The Effect of Parkinson Disease Tremor Phenotype on Cepstral Peak Prominence and Transglottal Airflow in Vowels and Speech

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Summary: Objectives: The physiological manifestations of Parkinson disease are heterogeneous, as evidenced by disease subtypes. Dysphonia has been well documented as an early and progressively significant impairment associated with the disease. The purpose of this study was to investigate how acoustic and aerodynamic measures of vocal function were affected by Parkinson tremor subtype (phenotype) in an effort to better understand the heterogeneity of voice impairment severity in Parkinson disease.

Study Design: This is a prospective case-control study.

Methods: Thirty-two speakers with Parkinson disease assigned to tremor and nontremor phenotypes and 10 healthy controls were recruited. Sustained vowels and connected speech were recorded from each speaker. Acoustic measures of cepstral peak prominence (CPP) and aerodynamic measures of transglottal airflow (TAF) were calculated from the recorded acoustic and aerodynamic waveforms.

Results: Speakers with a nontremor dominant phenotype exhibited significantly ($P < 0.05$) lower CPP and higher TAF in vowels compared with the tremor dominant phenotype and control speakers, who were not different from each other. No significant group differences were observed for CPP or TAF in connected speech.

Conclusions: When producing vowels, participants with nontremor dominant phenotype exhibited reduced phonation periodicity and elevated TAF compared with tremor dominant and control participants. This finding is consistent with differential limb-motor and cognitive impairments between tremor and nontremor phenotypes reported in the extant literature. Results suggest that sustained vowel production may be sensitive to phonatory control as a function of Parkinson tremor phenotype in mild to moderate stages of the disease.

Key Words: Parkinson disease−Dysphonia−Acoustic analysis−Cepstral peak prominence−Transglottal airflow.

INTRODUCTION

Idiopathic Parkinson disease (PD) is one of the most common progressive neurologic conditions affecting the elderly, with estimates that up to 1.5% of individuals over the age of 60 will develop the disease.[1] The onset and progression of PD is characterized by a constellation of motor and nonmotor impairments across multiple pathways of the central and peripheral nervous systems.[2] However, the initial presentation and subsequent advancement of motor and nonmotor impairments is not uniform throughout the population of individuals with PD.[3,4] As an example, while clinical diagnosis is typically made when there is a presence of two or more motor symptoms associated tremor, rigidity, bradykinesia, or postural impairment, and where those symptoms respond favorably to dopamine replacement therapy, the specific symptom clusters at time of diagnosis and their corresponding severity differ widely across large groups of patients.[1,3,5]

To better understand the clinical heterogeneity of PD, investigators have sought to develop methods for organizing individuals into clinical phenotypes (aka “subtypes”). Age of onset (young vs. old), dominant motor symptom (tremor vs. nontremor), postural stability and gait impairment, the presence versus absence of cognitive-motor complications, and presenting psychopathology are among the domains that have been used for phenotyping individuals with PD based on dominant clinical symptomatology.[3,6−8] Specific PD phenotypes have been found to predict a number of disease characteristics including the rate and severity of limb-motor impairment progression and the degree of cognitive decline.[8−10] Varying PD phenotypes have also been associated with different morphological and neurochemical changes in the central nervous system throughout the progression of the disease, supporting a theory that idiopathic PD actually consists of a cluster of variant forms whose early disease and midstage motor impairments, nonmotor impairments, and progressive patterns are different.[6,11,12]

The rest tremor of PD is present for many individuals in the early stages of the disease.[13] In a majority of cases, PD tremor initiates in the upper extremities, most often in a unilateral hand.[14,15] The tremor can spread axially through the ipsilateral limb, progress toward the lower limb, or eventually influence extremities bilaterally. The pattern of tremor progression is variable across individuals with PD, and current methods of assessment make it difficult to predict whether the initial presence of tremor will be a persistent or progressively severe symptom of the disease in any single individual.[14−16] In others, tremor will not be present at disease onset and may develop as a minor secondary symptom in comparison with bradykinesia, rigidity, or postural instability.[9,13]

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Tremor dominant (TD) PD phenotype is exemplified by a significant and persistent resting tremor which is usually present at onset and progresses as a substantial motor impairment throughout the course of the disease.[3,9] The neuropathology for TD PD includes severe cell loss in the medial substantia nigra pars compacta.[7] Brain imaging has revealed clear blood flow differences between TD and non-tremor dominant (NTD) PD phenotypes, in addition to dissimilarities in dopaminergic levels within the basal ganglia and abnormal protein deposits such as tau pathologies and β amyloids.[5,11,12] Assignment of individuals into TD or NTD phenotypes has been based on varied methods, including motor scores from the Unified Parkinson's Disease Rating Scale (UPDRS), patient history, and symptomatology derived from other clinical assessments.[3,9,17−19] It has been suggested that individuals with TD PD have a slower progression of degeneration than NTD phenotype, as well as less severe cognitive deficits through the first 8 years after diagnosis.[3,8] Additionally, the rate of progression, dementia, and life expectancy are suggested to be more favorable in individuals with TD phenotype compared with the NTD phenotype.[4]

The progression of PD will eventually impact articulation, voice, and swallowing. Approximately 90% of affected individuals with PD will manifest some form of speech abnormality (ie, dysphonic voice, reduced speech prosody, imprecise consonant and vowel articulation, reduced vocal loudness, vocal tremor, and dysfluency) over the course of the disease.[20−23] It is believed that voice is impacted early in disease progression, perhaps as early as Hoehn & Yahr (HY) stages 1 and 2, due to involvement of nuclei associated with the vagus nerve in the lower brain stem.[2,22,24]

Logemann et al. proposed that speech impairment in PD progresses in a caudal to rostral pattern, initiating at the level of the larynx and advancing to the tongue dorsum, lips, and tongue tip.[20] This pattern has been supported by Ho et al. in an analysis of voice and articulation impairments in a cohort of 200 speakers with PD.[25] Furthermore, impairments associated with vocal function are a common finding in the majority of acoustic studies of hypokinetic dysarthria.[26−29] Aerodynamic measures of subglottal pressure and transglottal airflow (TAF) have also differed in speakers with PD, especially those in more severe stages of the disease with perceptual hypophonia compared with healthy controls.[30] Sapir suggested the possibility of speech impairments being early manifestations in the progression of PD neuropathology, but may be too subtle for detection due to the ability of speakers in early stage PD to compensate.[22]

PD tremor manifests in the larynx in addition to the limbs. Laryngeal tremor has been documented via laryngeal imaging in up to 55% of individuals with PD in stages I−III.[31,32] The laryngeal tremor of PD is primarily a vertical tremor, although horizontal tremulousness of the arytenoid cartilages has also been reported.[32] Acoustically, the laryngeal tremor in speakers with PD has been characterized by excessive modulation in fundamental frequency of approximately 5 Hz.[33] This tremor rate has been found to be significantly higher in PD than male and female controls, although similar differences have not been consistently demonstrated in amplitude tremor. The auditory-perceptual consequence of laryngeal tremor in PD is not uniformly clear, and some acoustic studies have found contradictory evidence in the rate of vocal tremor in speakers with PD compared with control speakers.[34] In addition, some authors have questioned whether reports of vocal tremor in PD originates from laryngeal structures, based on evidence from laryngeal electromyography and observation of supraglottal structures which also oscillate during phonation in speakers with PD.[35,36]

As with limb tremor, the degree and pattern of voice impairment progression in PD is not homogeneous. For example, some studies have reported reduced habitual vocal intensity in samples of speakers with PD, whereas others have reported equivalent vocal intensity compared with healthy control speakers.[30,37,38] Matheron et al recently suggested that some perceptual features of PD voice (ie, hypophonia) may be influenced by multidimensional factors, which are not yet fully understood, a suppositions that has been supported also by Sapir.[22,30] The effect of PD tremor phenotype on voice and speech function is not clear due to a limited evidence base. Our laboratory's working hypothesis is that tremor phenotype may explain some of the variable findings associated with clinical voice measures in samples of speakers with PD. Although speech treatments are known to improve voice and speech function in speakers with PD, it is not known if PD phenotype influences a patient's response to treatment. If speech and voice are affected differently as a function of phenotype for a certain window of time after diagnosis, those phenotypic characteristics may serve as biomarkers which might facilitate application of prophylactic or rehabilitative treatments customized to specific PD clinical profiles.[5]

Aerodynamic and acoustic characteristics of voice production are among the impaired dimensions of voice in PD.[30,39] We suggest that it is essential to better understand how PD phenotype influences the physiological substrates of voice and speech as a strategy for improving current assessment batteries and choosing the most effective and customized intervention strategies. To address this need, the current study investigated acoustic and aerodynamic characteristics in speakers with TD and NTD PD phenotypes, and compared both with a group of control speakers. We investigated these variables by recording vocal productions in two commonly utilized clinical contexts: vowel and connected speech production. The specific research questions included (1) Does tremor phenotype influence acoustic measurements of cepstral peak prominence (CPP) in vowels and connected speech? (2) Does PD phenotype influence aerodynamic measurements of TAF in vowels and connected speech?

METHODS

Participants

A total of 45 participants were initially recruited for this study: 34 speakers with PD (22 males, 12 females) and 11 healthy older adult (HOA) controls (4 males, 7 females). Speakers with PD were recruited from regional speech-language pathology practices, flyers, support groups, neurology medical practices, and snowball sampling. HOA control participants were recruited from flyers and snowball sampling. Inclusion criteria for PD speakers consisted of a diagnosis of PD made by a neurologist and no other diagnosed neurologic illness separate from or related to PD. The HOA controls were required to be greater than or equal to age 50 at time of testing, and no self-reported history of speech, language, hearing, cognitive, or neurologic impairments. All participants were native speakers of American English. The methodology for this study was approved by a university institutional review board.

Speakers with PD were assigned to one of two phenotype groups based on motor signs and symptoms. Phenotype assignment was based on a similar method used by Selikhova et al.[9] We chose not to use the UPDRS as an assessment tool because previous research did not find an effect of tremor phenotype on speech intelligibility when using that tool to stratify speakers with PD.[19] TD phenotype was defined as a participant reporting tremor as (1) the predominant initial sign of the disease, (2) progression of tremor severity since diagnosis, and (3) tremor as a current major manifestation and impairment associated with PD in relation to other motor signs. NTD phenotype was defined as a participant reporting (1) no tremor at onset, (2) minimal (if any) progression of tremor since diagnosis, and (3) a negative report of tremor as a current major manifestation or impairment associated with PD.

Phenotype assignment was based on a combination of participant history, responses to a motor questionnaire (see Appendix), neurologist reports, and informal assessment conducted at the time of testing. All participants with PD were scheduled at a time of the day when they self-reported that their medication cycle was effective. Other characteristics of PD medication variety and dosage were not controlled. We excluded two participants with NTD PD from the final data cohort because their data sets contained substantial outliers in the airflow data (defined as greater than twice the interquartile range for any dependent variable, verified by *SPSS* Statistical software, IBM Analytics, Armonk, New York). We also excluded one HOA control participant due to diagnosis of a midmembranous vocal fold lesions after participation in the study. This left the final participant cohort with 16 TD, 16 NTD, and 10 HOA control participants, whose demographic data are illustrated in Table 1.

TABLE 1.
Demographic Characteristics of Tremor Dominant PD Phenotype (TD) and Nontremor Dominant Phenotype (NTD) Along With Control (Healthy Older Adult) Participants

Group	Yrs. Post Dx	Dx Age	HY Stage	Speech Severity
TD (n = 16)				
Mean	6.23	64.12	2.62	146
SD	4.5	10.96	0.61	45
Median	4.05	67.5	3.0	156
Range	13.6	40	2.0	174
NTD (n = 16)				
Mean	4.04	65.19	2.75	140
SD	2.78	7.42	0.44	49
Median	3.11	65.5	3.0	130
Range	7.70	25	1.0	197
Control (n = 10)				
Mean				50

Years postdiagnosis age (Yrs. Post Dx) represents years post at time of testing.

Instrumentation and procedures

This study utilized acoustic and aerodynamic instrumentation to acquire measurements of phonation periodicity and TAF in vowels and connected speech. Acoustic hardware included the Computerized Speech Lab (CSL—Pentax Medical, Montvale, NJ) along with a head-mounted condenser microphone (model C520; AKG Acoustics, Northridge, CA). Software used to acquire and analyze acoustic and aerodynamic recordings included the Analysis of Dysphonia in Speech and Voice (*ADSV*) program associated with the CSL system. Aerodynamic hardware included the Phonatory Aerodynamic System (PAS—Pentax Medical, Montvale, NJ) along with the associated *PAS* software.

For acoustic recordings, participants were asked to produce a sustained /a/ vowel and a standard clinical sentence ("We were away a year ago"). During recording, participants wore the head-mounted microphone with the microphone head placed approximately 3 cm from the left corner of the mouth. The microphone had a direct line input to the CSL, and the core program of the CSL was used to record all productions at default settings (44-kHz sampling rate). Speaker instructions for sustained vowels prompted them to "Take an easy breath and say the vowel /a/ at a comfortable pitch and loudness, as steady as you can, until I say stop. I will say stop after four or five seconds." Speaker instructions for the sentence prompted them to produce stimuli "At a comfortable pitch and loudness, as if you were speaking in conversation." Similar to aerodynamic stimuli, the vowel and sentence stimuli were chosen to reflect the more common prompts used to investigate acoustic properties of voice in clinical practice and in previously published research.

For aerodynamic recordings, participants were asked to produce a series of /pa/ repetitions at a modeled rate of 1.5 syllables/s and at a comfortable pitch and loudness. Participants repeated three trials of these utterances. Productions were elicited with the participant placing the PAS facemask firmly over the mouth and nose. Target airflow measures were acquired from the vocalic portion of each /pa/ syllable using the voicing efficiency protocol of the *PAS* software. This stimulus was used to reflect methods in the large body of existing literature where measures of TAF have been obtained from the vocalic portion of CV syllables. Participants were also asked to produce the sentence "We were away a year ago" at a comfortable pitch and loudness, "as if you were speaking in conversation." Target airflow measures were acquired from the entire duration of that all-voiced sentence. Participants repeated three trials of the sentence stimulus.

As part of a larger ongoing program of research, we determined baseline perceptual speech impairment severity for each speaker using a direct magnitude estimation procedure following the protocol of Weismer and Laures.[40] Three second-year graduate students served as perceptual judges and were instructed to make a rating of overall speech severity (ie, perceptual evaluations were not specific to voice characteristics only). Perceptual judges were instructed to consider their ratings in the context of a gestalt perception including voice quality, articulation accuracy, articulation rate, resonance, and intelligibility. The magnitude estimation task utilized a perceptual anchor consisting of a speaker with PD manifesting a moderate degree of speech severity, based on productions of the Consensus Auditory-Perceptual Evaluation of Voice (CAPE-V) sentences. This specific anchor was chosen by the investigators based on their consensus opinion that overall perceived severity of the speaker's productions fell within the moderate range. The speech severity of the perceptual anchor was assigned a rating of 100. Judges were instructed to rank recordings for the rest of the speakers based on this scale. (For example, if the speaker was twice as severe as the anchor, they were to give a score of 200; one-half severe, a rating of 50.) Connected speech samples consisting of the six CAPE-V sentences produced by each of the participants were played via free field speaker in randomized order with the anchor played approximately every five samples for perceptual calibration. For reliability calculations, five recordings were repeated in the stimulus set to compare inter-rater reliability. Mean speech severity ratings for each speaker are illustrated in Table 1.

Analyses

Four dependent variables were obtained from the acoustic and aerodynamic recordings. For acoustic measurements, CPP in dB, representing phonation periodicity, was computed from the midportion of the sustained vowel and for the entire duration of the sentence using the *ADSV* program. Measures of CPP were chosen to represent phonation periodicity because they have been shown to correlate strongly with perceptions of voice quality and are robust across speech sample type, including vowel and connected speech production.[41,42] For aerodynamic measurements, target airflow in milliliters/second (mL/s) was obtained from the vocalic portion of /pa/ syllables and across the entire production of the all-voiced sentences using the *PAS* program. TAF from the vocal portion of /pa/ syllable trains was utilized as it translates well to methods of airflow assessment in a large body of existing literature, and is also a commonly employed method for clinical assessment of airflow.

Data analysis resulted in CPP measures for vowel and connected speech, and airflow measures for vowel and connected speech. Separate multivariate analyses of variance (MANOVA) were applied to the acoustic variables and aerodynamic variables, with group as a between-subject factor. Follow-up pairwise comparisons using Fisher least square difference were applied to significant main effects. Although the MANOVA can protect against type I error, this was a preliminary study in this line of investigation and so all statistical analyses used an alpha level of 0.05 against which to determine statistical significance.

Reliability

Measurement reliability for acoustic and aerodynamic data was assessed by reanalysis of 10% (five participants) of all recorded productions. The strength of association between original and follow-up measurements was computed using Pearson product-moment correlations. Correlations were strong regarding CPP in both sustained vowels ($r = 0.99$) and speech ($r = 0.99$). Correlations for TAF in both sustained vowel and speech were completed. Again, correlations were strong for both vowel ($r = 0.98$) and speech ($r = 0.96$).

RESULTS

Average age at diagnosis, HY staging, and mean speech severity ratings are provided in Table 1. To determine group equivalence, a series of one-way analyses of variances were applied to these data and revealed no significant differences in diagnosis age, HY stage, or speech severity level between the two PD groups. However, both PD groups manifested significantly greater speech severity ($P < 0.05$) compared with the HOA controls, which was anticipated.

Figures 1−4 illustrate group statistics on the four dependent variables. With regard to CPP in vowels (Figure 1), control speakers exhibited the largest CPP vowel measures (mean = 12.30 dB, standard deviation [SD] = 1.09) compared with the TD (mean = 11.53 dB, SD = 1.95) and NTD (mean = 9.90 dB, SD = 2.92) groups. Results of the MANOVA and follow-up tests indicated a significant main effect of group (Pillai's trace = 0.271, $F = 3.05$, $P = 0.02$), with a statistically significant difference between NTD and TD groups ($P = 0.04$), in addition to a difference between the NTD and the control group ($P = 0.01$). The effect size for the difference between NTD and TD groups was moderate ($d = 0.65$), whereas the effect size for the difference between NTD and control groups was large ($d = 1.09$). There was no CPP vowel difference between the TD and the control group. With regard to CPP in speech (Figure 2), measures between the three groups were roughly equivalent (TD mean = 7.65 dB, SD = 1.38; NTD mean = 7.96 dB, SD = 1.37; control mean = 7.06 dB, SD = 1.30). There were no statistically significant group differences in CPP in speech measurements.

Airflow measures in vowels (Figure 3) revealed the largest mean values exhibited by the NTD group (mean = 244 mL/s,

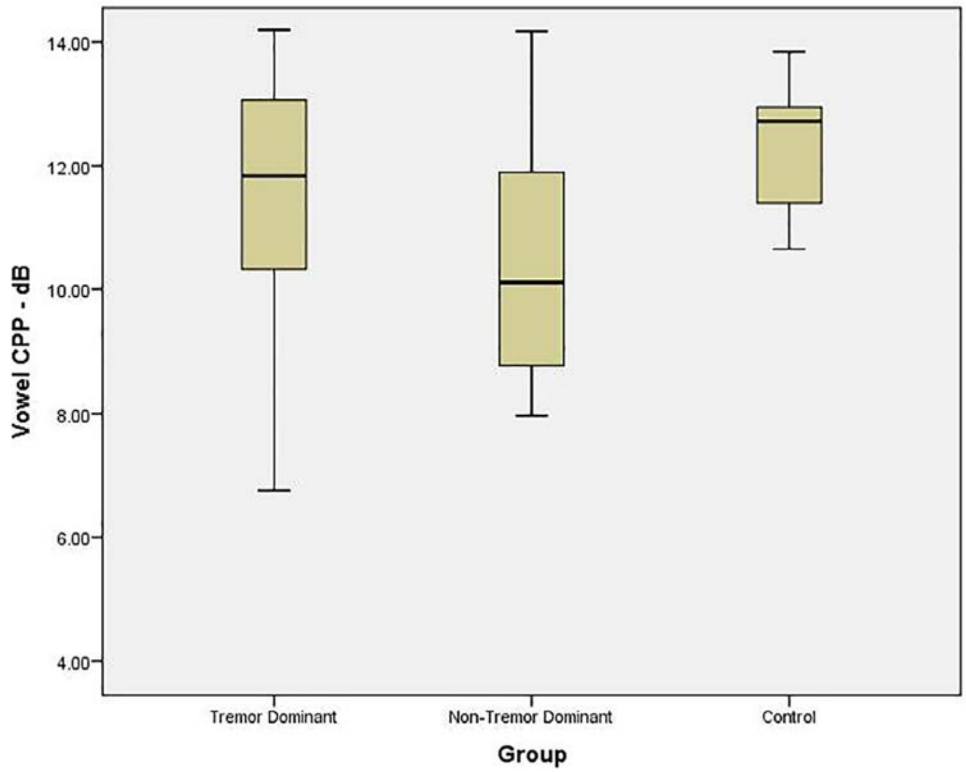

FIGURE 1. Box-and-whisker plots illustrating the interquartile range (*shaded area within box*), median (*horizontal line within box*), and maximum/minimum data ranges falling within 1.5 times the interquartile range (*whiskers extending from the box*) for measures of cepstral peak prominence in sustained vowels (CPP—in dB) for the three groups.

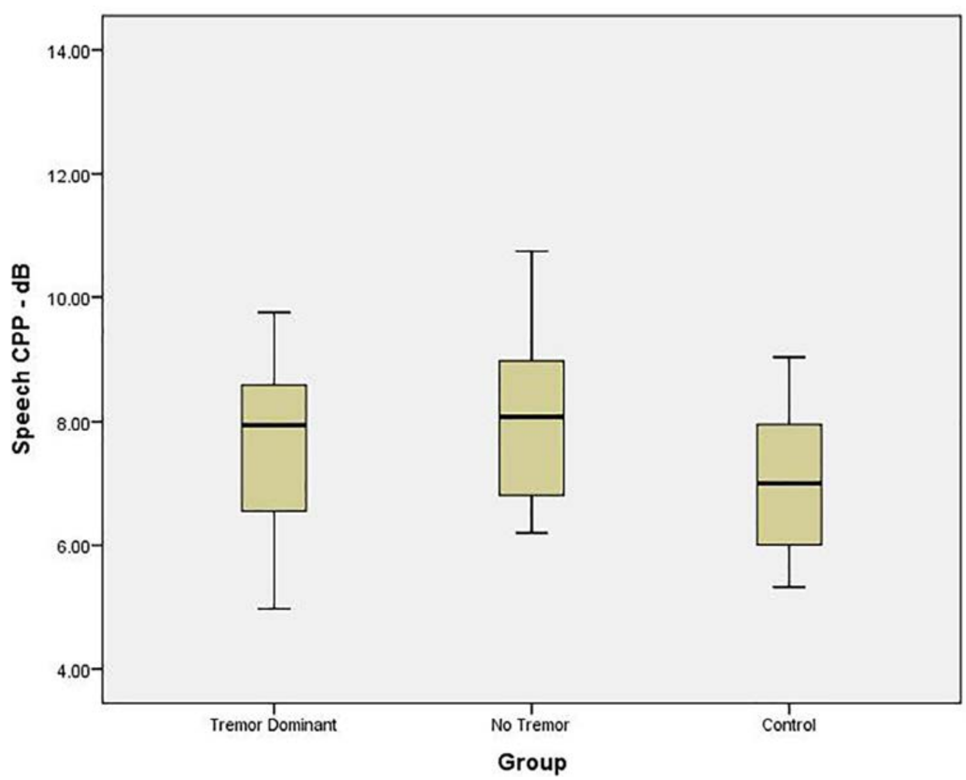

FIGURE 2. Box-and-whisker plots illustrating measures of cepstral peak prominence (CPP—in dB) in connected speech for the three groups.

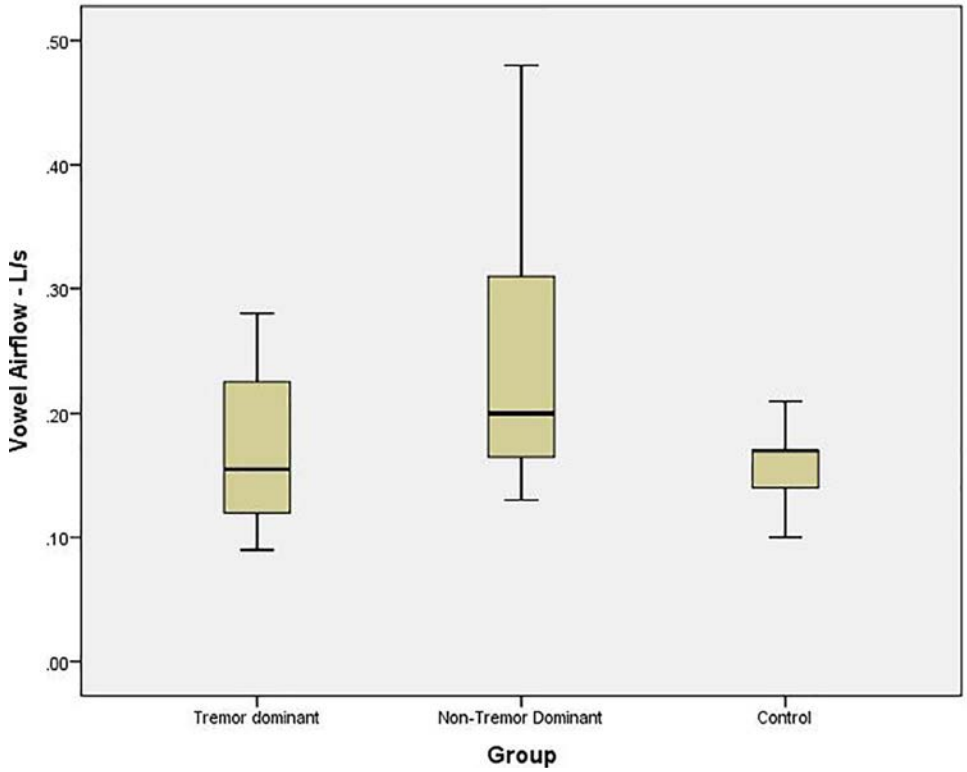

FIGURE 3. Box-and-whisker plots illustrating measures of transglottal airflow (in L/s) in sustained vowels for the three groups.

SD = 104), followed by the TD (mean = 169 mL/s, SD = 61) and control (mean = 156 mL/s, SD = 34) groups. Results of the MANOVA and follow-up tests indicated a significant main effect of group (Pillai's trace = 0.238, F = 2.56, P = 0.04), with a statistically significant difference between TD and NTD groups (P = 0.01), in addition to a difference between the NTD and the control group (P = 0.01). The effect size for the difference between NTD and TD groups was large (d = 0.88), as was the effect size for the difference between NTD and control groups (d = 1.14). With regard to airflow in speech (Figure 4), the NTD group manifested the largest measures (mean = 209 mL/s, SD = 101) followed by the TD (mean = 165 mL/s, SD = 55) and control (mean = 163 mL/s, SD = 69) groups. However, similar to the acoustic speech measures, there were no statistically significant group differences in airflow measures in connected speech.

DISCUSSION

The purpose of this study was to compare the acoustic and aerodynamic properties of voice between individuals with TD and NTD phenotypes of PD in addition to HOA controls. The first research question asked: does PD tremor phenotype influence acoustic measurements of CPP in vowels and connected speech? Results indicated that participants classified as NTD manifested significantly lower measures of CPP in vowels compared with both TD and control groups, who did not differ from each other. The acoustic CPP measure is influenced by phonation periodicity and acoustic noise energy. In general, as phonation periodicity decreases or acoustic noise increases, measures of CPP decrease and correspond to perceptions of greater dysphonic severity.[42–44] However, the measures of CPP in speech were equivalent across the three groups of speakers, suggesting a selective effect of stimulus on the acoustic dependent variable.

The second research question asked: does PD tremor phenotype influence aerodynamic measures of TAF in vowels and connected speech? Results fell into a similar pattern to those for acoustics, where main effects were found for vowels but not connected speech. Specifically, the participants classified as NTD manifested significantly elevated measures of airflow compared with the TD and control groups, who did not differ from each other. However, this finding was not consistent in connected speech, where groups were equivalent on the airflow measures. Measures of TAF are influenced by numerous factors, among which include respiratory drive, glottal configuration, medial compression force, and tissue stiffness. Elevated measures of airflow are typically reported in conditions associated with glottal insufficiency, although differences in TAF between speakers with PD and HOA have not been consistently described.[30,39,45–47]

Collectively, two salient patterns emerged from the data of this study. First, when producing vowels, participants with NTD phenotype manifested reduced phonation periodicity (indicated by lower CPP measures) and elevated TAF compared with TD and control participants, who did not differ from each other. Second, groups were equivalent on measures of CPP and airflow when producing connected

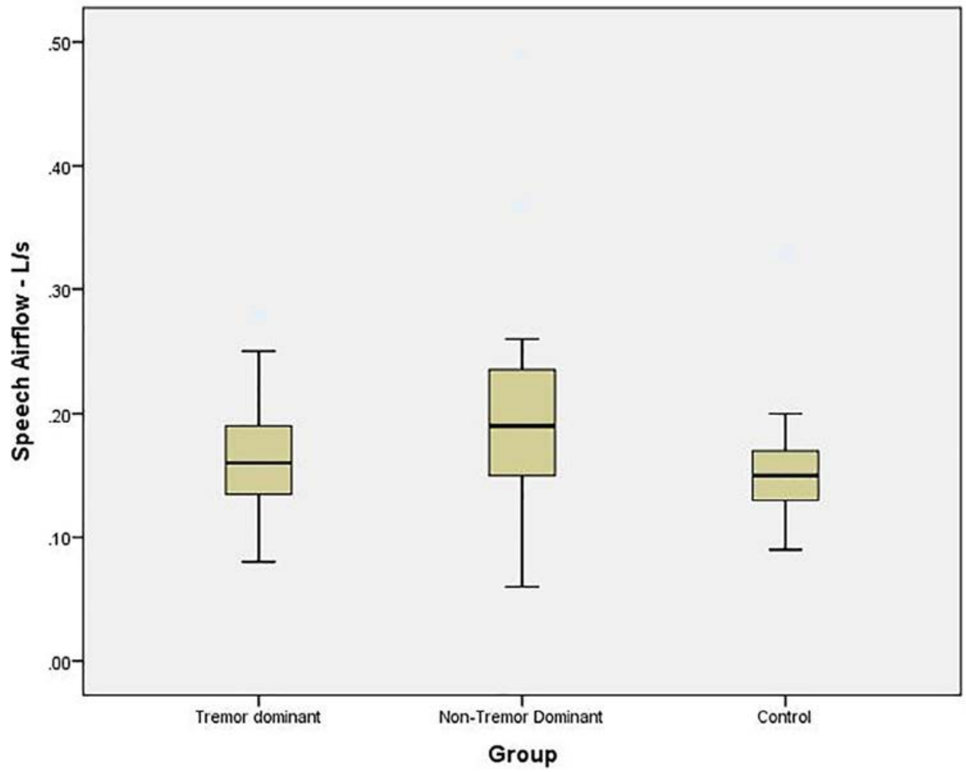

FIGURE 4. Box-and-whisker plots illustrating measures of transglottal airflow (in L/s) in sustained vowels for the three groups.

speech. The value of connected speech acoustic analyses for quantifying vocal function has recently been questioned.[48] In contrast, many authors have noted the neuromuscular control differences required for sustained vowel production and connected speech, and have suggested that analyses of both provide separate and complimentary information for the clinical characteristic of voice impairments.[49,50] Given that findings in the current study noted group differences in vowels but not connected speech for both acoustic and aerodynamic measures, our interpretation is that sustained vowel production is sensitive to phonatory control as a function of PD tremor phenotype in mild to moderate stages (eg, HY stages 1−3, reflecting the sample studied in this investigation) of the disease. This may imply that speakers with NTD phenotype experience greater impairment in sustained neuromuscular control of the vocal subsystems. However, this level of impairment is either reduced or the effect was not measureable when analyzing rapidly alternating movements in connected speech. This question will need to be pursued in future studies.

Interestingly, previous studies have reported no difference between speakers with PD and normal controls on measures of airflow obtained from vowels when using an airway interruption method.[39,47] However, these studies did not control for tremor phenotype, which has been shown to influence limb-motor disease progression and severity.[3] To our knowledge, only one previous study has prospectively investigated the effect of tremor phenotype on speech. Miller et al compared 38 TD speakers, 62 NTD speakers (postural instability or gait dominant), and 97 controls on measures of speech intelligibility. This study reported no statistically significant difference in intelligibility scores between the two PD phenotypes.[19] However, that study utilized scores from the UPDRS to assign phenotype groups, which has been found to be less sensitive to the relationship between speech impairment and motor disabilities.[19,27,51,52]

Differential effects of PD tremor phenotype on vocal function may be associated with divergent neuropathological impairment in motor and nonmotor pathways associated with TD and NTD forms. It has been demonstrated that individuals classified as NTD PD manifest lower levels of striatal dopamine and higher levels of pathological proteins within motor and nonmotor pathways compared with individuals with TD PD phenotype.[11,12] The neurodegenerative process affecting individuals with TD PD might also involve, to a greater extent, the cortical-cerebello-thalamic circuits. Recent evidence has demonstrated that tremor in PD is driven by reduction of dopamine supplied to the basal ganglia from the retrorubral area of the midbrain, triggering the onset of tremor via palladial-cortical connections and negatively influencing the "dimmer switch" tremor amplitude control mechanism of the cortical-cerebello-thalamic pathway.[51−53] This supports the supposition that direct and indirect pathways in the basal ganglia, and their associated thalamic, cortical, and brainstem connections, are undergoing different patterns and degrees of changes as a function of PD phenotype.

STUDY LIMITATIONS

A number of study limitations should be recognized and necessitate guarded generalizations from this investigation. The collective sample size was small, and the results could be influenced by sampling bias. Additionally, the mean age of the HOA controls was approximately 10 years younger than that of the two PD groups, whose ages were equivalent. Medication variety and dose were not controlled for in this study—all participants reported taking levodopa alone or in combination with other medicines, and were studied during self-reported "on" periods. Whether or not medication variables affect the acoustic and aerodynamic measures studied in this investigation will need to be explored in subsequent studies. This study used a binary assignment method to stratify speakers with PD into TD and NTD phenotypes. Other authors have further divided groups into three or more motor phenotypes. Although our method of assignment was sensitive to vocal differences in sustained vowels, whether or not our findings were confounded by other phenotypic characteristics will need to be investigated in future studies. Finally, the participant sex was not controlled for in this study, and as such, we do not know if this factor influenced measurements within the two PD phenotypes. This study did not compare auditory-perceptual voice quality differences between TD and NTD groups. Tremor has been reported as a salient perceptual feature of voice production in PD. Planned future studies will investigate the question of whether PD phenotype influences auditory-perceptual impressions of voice production.

CONCLUSIONS

Although investigations of tremor phenotype effects on vocal function are sparse, our findings are aligned with previous reports of physical and neurologic differences in TD and NTD phenotypes. NTD phenotype has been associated with a faster rate of disease progression (ie, severity) in motor and cognitive domains within the first 8 years after diagnosis, and faster progression has been associated with the emergence of speech and swallowing symptoms earlier in the course of the disease.[3,9] The NTD phenotype has also been found to exhibit greater densities of Lewy body, tau protein, and β amyloid in cortical neurons. Collectively, the evidence suggests that TD and NTD phenotypes represent variant forms of idiopathic PD characterized by marked differences in neuropathological progression and clinical symptomatology, and the results of the present study support the notion that acoustic and aerodynamic measurements of vocal function are sensitive to those differences in earlier stages of the disease in the context of sustained vowel production. Specifically, speakers with an NTD phenotype exhibited less phonation periodicity and greater TAF in sustained vowels than speakers with TD phenotype. Future research is needed to replicate and extend findings from this study. As more research is added to the body of evidence regarding how PD phenotype impacts voice and speech, there is potential that aerodynamic and acoustic measures could be used as a way to identify PD voice impairment earlier rather than waiting on symptoms to progress to a level in need of therapeutic intervention.

APPENDIX

Parkinson disease motor questionnaire. Participants were asked to report "Yes" or "No" when prompted to indicate whether they have recently experienced the symptoms.

Problem	No	Yes
Speech		
Speaking volume is low		
Voice sounds hoarse		
Pitch does not vary—monotone		
Articulation is slurred or mumbled		
Speech rate is too fast		
Speech rate is too slow		
Air comes out of nose when speaking		
Difficulty being understood by others		
Eating/Swallowing		
Drooling		
Food falls out of mouth		
Food gets stuck in cheeks		
Clear throat frequently when drinking		
Clear throat frequently when eating		
Cough frequently when drinking		
Cough frequently when eating		
Food or pills gets stuck in throat		
Motor		
Tremor in hand		
Tremor in arm		
Tremor in foot		
Tremor in leg		
Tremor in head or neck		
Tremor in face or tongue		
Movements are slow		
Muscles are stiff		
Balance problems		
Falling over		
Difficulty getting up from chair		
Posture is slumped when standing		
Shuffling feet when walking		

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