# Hypokinetic Dysarthria in Advanced Parkinson's Disease: Treatment Effects of Dopaminergic Medication and Deep Brain Stimulation

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**Abstract**

**Objective** Motor symptoms in Parkinson's disease (PD) can be effectively improved by dopaminergic medication and deep brain stimulation of the subthalamic nucleus (STN-DBS). However, the impact of these therapies on hypokinetic dysarthria is still controversial. The objective is therefore to elucidate the impact of dopaminergic medication therapy and DBS on hypokinetic dysarthria in PD on an acoustic level.
**Method** Semi-spontaneous speech of 37 patients with PD was recorded in two conditions: once before morning intake of dopaminergic medication and directly following dopaminergic administration. A subgroup of the PD participants (n = 9) underwent a third measurement after at least 6 months of bilateral STN-DBS. Additionally, speech of 37 healthy controls was recorded. Nine parameters representing speech dimensions that are affected in PD (i.e., tempo, prosody and voice quality) were extracted from the speech data using automatic acoustic voice analysis. These speech parameters were compared in three analyses: Parkinson vs. healthy controls, on-medication vs. off-medication and on-medication vs. DBS.
**Results** Speech production of PD patients off-medication was found to be significantly worse than that of healthy controls. Further, the results revealed no difference between speech production of PD patients before and after dopaminergic medication administration. Lastly, speech parameters were not found to differ following DBS when compared to the on-medication state in PD patients.
**Conclusion** Speech production of PD patients does not seem to be affected by either dopaminergic medication or STN-DBS. From the results it appears that hypokinetic dysarthria is not affected in the same manner as limb motor symptoms and therefore is not solely caused by dopaminergic depletion. More experimental investigations are needed to gain further insight into the impact of therapies and the underlying pathophysiology of hypokinetic dysarthria.

*Keywords*: Parkinson's disease; hypokinetic dysarthria; levodopa; Deep Brain Stimulation; acoustic analysis

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## Introduction

In approximately 90% of individuals with Parkinson's disease (PD) speech impairments, collectively referred to as hypokinetic dysarthria, are present (e.g. Saifer & Ali, 2018). Impairments related to speech can have a negative impact on the quality of life (Fabbri et al., 2017). Hypokinetic dysarthria includes impairments in speech dimensions such as prosody, fluency, phonation and faciokinesis (Mekyska et al., 2011) that can worsen as the disease progresses (Ho et al., 1999). As a result, deviations in measures such as intensity, pitch and speech rate are commonly visible in the acoustic signal of PD patients' speech (Duffy, 2013; Ho et al., 1999; Baker et al., 1998; Darley et al., 1969). It is as of yet unclear what pathophysiology underlies parkinsonian dysarthria, with both motor problems and cognitive deficits having been hypothesized to underlie speech problems in PD. Specifically, some studies suggest that speech problems are caused by hypokinesia of the speech apparatus (Ho et al., 1999; Smith & Caplan, 2018), while others consider higher order processing to play a role in the emergence of speech impairments through deficits in motor planning (Skodda et al., 2011). Yet it has also been suggested that while in early stages PD may be linked to dopaminergic depletion and therefore motor impairment, non-dopaminergic pathology of speech problems is involved in an advanced stage of PD (Rusz et al., 2016).

In line with this gap in knowledge, is the fact that research on the effect of pharmaceutical treatment on hypokinetic dysarthria has yielded mixed results. Parkinsonian medication consists of several forms of levodopa that are often combined with supplementary medication such as dopamine agonists (Santos et al., 2010). Some studies investigating the effect of dopaminergic medication report speech improvements after levodopa intake including fundamental frequency (F0) and jitter (Pinho et al., 2018), dynamic intonation (Skodda et al., 2011b) and F0 and speech intensity (only individually; Goberman et al., 2002). In contrast, others report no change in speech production either after short-term (Azevedo et al., 2013; Santos et al., 2010) or long-term dopaminergic medication treatment (Skodda et al., 2010; Tykalova et al., 2015).

In addition to administration of dopaminergic medication, deep brain stimulation (DBS) of the subthalamic nucleus (STN) is a commonly used treatment option for PD patients in an advanced stage of PD. Treatment with DBS involves the placement of electrodes in the brain that are coupled to a neuropacemaker to release electrical impulses. The STN is the most effective DBS electrode location to treat motor symptoms (Benabid, 2003). Like medication, the effect of DBS on hypokinetic dysarthria is still controversial. In the majority of research papers, DBS is reported to have an adverse effect on speech intelligibility. Examples are findings of deterioration of articulation, prosody and temporal parameters (Tsuboi et al., 2014) and reduced speech intelligibility (Aviles-Olmos et al., 2014; Tripoliti et al., 2011) after DBS.

While it is mainly reported that DBS causes speech deterioration, a study in 2008 found STN-DBS to leave the speech measures prosody, intensity and articulation unaffected. Furthermore, speech measures related to tremor were reduced by stimulation (d'Alatri et al., 2008). In contrast, one longitudinal study showed improvement in the speech measures intensity and fundamental frequency variability after STN-DBS, albeit in a sample limited to 7 patients (Dromey et al., 2000).

Whereas the goal of subscribing levodopa or applying DBS to PD patients is to alleviate or even remove motor symptoms, it is still unclear what the exact influence of these therapies on hypokinetic dysarthria is. The extent to which speech impairments in PD can be attributed to motor and/or cognitive impairments is also yet to be identified. The main aim of the current study is therefore to investigate the relation between both treatments and acoustic speech parameters based on semi-spontaneous speech to gain further insight into hypokinetic dysarthria and its pathophysiology. It is hypothesized that PD patients show speech impairments when compared to healthy controls. Further, because findings on a medication effect on speech have so far been mixed, it leaves an unanswered question this study attempts to clarify. Based on results of the majority of previous data, DBS is hypothesized to have an adverse effect on speech.

## Method

### *Participants*

A total of 37 Dutch native subjects (22 male, 15 female; mean age 62.2, SD 6.0) diagnosed with PD were included in the study. PD participants in the research underwent speech assessment twice: with (on-state) and without medication (off-state). This group of participants is referred to as the PD-med group. A subgroup of these patients (PD-DBS group) was tested an additional third time at least 6-months following DBS surgery. The PD-DBS subgroup consisted of 9 patients (4 male, 5 female; mean age 59.4, SD 6.7) with electrodes for DBS implanted bilaterally in the subthalamic nucleus. In addition to examining the effect of medication and DBS in PD patients, speech data of the PD group in the off-state was also compared

to 37 healthy controls (22 male, 15 female) of comparable age (mean age 62.2, SD 7.3). Exclusion criteria for all participants included: having speech or language impairments (in case of the PD group: only prior to PD onset), speech deficits such as stuttering, uncorrected hearing loss, a history of neurological or communication disorders other than PD or a current depressive episode or psychiatric diagnosis.

The study was approved by the Ethical Review Board of the University Medical Center Utrecht. Signed informed consent was obtained from all participants.

*Measures*

In order to compare different dopaminergic drug regimens of participants, the daily levodopa equivalent dose (LED) was calculated with conversion factors provided by Tomlinson and colleagues (2010). Motor functioning was assessed by taking scores of patients on the third section of the Movement Disorders Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS-III; Goetz et al., 2007). For the majority of PD participants, cognitive functioning was measured with the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005). Six patients were tested with the Scales for Outcomes in Parkinson's disease-Cognition (SCOPA-cog; Martinez-Martin et al., 2008). Details of all participants are provided in Table 1.

**Tabel 1** *Participant Characteristics*

| | **PD-med (N = 37)** | **PD-DBS (n = 9)** | **Healthy controls (N = 37)** |
|---|---|---|---|
| Age[a] (years) | 62.2 ± 6.0 | 59.4 ± 6.7 | 62.1 ± 7.3 |
| Education in years | 13.3 ± 2.5 | 14.6 ± 1.6 | 14.4 ± 1.8 |
| Disease duration[b] (years) | 9.6 ± 4.6 | 9.6 ± 2.3 | – |
| Daily LED (mg) | 1445.6 ± 612.6 | 817.0 ± 205.1[c] | – |
| MDS-UPDRS-III | On 20.3 ± 11.6<br>Off 40.6 ± 14.2 | On 16.9 ± 5.0<br>Off 41.8 ± 8.0 | – |
| MoCA | 26.2 ± 2.3 | – | – |
| SCOPA-cog | 23.7 ± 3.1 | – | – |
| Post surgery period (months) | – | 9.7 ± 3.9 | – |

*Note.* Values are mean ± SD. [a] Age of participants refers to age at the time of the first examination. [b] Disease duration is the period between diagnosis and the first examination. [c] Daily LED of the PD-DBS group is measured at the second assessment following DBS surgery. Abbreviations: LED = levodopa equivalent dose; MDS-UPDRS = Movement Disorder Society Unified Parkinson's Disease Rating Scale; MoCA = Montreal Cognitive Assessment; SCOPA-cog = SCales for Outcomes in PArkinson's disease-COGnition.

*Speech Examination*

Speech assessment consisted of a 5- to 10-minutes long interview with general questions to collect semi-spontaneous speech data. Testing took place in a quiet environment. The interview consisted of three sets of questions that were counterbalanced across participants and conditions. To record the produced speech of participants a TASCAM DR40 recording device was used, storing 16-bit .WAV files with a sampling rate of 44.1 kHz. Speech of the participant and interviewer were recorded with head-worn microphones separately on two tracks. Speech samples of patients in the PD-med group were collected twice: first prior to morning intake of levodopa (off-state), and a second time, approximately one hour after intake of levodopa (on-

state). Due to this time difference, dopamine levels were optimal at the second assessment (Goberman et al., 2002). The subgroup of PD patients that were included in the PD-DBS group underwent an extra follow-up recording performed within an interval of 6-16 months after DBS-surgery. During the follow-up recording under DBS stimulation, patients were on medication.

*Acoustic Speech Analysis*

Acoustic voice analysis of the speech data focussed on three main speech dimensions affected in hypokinetic dysarthria: tempo, prosody and voice quality. The temporal parameters included net speech rate (NSR), pausing rate and pausing duration. Prosody-related speech parameters that were extracted from the speech data were mean pitch, pitch variability and intensity variability. Voice quality was covered by the parameters jitter, shimmer and harmonics-to-noise ratio (HNR). Acoustic voice analysis was employed by extracting speech parameters from the recorded spontaneous speech data with the 'extended Geneva Minimalistic Acoustic Parameter Set' (eGeMAPS; Eyben et al., 2015) in openSMILE (Eyben et al., 2010). Exceptions are pausing duration and pausing rate, which were extracted with PRAAT software (Boersma & Weenink, 2018). All speech measures included in the current study have previously been investigated in PD patients (e.g. Elfmarková et al., 2016; Rusz et al., 2016). Definitions of the speech parameters are given in Table 2.

**Table 2** *Definitions of Speech Parameters*

| **Speech dimension** | **Speech parameter** | **Definition** |
|---|---|---|
| Tempo | Net speech rate (NSR) | Number of continuous voiced regions per second (pseudo syllable rate). |
| | Pausing rate | Number of pauses per second. |
| | Pausing duration | Mean length of unvoiced regions. |
| Prosody | Mean pitch | Logarithmic F0 on a semitone frequency scale, starting at 27.5 Hz (semitone 0). Arithmetic mean. |
| | Pitch variability | Logarithmic F0 on a semitone frequency scale, starting at 27.5 Hz (semitone 0). Coefficient of variation. |
| | Intensity variability | Estimate of perceived signal intensity from an auditory spectrum. Coefficient of variation. |
| Voice quality | Jitter | Deviations in individual consecutive F0 period lengths. |
| | Shimmer | Difference of the peak amplitudes of consecutive F0 periods. |
| | Harmonics-to-noise ratio (HNR) | Relation of energy in harmonic components to energy in noise-like components. |

*Note.* Definitions of speech parameters evaluated with automatic acoustic analysis. Definitions of speech parameters extracted by openSMILE are adopted from Eyben et al., (2015).

*Statistical Analysis*

The first study objective was to investigate differences between speech of PD patients in the off-state and healthy controls. For this goal, a multivariate analysis of covariance (MANCOVA) with group (PD vs. healthy controls) as between-subject factor was used to examine group differences for the speech parameters. A second MANCOVA was performed to study possible speech differences between the two medication states (on- and off-state) in PD patients. To detect a possible impact of sex and age, these sociodemographic variables were entered as a covariate in the analyses of group and medication state. Lastly, a MANCOVA was carried out to assess the influence of DBS therapy on the speech dimensions by comparing the PD-ON and PD-DBS measurements. During the follow-up recording after DBS-use (PD-DBS measurement), medication dosages were lowered due to DBS allowing for reduction of levodopa intake (Krack et al., 1997). To correct for the medication dosage during this recording, the percentage of LED reduction was included as a covariate in the analyses of therapy. Furthermore, duration of DBS-use was entered in the model as a covariate as well. DBS duration was included in the model as an interaction effect with therapy. Medication reduction could, however, only be included as a main effect due to an otherwise saturated model. Additional correlations between the speech parameters and medication reduction were carried out and compared between the PD-ON and PD-DBS condition in order to explore a possible interaction with medication reduction. Also, if a significant main- or interaction effect was detected, follow-up tests using correlation were performed to investigate the direction and size of the effect. Statistical analyses were conducted in the R environment (version 4.0.5, 2021). The threshold used to determine statistical significance was set at an alpha of .05.

**Results**

*PD vs. HC*

The results from the MANCOVA comparing PD patients in off-state with healthy controls showed that speech parameters significantly differed between the groups (Pillai's trace = .46, $F(9, 58) = 5.62$, $p < .001$). Specifically, compared to HC, PD patients showed increased intensity variability ($F(1, 66) = 8.79$, $p = .004$), speech rate ($F(1, 66) = 4.23$, $p = .044$), and pausing duration ($F(1, 66) = 14.92$, $p < .001$). The results of the main effects for group of the MANCOVA for each speech parameter are presented in Table 3.

In addition, the analysis revealed a main effect for age (Pillai's trace = .28, $F(9, 58) = 2.45$, $p = .020$) but no interaction effect with group (Pillai's trace = .20, $F(9, 59) = 1.65$, $p = .12$) on the combined speech parameters. Follow-up testing showed that pitch variability decreased with advancing age, $F(1, 66) = 33.21$, $p = .032$. Also, a significant interaction effect for age with group was found on pausing rate ($F(1, 66) = 4.72$, $p = .033$. Follow-up tests per group showed a negative correlation between age and pausing rate, only in the PD group ($r(35) = -.37$, $p = .02$).

There was a main effect for sex on the combined speech parameters (Pillai's trace = .67, $F(9, 58) = 12.94$, $p = .020$), but no interaction effect with group was found (Pillai's trace = .23, $F(9, 58) = 1.92$, $p = .067$). For mean pitch and pitch variability, a significant main effect for sex was found, $F(1, 66) = 52.78$, $p = < .001$ and $F(1, 66) = 30.21$, $p = < .001$ respectively. Female participants showed a higher mean pitch ($M = 27.47$, $SD = 2.37$) and pitch variability ($M = 0.24$, $SD = 0.05$) than male participants ($M = 23.44$, $SD = 2.52$) and ($M = 0.18$, $SD = 0.03$). Also, for jitter a significant main effect for sex was found with females ($M = 0.08$, $SD = 0.02$) showing more jitter than males ($M = 0.07$, $SD = 0.02$), $F(1, 66) = 6.08$, $p = .016$.

*PD-on vs PD-off*

The MANCOVA testing for differences between the two medication states (on and off) revealed no statistically significant effect on the speech parameters, Pillai's trace = .15, F(9, 58) = 1.15, p = .34. In other words, there were no differences between the on-state and the off-state regarding tempo, prosody and voice quality dimensions of patients with PD. Results of the main effects for each speech parameter of the MANCOVA for medication state can be found in Table 3.

*PD-on vs PD-DBS*

The MANCOVA on the influence of DBS on the different speech variables, did not reveal a main effect for therapy (medication or DBS) on the combined speech parameters (Pillai's trace = .77, $F(9, 3) = 1.14$, $p = .51$). This indicated that no effects of therapy were found on the individual speech parameters of the temporal, prosodic and voice quality dimension. Table 3 depicts the main effects of the MANCOVA for therapy separately for each speech parameter.

In the model, percentage of medication dose reduction following DBS and duration of DBS-use were entered as covariates. The analyses revealed no main effects on combined speech parameters for either

medication reduction (Pillai's trace = .78, $F(1, 11) = 1.19$, $p = .49$), or DBS duration (Pillai's trace = .73, $F(1, 11) = 0.90$, $p = .60$). For DBS duration, no interaction effect with therapy could be detected, (Pillai's trace = .34, $F(1, 11) = 0.17$, $p = .98$). A main effect of medication reduction was found on the individual speech parameter pausing duration, $F(1, 11) = 8.04$, $p = .016$, with increasing medication reduction relating to shorter pausing duration. For DBS duration, main effects were found on all voice quality parameters. Longer DBS durations related to an increase in jitter, $F(1, 11) = 10.51$, $p = .008$ and shimmer, $F(1, 11) = 5.87$, $p = .033$ and a decrease in HNR, $F(1, 11) = 5.25$, $p = .042$.

As before-mentioned, the variable medication reduction could not be added to the model as an interaction effect. In order to gain more insight into the possible interaction between medication reduction and therapy, additional correlations were carried out. Correlations were performed between medication reduction and the speech variables. This was done in both the PD-ON and the PD-DBS condition to investigate if a difference could be detected between the conditions. As the correlations were not significant (all $r$s < -.49; $p$s >.18), it could not be demonstrated that medication reduction affected the analyses on speech differences between the PD-ON and PD-DBS condition.

**Table 3** *Results of Acoustic Analysis*

| Speech parameter | Healthy controls (HC) | Parkinson's disease (PD) | | | | Group comparisons: P-value | | |
|---|---|---|---|---|---|---|---|---|
| | (N = 37) | Off (N = 37) | On (N = 37) | DBS (N = 9) | On (N = 9) | PD vs HC | On vs Off | DBS vs. On |
| Net speech rate | 1.48 ± 0.36 | 1.65 ± 0.36 | 1.52 ± 0.35 | 1.84 ± 0.52 | 1.69 ± 0.42 | **.044*** | .086 | .582 |
| Pausing rate | 4.86 ± 5.37 | 6.97 ± 3.61 | 5.84 ± 3.53 | 7.40 ± 3.14 | 6.78 ± 4.87 | .088 | .145 | .779 |
| Pausing duration | 0.21 ± 0.07 | 0.28 ± 0.10 | 0.32 ± 0.13 | 0.30 ± 0.17 | 0.31 ± 0.12 | **<.001**** | .149 | .457 |
| Mean pitch | 24.70 ± 3.28 | 25.5 ± 3.00 | 26.23 ± 2.99 | 25.93 ± 3.01 | 26.07 ± 1.92 | .130 | .239 | .897 |
| Pitch variability | 0.21 ± 0.04 | 0.20 ± 0.05 | 0.21 ± 0.05 | 0.22 ± 0.04 | 0.23 ± 0.05 | .595 | .462 | .346 |
| Intensity variability | 0.91 ± 0.14 | 1.00 ± 0.11 | 1.06 ± 0.18 | 0.96 ± 0.30 | 1.06 ± 0.26 | **.004**** | .052 | .185 |
| Jitter | 0.08 ± 0.02 | 0.07 ± 0.02 | 0.07 ± 0.02 | 0.07 ± 0.02 | 0.08 ± 0.02 | .767 | .310 | .394 |
| Shimmer | 1.55 ± 0.18 | 1.44 ± 0.28 | 1.37 ± 0.23 | 1.34 ± 0.23 | 1.40 ± 0.18 | .054 | .176 | .332 |
| HNR | 3.75 ± 1.87 | 4.40 ± 2.03 | 4.85 ± 1.76 | 4.97 ± 1.81 | 4.73 ± 1.36 | .114 | .319 | .467 |

*Note.* Data are mean ± standard deviation. P-values are given for each statistical comparison: group (PD vs HC), medication state (on- vs off-state) and therapy (DBS vs on-state). Statistically significant differences are indicated with asterisks (* significance at $p < .05$; ** significance at $p < .01$; *** significance at $p < .001$).

**Discussion**

The main purpose of the study was to investigate the impact of DBS and Parkinsonian medication on the production of speech in patients in an advanced stage of PD. To study this, firstly, speech of 37 PD patients was compared to 37 healthy controls with regard to multiple speech parameters that represent the speech dimensions tempo, prosody and voice quality. Next, in the same way, speech of all PD patients was compared between conditions with and without medication. Finally, for 9 PD patients, speech in the on-medication condition was compared to speech after at least 6 months of DBS-use.

*Parkinsonian Speech Outcomes*

Comparisons between the PD group and the healthy control group revealed several differences between the groups. In the temporal dimension, differences in two speech parameters were found. The first was net speech rate, which was found to be significantly higher in PD patients compared to healthy controls. Higher speech rate in PD patients has been found in other studies examining continuous speech as well (De Letter et al., 2006; Ho et al., 2008; Rusz et al., 2022). Additionally, Skodda and Schlegel (2008) have also reported a higher speech rate in PD patients when measured towards the end of a reading task, representing acceleration in the course of speaking. Increased speech rate as found in PD patients presumably reflects oral festination: a tendency to accelerate when performing repetitive movements that has previously been found to impact gait and, as demonstrated here, also affects speech. It has to be noted that despite similarities with previous papers, data from earlier literature is inconsistent: in some research no deviation from healthy speakers (Duez, 2006) or even a reversed effect, namely significant reduction in speech rate of PD patients (Martínez-Sánchez et al., 2016) is reported.

The second significant finding in the temporal speech dimension was the prolonged pausing duration found in PD patients. This finding is in line with the general agreement that PD patients produce pauses with a longer duration compared to healthy speakers (Nishio & Niimi, 2001). Longer pausing duration likely reflects hypokinesia of the speech apparatus which makes it hard to initiate speech production (Rusz et al., 2022). In contrast to pausing duration, pausing rate was not found to significantly differ between speech of PD patients and healthy controls. There is however no consensus on pausing rate in individuals with PD, with literature on both increased (Torp & Hammen, 2000) and reduced pausing rate (Skodda & Schlegel, 2008) being present. Other studies even demonstrate high interindividual variability concerning pausing rate (Metter & Hanson, 1986) which might explain why no deviations were detected for this speech parameter in the current study.

Results from the prosodic dimension demonstrated that intensity variability was higher in PD patients than healthy controls. Changes of intensity in speech are an indication of a deficit in prosody (Goberman et al., 2002). The current finding concerning intensity variability is not in agreement with previous studies reporting reduced variability of loudness (monoloudness) in speech of PD patients (e.g. Jimenez-Jimenez et al., 1997; Rusz et al., 2022). Further, in contrast to previous work, no differences were detected with regard to the other two prosodic parameters mean and variability of pitch.

Lastly, none of the speech parameters of the voice quality dimension (i.e., jitter, shimmer and HNR) were found to be impaired in PD patients as compared to HC. The results contradict the expected reduced voice quality in speech of PD patients that was previously reported (Santos et al., 2010). Nevertheless, not all papers find this reduction of voice quality. An example is a paper by Rusz et al. (2022) in which no deviation in voice quality for PD patients was found either. To summarise, in two out of the three investigated speech dimensions, tempo and prosody, PD patients were found to produce speech significantly different than healthy controls.

*Influences on Speech Outcomes Following Medication and DBS*

From the comparisons within PD patients in two medication conditions, it appeared that speech production was not significantly affected by dopaminergic medication in PD patients. The lack of an effect of levodopa is in accordance with other studies failing to detect an impact of Parkinsonian medication on speech (e.g. Elfmarková et al., 2016; Tykalova et al., 2022). In addition to this, and in contrast with existing data that reports deterioration of hypokinetic dysarthria (Tsuboi et al., 2014; Tripoliti et al., 2011), no effect of DBS on the studied speech dimensions could be detected. The present results do however confirm the findings of d'Alatri et al. (2008) who studied the prosodic and temporal dimension and found no effect of STN-DBS on speech production (d'Alatri et al., 2008). Next to these results, none of the socio-demographical factors studied (age, sex, DBS duration and reduction of L-dopa dose after DBS) were affecting speech changes due to L-dopa administration or DBS. The lack of an interaction between the reduction of medication dose

post surgery, and speech change caused by DBS, further strengthens the result that medication does not influence speech production in the current study. Next to this, even though no effect of DBS was found after comparing conditions, main effects were found for DBS duration on all three speech parameters related to voice quality. This might indicate that longer DBS duration negatively impacts voice quality.

*Pathophysiology of Hypokinetic Dysarthria*

In contrast to earlier findings on motor symptoms in PD (Benabid 2003; Tomlinson et al., 2010), hypokinetic dysarthria thus appears to be non-responsive to pharmacological treatment and DBS. These outcomes provide information about the underlying pathophysiology of hypokinetic dysarthria. Previously, it has been suggested that motor symptoms and speech symptoms have shared pathophysiology. As motor symptoms in PD originate from hypokinesia and bradykinesia of limb motor control (Ackermann et al., 1997), it has been theorized that a similar underlying impairment causes speech production issues, which is described as hypokinesia of the speech apparatus (Rusz et al., 2013, 2022). Hypokinesia of the speech apparatus would result in less range of motion in speech muscles which induces undershooting of articulation (Goberman et al., 2002).

The present results do not show an effect of dopaminergic treatment or DBS on speech production. Therefore, at first glance, the outcomes do not appear to support the abovementioned theory of hypokinetic dysarthria resulting from hypokinesia of the speech apparatus. However, other axial symptoms, aside from hypokinetic dysarthria, have previously been found to be poorly responsive to these therapies as well (Fasano et al., 2015). This suggests that motor and speech symptoms do not completely share the exact same pathophysiology. Indeed, this is confirmed by papers revealing differences in neural circuits at an organisational level: while limb control is performed by corticospinal pathways, speech production is controlled by corticobulbar circuits (Dromey et al., 2000). Even though similarities might exist, the difference in anatomical-functional pathways could explain why both therapies do not impact speech while motor symptoms are ameliorated effectively. The present results thus confirm research in which it is proposed that pathophysiology of hypokinetic dysarthria might partly overlap with that of motor symptoms, but is not entirely similar (Pinto et al., 2004; Smith & Caplan, 2018). Subsequently, in some papers, it is suggested that the absence of an effect of medication or DBS can be attributed to nondopaminergic pathology (e.g. d'Alatri et al., 2008; Brabenec et al., 2017). In addition, it has already been established that speech production is among the axial motor symptoms that are less dependent from global motor control and hence levodopa, in an advanced disease stage (Espay et al., 2001; Rusz et al., 2016; Jacobi et al., 2019). As only patients in an advanced stage of PD were enrolled in the present study, this could explain why neither medication nor DBS had an effect on speech production.

*Alternative Explanatory Factors*

Although general theories on the underlying pathophysiology of hypokinetic dysarthria are developed, high interindividual variability is often reported in papers on how Parkinsonian speech is influenced by DBS (Tripoliti et al., 2011) and levodopa (Elfmarková et al., 2016; Skodda et al., 2013). This variability might explain why neither of the therapies was found to affect speech on a group level, while an effect might have been present in individual patients. Indeed, speech change due to medication and DBS was found to be variable between individuals in almost all speech parameters: both positive and negative changes were observed in individuals. It is however important to emphasise that no statistical models were used to examine individual variation.

Another possible explanation for the lack of an effect of dopaminergic medication is the fact that the enrolled patients were chronically treated with levodopa. Some researchers argue that even though assessment in the off-state took place prior to the morning intake of medication, an effect of medication could still be present (Elfmarková et al., 2016). This might have reduced differences between the on- and off-state.

Finally, the finding that DBS has no impact on hypokinetic dysarthria could be influenced by the settings of the DBS. Although this is not very likely, previously, indications have been found that side-effects of DBS, such as speech deterioration, can be limited by ensuring that tuning of basal ganglia circuits is balanced bilaterally (D'Alatri et al., 2008).

*Limitations*

There are some limitations that might have impacted the obtained results. First of all, a strong point of the current study is the fact that in the DBS group speech was assessed prior to and following DBS. However, an additional post-surgery measurement

where DBS stimulation was turned off was not included. Adding such a condition would allow for eliminating the possible effect of surgery. Further, even though evaluation after DBS-use was done within-subjects, the number of participants undergoing this speech assessment might have been too limited to make firm conclusions about DBS-effects on speech. Next to this, patient selection criteria could explain the discrepancy between the current results and previous work reporting an effect of DBS or, in some cases, medication. Patients were enrolled in the current study because they were candidates for DBS based on their impairment in motor function. Consequently, severity of speech impairment was irrelevant for inclusion in the experiment. The lack of an inclusion criterion on the presence of hypokinetic dysarthria may therefore have impacted the obtained results (d'Alatri et al., 2008). This is especially likely as it was found that the included PD patients only significantly differed from healthy controls on three individual speech parameters. This potentially reflects the inclusion of patients without severe dysarthria. Without severe speech problems, there may have been little room for improvement if speech were to be responsive to DBS or dopaminergic medication. A last limitation that warrants prudence in data interpretation has to do with the effect of progression of PD. Although the duration of DBS-use was controlled for in the statistical model, speech may have changed between the on-state measurement and the DBS surgery, possibly influencing the obtained results.

*Directions for Future Research*

In future research, the so far inconsistent results regarding impact of medication and DBS may be resolved by paying attention to factors causing this variation. These are for example the sample size, disease severity of patients, electrode location of DBS and differences in methodology such as time intervals of speech assessments and the way in which speech is collected and analysed. Also, there should be more focus on results in individual patients as many papers report high interindividual variation. Accounting for these factors could make research more consistent and therefore more reliable and comparable. As a result, more informative conclusions can be drawn from papers in this field. On a wider level, developments with regard to acoustic analysis could lead to application of the technique in clinical settings by using it for diagnosis and monitoring of disease progression, and even for programming of DBS settings and estimating optimal medication doses.

**Conclusion**

Patients with PD were found to display speech impairments in the temporal and prosodic speech dimensions. None of the investigated speech parameters was affected by dopaminergic therapy or STN-DBS, which are therapies that are effective for motor symptoms. The results thus indicate that the pathophysiology of impairments in speech function in PD is not entirely similar to that of global motor function. Consequently, this indicates that nondopaminergic pathways might play a role in speech production problems in advanced PD. Extending knowledge in the future on the impact of therapies and the underlying neurobiology of hypokinetic dysarthria is important to find the optimal balance between STN-DBS, dopaminergic medication and forms of rehabilitation. Such developments are required to reduce speech side-effects, which can ultimately contribute to improvement of quality of life in PD patients.

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