The effect of Levodopa on articulation in Parkinson's disease: A cross-linguistic study

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ABSTRACT

Parkinson's disease (PD) is a neurological disorder that is characterized by a decay in global motor performance, manifest in tremor, abnormal gait, and dysarthria. PD dysarthria characteristics include monoloudness, pathological voice quality, and imprecise articulation. Standard treatment for relieving PD symptoms is the drug Levodopa, but it is currently unknown how it affects speech. We investigated the effect of Levodopa on the vowel space of 4 Dutch and 6 Slovenian PD participants. They recorded their speech on twenty occasions distributed over four days across 2-4 weeks. First and second formants of corner vowels [i-a-u] produced in isolated words were measured at acoustic midpoints of 4043 tokens. VAI [13], a metric of vowel space dispersion, was calculated for each speaker. VAI was not significantly affected by Levodopa in either language, which may indicate that the motor control underlying vowel articulation is not as sensitive to Levodopa as other motor symptoms.

Keywords: Parkinson's disease, vowel production, levodopa, dysarthria, vowel acoustics

1. INTRODUCTION

Parkinson's disease (PD) is a neurodegenerative disorder estimated to affect more than 10 million people worldwide, predominantly the elderly [9]. With the world-wide ageing of the population, the number of people diagnosed with Parkinson's disease will continue to increase. About three quarters of all PD patients experience not only motor symptoms such as bradykinesia, tremor, postural instability and freezing, but also speech difficulties in the form of hypokinetic dysarthria, which may occur at various stages of the disease. For these patients, voice quality is often affected first, followed by articulatory difficulties [4]. Their speech is characterized by monopitch, monoloudness, breathy voice and imprecise articulation [23].

At present, the gold standard for alleviating the symptoms of Parkinson's disease is the drug Levodopa, a natural substance that supplies dopamine to the brain. After the intake of Levodopa, patients experience less tremor and improved motor coordination (the ON state). However, the response of the body to Levodopa fluctuates over the course of the drug's lifecycle. Although the effect of Levodopa on general limb movement has been well-documented [10, 22], it is currently unclear if and how Levodopa affects speech production.

The research to date on the effect of Levodopa on articulation has produced varied and even contradictory findings. Some studies have found a small effect on consonant production and no effect on vowel production [14], whereas other studies have found the reverse effect [18] or no effect at all [21]. These differences can partly be explained by methodological factors such as the inclusion of different speech tasks, acoustic analyses, stage of disease [18, 14] and the timing of recording.

Dysarthric patients have been shown to produce an acoustically-reduced vowel space area (VSA) [16, 3]. Another acoustic index used to assess dysarthric speech is the Vowel Articulation Index (VAI), designed to reduce inter-speaker variability through normalization [13]. Because it has been argued that VAI is more sensitive to hypokinetic dysarthria than the VSA [17], the present study reports only VAI, although analyses of the same speech data with VSA showed a similar pattern.

In the present study, the speech of PD patients was measured at various time points throughout the day across four different days. The four days spanned a period of two to four weeks, and the recordings captured a wide array of speech tasks. The study was performed on two languages: Dutch and Slovenian, using comparable tasks and the same experiment design. Cross-linguistic research is especially important when dealing with pathological populations, as it allows us to identify whether the speech production difficulties are induced by the disease or by linguistic constraints [11].

In sum, the goal of this study is to shed more light on the effect of dopaminergic therapy on speech production in PD by:

- measuring a Vowel Articulation Index at several time points across a drug cycle;
- including two populations with different native languages;
- and making use of automatic tools to characterize dysarthric speech.

- Our hypothesis is that the VAI will be lower during the OFF state than during the ON state.

2. METHOD

2.1 Participants

In total, 10 participants (2 female) diagnosed with idiopathic Parkinson's disease were included. Participants were native speakers of either Standard Dutch (n=4), or Slovenian (n=6), recruited from Ljubljana and surrounds. No participant had a history of neurological disorder or depression, and they were all treated with Levodopa in the form of a pill. None of the participants had undergone Deep Brain Stimulation. Age of participants ranged from 57 to 71 for Slovenian speakers (mean = 61.0) and 61 to 83 (mean = 69.3) for Dutch speakers. The duration of disease ranged from 2 to 12 years (mean = 6.8 years) for Slovenian speakers and 5 to 9 (mean = 6.5) for Dutch speakers.

2.2 Procedure

After the experimenter delivered the equipment and provided the instructions for use, the participants recorded themselves on four different days spread over a period of 2 (Slovenian) or 4 (Dutch) weeks. Each recording day consisted of 5 recording sessions. These sessions were scheduled in such a way that they included the OFF state (15 minutes prior to Levodopa intake in the morning) and four ON states (60 and 120 minutes after the morning Levodopa intake, and 60 and 120 minutes after the late afternoon or evening Levodopa intake). Specific times were adapted to each participant's intake schedule. During every session, the participants performed four tasks: they read sentences containing target words out loud; they played two games designed to elicit semi-spontaneous speech with their partner; and they performed an oral diadochokinesia task. Here, we present an analysis of vowels produced in target words in the sentence reading task.

Whereas previous studies have only included measures made around the same time of day, or at most one measure made during the OFF state and one during the ON state, patients in the present study made recordings at five different time points distributed over four days. By doing so, we were able for the first time to investigate speech variation throughout a day. In order to achieve the most naturalistic setting possible, speech recordings were made at patients' homes without the presence of an experimenter. Since it is known that anxiety can worsen PD symptoms [6] this approach was least likely to influence the speech of the patient.

2.3 Experimental materials

The phonologies of the two languages in this study differ in some important ways which informed experiment design. Dutch (Germanic) uses 13 monophthongs and three phonemic diphthongs in a vocalic inventory which includes length distinctions [2]. Slovenian (Slavic) uses eight vowels and no phonemic diphthongs, and does not differentiate between long and short vowels [20]. It only has one open low vowel (/a/), where Dutch has two (/a:/ and /ɑ/). Both languages use lexical stress, which is realized as pitch accent in Slovenian.

Participants produced utterances with target words containing stressed corner vowels /a/, /u/ and /i/ in C_1_C_2 contexts. Liquids and sibilant fricatives were avoided at C_1 positions, where possible, to minimize coarticulatory influences on the vowel. C_2 was always a plosive consonant, and two words were used for every possible VC_2 combination. Dutch vowels were elicited in 30 disyllabic words, where stress always falls on the first syllable and the second syllable contains a schwa (e.g. *bieten* /ˈbi.tən/ 'beetroot'; *vaten* /ˈfa:.tən/ 'barrels'; *voeten* /ˈfu.tən/ 'feet'). Slovenian vowels were elicited in 36 words of variable syllable length (1 to 4), so that the target syllable always carried primary stress (e.g. *pita* /ˈpi.ta/ 'pie'; *solata* /so.ˈla.ta/ 'salad'; *tuba* /ˈtu.ba/ 'tuba (instrument)').

Target words were elicited in carrier phrases of the form "He has said __ again". The order of the carrier phrases was randomized for each session. In total, 70 to 80 repetitions of every target word were elicited from the Dutch participants, and between 50 and 60 repetitions from the Slovenian participants. In every session, approximately 10 tokens containing each target vowel were recorded for each Dutch participant and 6 instances for each Slovenian participant.

2.4 Recordings

All recordings were made by the participants themselves in their homes, without experimenters present. Shure WH20 headset microphones were used, connected to an iRig Pro Duo audio interface which digitized and transferred the speech recordings to a Motorola Moto C Plus smartphone. Recordings were automatically uploaded to a cloud server, allowing the experimenter to monitor remotely and provide assistance if needed. Permission to do so was obtained from the participants beforehand in order to comply with the new European GDPR regulations. Ethical approval for both studies was obtained via the Faculty of Arts Research Ethics Review Committee of the University of Groningen.

3. ANALYSIS

3.1 Software

For all Dutch recordings, word boundaries were identified in ELAN [19] and acoustic segmentation was conducted automatically using forced alignment with WebMAUS [22]. For all Slovenian recordings, word and sound segmentation of target words was done manually in PRAAT [1], as there is no trained acoustic model available for this language. Signal analysis was performed in MATLAB [7], and the statistical analysis was conducted in R [12] using mixed-effects regression modelling including the appropriate random intercepts and slopes (assessed via model comparison, using the ANOVA function in R).

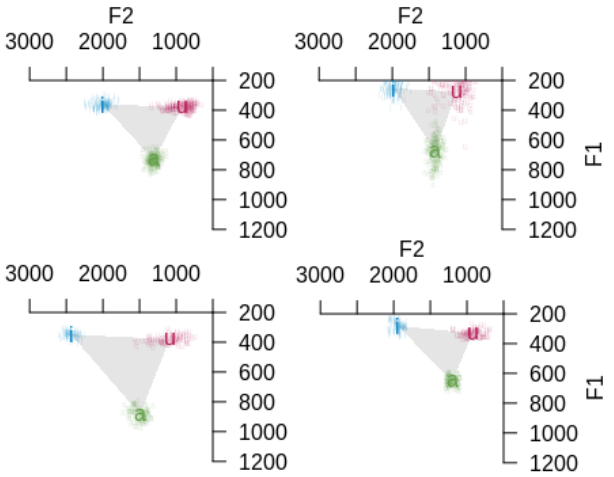
3.2 Pre-processing and data selection

In total 1321 tokens of /i/, 1330 of /u/ and 1392 of /a/ were analysed, amounting to approximately 130 exemplars of each vowel per participant. Formant frequencies were automatically tracked over each vocalic interval, estimated from 9 LPC coefficients using a 10ms analysis window and a 2ms window-shift, with configurable cut-off frequencies and lower and upper bounds for F3-F4 cut-off . After evaluation of several configurations, we found that for Dutch, the combination of a lower bound of 2400 Hz, an upper bound of 3900 Hz and 5 cut-off frequencies produced best results.

For Slovenian, a lower bound of 3000 Hz, upper bound of 4500 Hz and 8 cut-off frequencies was found to be optimal. First and second formant values were extracted from the temporal midpoint of each vowel token. Acoustic distributions of the entire vowel space for male and female speakers of each language are illustrated in Figure 1.

Since we used automatic formant tracking, we reduced outliers per speaker by excluding formant values exceeding 150% of the interquartile range below the first quartile or above the third quartile were removed from the dataset. In total, 142 values were excluded from the Dutch data. No values were excluded from the Slovenian data.

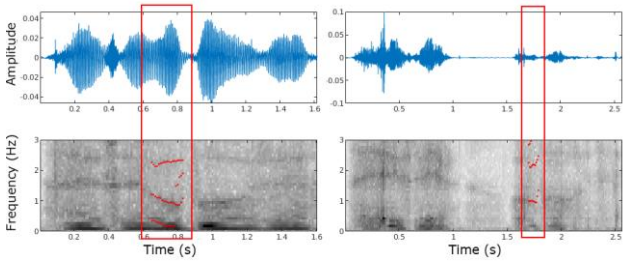
Figure 1: Vowel space areas for female (left), male (right), Dutch (above) and Slovenian (below) speakers. The top right picture shows the vowel space area of the participant discussed in section 3.3, after outliers had been removed.



3.3 Difficulties characterizing dysarthric speech

For one Dutch participant, 60 outliers had to be removed from the data. Further examination revealed that these outliers mainly occurred during intervals of devoiced speech. Because of the absence of a modal fundamental frequency, the formant tracker had difficulty reliably tracking formants in these segments, and often misidentified F2 as F1 (see Figure 2). Criteria for exclusion of outliers were refined (Sec 3.2) to cope with vowel tokens with erroneous formant values arising from this issue, so that after data cleaning, data from all speakers could be processed in the same way.

Figure 2: Automatic formant tracking in voiced and devoiced speech. Left: robust formant tracking in an utterance with a strong modally voiced component. Right: mis-tracking of F1 and F2 in devoiced dysarthric speech.



3.4 Quantifying Vowel Production

The Vowel Articulation Index (VAI) was calculated for each participant per session using Formula (1) [ref]. F2i represents the second formant frequency of [i]; F1a: the first formant frequency of /a/, etc. A larger value of VAI corresponds to configurations in which corner vowels are more dispersed in the F1-F2 plane, so that greater articulatory differences between a speakers' [i-a-u] vowels should be reflected in a larger VAI [ref].

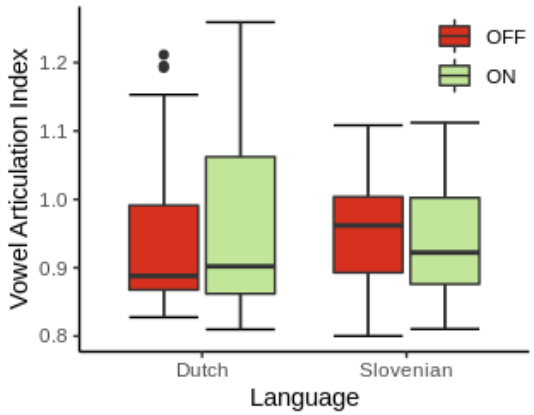
$$(1) \qquad VAI = \frac{F2i+F1a}{F2u+F2a+F1i+F1u}$$

4. RESULTS

4.1 VAI

VAI scores were calculated from mean F1 and F2 values for each vowel, per speaker, day, and session. The best linear mixed-effect regression model included state (included due to our hypothesis; ON or OFF; non-significant, β = 0.004; $F(1,188) = 0.35$, $p = 0.56$; see Figure 3) and sex (β = 0.19; $F(1,8) = 9.73$, $p = 0.014$) as fixed factors with random intercepts for each participant. Models including interactions between state and language or language separately did not significantly improve fit, nor did models that included session number (1, 2, 3, 4 or 5) as a predictor instead of state.

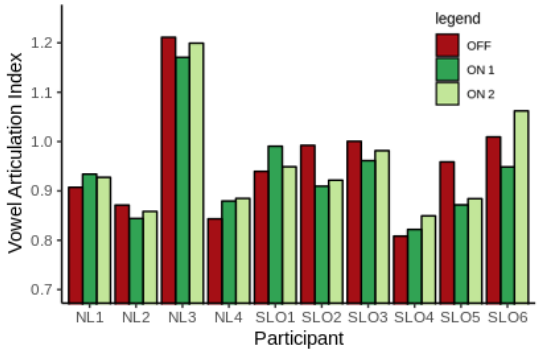
Figure 3: VAI measures for ON-OFF states in Dutch and Slovenian participants.

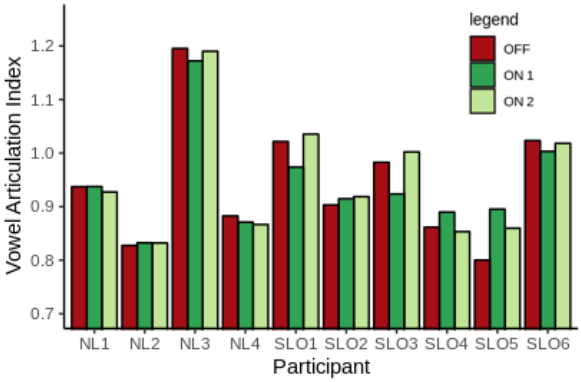


4.2 Individual variability

These data suggest that there was no effect of State on VAI; however, this might be due in part to the small sample size. Considerable individual variation can be observed in the relationship between VAI and state, when compared across three (out of five) timepoints of two (out of four) different days (Figure 4).

Figure 4: Individual variation in VAI measures for the OFF and two ON sessions. Top: Day 1; Bottom: Day 2.





5. DISCUSSION

The purpose of this study was to investigate the effect of Levodopa on articulation in PD. Articulation was assessed by computing VAI scores for each individual at 20 time points. Although previous studies have found evidence for a beneficial effect of Levodopa on phonation [24, 15], which we took as our hypothesis, we did not find a measurable effect on vowel articulation using this metric. We did, however, find different patterns in individual responses. It is possible that the articulation required for vowel production can be considered as one of the axial motor symptoms, which are less responsive to dopaminergic treatment (as suggested in previous work [17]).

The inclusion of two languages in our study provides more insight than one language could alone. As Dutch and Slovenian have different phonotactic constraints and sound inventories, the ability to draw the same conclusion for both strengthens it. Furthermore, most previous work on dysarthria in PD included only English as the subject of study, which makes generalization across languages problematic. The more cross-linguistic studies are carried out, using the same methods and measurements, the more can be discovered about hypokinetic dysarthria and articulation in PD, independent of language.

In conclusion, we believe that the absence of a clear effect of medicine state may be due to the fact that the articulation involved in vowel production is less responsive to dopamine. However, to make a stronger claim, additional research is required, measuring articulation directly, which should also include patients in earlier stages of the disease as that is when speech might be more responsive to Levodopa.

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