in the off phase was performed in the morning period, at least 12 hours after the last administration of levodopa, while the other anti-parkinsonian drugs were maintained. Some patients showed great incapacity if they did not receive the levodopa dose, being unable to get to the hospital for evaluation in the off phase. They were asked then to return for evaluation at another time. However, this was not possible for some patients and the evaluation of the off phase was not done without excluding the patient from the sample. For this reason, patients 4, 8 e 11 were not assessed on the off phase of third month postoperative evaluation.

After evaluation in the off phase, the patient was requested to take his or her usual dose of levodopa, and underwent a new evaluation during the on phase, approximately 40 minutes to 2 hours after the ingestion. Sometimes, when the patient did not reach an on phase, his evaluation was repeated under the expected conditions on another day. In patients who did not reach the on phase, this evaluation was not done without excluding them from the sample. Patients 8 and 11 were not assessed during the on phase of third month post-operative evaluation.

**Acoustic voice measurements** – After the neurological evaluation, the oral communication evaluation was carried on. We recorded the following phonation tasks: the emission of the oral vowel, open and central /a/, like father, isolated and sustained in the habitual pitch and loudness and in comfortable way. The patients' phonation tasks were recorded by a digital Mini-Disc recorder, model MDS-520 (Sony trademark), unidirectional; a stereo microphone, model SM-58 (Shure trademark), sited 15 cm distant from the speaker's mouth, and a 74 minute mini disk (Sony trademark). Due to the motor and balance difficulties and the presence of disabling dyskinesias in some patients, all of them were asked to be sitting while recording their tasks.

The Multi-dimensional Voice Program software, model 5105 (Kay Elemetrics Corp.) performed the computerized acoustic analysis. The fundamental frequency measurements ( $F_0$ ), frequency (jitter and PPQ) and intensity perturbation (Shimmer and APQ) and noise (NHR) were extracted from the emission of central, low, open oral vowel /a/, isolated and sustained in the habitual pitch and loudness. The most stable portion of an average of 3 seconds was selected as vocal sample and whenever possible, the beginning and the end of the emission were eliminated.

**Statistical method** – The analysis of variance for a randomized block design test was used to analyze the levodopa dose over the period of time, to compare the global UPDRS motor scores and the acoustic measurement. A 0.05 significance level was considered for all analyses. Reliability analysis was performed using the intraclass correlation coefficient test and was assessed by re-measuring 80% of the data of acoustic measurement. Correlation coefficient ranged from 0.88 to 0.9979. The score of UPDRS III - scale was not submitted to reliability analysis.

## RESULTS

The selected parameters were analyzed in groups and the data were expressed by the average of the total sample.

In general, the surgeries performed did not induced a reduction in the daily dose of levodopa (pre-op=625mg, 1<sup>st</sup> po=640mg, 3<sup>rd</sup>=688mg -  $p=0.912$ ). However, when comparing the UPDRS (Part III- motor scores), we noted a trend towards improvement between the pre-op and the 1<sup>st</sup> po in the off phase ( $p=0.052$ ). In the on phase, the UPDRS scores showed a statistically significant deterioration ( $p=0.007^*$ ) (Fig 1).

The acoustic measurements of the voice in the off phase at the pre-op period compared with 3<sup>rd</sup>po revealed statistically significant differences, specially in  $F_0$ , despite the small increase of 16Hz observed in the 3<sup>rd</sup> po, this difference was statistically significant ( $p=0.009^*$ ). The amplitude perturbation meas-

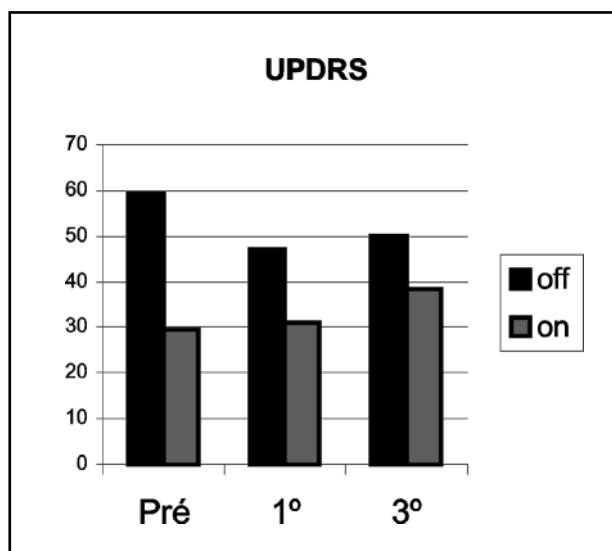


Fig 1. Data of the global motor score, in the pre-operative, in the 1<sup>st</sup> month and 3<sup>rd</sup> month postoperative. Pré, pre-operative period; 1<sup>o</sup>, first post-operative month; 3<sup>o</sup>, third post-operative month.

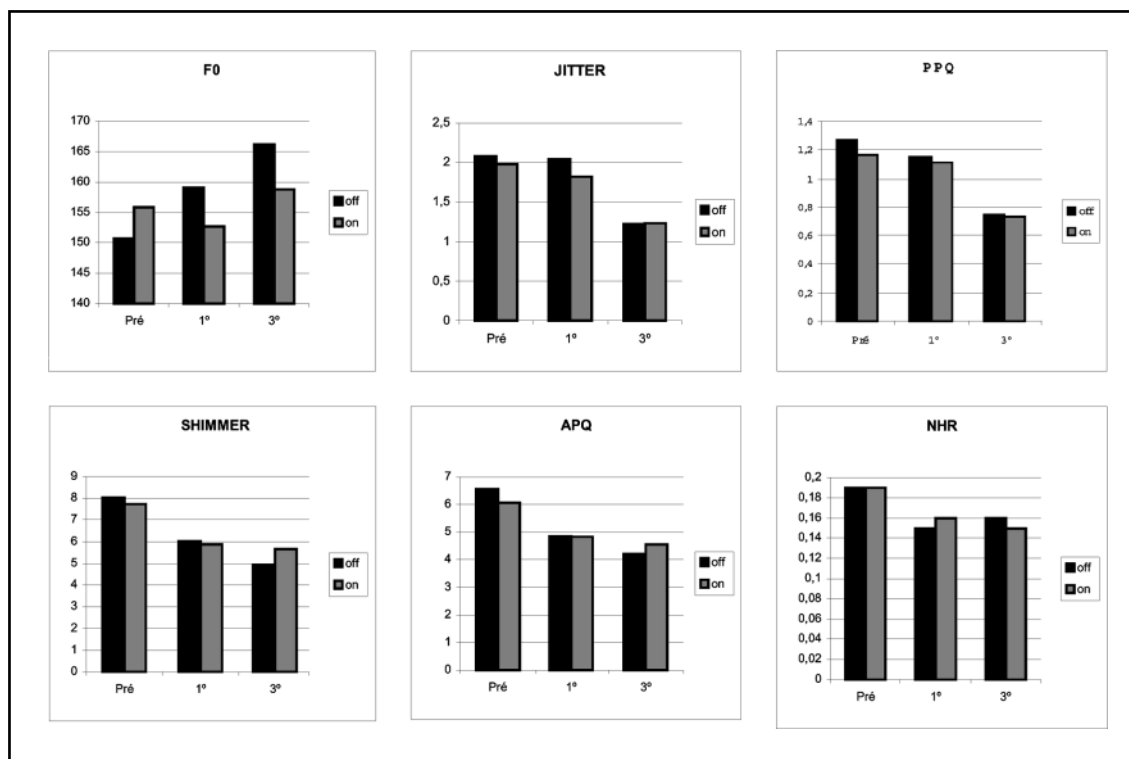


Fig 2. Data of the acoustic measurements:  $F_0$ , jitter, PPQ, shimmer, APQ and NHR, in the pre-operative, 1<sup>st</sup> month and 3<sup>rd</sup> month postoperative, on the off and on phases.

measurements shimmer and APQ were reduced, characterized by a statistically significant improvement up to the 3<sup>rd</sup> po ( $p=0.038^*$  and  $p=0.027^*$ , respectively) (Fig 2).

High values were found in the frequency perturbation measurements (jitter e PPQ) on the all phases and periods (Fig 2). The noise NHR measurement revealed slightly increased values. Both measurements presented some reduction at the postoperative period, although not a statistically significant one (jitter:  $p=0.212$ ; PPQ:  $p=0.159$ ; NHR  $p=0.071$ ) (Fig 2).

## DISCUSSION

After the PVP we observed no change in the severity of dysarthrophonia in seven subjects, worsening in three and improvement in only two, suggesting that PVP neither interfere in the voice nor in the speech of these patients. The UPDRS (Part III-motor score) was used because it allows data comparisons between different studies, as it is a widely used scale. The mean UPDRS score was lower after PVP, which is in accordance with the literature<sup>5,11,14</sup>. The different studies that reported neurological evaluations in the off and on phase observed an improvement only in the off phase<sup>5,11,14-16</sup>. Ondo et al<sup>14</sup> speculated that the improvement in the off

phase is consistent with the traditional model of the basal ganglia physiology in PD, which determines the presence of tonic thalamic hypo activity resulting from the excessive inhibition induced by the internal palladium. The Gpi efferent is somatotopically connected to the ventro-lateral thalamus via ansa lenticular (anteriorly) and the lenticular fasciculus (posteriorly). Excessive Gpi activity is (believed to be) the result of a reduction of striatal inhibition (direct via) and of the increase in subthalamic excitation (indirect via).

A small change was observed in voice assessment, although it revealed values lower than those observed in the off phase. According to our clinical experience and some studies<sup>17</sup>, the effect of levodopa on the symptoms of voice and speech still appears to require more detailed studies, bearing in mind the great variability of symptoms shown by patients treated with this drug. The changes observed in the off phase, in the neurological, voice assessment suggest that the ideal period for evaluating motor symptoms and the interference of voice treatment in PD is in the off phase.

With regard to  $F_0$ , studies show  $F_0$  to be higher in men and lower in women with PD<sup>18</sup>. However, this study did not show evidence of changes in the

usual frequency range, which is similar to the study of Ramig et al.<sup>19</sup>. In the studied periods, it was observed an increase in  $F_0$  as Schulz et al.<sup>8</sup> that observed an increase in the fundamental frequency in three out of six cases evaluated.

The laryngeal physiopathology in PD can be considered in this case. Laryngeal changes are frequently explained by the presence of bradykinesia or rigidity. Hirose, and Joshita<sup>18</sup> observed in a single individual the loss of reciprocal suppression of the thyroarytenoid muscle during inspiration, which is indicative of rigidity. Baker et al.<sup>20</sup> attributed hypokinesia and bradykinesia to the presence of changes in the laryngeal function. Thus, the increase in  $F_0$  may be associated with the increase in loudness. There is an intimate relationship between  $F_0$  and vocal intensity; although increases in intensity are measured by greater glottal coaptation and activity of the respiratory mechanism, variations in intensity are dependent on the frequency and vice-versa. Regarding the evaluation of vocal intensity, some studies described a reduction in loudness after PVP<sup>5,8,15</sup>, while Laitinen et al.<sup>6</sup> observed an increase. Schulz et al.<sup>8</sup> did not observe a correlation between the increase of  $F_0$  and the increase in vocal intensity. They only perceived that vocal intensity was greater after PVP in patients that showed mild dysarthrophonia<sup>9</sup>.

Frequency perturbation measurements changes are found in PD patients<sup>19</sup>; NHR also showed increased values. One could suppose that the NHR would be ideal in evaluating changes in the glottal source and less sensitive in analyzing in the dysarthrophonia. The amplitude perturbation shimmer and APQ measurements improved, though without reaching normality. The surgical procedure may have helped in the greater control of the phonation system. However, the improvement in measurement was not sufficient to interfere in the functional use of communication in PD patients. The frequency perturbation and intensity measurements represent the efficiency of motor control of the laryngeal system in maintaining an emission as stable as possible, apart from correlating the changes in glottal coaptation and the presence of roughness and breathness in voice<sup>21</sup>. Nevertheless, Kent et al.<sup>22</sup> discussed the feasibility of correlating the acoustic measurements with the phonation characteristics of the auditory perceptual analysis in the neurological dysphonia. So it remains unknown whether the acoustic properties always correlate to the perceptive descriptions.

Analyzing the surgical interference in the UPDRS scores (Part III) and the voice parameters, slight differences were observed throughout the postoperative periods. The total average score of the UPDRS, in the off phase revealed an improvement in the 1<sup>st</sup> po and a small deterioration in the 3<sup>rd</sup> po. However, in relation to the voice and speech parameters evaluated, the averages showed statistically significant improvement only when the pre surgery period was compared to the 3<sup>rd</sup> po.

Discrepant data regarding surgical interference with the motor symptoms of the members and voice and speech were also observed by Buck, and Cooper<sup>7</sup>, who showed similar improvement of tremor, rigidity and speech in only 20.0% of the patients.

Some questions may be raised. The variation in hypokinetic dysarthrophonia and the neurophysiological and neuroanatomical differences of the voice and speech sensorymotor organization in relation to the limbs may distinctly affect individuals with PD and thus, generate differences in the responses to the surgical procedure<sup>23</sup>.

In conclusion, this study showed improvement in some selected phonation parameters, but the surgical procedure did not promote major facilitation of the functional use of communication, since no improvement was observed in dysarthrophonia. This study revealed slight changes on voice parameters evaluated after unilateral posteroventral pallidotomy. According to some authors, the changes in voice and speech may be a consequence of the size of the lesion and the perilesional edema in unilateral surgical interventions, as well as of different neurophysiologic and neuroanatomical mechanisms responsible for sensory-motor organization of voice and speech in relation to limbs<sup>15,23</sup>. However we found no correlation between the side of the lesion and worsening of voice, as observed by Wang and colleagues<sup>24</sup>.

Numerous researches and modern techniques have been employed in the search for improving PD treatment. However, nowadays the therapeutic options present inherent limitations to the disease and the treatment itself. Thus, recent and controlled studies have shown that changes in voice and speech in PD patients seem to respond satisfactorily to speech therapy<sup>25,26</sup>. Therefore, studies that analyze specific effects of different treatment interventions help us not only to understand PD, but also to define medical and speech therapy .

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