Correlation between levodopa response and acoustic parameters of prominence marking as well as tongue body movements in patients with Parkinson's disease

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Abstract

This study investigates the prominence production strategies of 12 patients with Parkinson's disease on the acoustic and articulatory level by using Electromagnetic Articulography. The ability to mark prominence is tested in two conditions to further examine the influence of motor performance on speech production: without dopaminergic medication and with dopaminergic medication. The data reveals that patients with Parkinson's disease are able to mark prominence in both conditions. They maintain prominence relations across and within accentuation by adjusting acoustic prosodic markers. Under prominence, tongue body movements were modulated in the temporal rather than the spatial domain to mark prominence. Most patients responded to the levodopa intake, improving the gross motor performance by 43 %. The improved gross motor performance was accompanied by an improvement of speech motor performance in terms of faster tongue body movements.

Keywords: acoustic, articulation, prominence, speech production, Parkinson's disease, levodopa

1. Introduction

1.1. Parkinson's disease

Parkinson's disease (PD) is a movement disorder caused by a reduced dopamine concentration in the brain. The progressive loss of dopaminergic neurons affects neural circuits which further affect non-motor and motor functions (Deuschl 2017). Motor impairment influences gross motor but also speech motor control. Gross motor symptoms are manifested in smaller, slower and less extended movements (bradykinesia) of the limbs, increased muscle tone (rigidity) and/or a resting tremor. Due to a reduced control over muscles necessary for speech production, many patients develop a speech disorder, namely hypokinetic dysarthria. This hypokinetic dysarthria affects all motoric subsystems of speech and leads to a reduced modulation of intensity and pitch, slower and unprecise articulation as well as an overall reduced articulation space (Duffy 2019). To increase motor ability, patients are treated with dopaminergic medication such as levodopa. Levodopa increases the amount of dopaminergic neurons and improves neural activity in the brain circuits. Whereas it is proven that levodopa is an effective treatment for improving gross motor performance (Katzenschlager & Lees 2002), it remains unclear to what extent it influences speech production.

1.2. Prominence marking in patients with PD

Prominence marking is a strategy for highlighting important information in communicative contexts. In intonation languages, such as German, parameters within a syllable, e.g. segment duration, intensity, pitch movement, are adjusted to signal prominence (Baumann et al. 2006, Mücke & Grice, 2014). Underlying movements of respective articulators are observed to be more distinct, by moving longer as well as with higher velocities and amplitudes. Adjustments of prosodic parameters evoke a contrast between accented (prominent) and unaccented (non-prominent) syllables but also a differentiation between focus types, such as broad and contrastive focus. Previous studies investigating prominence marking in PD have shown that prominence marking can vary in speakers with PD compared to healthy controls (Cheang & Pell 2007; Tykalova et al. 2014). A recent study by Thies et al. (2020) showed that patients with PD can mark prosodic prominence by modulating F0, intensity and vowel articulation in prominent positions, but the prosodic modifications are less efficient than in healthy control speakers. While patients performed with a reduced vowel space in terms of *hypo*articulated vowels, they *hyper*articulated prosodic parameters such as intensity and tonal height. While the study of Thies et al. (2020) is restricted to patients with medication, the present study investigates prominence production in patients with medication (med-ON) and without medication (med-OFF). The aim is to determine the influence of the drug levodopa on speech performance using acoustic but also articulatory measurements.

2. Method

2.1. Participants and assessments

Twelve native German speaking patients with idiopathic PD (7 male, 5 female) aged between 51 - 70 years (μ = 59 years $\pm$ 6) participated in the study. On average, patients were diagnosed with PD for 7 years ($\pm$ 5). Participants were assessed in two conditions: (1) without drug intake (med-OFF) - 12h after cessation of all dopaminergic medication - and (2) with drug intake of 200 mg of soluble levodopa (med-ON).

2.1.1. Elicitation of speech data

Speech data was recorded acoustically and articulatorily with an Electromagnetic Articulograph (AG 501, Carstens system). The acoustic signal was captured using a condensator microphone headset keeping the mouth-to-microphone distance of about 7 cm constant during the whole recording session. As gain levels were adjusted from med-OFF to med-ON recordings and between the participants, a reference tone was recorded as first stimulus in each recording condition from which the intensity values for the analysis get controlled. The acoustic signal was recorded at 44.1 kHz/16 bit. To capture kinematic data, sensors were placed on the (1) lower lip, (2) upper lip, (3) tongue body and (4) tongue tip. The tongue sensors were placed approximately 1 cm and 4 cm from the beginning of tongue tip.

2.1.2. Elicitation of motor function and levodopa response

Motor performance of the participants was evaluated using part III of the 'Unified Parkinson's Disease Scale' (UPDRS, Goetz et al., 2008), a standard assessment for monitoring the motor ability of PD. For this motor assessment a video is taken from the patient while he/she is doing different tasks, such as finger tapping, arising from chair, walking, etc.. Motor signs are rated on a 0 – 4 scale (0 = normal, 4 = severe). A comparison of the motor scores in both conditions determines the influence levodopa had on the patients' gross motor ability. The levodopa response indicates the percentage of motor improvement from med-OFF to med-ON condition.

2.1.3. Test procedure

Assessments were performed in a fixed order and started in med-OFF condition, followed by med-ON condition (Table 1). In each condition the video for motor assessment was taken first. Afterwards, the speech recordings were made.

Table 1: *Procedure of recording session.*

UPDRS video Speech recordings	med-OFF
200 mg levodopa intake and break	
UPDRS video Speech recordings	med-ON

The defined 'OFF' state is achieved after abstaining 12 hours from levodopa. Therefore, the patients received the last dose of medication at 6 pm on the evening before the experiment. In order to receive the med-ON condition, patients received 200 mg of soluble levodopa before pausing. 30-45 minutes after drug intake, the second test session started.

2.2. Speech material

The speech task was designed as a question-answer-scenario to elicit target words in three different focus structures (Figure 1): background, broad focus and contrastive focus. The target words were disyllabic girl names ($C_1V_1.C_2V_2$) with word stress on the first syllable.

Figure 1: *QA-scenario in a game-like setting.*
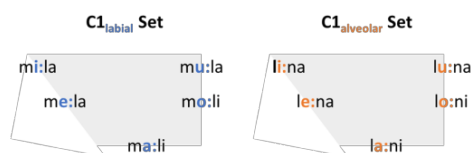

Figure 2: *Target words.*

Target words were embedded in a predefined sentence structure, such as: 'Die Schwester hat der Mela gewunken' *(The sister was waving to Mela)* or 'Der Opa hat die Mali verlassen' *(The grandpa has left Mali)*. In total 12 target words consisting of 5 different cardinal vowels were recorded in each focus condition (Figure 2).

2.3. Data processing and measurements

The speech data was displayed and annotated using the EMU-webApp (Winkelmann et al. 2017). Target words, syllables and the respective segments were determined according to the speech waveform and the wide-band spectrogram. For the articulatory gestures of the tongue body three landmarks were annotated in the vertical plane: onset, target and peak velocity (Figure 3). The following prominence markers on the acoustic level were calculated:

Acoustic syllable duration (ms): Temporal interval between the start of the first consonant C1 until end of the first vowel V1 of each target word. Longer syllables are associated with an increase in prominence.
Tonal height (st): The frequency difference between the starting point and the high target point of the F0 movement occurring in the vicinity of the target word. Positive values indicate a rising F0 movement, negative values a falling F0 movement. An increase in tonal height is associated with a higher degree of prominence.
Intensity (dB): The mean intensity of the vocalic segment V1 was computed in relation to the reference tone to control for speaker variation. Increased intensity values are associated with an increase in prominence marking.
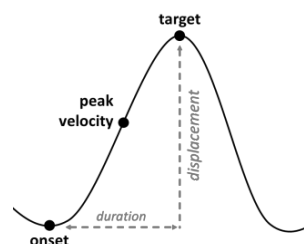

Figure 3: *Gestural landmarks and measurements.*

The articulatory analysis is limited to the production of the first vowel V1 as main domain of focus production. Tongue body movements were investigated by including the following variables (Figure 3, Browman & Goldstein 1986).

Gestural duration (ms): Temporal interval between the start of the vocalic gesture until the gestural target. Longer gestures are associated with an increase in prominence.
Displacement (mm): Spatial difference between onset and target of the gestural movement. Higher displacements are associated with the production of more peripheral vowels, leading to an increase in prominence.
Peak velocity (mm/s): Maximum velocity of the movement. Faster movements are associated with an increase in prominence, even though the role of peak velocity is inconclusive in the literature (Pagel et al. 2020).

For calculating the percentage change of the UPDRS III motor score from med-OFF to med-ON condition, the following calculation was used:

$$Percentage\ change = \frac{(V2-V1)}{V1}x100 \qquad (1)$$

In this equation V2 represents the value in med-ON condition, and V1 respectively in med-OFF condition.

2.4. Statistical analysis

The data was analyzed using R Studio (RStudio Team 2020) and the package lme4 (Bates et al. 2015) to perform linear mixed effect models. Continuous dependent variables of interest were fitted to two critical predictors: focus condition (background vs. broad focus vs. contrastive focus) and medication condition (med-OFF vs. med-ON). The fixed factor 'vowel' was additionally added when fitting models for articulatory data. Random intercepts were included for word and patient as well as random slopes for patient by medication condition. Effect of predictors were tested by comparing the test model (with predictor) to a reduced model (without predictor) via likelihood-ratio tests. P-values are based on these comparisons. Statistical output was corrected for multiple testing using the Dunn-Šidák correction, which lowers the alpha level to 0.0167.

3. Results

3.1. Motor ability

The motor performance was evaluated with the UPDRS III. In med-OFF condition a mean value of 34 (± 11), ranging from 16 to 48 (out of max. 108 points to reach), was determined. Under medication the mean score is 18 (± 6), ranging from 8 to 29 points. The calculated mean levodopa response from med-OFF to med-ON is - 42.52 (± 20.55).

3.2. Acoustics

Plots for the acoustic parameters are provided in Figure 4. The presentation of the results will combine the analysis of prominence production (background, broad focus, contrastive focus) with the influence of levodopa (med-OFF, med-ON).
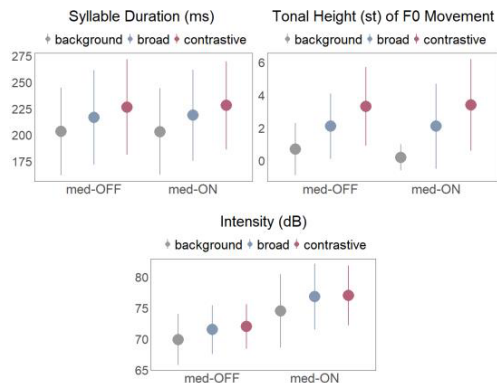
Figure 4: *Acoustic parameters of prominence marking.*

3.2.1. Syllable duration

Syllable durations increase comparing non-prominent and prominent productions in both conditions (Figure 4, top left). As the statistical model confirms syllable durations increases from background to broad focus (by 13 ms in med-OFF; by 16 ms in med-ON) and further from broad to contrastive focus (by 9 ms in med-OFF; by 10 ms in med-ON; $X^2(2)$=149.68; p<.001). No difference in syllable duration is found comparing medication conditions med-OFF and med-ON ($X^2(1)$=0.0788; p>.05).

3.2.2. Pitch height of F0 movement

Tonal height of F0 movement is adjusted in prominent productions (Figure 4, top left). The statistical model reveals an

effect of focus condition with increasing tonal height from background to broad (by 1.4 st in med-OFF; by 1.9 st in med-ON) and from broad focus to contrastive focus (by 1.2 st in med-OFF; by 1.3 st in med-ON; $X^2(2)$=284.75; p<.001). There is no significant difference between med-OFF and med-ON condition ($X^2(1)$=0.248; p>.05).

3.2.3. Intensity

Figure 4 (bottom) illustrates the intensity values within the vocalic segment. The figure gives the impression that intensity values are higher (background: by 4.6 dB, broad: by 5.3 dB, contrastive: by 5 dB) in med-ON condition. Nevertheless, the statistical model does not reveal a significant difference with corrected alpha level ($X^2(1)$=5.6578; p=0.01738). In contrast, the model states that intensity values differ between non-prominent and prominent productions ($X^2(2)$=193.88; p<.001).

3.3. Articulation

In this section, the gestural characteristics of the tongue body movement are presented (Figure 5). As before, the results will report whether there is an effect of medication and of focus structure for the parameters of interest.
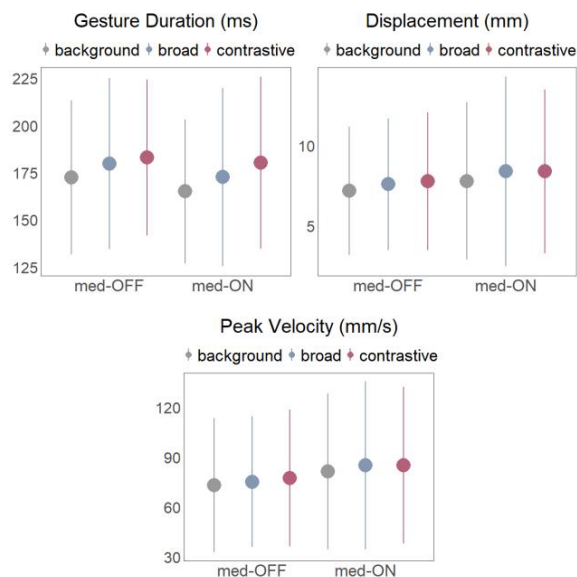
Figure 5: *Articulatory parameters of tongue body movement.*

3.3.1. Gestural Duration

The gestural duration of the vocalic gesture is presented in Figure 5 (top left). The mixed model reveals an effect of focus condition, increasing the duration from background to broad (by 7 ms in med-OFF; by 8 ms in med-ON) and further from broad to contrastive focus condition (by 3 ms in med-OFF; by 7 ms in med-ON; $X^2(2)$=18.951; p<.001). The model output indicates further, that the medication condition does not have an influence ($X^2(1)$=4.0895; p=0.04322).

3.3.2. Displacement

Although it seems that displacements are higher in prominent productions (Figure 5, top right), the statistical model does not reveal an influence of focus condition ($X^2(2)$=7.459; p=0.024) nor of medication condition ($X^2(1)$=3.5317; p>.05).

3.3.3. Peak velocity

The data for the parameter peak velocity is presented in the bottom row of Figure 5. While focus condition does not have an effect on peak velocity ($X^2(2)=3.3713$; p>.05), the peak velocity increases from med-OFF to med-ON condition (background: by 8 mm/s, broad: by 10 mm/s, contrastive: by 8 mm/s; $X^2(1)= 7.7488$; p<.01).

4. Discussion

Parkinson's disease as a movement disorder affects motor ability. Motor impairment is reflected in smaller, slower, less extended and unprecise movements of limbs and articulators. As speech production may depend on overall motor ability, the influence of levodopa, a drug which improves the motor ability in patients with PD, was tested. Patients were recorded in two conditions: without an effect of medication and with intake of the drug 'levodopa'. In addition, the speech material surveys the prominence production across three different focus conditions. The modulation of prosodic parameters was investigated on the acoustic level as well as on the articulatory level.

Effect of levodopa: On average, levodopa improved motor symptoms by 43 %. Only 2 out of 12 patients did not respond to the drug intake, as they had a response below 30 %. In this data, levodopa did not have an effect on the acoustic parameters: syllable duration, tonal height and intensity. However, there is a clear tendency that patients speak louder in med-ON condition possibly due to improved pulmonary function as well as stronger respiratory muscles, resulting in a better breath support (Monteiro et al. 2012). This leads to an increase in overall intensity of the target syllables. On the articulatory level, levodopa has an influence on the maximal velocity of the tongue body movement, as the tongue moves faster, probably due to less rigid muscles.

Prominence marking: Patients were able to produce prosodic prominence with and without medication. They adjusted parameters of speech production systematically to maintain prominence relations within and across accentuation. On the acoustic level, syllable duration, intensity and tonal height of rising F0 movement were modulated (Thies et al. 2020). When looking at the articulatory level, the duration of the gestural activation interval increases to signal prominence leading to longer vowel durations in prominent position. Surprisingly, the modulation in the spatial domain in terms of increasing amplitudes of the vocalic gestures were rather small in both conditions. This is probably due to the reduced vowel space reported for patients with PD in the literature. The lacking levodopa effect on prominence marking could also be explained by the fact that patients with PD can also achieve good motor performance in med-OFF, comparable to walking, as long as they focus on the task. A certain reserve can often be retrieved.

Variability: One factor that should be taken into account is the strikingly high variability of the data, indicating speaker specific behavior. Individual speaker behavior can be one reason why some levodopa influences could not be statistically validated. Some tendencies indicate that levodopa has an effect on tonal pattern as well as displacement and duration of tongue body movements. Tonal strategies seem to change especially in background and broad focus condition, comparing med-OFF and med-ON condition. Some patients cannot differentiate between prominent and non-prominent constituents in med-OFF, as they unexpectedly modulate F0. This behavior improves in med-ON, as pitch movements are reduced. In addition, patients increase their pitch accent inventory in broad focus condition from only rising to sometimes falling, comparing med-OFF and med-ON. Especially for gestural parameters, some effects were missed due to the fact that the presented data was pooled over vowels.

5. Conclusion

Patients with Parkinson's disease mark prosodic prominence by changing parameters of speech production systematically across and within accentuation to encode different degrees of prominence. The data suggests that levodopa has an influence on patients' speech performance by producing sounds more louder and increasing the velocities of articulatory movements.

6. Acknowledgements

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