

Speech Characteristics of Patients with Parkinson's Disease—Does Dopaminergic Medications Have a Role?

Valiyaparambath Purushothaman Vandana¹ Jeevendra Kumar Darshini¹ Venkappayah Holla Vikram² Kamble Nitish² Pramod Kumar Pal² Yadav Ravi²

¹ Department of Speech Pathology and Audiology, National Institute of Mental Health and Neurosciences (NIMHANS), Bengaluru, Karnataka, India

²Department of Neurology, National Institute of Mental Health and Neurosciences (NIMHANS), Bengaluru, Karnataka, India Address for correspondence Valiyaprambath Purushothaman Vandana, PhD, Department of Speech Pathology and Audiology, National Institute of Mental Health and Neurosciences (NIMHANS), Bengaluru, Karnataka 560029, India (e-mail: vpvandana@qmail.com).

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Abstract

Objective The present study aimed to investigate the effects of dopaminergic medication on voice, speech motor functions, and motor impairment in patients with Parkinson's disease (PD).

Materials and Methods Twenty-five individuals (16 males and 9 females) with PD underwent comprehensive assessment of voice, speech, and motor functions in levodopa medication ON and medication OFF conditions. Age- and gender-matched healthy controls were recruited to compare speech and acoustic parameters. Multi-Dimensional Voice Program (MDVP) from Computerized Speech Laboratory (Model: 4500) was utilized for acoustic analysis of voice and the Voice Handicap Index (VHI) for the self-assessment of vocal function. Frenchay Dysarthria Assessment (FDA-2) and Unified Parkinson's Disease Rating Scale-III (UPDRS III) were used to evaluate speech motor and motor functions, respectively.

Statistical Analysis The mean and standard deviation were used as descriptive statistics measures. Raw scores were obtained for FDA-2, DRS, VHI, MDVP parameters, and UPDRS-III in either medication condition. The Wilcoxon signed-rank test was performed to determine the statistical significance of the above measures in both genders across the medication conditions. Spearman's rank correlation coefficient was used to determine the relationship between motor speech function and motor impairment and between VHI and MDVP parameters across both medication conditions. The interrater reliability rating was established using Cohen's kappa.

Keywords

- Parkinson's disease
- dopaminergic medication
- ► speech
- ► Voice Handicap Index

ditions. The interrater reliability rating was established using Cohen's kappa. **Results** An improvement in lip and laryngeal functioning was found in the medication ON over medication OFF state in both males and females with PD. A few frequency and amplitude-related measures improved in the medication-ON state over the medication-OFF state. UPDRS-III scores reduced from the OFF state to the ON state, and no change in dysarthria severity or VHI was found in either gender or medication condition. No correlation was found between speech motor function and motor

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function or between VHI and acoustic parameters of voice in either medication condition.

Conclusions Improvement in motor symptoms with levodopa was predominantly observed when compared with the minor improvements in a few aspects of speech motor function and vocal parameters. The results of this study suggest the need for speech therapy as a nonpharmacological treatment method for speech impairments in PD.

Introduction

Parkinson's disease (PD) is a condition associated with the degeneration of dopaminergic neurons in the basal ganglia and associated areas of the brain. Reduction in dopamine leads to several motor and nonmotor symptoms.¹ The primary motor symptoms associated with PD include resting tremor, rigidity, akinesia (bradykinesia), and postural deficits. In addition, PD is associated with dysphagia, cognitive deficits, depression, and hypokinetic dysarthria. Hypokinetic dysarthria is characterized by hypophonia, abnormal speech rate and voice quality, imprecise consonants, and reduced pitch and loudness variation in connected speech.² Voice problems may be seen in as many as 89% of individuals with PD. They have been described qualitatively as breathy, hoarse, tremulous, abnormally pitched, and having a reduced pitch range.³

Individuals with PD are commonly treated with levodopa, which increases their dopamine content.⁴ It is reported to have beneficial effects on motor symptoms, but its effect on speech motor control is inconclusive.⁵ Some studies have found positive effects of levodopa on speech in terms of improved loudness, speech intelligibility, and articulation.^{6–8} However, other studies did not report a consistent positive outcome in speech with the intake of levodopa.^{2,9–13}

A survey of the literature reveals that there is considerable variability in the assessment procedures to investigate the speech characteristics of individuals with PD. This variability is considered in terms of only the perceptual evaluation of speech or the acoustic analysis of the vocal function or investigating specific subsystems for speech such as respiratory or vocal function before (medication-OFF) and after (medication-ON) the intake of levodopa.^{2,9,10,14} Although these studies contribute to the understanding of the changes in the specific speech subsystems, a comprehensive understanding of the alterations, if any, in the overall speech characteristics secondary to the intake of dopaminergic medications, is required. An investigation that employs a

standardized protocol to investigate the specific speech motor functions at rest, during sustained postures, and during speech production, along with the perceptual, acoustic, and the patients' perception of their global vocal function in the ON and OFF conditions can contribute to a holistic understanding of the effect of dopaminergic medications on the speech characteristics of these patients.

Thus, aim of this study was to investigate

- (1) The role of dopaminergic medication in patients with PD on vocal, speech motor function, and motor impairment by acoustic and perceptual analysis of voice.
- (2) The relationship between speech motor functions, vocal parameters, and motor impairment in individuals with PD in the ON and OFF conditions.

Methods

Twenty-five individuals (16 males and 9 females) with PD in the age range of 26 to 75 years were recruited from the Movement Disorder Clinic in a tertiary hospital in India. Patients with PD who were on medical management (i.e., levodopa medications, minimum dosage: 200 mg) without any other associated neurological or medical condition and who spoke any of the Indian languages with a working knowledge of Hindi or English were included in the study. Patients with dementia, apathy, psychiatric disorders, hearing impairment, or language disorders, and those aged >75 years were excluded from the study. A complete medical history and a thorough clinical examination of all the patients were done by a neurologist. Evaluation of the speech characteristics was done by an experienced speech-language pathologist (SLP). The demographic profile of individuals with PD is described in -Table 1. Individuals with PD have a range of disease severities. Of the 25 participants, 7 had no speech impairment, 9 had slight speech impairment, 6 had mild speech impairment, and 3 had moderate speech impairment based on subsection 2.1 of the Unified Parkinson's Disease Rating Scale-III (UPDRS-III), a 31-item rating scale

Tab	le 1	Demograp	hic c	letails	of	the	indiv	idual	s witl	n PD
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SI no.	Gender	n	Mean age	Age at onset	Duration of disease
1.	Males	16	57.93 ± 7.88	46.61 ± 8.45	11.30 ± 4.19
2.	Females	9	54.55 ± 10.94	56 ± 10.14	9.74 ± 4.59

Abbreviation: PD, Parkinson's disease.

that evaluates behavior, mentation, mood, motor functions, and activities of daily living (ADL). None of the individuals with PD reported severe speech impairment (score of 4 on UPDRS subsection 2.1). Reports of PD-related speech impairment were relatively similar in males and females and none had received speech or language interventions prior. The mean UPDRS subsection 2.1 score was 0.79 for females and 1.09 for males, both of which are indicative of "slight" impairment.

Twenty-five volunteers (16 males [mean age = 56.87 ± 8.71] and 9 females [mean age = 54.88 ± 13.33] years) with no past history of neurological, psychiatric, or speech-language disorders were recruited as healthy controls (HC). Only speech (motor speech and voice) evaluation was done for the HC group and no follow-up testing was suggested. The participants in both the groups, that is, PD and HC groups did not differ significantly for age. All participants provided written informed consent. The study complied with the Helsinki Declaration and was approved by the institutional ethics committee.

General Procedure

The participants with PD were evaluated for vocal, speech, and motor impairments in two conditions: medication ON and medication OFF states. The ON state refers to the condition 1 hour after intake of the first dose of levodopa in the morning, while the OFF state refers to the condition 12 hours following the withdrawal of levodopa. Each participant with PD was tested first off and then on medication.

Evaluation of Motor and Speech Impairments

Motor skills were assessed using the UPDRS-III. This was administered by a neurologist at the Movement Disorders Clinic. Speech motor function was evaluated by administering the Frenchay Dysarthria Assessment-2 (FDA-2; Pam Enderby and Rebecca Palmer, 2008).¹⁵ It is a standardized 9-point rating scale for the evaluation of motor speech systems in the following domains: reflex, respiration, lips, tongue, soft palate, larynx, and speech intelligibility on a 5-point rating scale (a–e) where "a" is normal and "e" indicates profound severity. The severity of dysarthria was established using the Dysarthria Rating of Severity (DRS)¹⁶ by an experienced SLP.

Perceptual Evaluation of Speech

The perceptual judgment of speech intelligibility across the two medication conditions, that is, ON-OFF, was done by administering the Speech Intelligibility Rating Scale developed at Ali Yavar Jung National Institute of Speech and Hearing Disabilities, Mumbai (2003). It is a 7-point rating scale, where 0 represents normal speech intelligibility and 6 poor speech intelligibility. The speech samples recorded in both medication conditions were randomized, anonymized, and subjected to perceptual analysis by three SLPs. They were aware of the PD diagnosis of the patients but were blinded to the states (Medication-ON and Medication-OFF) in which the samples were recorded.

Self-Assessment of Global Vocal Function

Patients were asked to evaluate their vocal function by the administration of Voice Handicap Index-10 (VHI-10,¹⁷ which is a 10-item questionnaire evaluating the patients' self-perception of vocal difficulties across three domains: (a) functional, (b) physical, and (c) emotional on a 5-point rating scale, that is, 0—never and 4—always. The maximum score is 40, and a score >11 is considered abnormal.

Acoustic Analysis of Voice

The acoustic analysis of voice was performed by recording the voice onto the Multi-Dimensional Voice Program (MDVP) module on the Computerized Speech Laboratory (CSL; Model: 4500) for analysis. Each patient was seated in the upright position and instructed to phonate /a/ at a pitch and loudness level comfortable for each of them for a minimum duration of 3 second. For acoustic analysis, the sustained vowel /a/ was selected as it enabled the understanding of laryngeal function primarily by reducing the effect of coarticulation that would otherwise be a factor in connected speech. Further, this task requires limited participant training. To control for the phonatory onset and offset, only the midsection of the vowel was considered for analysis. The recording of the speech signal was done by placing the microphone 10 cm away from the participant's lips. Acoustic parameters considered for analysis were the average fundamental frequency (F0) in Hertz, period to period variability in pitch-absolute jitter (µs), frequency tremor intensity index in percent(FTRI%), period to period variability in amplitude-shimmer (dB), and soft phonation index (SPI). The recording was performed in a well-lit and soundproof room.

Data Analysis

Descriptive statistics were used to determine the mean and standard deviation (SD) for the values obtained in the FDA-2, DRS, VHI, MDVP parameters, and UPDRS-III in either medication condition. To determine the statistical significance of the above measures in both genders across the medication conditions, Wilcoxon signed-rank test was performed. To determine the relationship between motor speech function and motor impairment and between VHI and MDVP parameters across both medication conditions, Spearman's rank correlation coefficient was used. The interrater reliability rating was established using Cohen's kappa. Statistical analysis was performed using SPSS 20.0. Level of Statistical significance was set at p < 0.05.

Results

Comparison of Acoustic Parameters between HC and Individuals with PD

There was a significant difference between HC and PD with respect to lip function, laryngeal function, and speech intelligibility (p < 0.05) in the FDA-2. The acoustic parameters of F0 (Hz) for males and SPI for females were also significantly different (p < 0.05) between the two groups.

	Medication-OFF		Medication-ON		
	Mean	SD	Mean	SD	p-Value
Reflexes (M)	8.02	1.17	8.15	1.07	0.04 ^a
(F)	8.32	0.75	8.32	0.75	1.00
Respiration(M)	7.43	1.38	7.62	1.16	0.06
(F)	7.55	1.23	7.55	1.26	1.00
Lips (M)	7.34	0.80	7.66	0.72	0.01 ^a
(F)	7.21	0.94	7.83	0.83	0.01 ^a
Palate (M)	8.61	0.61	8.68	0.49	0.10
(F)	9.00	0.00	9.00	0.00	1.00
Laryngeal (M)	6.15	1.08	6.56	1.07	0.01 ^a
(F)	6.02	1.31	6.52	1.08	0.01 ^a
Tongue (M)	7.24	0.85	7.37	0.91	0.06
(F)	7.61	1.13	7.67	1.08	0.31
Intelligibility(M)	7.00	0.87	7.21	0.75	0.08
(F)	7.16	0.43	7.27	0.36	0.15
DRS(M)	2.93	0.77	2.81	0.65	0.15
(F)	2.77	0.44	2.77	0.44	1.00
UPDRS-III(M)	48.38	14.64	18.81	7.82	0.01 ^a
(F)	39.80	11.23	20.43	14.50	0.05 ^a

Table 2 Mean, SD, and *p*-values for the speech motor function, severity of dysarthria and motor impairment between the two medication conditions in males (M) and females (F)

Abbreviations: DRS, Dysarthria Rating of Severity; SD, standard deviation; UPDRS-III, Unified Parkinson's Disease Rating Scale-III. $^{a}p < 0.05$.

Comparison of Speech Motor Function, Severity of Dysarthria, and Motor Impairment between Medication ON and OFF Conditions

The mean and SD values for the individual subsections of FDA-2, DRS, and UPDRS-III across the two medication conditions and their *p*-values are shown in **-Table 2**. A significant difference in the lip and laryngeal functions in FDA-2 and UPDRS-III was found in both males and females between the two medication conditions. However, there was no significant difference in the severity of dysarthria between the two medication conditions in either male or female patients.

Comparison of Acoustic Parameters of Voice and Patients' Self-Assessment of Vocal Function between Medication ON and OFF Conditions

The mean and SD values for the acoustic parameters of voice and the VHI prior (medication-OFF) and after (medication-ON) the intake of medication for both males and females are shown in **- Table 3**. A significant difference was found for the following acoustic parameters of voice for males between the two medication conditions: F0 (Hz), FTRI (%), and vAm (%) (p < 0.05). A significant improvement in frequency parameters mainly the fundamental frequency (p < 0.05) that represents the number of times the vocal cords vibrate per second was noticed in medication-ON state for males. The tremor parameter of frequency (i.e., FTRI%) and amplitude parameter of peak amplitude variation (vAm%) reduced from the OFF state to the ON state. There was no significant difference in the acoustic parameters of voice in females between the two medication conditions.

Spearman's correlation coefficient for evaluating the relationship between motor speech function and motor impairment, as well as acoustic parameters of voice with VHI in both males and females in the two medication conditions, revealed no correlation between any of these parameters. The interrater reliability for the speech intelligibility ratings in either medication condition for both males and females was determined using Cohen's kappa coefficient. Substantial to near perfect agreement (0.73–0.91) was established for the intelligibility ratings by the three raters in either medication condition for both genders.

Discussion

The present study aimed to evaluate the voice, motor speech, and motor functions of individuals with PD in the ON and OFF states. Gender significantly influences voice and speech;^{18–20} hence, males and females were evaluated separately. HC and patients with PD differed significantly for lip and laryngeal functioning and with reference to the acoustic parameters; there was a difference only for F0 in males and SPI in females. The difference between the two groups for only specific speech subsystem functioning can be due to the lack of significant

	Medication-OFF		Medication-ON		
	Mean	SD	Mean	SD	p-Value
F0 (Hz) (M)	141.5	43.05	149.9	38.9	0.04 ^a
(F)	183.73	32.96	180.9	48.21	0.51
Jitter(µs) (M)	109.8	77.91	97.05	100.05	0.06
(F)	65.15	56.15	62.74 78.54		0.31
Shimmer(dB) (M)	0.57	0.30	0.45	0.24	0.20
(F)	0.38	0.24	0.39	0.20	0.62
FTRI(%) (M)	3.09	9.8	0.40	0.47	0.01 ^a
(F)	0.37	0.33	0.46	0.46	0.57
SPI (M)	16.98	5.62	17.18	6.55	0.87
(F)	16.59	11.19	13.79	4.69	0.67
vF0 (M)	2.09	1.35	1.79	1.89	0.05
(F)	1.67	0.76	2.89	4.07	0.95
vAm (M)	10.87	5.71	7.76	2.99	0.03 ^a
(F)	10.16	4.78	9.19	3.71	0.59
VHI (M)	25.68	7.04	22.81	7.20	0.43
(F)	25.33	6.02	23.77	2.58	0.37

Table 3 Mean, SD, and *p*-values for the acoustic parameters of voice and patients' self-assessment of vocal function (VHI) between the medication ON and OFF conditions across males and females

Abbreviations: F0, average fundamental frequency; FTRI, Frequency Tremor Intensity Index; Jitter, frequency perturbation; SD, standard deviation; Shimmer, amplitude perturbation; SPI, soft phonation index; vAm, variation in amplitude; vF0, variation in F0; VHI, Voice Handicap Index. ^a*p*-Values are significant at 0.05.

speech impairment in our PD cohort, which would otherwise have affected the other speech subsystems as well. An increase in F0 in males with PD is consistent with the findings of the studies revealing the same in those in the early and later stages of PD.²¹ An increase in SPI in women with PD is suggestive of incomplete glottal closure and loose adduction of vocal folds compared with HC.²²

Lip and laryngeal functions significantly improved in the medication-ON over the medication-OFF state in both males and females with PD. Rusz et al²³ reported improved pitch flexibility and lip and laryngeal function in the ON state. They ascribed this to improvement in postural tension, thus improving the range of oromotor and laryngeal movements. Labial function improved from the OFF state to the ON state. This finding was similar to that of Lechien et al,²⁴ who reported that levodopa significantly improved lip strength, frequency of labial movement, and labial motility. Pinto et al²⁵ also indicated that levodopa treatment decreased nonspeech labial rigidity and increased the amplitude of labial movements. A trend toward a significant difference in tongue function was observed for males between the two medication states. A reduction in rigidity and bradykinesia in the ON state can explain this difference.

The UPDRS scores showed significant improvement following intake of levodopa, whereas the speech intelligibility and severity of dysarthria remained the same (**-Table 2**). There was no correlation between any of the acoustic parameters and UPDRS. Several previous studies have found stable or poorly responsive speech and phonatory measurements, despite levodopa-related motor changes from OFF to ON states.^{6,22,26–28} This is in contrast to the significant correlations found between acoustic findings and both the ADL and motor portions of the UPDRS by Silbergleit et al.²⁹ Levodopa treatment has had mixed and contradictory results with respect to changes in speech impairments in PD.^{30,31} Some studies reported a slight improvement in intonation, vowel articulation, and speech intelligibility,6,8,9,28 while other studies^{11,12} showed no significant effect of levodopa. Increased speech volume and improved speech intelligibility were noted in some patients, while no improvements were seen in others by Fabbri et al.³¹ Ma et al³² reported an inconsistent effect of dopaminergic medication on speech prosody. They speculated about the role of nondopaminergic mechanisms in improving speech prosody. In contrast to reports that showed no changes in F0 SD or jitter to levodopa intake,^{7,10,12} Pinho et al³³ reported that the use of levodopa improves vocal parameters such as fundamental frequency (F0) and jitter, but not vocal intensity. The results of our study also indicate similar findings with few acoustic voice parameters such as F0, FTRI lrb%), and vAm improvement, but other parameters remained stable. A trend for voice improvement was noticed following the treatment with levodopa. This was with respect to pitch and intensity variability and articulation. Inconsistency across studies may be due to participant-related variances, intake of other medications, and differences in dysarthria severity.

There may have been some dissociation between the influence of levodopa on motor symptoms and certain speech characteristics in patients with PD. The differences in the response of motor and certain speech characteristics may be due to the presence of both dopaminergic and nondopaminergic lesions associated with speech production in PD.^{32–35} The presence of a unique levodopa dose-based response curve for individual symptom in PD might be another possible explanation.³⁶ This suggests that speech symptoms with a flat dose-response curve may be underdosed; hence, it may not be considered that these are resistant to levodopa. The need to conduct systematic dosage increase studies on speech symptoms to explore this was emphasized in their study. Alternatively, other studies identify nondopaminergic mechanisms such as defects in vocal loudness perception and altered sensory processing as the underlying pathophysiological mechanisms of voice and speech impairments.^{36–38}

No correlation between VHI and a measure of voice disability with acoustic voice tremor measures was found. This finding is not unexpected, since it is challenging to compare acoustic measures that are objective in nature to the self-perceived measure of a voice problem. This is because VHI varies for each patient depending on their social connections, family interactions, job, and personality.³⁹ There was no change in the VHI between the ON and OFF states in our study. Cushnie-Sparrow et al¹³ speculated that irrespective of the order of withdrawal of medication, the exacerbated symptoms of PD in the OFF state may lead to mood fluctuations and physical distress that can possibly affect the speech and voice in these individuals in the ON state as well.

Conclusion

The purpose of this study was to examine the acoustic, perceptual, and motor characteristics of individuals with PD before and after taking dopaminergic medication. The PD patients' improvement in motor skills was predominant compared with minor improvements in measures of voice and articulation, when examined in their OFF to ON states. No significant correlations were found between PD disease duration and any of the parameters. The results of this study suggest the effectiveness of nonpharmacological treatments such as speech therapy for the management of speech impairments in PD.

Counterbalancing the order of medication states would strengthen the findings of this study. Studies should also be conducted to examine changes in speech symptoms across a range of levodopa doses. The PD subjects studied had a wide age range and disease characteristics, and none of the patients showed severe speech impairments. Differences between ON and OFF states tend to be higher when there is severe speech impairment, suggestive of a ceiling effect. A similar study with individuals with PD with severe speech intelligibility should be performed to answer the research questions posed. Analysis of individual patient data may shed more light on the causes of speech variability.

Authors' Contributions

V.P.V. was involved in conception and design, acquisition of data, drafting of the article or critical revision of the manuscript for important intellectual content; J.K.D. was involved in acquisition of data, analysis and interpretation of data, drafting of the article, and critical revision of the manuscript; V.H.V. was involved in acquisition of data and critical revision of the manuscript; K.N. was involved in data interpretation and critical revision of the manuscript for important intellectual content; P.P.K. was involved in critical revision of the manuscript for intellectual content; Y.R. was involved in critical revision of the manuscript for intellectual content. All authors read and approved the final manuscript.

Ethical Approval

The study is in compliance with the Declaration of Helsinki and was approved by the Research Ethics Committees of NIMHANS, Bengaluru.

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Conflict of Interest None declared.

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