The effect of levodopa on speech in Parkinson's disease: musical' scale study

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Abstract

This paper aims to examine the effect of levodopa on speech in patients with Parkinson's disease. Our hypothesis is that, in such a task, speech production should be phonetically affected for parkinsonian patients and improved by L-Dopa treatment.
In order to determine dopamine effect, oral productions of 14 parkinsonian patients of the akinetic type have been collected, in the OFF and ON states. They have then been compared to those of control subjects. The specific aim of this study is (a) to examine the ability of patients to handle the variations in fundamental frequency of their voice as well as to master the rise in frequency required by the task , i.e. production of the musical scale (b) to measure the palliative effects that can be induced treatment based on L-Dopa.

Effects relating to the L-dopa administration diverge according to the patients, the year post diagnosis and the Parkinson's disease severity degrees. Compared to our control population, our parkinsonian subjects present prosodic disorders, in particular on the level of the fundamental frequency management. This dysfunction would come from the akinesy, the breathing deficit and the problems of vocal cords vibration. These results confirm in part Darley hypothesis, knowing that the parkinsonian "dysprosody" would come from a peripheral neuro-engine dysfunction affecting the larynx motor activity.

1. Introduction

Parkinson disease (PD) is commonly characterized by a reduction in motor activity, and at the speech production level, by a "dysprosody" [1]. The speech disorders occurring as a result of PD are a form of hypokinetic dysarthria. Darley [2] explains the origin of the parkinsonian dysarthria by the execution limitation of respiratory movements, due to aweakness of muscular rigidity. The disorders would thus affect speech production and in particular the handling of fundamental frequency (F0). The fact that voice can't correctly be used depends on various factors, mainly of physiological nature (defect of the vocal cords vibrations for example). Gentil [3] affirms that the F0 of parkinsonian subjects is conventionally associated with global increase in pitch and reduction in range. This phenomenon is likely due to a greater stiffness and a hypokinesia of the muscle controlling the tension of the vocals folds.

2. Dysprosody

Critchley [4] classified the speech disorders of parkinsonian subjects into an akinetic, rigid, hyperkinetic, and iterative (or repetitive) forms of dysarthrophonia. This symptomatic classification suggests that the two main elements of PD, bradykinesia and rigidity, exert an influence on the motor speech system.The equivalents of hypokinesia or rigidity has been described as monopitch, reduced stress, imprecisely produced consonants breathless voice, monoloudnesss and inappropriate silences [5], [3].

Prosody pervades all aspects of a speech signal, both in terms of a raw acoustics outcomes and linguistically meaningful units from the phoneme to the discourse unit. It can be defined as the phrase, accent, and tone structure of speech. It is carried out by the suprasegmental features of fundamental frequency, loudness and duration [6]. Measurements of fundamental frequency and its variation providing statistical data related to the defect of the melody, is a dominant feature of parkinsonian subjects [3].

3. Speech and subject data base

We use medical data, neurological and speech bases constituted in collaboration with the Purpan Hospital of Toulouse within the framework of a project granted by the INSERM (French Institute of Health and Medical Research). The data base contains several kinds of stimuli according to the experimental protocol [7]

3.1. Patients

Currently, 14 subjects (in OFF vs ON state L-dopa treatment) underwent the linguistic protocol (5 females and 9 men between the stage II and IV towards Hoehn and Yahr scale [8]). The selected parkinsonian patients are all of the akinetic type. They are all French, aging from 60 to 75 years old, they show evidence, in all cases, of speech (phonetic) disturbances on the basis of a first-level perceptual analysis.

To be considered clinically significant the improvement due to pharmacological treatment must be at least 30%. However, it appears that, among the 14 patients who passed the protocol, ten benefit from this improvement. Indeed, the treatment improves the UPDRS motor score of four females patients. Among men, three patients benefit from a 50% improvement, two of 30%. Among the remaining four, three show an improvement, but which does not exceed 30% One patient does not reach the ON state and another was unfortunately unable to complete the ON state protocol.

In order to free us from the aging fourteen participants are chosen as controls. The age and gender characteristics of these participants were matched as closely as possible with those from the participants with PD.

3.2. Levodopa administration

The patients are convened the day before the investigation, and are hospitalized for 24 hours. They stop their antiparkinsonian treatment 16 hours after their arrival. They are observed the next morning in period of "freezing, without any treatment". At the end of this first exercise series, they receive their usual antiparkinsonian treatment and can have a rest. As soon as they are unfreezed, they repeat exactly the same procedure as previously (series of phonetic exercises) so to evaluate their production in phase "ON".
A number of acoustics studies have found that patients with PD (undedicated or off medication) have impaired speech prosody [9]. Nevertheless, prosody and acoustic parameters

could be improved by L-dopa treatment. Currently the standard medication for treatment of PD is a combination of levodopa and carbidopa, in the form of Sinemet [10].

4. Methods

The three main stages of our study are the phonetic annotation of the signal, extraction of the prosodic parameters, and statistical analyses.

4.1. Data recording / Analysis

Speech signal is annotated at orthographic and phonetic levels according to the visualization of the frequency curves, of formant transitions and intensity obtained by the signal editor "Winsnoori" (1994-1997 by S.Q.L.A.B).
The speech signal is analyzed using a 22 kHz sampling. The mean, standard deviation, maximums and minimums F0 and intensity values are computed five milliseconds using the LPC algorithm.

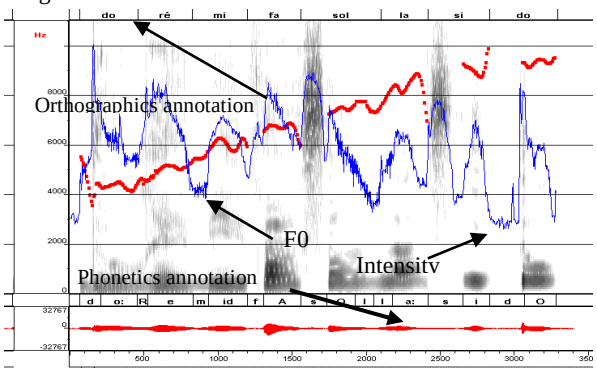

Figure 1: *phonetics and orthographic annotation of musical' scale*

4.2. The Stimuli

We study the diatonic scale. The patients must ascend the diatonic scale: DO, RE, MI, FA, SOL, LA, SI, DO (english: C, D, E, F, G, A, B, C) going from the gravest to the acutest. Thus, the patients' voice quality should be observed.
Indeed, the aim here is to not to show if patients sing right or wrong but testing the capacity of patients to vary the fundamental frequency of their voice as well as to control rise in frequency. Our hypothesis is that, in such a task, speech production should be phonetically affected for parkinsonian patients and improved by L-Dopa treatment.Each element of the stimulus is theoretically separated from a tone or from an half, as illustrated in the table 1. For example the note "DO" and the not "Re" differ from a tone whereas the note "FA" is different from the "MI" note of a half tone.

C	D	E	F	G	A	B	C
1	T	T ½	T 1	T 1	T 1	T ½	T

Table 1. *Theoric musical scale's evolution.*

5. RESULTS

This investigation examines a corpus of speech collected from two groups. First 14 Parkinsonian patients in OFF and ON state (5 females: P1 to P5 and 9 men: P6 to P14) at level 3 and 4 of the Hoehn and Yahr scale (1967). Then a control group including 14 subjects (5 females: S1 to S5 and five men, S6 to S14). For better readability during the presentation of various results, including averages, we grouped the results by state of Parkinsonian Disease Females or Men: OFF (PDF or PDM OFF) and ON state (PDF or PDM ON) and females and men subjects control under the generic term " FSC" and "MSC".

The perceptual and phonetic analyses are presented below according to: 1) a first comparison of vocalizations between OFF and ON states for PD subjects and for control subjects, 2) a second comparison to identify potential strategies patients could produce between frequency and intensity.

We will conclude this comparison by discussing for a couple of parameters acoustic analysis curves of F0, and intensity.

5.1. Musical' scale: F0 curves

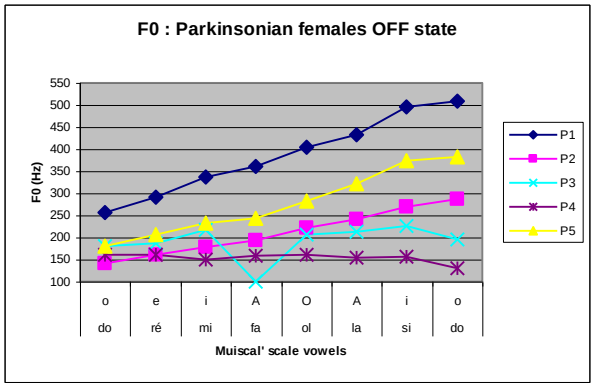

Figure 2: *Musical' scale representation: F0 curves: OFF State.*

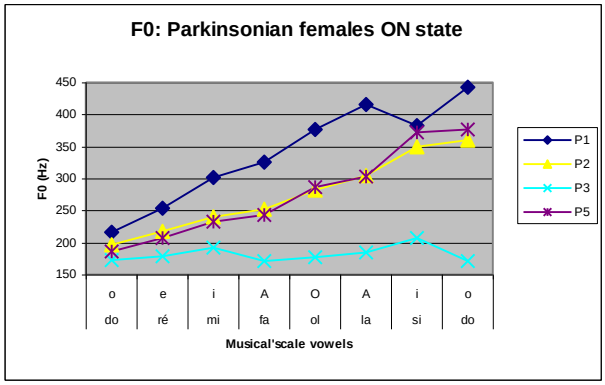

Figure 3: *Musical' scale representation: F0 curves ON State.*

The female patient P4, and men patients P8, P11, P12 and P13, are not included in the comparisons about intra-OFF-ON. Indeed, they do not benefit from an improvement of 30%. Consequently, comparisons OFF-ON are carried out on 4 females patients and 5 men patients.

5.1.1. Parkinsonian Disease patients and control females

We find 3 profiles at the level of the realization of F0 curve, in OFF and ON state: rising, flat and descending realization.

We calculated the mean values of F0 for each vowel of the stimulus. The aim is to observe the evolution of the oral realization according to the drug intake.
In state OFF three Parkinsonian Disease Females (P1, P2, and P5) have a **rising realization**, whatever in OFF or ON state.

In ON state, P1 and P5 productions still rise but dopamine does not improve the main values of the F0 on the entire stimulus. Means of F0 for these two patients are respectively 385.57 and 277.80 Hz in OFF state and 339.35 Hz 275.96 Hz in O state). The patient P2 does not improve her realization after the drug intake (211.84 Hz in OFF state; 182.01 Hz in ON state), her realization is decreasing.

Flat realization: Patients P3 and P4 produce the musical scale without any change in fundamental frequency between different notes. This occurs both in ON or OFF state. The musical scale is then produced like a monotonous sentence, "recto tono".

The treatment appears benefit to the P3 patient as the mean of phonemes is higher in ON and achieves an ascending scale. In OFF state her F0 values are first ascending and then a stage (pause) is made on the note "SI" after which the frequency values are decreasing., we observe the same phenomenon for patient P2 in ON state**.**
We note the opposite effect for patient P1 patient the frequencies raise just after the pause accomplished on note "SI".

Our results show that, on the entire population of control females, only subject S2 presents some difficulties to achieve an ascending scale.

5.1.2. Parkinsonian Disease patients and control Men

Ascending realization: whatever ON or OFF state, four patients (P7, P9 and P10 and P13) produce an ascending scale. Among them two (P7 and P10) present a best production after taking medication On the other hand dopamine does ameliorate P9 production. F0 mean of P7 and P10 represent respectively 169.34 and 225.70 Hz in OFF state and 170.95 Hz 233.70 Hz in ON state.
Means of P9 and P13 are 132.19 and 131.67 Hz in OFF state and 172.56 and 136.14 Hz in ON state.

P13 patient makes a pause at the level of "LA" note and uses this one to rise in frequency over the two last notes.
In ON state, patient P10 also makes a pause at the level of the "SI" note following; the values of frequency drop.

Decreasing realization: Only one patient has a decreasing realization this is P12.

Two patients (P6 and P14) present **descending achievements**, whatever OFF or ON state. Besides, they do not manage to make the fundamental frequency of their voice varying. Among these patients, one improves his production in the ON state; mean of his production is 129,78 Hz in OFF state and 136.16 in ON state.

Among the men control subjects, two shows an ascending achievement S5, S6, S8, and S9. Subjects S10 and S12 have a completely flat realization, and the mean of the range for these subjects is higher than for the patients (OFF: 127.Hz; ON: 125.52Hz; Control: 137.39Hz). S7, S11 realizations is firstly decreasing on the "LA" note, then rising until the end of the stimulus.

5.2. Musical' scale: intensity results

5.2.1. Parkinsonian Disease patients and control females

As already indicated, we study the variations in intensity. Indeed, we hypothesize that in the ON state, patients compensate for the difficulties in the management of vocal cords by a sur articulation of voice production resulting by an increased intensity.
It could be therefore a palliative strategy, such as the definition is given in the article of Nespoulous [11]: a strategy to overcome a deficit that is the result of disease or a "deteriorated" situation".

If we compare the mean intensity values of vowels among the 3 populations, mean for patients in OFF state is 53.14 dB against 55.40 dB for patients in ON state and 57, 35 dB in control subjects. It is slightly higher after administration of dopamine, but there is no really significant difference.

Our hypothesis is confirmed by two patients (P1 and P5). The mean F0 is lower in the ON state than in the OFF state. On the other hand, the intensity values are more important in ON state. The patient P3 is the only one who sees his achievement improved in terms of F0 intensity after taking medication.
This is not the case with the last patient P2, whose average F0 and intensity decline in the ON state.

5.2.2. Parkinsonian Disease patients and control Men

In Parkinsonian Disease population, mean intensity values represents in OFF state 58.85 dB, against 59.91 for patients in ON state, and 55 dB for control group. On the contrary, the intensity values are greater in the ON state.

P6: Mean F0 and intensity OFF state: 158.70 Hz and 57.70 dB, ON state: 152.88 and 60.23 dB.
P9: Mean F0 and intensity OFF state: 132.19 Hz and 62, 47 dB; ON state: 131.67 Hz and 65, 68 dB.

P10 patient improved both his achievements in terms of F0 and intensity after taking medication: mean F0 and intensity OFF state: 225, 63 and 52 Hz, 91 dB, ON state: 233.70, 55, 75 dB. The patient P7's frequency values increase between ON and OFF state, but the intensity values fall (169.34 and 56.67 Hz in OFF state and 170.95 Hz and 55.15 dB in the ON state) .

6. Discussion

The aim of this work is to examine the acoustic characteristics of the prosody for parkinsonian patients in OFF and ON state of drug intake. Among the entire patient population only P4, P5, P6, P8 and P14 have difficulty achieving an ascending

scale. This phenomenon is also found with control subjects and for subjects S2, S10 and S12, during the musical scale production. Our paramount objective is to determine if the subject is able to make the frequency of his voice varying between each note and thus to carry out a rising scale. Our specific goal is to determine if the mean of the notes, and more precisely of the final vowels, improved after the dopamine intake. So,we also studied the effect of treatment with L-dopa on the average F0 and intensity for all the patients' gender.

For all female patients, mean F0 is higher before the treatment and control subjects have an higher mean than average patient females and that whatever their state of drug intake. With regard to intensity, the mean for all patients female is higher in ON state, and the average for control subjects is higher. As for the average F0, the control subjects men have a lower intensity than Parkinsonian men and whatever their condition.
Actually, the dopamine seems to have a clear effect among 4 patients (P2, P7, P10 and P14) with regard to the mean of F0 on the stimuli musical scale. The 5 others have a more raised mean in OFF.

7. Conclusions

The purpose of this study was to examine the acoustic characteristics of speech prosody in participants with PD before and after taking medication. Previous studies have found a reduction in speaking F0 variability in subjects with PD compared to controls [12,13,]. In addition to F0 variability, individuals with PD

Our Parkinsonian population confirmed deficits in speech prosody compared to age-matched controls. The participants with PD demonstrated increased mean F0 values.on the musical scale production. Patients have some problems in handling adequately assertion patterns. Effects relating to the L-dopa administration diverge according to the patients, the year post diagnosis and the Parkinson's disease severity degrees.

Compared to our control population, our parkinsonian subjects present prosodic disorders, in particular on the level of the fundamental frequency management. This dysfunction would come from the akinesy, the breathing deficit and the problems of vocal cords vibration. These results confirm in part Darley hypothesis [2], knowing that the parkinsonian "dysprosody" would come from a peripheral neuro-engine dysfunction affecting the larynx motor activity.
Intensity is the most difficult parameter to identify, which is certainly due to its correlations with F0 values [14].The weakening of the intensity can go until whisper. It can settle from the start or only at the end of production and it can be accompanied by a deceleration of the articulation rate [15].
In this study one of our hypothesis is that the patients would hide their deficit of vocal cords vibration by an increase in intensity. It would be thus a palliative strategy. Our hypothesis is checked in particular among the females.

These results reinforce the importance of examining the palliative strategy adopted by the subject to hide their vocal cords deficit, we want observe and compare duration, percent pause time and pauses strategy. The we make the hypothesis that musical scale production would be an indicator of the subjects' capacity to produce intonation schemas according to a given instruction: that's why we will continue our data base exploitation on the remaining speech tasks. We also observe the phonological disturbances. Indeed, actually we create a specific "diacritic" alphabet to describe the Parkinson's dysarthria. The aim of these diacritics is to describe the phenomenon of lengthening, diphthongization of the vowel, resumptions of breath, breathlessness, quavering, freezing, husky devoicing.

8. Acknowledgements

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