Phonatory Impairment in Parkinson's Disease: Evidence from Nonlinear Dynamic Analysis and Perturbation Analysis

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Phonatory Impairment in Parkinson's Disease: Evidence from Nonlinear Dynamic Analysis and Perturbation Analysis

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Summary: Many persons with Parkinson's disease (PD) will eventually experience vocal impairment as their condition advances. Using standard perturbation analyses (parameters like jitter and shimmer) to measure fluctuations in phonatory signal may inhibit researchers from recognizing severely disordered patterns that seem to be present in the voices of some PD patients. Nonlinear dynamic analysis can quantify these aperiodic patterns, which indicate severe pathology that is usually characterized perceptually by hoarseness. Here, sustained vowel phonations of a heterogeneous group of PD subjects (20 women and 21 men) were compared with those of a control group (22 women and 18 men) based on results of nonlinear dynamic analyses (D_2) and perturbation analyses. Results showed PD subjects as a whole to have significantly higher D_2 values than control subjects ($P = 0.016$), which indicates increased signal complexity in PD vocal pathology. Differences in the comparison of these two groups were significant in jitter ($P = 0.014$) but nonsignificant in shimmer ($P = 0.695$). Furthermore, the performance on these three measures was affected by subject sex. Nonlinear dynamic analysis showed significantly higher D_2 in the female PD group than in the female control group ($P = 0.001$), but jitter and shimmer did not show such a difference. The male PD group had statistically higher jitter than the male control group ($P = 0.036$), but these groups did not differ in D_2 or shimmer. Overall, nonlinear dynamic analysis may be a valuable method for the diagnosis of Parkinsonian laryngeal pathology.

Key Words: Parkinson's disease—Phonation—Perturbation analysis—Nonlinear dynamic analysis.

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INTRODUCTION

Parkinson's disease (PD) is a neurodegenerative disease characterized by muscle rigidity, tremor, and slowed movement (bradykinisia) resulting from a dopamine imbalance in the nigrostriatal region of the brain. Surveys have found 70% of PD patients to report onset of speech impairment after their development of PD,[1] often as one of the earliest symptoms of the disease.[2] PD vocal pathology stems from impaired function of the laryngeal, articulatory, and respiratory muscles—likely as a manifestation of the core symptoms of PD—but PD patients' vocal symptoms do not necessarily parallel their motoric limb symptoms.[3] PD speech has been described subjectively as breathy, tremulous, high-pitched, monotone, quiet, and hoarse.[4,5]

Researchers and clinicians often use acoustic analysis to objectively evaluate speech function by measuring properties of recorded sustained phonation from vocal pathology patients (including PD patients). For nearly periodic samples, short-term fluctuations in phonatory signal can be quantified using acoustic perturbation measurements. These fluctuations are given as cycle-to-cycle variation in frequency (jitter) or cycle-to-cycle variation in amplitude (shimmer). Some studies using these perturbation analyses have suggested that PD subjects have higher jitter and shimmer values than control subjects.[5–7] However, using perturbation methods to determine the degree of vocal pathology present in severely disordered voices can be difficult because a pitch cannot be reliably extracted.[8,9]

Aperiodic voice segments usually sound perceptually rough or hoarse and have been identified, for example, in patients with vocal polyps[10] and laryngeal paralysis.[11] Hoarseness is a common feature of dysarthrias, including PD.[2,4–6] Heterogeneous samples of vocal pathology subjects (including PD subjects) may show an elevated incidence of aperiodic phonation. Categorization of spectrograms (visual signal displays from voice samples) from electroglottographic (EGG) recordings has found elevated percent composition of aperiodic phonation in male and female PD subjects.[6] Such vocal-fold vibratory data support the hypothesis that aperiodic phonation may occur more often in acoustic samples from PD subjects than in subjects without vocal pathology.

Recently, application of nonlinear dynamic analysis has been shown to be a valuable way to study phonation with aperiodic segments.[10,12–14] Nonlinear dynamic analyses of EGG signals have been employed to measure PD vocal pathology.[15] This nonlinear analysis complimented prior spectrographic categorizations of elevated aperiodic properties in the EGG signals of some persons with PD.[6] Nonlinear dynamic analysis provides complementary information to perturbation analysis in the objective study of voice. Therefore, the application of nonlinear dynamic analysis in combination with perturbation analysis may improve our ability to describe pathological voices from PD as well as aid in the diagnosis of laryngeal pathologies from PD.

In this study, we apply nonlinear dynamic analysis and a perturbation analysis to describe the vocal deficits in PD patients. Correlation dimension, jitter, and shimmer of acoustic signal are employed to compare sustained vowel phonations of PD subjects with those of control subjects. As past observations of PD phonation suggest that results of this analysis might differ based on sex,[15] comparisons are also made based on this factor.

MATERIALS AND METHODS

Subjects

An attending neurologist obtained consent and referred consecutive idiopathic Parkinson's disease (IPD) patients to an ear, nose, and throat (ENT) clinic for participation in the study. Healthy persons with no signs of voice or speech disorders were recruited to be a control group. Both groups of subjects underwent a laryngeal endoscopy by an otolaryngologist to check for any exclusionary laryngeal conditions (eg, nodules, paralysis, or inflammation) outside of the vocal fold bowing often observed in PD.[16] PD subjects were chosen based on their diagnosis of IPD, tolerance of laryngeal endoscopy, and absence of symptoms of cognitive impairment. With these criteria in mind, 20 female (age mean = 60, SD = 10.97) and 21 male (age mean = 56, SD = 8.58) PD subjects, along with 22 female (age mean = 51, SD = 6.48) and 18 male (age mean = 42, SD = 11.90) control subjects were selected to participate in this study.

PROCEDURE AND INSTRUMENTATION

A condenser microphone placed at approximately 15 cm from the mouth was used for acoustic recordings. Sustained vowel phonations were sampled at a sampling rate of 20 kHz using a 12-bit analog-to-digital converter (National Instruments AT-MIO-16, Austin, TX). Each subject was asked to sustain a steady phonation of the vowel /a/ at a comfortable pitch and loudness for at least 3 seconds. This procedure was repeated until three successful signal recordings were made. Then, from these sustained voices, 1-second segments were cut from the middle of phonation trials and processed using nonlinear dynamic analysis and perturbation analysis.

NONLINEAR DYNAMIC ANALYSIS

Phase space reconstructions and correlation dimensions were employed to describe the nonlinear dynamic characteristics of all voice samples. The reconstructed phase space shows the dynamic behavior of a signal; periodic signals produce a closed trajectory in phase space, whereas aperiodic signals look irregular and chaotic. Correlation dimension D_2 is a quantitative measure that specifies the number of degrees of freedom needed to describe a dynamic system; a more complex system has a higher dimension, which means that more degrees of freedom may be needed to describe its dynamic state.[17] Detailed descriptions of these nonlinear dynamic methods can be found in the literature.[13,18–22] In this study, phase space reconstructions and correlation dimension calculations were based on the numerical algorithms that we applied to analyze excised larynx phonations[18,23] and human voices.[10,14,24]

Briefly, for a time series $x(t_i)$, $t_i=t_0+i\Delta t$, $(i=1,2,\cdots,N)$ sampled at the time interval $\Delta t=1/f_s$ (Figure 1A), a phase space can be reconstructed with the time delay vector, $X_i=\{x(t_i), x(t_i-\tau),\cdots,x(t_i-(m-1)\tau)\}$, where τ is the time delay and m is the embedding dimension. Figure 1B shows the trajectory in the reconstructed $(x(t),x(t+\tau))$ phase space of a Parkinsonian voice, where the length of the sustained vowel is 1 s (N = 20000), and the time delay τ was estimated as $9\Delta t$ using the mutual information method.[25]

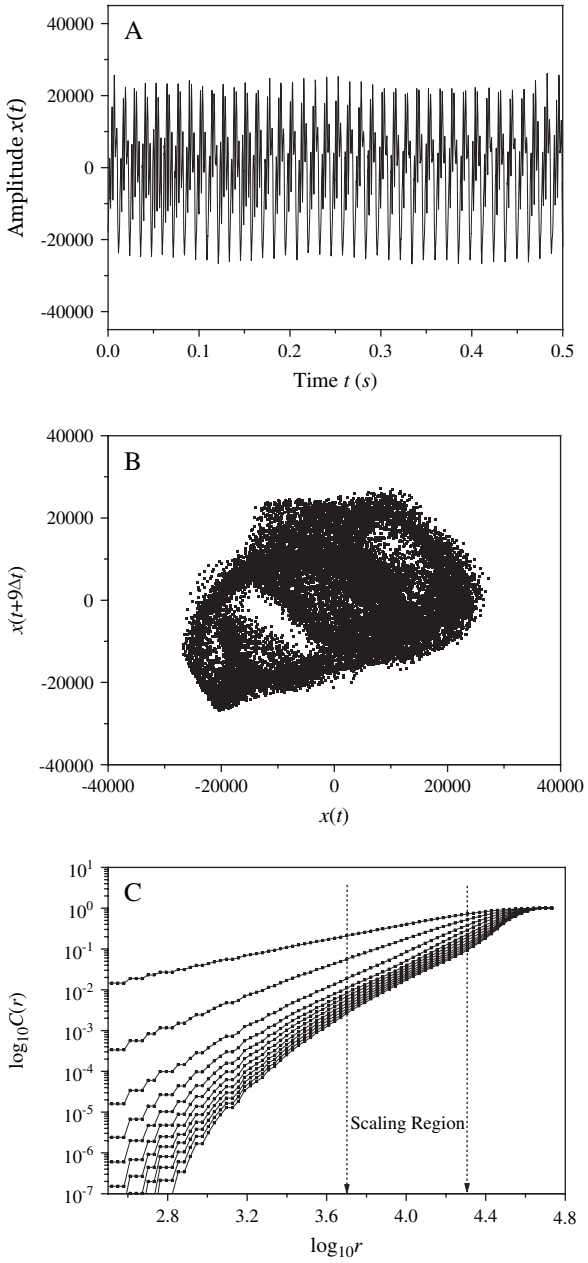

FIGURE 1. The acoustic waveform of a (**A**) Parkinsonian voice, the (**B**) reconstructed phase space, and the (**C**) correlation integral $\log_{10} C(r)$ versus $\log_{10} r$.

The correlation dimension can be calculated according to its definition,[17] $D_2=\lim_{r\to 0}\frac{\log C(r)}{\log r}$, where r is the radius around X_i and $C(W,N,r)=\frac{2}{(N+1-W)(N-W)}\sum_{n=W}^{N-1}\sum_{i=0}^{N-1-n}\theta(r-\parallel X_i-X_{i+n}\parallel)$

is calculated using the formula by Theiler.[26] W was set to be the time delay τ and $\theta(x)$ satisfies $\theta(x)=\begin{cases}1 & x>0\\ 0 & x\leq 0\end{cases}$.

Because of the finite signal length and finite measurement accuracy, there is a finite region in the curve of log *C(W, N, r)* versus log *r* termed as the scaling region, in which the slopes of log *C(W, N, r)* versus log *r* curves increase at first but eventually converge with the increase of *m*. We derived the dimension estimate and its standard deviation (less than 1%) using a linear curve fit to the curve of $\log_2 C(r)$ versus $\log_2 r$ in this scaling region. The correlation dimension of a time series can be obtained when the embedding dimension *m* is substantially large.

Figure 1C shows the graph of $\log_2 C(r)$ versus $\log_2 r$ of this Parkinsonian voice, in which the curves from top to bottom correspond to $m = 1, 2,\ldots,12$. In the scaling region ($3.7 < \log_{10} r < 4.3$), the slopes of the $\log_2 C(r)$ versus $\log_2 r$ curves approach 2.30 ± 0.01 with the increase of *m*, giving the estimate of the correlation dimension of this voice. Using the above procedure, the correlation dimensions of all voices from PD and control subjects were obtained.

PERTURBATION ANALYSIS

The 1-second segments of sustained phonation were also processed using *Cspeech* 4.0 software (Paul Milenkovic, Madison, WI).[27] Percent jitter (% Jitt) and percent shimmer (% Shim) were obtained for the nearly periodic phonations. It has been determined that values of percent jitter and percent shimmer are only reliable for nearly periodic voices and are invalid for aperiodic samples.[8] Therefore, eight aperiodic phonation segments (six from PD subjects and two from control subjects) were eliminated from the perturbation analysis.

STATISTICAL ANALYSIS

SigmaStat 3.0 and *SigmaPlot* 8.0 software (Jandel Scientific, San Rafael, CA), respectively, were used to statistically analyze and graph the results from correlation dimension (D_2), percent jitter, and percent shimmer. For each of these three parameters, Mann–Whitney rank sum tests were first used to give an overall comparison between the PD group and the control group. Furthermore, within each parameter, sex differences were evaluated by a comparison between male PD subjects and male control subjects, as well as a comparison between female PD subjects and female control subjects. Statistical significance was set at the level of 0.05.

RESULTS

Nonlinear dynamic analysis

Results of the correlation dimension (D_2) analysis of the acoustic phonatory samples are summarized in Table 1. As anticipated, PD subjects had significantly higher D_2 overall than control subjects ($P = 0.016$) (Figure 2A). D_2 of female PD subjects was significantly higher than that of female control subjects ($P = 0.001$) (Figure 2B), but the D_2 of male PD subjects did not significantly differ from that of male control subjects ($P = 0.92$) (Figure 2C).

Perturbation analysis

Findings from the perturbation analysis are summarized in Tables 2 and 3. Overall, PD subjects had statistically greater percent jitter than control subjects ($P = 0.014$) (Figure 3A), but they did not have significantly different levels of percent shimmer ($P = 0.695$) (Figure 4A). Looking at each sex

TABLE 1. *Correlation Dimension (D_2) in the Voices of PD Subjects and Control Subjects Compared by Sex and Globally*

	D_2		
	PD	**Control**	***P* Value**
Male	M = 1.86 SD = 0.46	M = 1.84 SD = 0.35	0.92
Female	M = 1.85 SD = 0.44	M = 1.46 SD = 0.28	0.001*
Total	M = 1.85 SD = 0.44	M = 1.63 SD = 0.36	0.016*

*Significant difference at the 0.05 level.

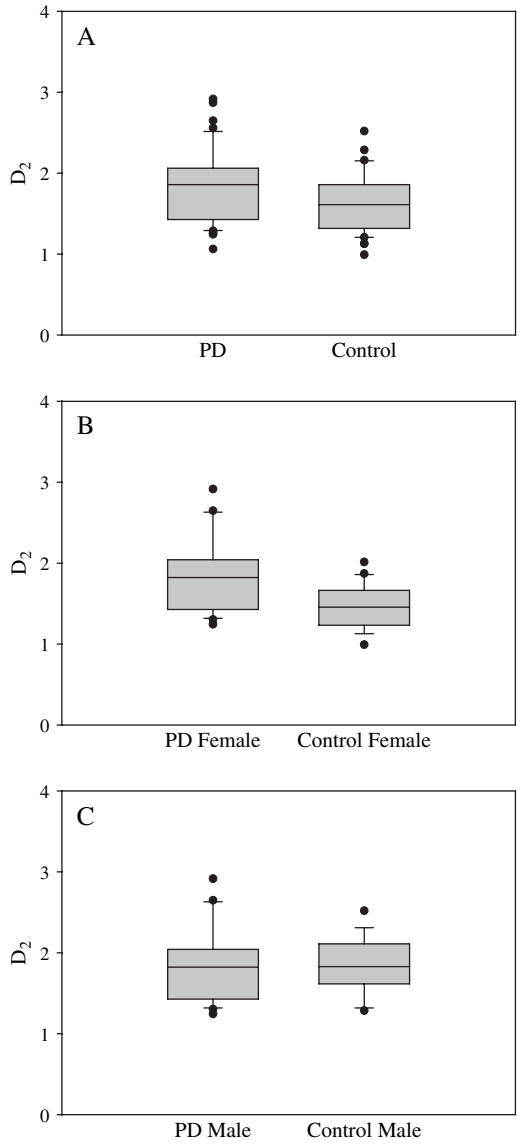

FIGURE 2. D_2 of acoustic signal in PD subjects and control subjects compared (**A**) globally, (**B**) among women, and (**C**) among men.

separately, female PD subjects and female control subjects had statistically indistinguishable levels of percent jitter ($P = 0.144$) (Figure 3B) and percent shimmer ($P = 0.488$) (Figure 4B). Male PD subjects had significantly higher percent jitter values than male control subjects ($P = 0.036$) (Figure 3C), but analysis of percent shimmer did not reveal a significant difference between these groups ($P = 0.574$) (Figure 4C).

TABLE 2. *Percent Jitter (% Jitt) in the Voices of PD Subjects and Control Subjects Compared by Sex and Globally*

	% Jitt		
	PD	**Control**	***P* Value**
Male	M = 0.58 SD = 0.84	M = 0.29 SD = 0.39	0.036*
Female	M = 0.76 SD = 1.27	M = 0.20 SD = 0.12	0.144
Total	M = 0.67 SD = 1.07	M = 0.24 SD = 0.27	0.014*

*Significant difference at the 0.05 level.

DISCUSSION

Evidence from the comparisons conducted in this study suggests that nonlinear dynamic analysis is a valuable method of detecting and describing the vocal pathology of PD. PD subjects showed significantly increased correlation dimension (D_2) in their phonatory signal when compared with control subjects. These findings in nonlinear dynamic analysis paralleled the results from comparisons of jitter (though not shimmer), which found PD subjects to have significantly higher jitter values than control subjects, as in previous studies.[5,6] Finding similar dimension estimates to those of the control subjects in this study, Baken[28] proposed that signal dimension is distinct from parameters like jitter and shimmer in that it measures irregularity rather than variability. This information was presented as support for the value of dimensional description of vocal pathologies.

TABLE 3. *Percent Shimmer (% Shim) in the Voices of PD Subjects and Control Subjects Compared by Sex and Globally*

	% Shim		
	PD	**Control**	***P* Value**
Male	M = 1.00 SD = 1.07	M = 0.74 SD = 0.44	0.574
Female	M = 0.89 SD = 0.89	M = 0.86 SD = 0.51	0.488
Total	M = 0.95 SD = 0.98	M = 0.81 SD = 0.48	0.695

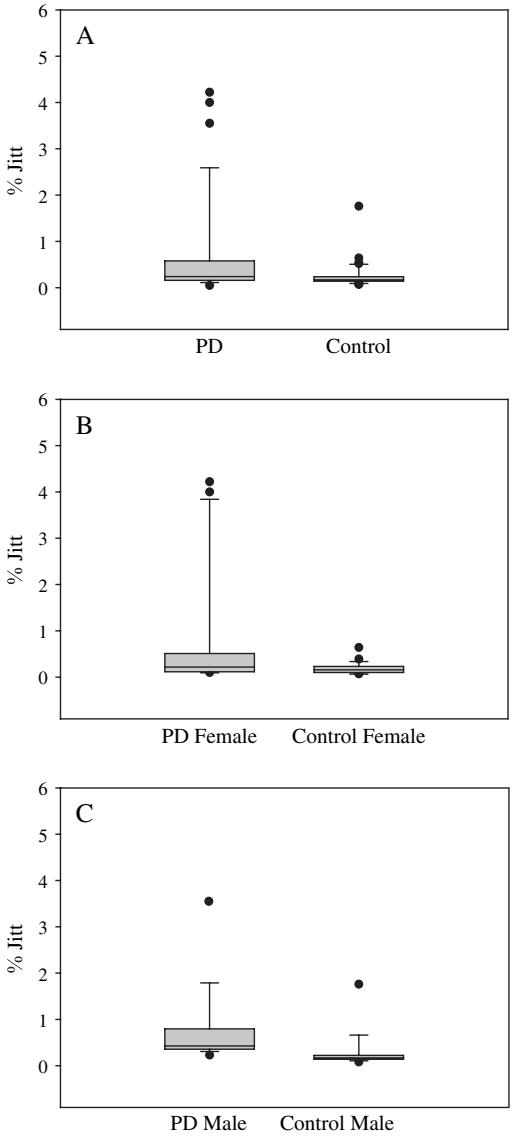

FIGURE 3. Percent jitter (% Jitt) of acoustic signal in PD subjects and control subjects compared (**A**) globally, (**B**) among women, and (**C**) among men.

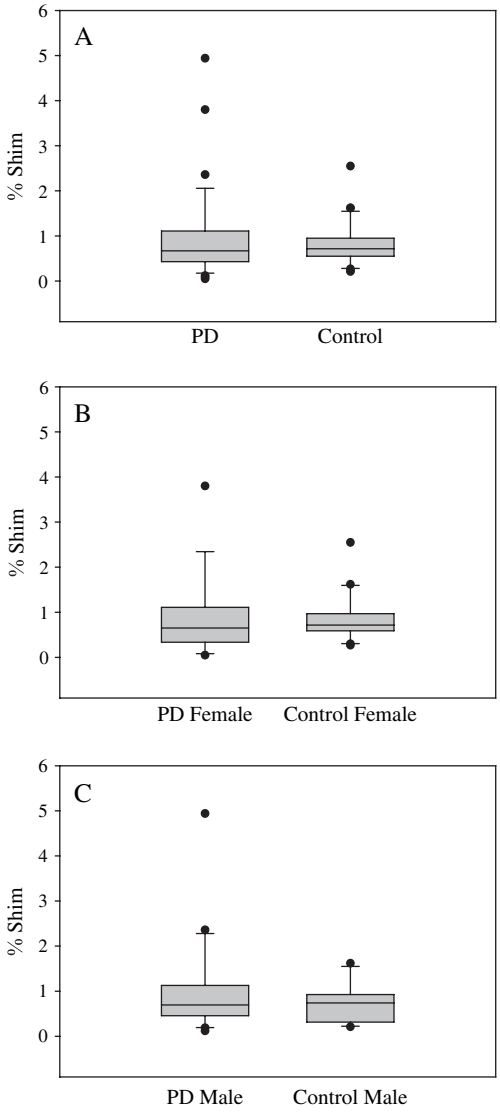

FIGURE 4. Percent shimmer (% Shim) of acoustic signal in PD subjects and control subjects compared (**A**) globally, (**B**) among women, and (**C**) among men.

D_2 can quantify both periodic and aperiodic voice samples, whereas perturbation methods cannot accurately measure aperiodic voices in PD.[8,9] Additionally, aerodynamic measurement has been applied to PD patients. Jiang et al[29] have found that PD patients require greater subglottal pressure to produce phonation because of greater laryngeal airflow resistance, but aerodynamic measurement cannot reveal aperiodic voice characteristics. Nonlinear dynamic methods provide quantitative analysis for aperiodic Parkinsonian voices. Therefore, nonlinear dynamic analyses may be able to add valuable information to other methods (eg, acoustic perturbation and aerodynamic measurement) of describing Parkinsonian vocal pathology.

Nonlinearity in human phonation has been attributed to nonlinearity of stress–strain curves of vocal fold tissues, nonlinearity associated with vocal fold collision, and nonlinearity of pressure-flow relations in the glottis.[13] The abnormal vocal fold rigidity and vocal fold stiffness that are commonly

observed characteristics in PD[4,7,29,30] might partially account for the increased dimension in the Parkinsonian voices of this study. Vocal fold stiffness and bowing in PD have been attributed to cocontraction of the opposing thyroarytenoid and cricothyroid muscles,[30] which function, respectively, to shorten and lengthen the vocal folds. Physiologically, coordinated motor control of muscle groups maintains normal vocal fold function, which can break down in persons with PD.

In this study, D_2 values of Parkinsonian voices were higher than those of normal subjects, which suggests that more degrees of freedom are needed to model Parkinsonian voices. In addition, D_2 values of PD voices were all between 1.00 and 3.00, which shows that finite degrees of freedom can be used to model Parkinsonian voices. A two-mass model with finite degrees of freedom was capable of studying the vibratory characteristics of vocal folds in PD, where increased vocal fold stiffness could induce aperiodic patterns of phonation.[31] Vocal fold systems may have a high number of variables, as observed in finite element models, but vocal fold vibration is only dominated by the first few modes (degrees of freedom).[32,33] These results based on nonlinear dynamic analysis of Parkinsonian voices show a qualitative consistency with these modeling studies.

Some interesting sex differences were observed in this study: female PD subjects had higher D_2 than female control subjects, but male PD subjects and male control subjects did not differ by this measure. Hertrich et al[15] applied another nonlinear parameter, fractal dimension, and did not find male or female PD subjects to have greater aperiodicity in acoustic signal than control subjects, but they did observe greater aperiodicity in the EGG signals of female PD subjects when compared with female controls. Sex differences in these nonlinear parameters have been attributed to sexual dimorphism in laryngeal motor function and size.[6] As in Hertrich et al,[15] this study found higher complexity of phonation in male control subjects than in female control subjects. The preceding sex differences are intriguing and warrant further investigation.

In studies of progressive, secondary vocal impairments, it is essential to consider how the inclusion criteria affect the applicability of the findings. In this investigation, a stage-variant, medication-variant group of PD subjects was analyzed, which suggests that this study's observations describe PD patients throughout the course of the disease. Several aspects of speech deterioration (although not percent jitter) have been correlated with disease progression among PD patients.[34] Whether nonlinear dynamic analyses would find phonatory pathology to be correlated with severity of PD is certainly of interest. Overall, evidence from this study suggests that nonlinear dynamic analyses may represent a useful new method in the study of Parkinsonian vocal pathology, complementing traditional methods of voice analysis.

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