Relationship Between Voice and Motor Disabilities of Parkinson's Disease

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Summary: To evaluate voice of Iranian patients with Parkinson's disease (PD) and find any relationship between motor disabilities and acoustic voice parameters as speech motor components. We evaluated 27 Farsi-speaking PD patients and 21 age- and sex-matched healthy persons as control. Motor performance was assessed by the Unified Parkinson's Disease Rating Scale part III and Hoehn and Yahr rating scale in the "on" state. Acoustic voice evaluation, including fundamental frequency (f0), standard deviation of f0, minimum of f0, maximum of f0, shimmer, jitter, and harmonic to noise ratio, was done using the *Praat* software via /a/ prolongation. No difference was seen between the voice of the patients and the voice of the controls. f0 and its variation had a significant correlation with the duration of the disease, but did not have any relationships with the Unified Parkinson's Disease Rating Scale part III. Only limited relationship was observed between voice and motor disabilities. Tremor is an important main feature of PD that affects motor and phonation systems. Females had an older age at onset, more prolonged disease, and more severe motor disabilities (not statistically significant), but phonation disorders were more frequent in males and showed more relationship with severity of motor disabilities. Voice is affected by PD earlier than many other motor components and is more sensitive to disease progression. Tremor is the most effective part of PD that impacts voice. PD has more effect on voice of male *versus* female patients.

Key Words: Parkinson's disease–motor disorders–UPDRS–voice–acoustic.

INTRODUCTION

Idiopathic Parkinson's disease (IPD) is a neurodegenerative disorder with motor and nonmotor clinical manifestations. Bradykinesia, rigidity, tremor at rest, and postural instability constitute core motor features,[1] whereas neuropsychiatric disorders, autonomic dysfunction, and sleep difficulties are common nonmotor symptoms.[2] Speech abnormality is a very common motor disorder in IPD. Hypokinetic dysarthria, a speech alteration that affects all speech subsystems such as respiration, phonation, articulation, and prosody,[3] is observed in almost 90% of the IPD patients.[4,5] It seems that voice is affected earlier in this process followed by articulation and fluency abnormalities.[6] Most distinct and frequent voice symptoms of PD are mono loudness, mono pitch, breathiness, harshness, and reduced loudness.[7] It is believed that perceptual features of hypokinetic dysarthria are related to pathophysiological motor deficits; for instance, mono loudness, mono pitch, variable rate, short rushes of speech, and reduced stress are in accordance with muscle rigidity,[8] and long and excessive pauses may result from bradykinesia.[9] In recent decades, some studies used the Unified Parkinson's Disease Rating Scale part III (UPDRS-III) to investigate any relationship between the IPD motor severity and the patients' voice characteristics. Whereas some studies have reported a strong relationship between UPDRS-III and acoustic voice parameters,[10–13] others have declined such a relationship.[14–17] A limited number of surveys were conducted to find a connection between voice and motor disabilities (UPDRS-III subscales) in PD patients.[15,18] The authors of these surveys tried to figure out whether the speech is a peripheral or an axial feature of PD and also to figure out what is the effect of dopaminergic medication therapy on speech. Because the authors studied small groups of patients,[18] and patients were in early stages of the disease,[15] their results are questionable.

As the disease progresses, deterioration of motor and nonmotor features is expected.[6,19] There has been a debate about the relationship between IPD duration and speech and voice characteristics. Some studies suggested the negative effect of disease duration on speech parameters,[20–22] whereas others detected no relationship between those factors.[14,16,17,23]

Because previous studies reported contradictory results and there is no survey on Farsi-speaking Iranian IPD patients, this study focused on the impact of disease duration and severity on the phonation features, and compared the vocal characteristics of patients with a normal group to find any changes resulting from PD in Farsi-speaking patients. In addition, the present study tried to answer the question whether the phonation system (voice) has a separate mechanism from other motor mechanisms in IPD.

MATERIALS AND METHODS

The study protocol was approved by the Ethics Committee of Tehran University of Medical Sciences. Informed consent was obtained from all study participants. This cross-sectional, nonexperimental study was carried out on 27 IPD patients and 21 healthy age- and sex-matched control subjects (Table 1). The patients were recruited by convenience sampling from the movement disorders clinic of Rasool-e-Akram Hospital, Iran University of Medical Sciences, and a private movement disorders clinic run by one of the authors (G.S.). The diagnosis of IPD was based on the UK Parkinson's Disease Society Brain Bank's clinical

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TABLE 1.
Basic Characteristics of PD Patients

Sex	Number	Age (Mean ± SD)	PD Severity (UPDRS-III) Min	Max	(Mean ± SD)	Severity (H&Y) Min	Max	(Mean ± SD)	Duration of Disease (Mean ± SD)
Male	15	61.6 ± 8.94	13	62	29.60 ± 14.237	2	3	2.07 ± 0.258	8.6 ± 4.5
Female	12	59.33 ± 7.3	11	84	35.42 ± 19.88	1	3	2.25 ± 0.622	11.41 ± 7.66
Total	27	60.59 ± 8.18	11	84	32.19 ± 16.88	1	3	2.15 ± 0.456	9.85 ± 6.15

Notes: The units of age and duration of disease: Year. Month (61.6 means 61 years and 6 months).
Abbreviations: H&Y, Hoehn and Yahr; max, maximum; min, minimum; PD, Parkinson's disease; SD, standard deviation; UPDRS-III, third part of the Unified Parkinson's Disease Rating Scale.

diagnostic criteria.[2] Inclusion criteria of this study were (1) no other neurological or movement disorders, (2) ages above 50 years, (3) at least 3 months of levodopa therapy, (4) disease duration more than 5 years, (5) no history of speech therapy, (6) being monolingual (only Farsi speakers), (7) no history of laryngeal cancer and endotracheal intubation, and (8) no history of surgery, chemotherapy, radiotherapy, or trauma to the head and neck. All participants had used levodopa as the main drug. Amantadine, dopamine agonists, benzodiazepines, and selective serotonin reuptake inhibitors were among the medications taken by participants. All healthy subjects were checked by a neurologist (S.K.) and an otolaryngologist for any neurological or voice disorder, respectively.

The disease severity was assessed by two sets of tests: UPDRS-III (score 0–132) and Hoehn & Yahr rating scale (H&Y; score 1–5). All participants were examined 45–90 minutes after taking their regular dose of levodopa-carbidopa, so they were in the "on" state during rating. After both ratings were completed, a speech and language pathologist (F.M.), not blinded to the study, assessed and recorded the subjects' voice in a quiet room (noise less than 35 dB).[20] The participants sat on a fixed armchair with a headset (Sony DR-320DPV, Japan) placed on their ears, and the microphone-to-mouth distance was 8 cm.[8] After being instructed by the examiner, all participants were asked to prolong the vowel /a/ (with their habitual pitch and loudness) two times, each time for 5 seconds (39), and the second sequence was recorded for acoustic parameters analysis. Voice samples were recorded on a laptop (MSI-CR420, China; OS: Windows XP, sound card 6.1.7600.16385, Paul Boersma). In the present study, *Praat* software version 5.1.17 was used to analyze mean fundamental frequency (f0), standard deviation of f0 (f0SD), minimum of f0 (min f0), maximum of f0 (max f0), shimmer, jitter, and harmonic to noise ratio (HNR). Both neurological and speech tests were done at the same center in a single visit.

Statistical analyses

SPSS Statistics 16 software was used for statistical analysis (Sun Microsystems, Inc., Santa Clara, CA, USA). We used the Kolmogorov-Smirnov test to determine the normality of the variables, and the Mann-Whitney *U* test and the independent sample *t* test to compare the mean variables in patient and in control groups. Pearson and Spearman correlation coefficients were used to evaluate any statistically significant relationship between voice features and total UPDRS-III and its subscales. Chi-square test was used to ascertain sex equality. The confidence interval was 95% ($P < 0.05$).

RESULTS

Gender, age, duration of PD, total UPDRS-III, and H&Y scores are shown in Table 1. Almost 65% of the patients were in the first decade of disease, 26% were in the second decade, and 8% were in the third decade. The independent sample *t* test and chi-square test showed that the patients and the controls were age ($P = 0.619$) and sex ($P = 0.585$) matched. The age at onset of the female patients (53 ± 11.25 years) was not different from that of the male patients (47.91 ± 10.29 years) ($P = 0.73$). The difference in the disease duration was not significant between male and female patients ($P = 0.055$). The highest H&Y and UPDRS-III scores were 3 (in both sexes) and 84 (in females), respectively. Although females had higher disease severity than males (84 *vs* 62), the difference was not statistically significant.

Acoustic voice evaluation

Independent sample *t* test was used to compare the mean f0, min f0, max f0, shimmer, and HNR between IPD and control groups, and Mann-Whitney *U* test was used for SDf0. We did not find any significant differences in the acoustic voice characteristics between the two groups before and after sex segregation (Table 2).

Relationship between voice, disease duration, and disease severity

Some variables like f0, max f0, min f0, shimmer, HNR, disease duration, UPDRS-III score, and severity of rigidity and leg agility in UPDRS-III had normal distributions, but other variables did not follow the same pattern. So, to investigate the relationship between voice, disease duration, disease severity, and motor disabilities, a parametric (Pearson correlation coefficient) and a nonparametric correlation test (spearman correlation coefficient) were used.

Table 3 shows the relationship between disease duration, voice characteristics, and disease severity of the patients.

In the IPD group, f0 (r = 0.440), SDf0 (r = 0.397), min f0 (0.448), and max f0 (r = 0.433) had a positive correlation with the disease duration. In female patients, there was a relationship between the duration of PD and f0 (r = 0.599) and shimmer (r = 0.626), but a similar relationship was not found in the male patients. There was no correlation between the PD duration and UPDRS-III (disease severity), but there was a positive

TABLE 2.
Voice Characteristics in PD Patients and Control Group

Voice Parameter	PD Male (n = 15) Mean ± SD	Control Male (n = 10) Mean ± SD	*P* Value	PD Female (n = 12) Mean ± SD	Control Female (n = 11) Mean ± SD	*P* Value	Total PD (n = 27) Mean ± SD	Total Control (n = 21) Mean ± SD	*P* Value
f0	138.5 ± 31.5	132.2 ± 25.5	0.603	190.7 ± 26.88	188.4 ± 29.7	0.849	161.7 ± 39.26	161.1 ± 39.53	0.997
SDf0	1.79 ± 0.098	1.37 ± 0.078	0.177	8 ± 14.71	7.88 ± 13.88	0.740	4.55 ± 10.10	4.78 ± 10.38	0.625
Min f0	133.2 ± 29.92	128.8 ± 24.06	0.703	169.05 ± 40.9	172.3 ± 50.73	0.865	149.1 ± 39.97	151.1 ± 45.19	0.839
Max f0	143.3 ± 32.93	136.3 ± 27.34	0.582	200.6 ± 31.33	197.2 ± 25.42	0.782	168.8 ± 42.91	168.2 ± 40.41	0.964
Jitter	0.475 ± 0.67	0.207 ± 1.33	0.531	0.22 ± 0.228	1.65 ± 0.73	0.833	0.361 ± 0.533	0.185 ± 0.106	0.412
Shimmer	3.11 ± 2.37	2.45 ± 2.16	0.485	2.40 ± 1.21	2.33 ± 0.97	0.874	2.85 ± 1.94	2.38 ± 1.60	0.438
HNR	19.67 ± 6.46	22.63 ± 4.14	0.213	22.2 ± 3.58	21.6 ± 3.07	0.670	20.83 ± 5.45	22.1 ± 3.56	0.348

Note: All of voice parameters' units are hertz (Hz).
Abbreviations: f0, average fundamental frequency; HNR, harmonic to noise ratio; max, maximum; min, minimum; PD, Parkinson's disease; SD, standard deviation.

TABLE 3.
The Results of Correlation Between Voice Characteristics, Disease Duration, and Disease Severity in PD Patients

	Duration of Disease			Disease Severity (UPDRS-III)			Disease Severity (H&Y)		
Parameter	Male (n = 15)	Female (n = 12)	Total (n = 27)	Male (n = 15)	Female (n = 12)	Total (n = 27)	Male (n = 15)	Female (n = 12)	Total (n = 27)
f0	0.214	0.599*	0.440*	–0.385	0.030	–0.013	0.244	0.655	0.456*
SDf0	0.322	0.274	0.397*	0.273	0.210	0.238	0.371	0.363	0.370
Min f0	0.208	0.501	0.448*	–0.396	0.085	–0.013	0.231	0.595	0.509†
Max f0	0.224	0.540	0.433*	–0.376	0.119	0.030	0.252	0.561	0.433*
Jitter	0.202	0.119	0.168	0.503	0.231	0.293	–0.186	0.267	–0.044
Shimmer	0.144	0.626*	0.232	–0.046	0.165	–0.007	–0.086	0.440	–0.088
HNR	–0.135	–0.378	–0.138	–0.231	–0.244	–0.162	0.155	–0.246	0.012
DOD	—	—	—	0.308	0.305	0.332	0.332	0.606*	0.557†

* Correlation is significant at the 0.05 (two tailed).
† Correlation is significant at the 0.01 (two tailed).
Abbreviations: DOD, duration of disease; f0, average fundamental frequency; H&Y, Hoehn and Yahr; HNR, harmonic to noise ratio; max, maximum; min, minimum; PD, Parkinson's disease; SD, standard deviation; UPDRS-III, third part of the Unified Parkinson's Disease Rating Scale.

TABLE 4.
The Results of Correlation Between UPDRS-III and its Subscales (Motor Disabilities) with Voice of Total Patients*

	f0	SDf0	Min f0	Max f0	Jitter	Shimmer	HNR
Speech	0.033	0.358	0.057	0.044	0.384†	0.445†	–0.312
Facial expression	0.221	0.469†	0.140	0.257	0.305	0.472†	–0.345
Rigidity	0.088	–0.074	0.044	0.090	–0.012	–0.364	0.177
Finger tapping	0.033	0.267	–0.241	0.099	0.305	0.205	–0.147
Hand movements	–0.045	0.168	–0.198	0.005	0.237	0.100	–0.053
Pron-supination of hands	–0.007	0.123	–0.143	0.033	0.266	0.217	–0.292
Toe tapping	0.292	0.168	0.084	0.330	0.101	0.082	–0.050
Leg agility	0.033	0.189	0.077	0.060	0.223	–0.005	–0.079
Arising from chair	0.249	0.320	0.229	0.227	0.205	0.292	–0.288
Gait	0.144	0.340	0.216	0.150	0.336	0.373	–0.299
Freezing of gait	–0.309	0.235	–0.237	–0.309	0.323	0.340	–0.302
Postural stability	0.277	0.193	0.301	0.273	0.028	0.321	–0.172
Posture	0.134	0.265	0.123	0.184	0.166	0.314	–0.232
Spontaneity of movement (body bradykinesia)	0.052	0.365	0.176	0.028	0.225	0.258	–0.155
Postural tremor of the hands	–0.120	0.184	–0.192	–0.119	0.200	0.021	–0.035
Kinetic tremor of the hands	–0.496†	–0.240	–0.261	–0.515†	0.151	0.037	–0.117
Rest tremor amplitude	–0.263	0.036	–0.211	–0.234	0.262	0.185	–0.256
Constancy of rest tremor	–0.219	0.091	–0.241	–0.167	0.283	0.225	–0.273
Total	–0.013	0.238	–0.013	0.030	0.293	–0.007	–0.162

* Correlation is significant at the 0.05 (two tailed).
† Correlation is significant at the 0.01 (two tailed).
Abbreviations: f0, average fundamental frequency; HNR, harmonic to noise ratio; max, maximum; min, minimum; Pron-supination of hands, pronation-supination movements of hands; SDf0, standard deviation of fundamental frequency; total, total score of UPDRS; UPDRS-III, third part of the Unified Parkinson's Disease Rating Scale.

correlation between the disease duration and the H&Y in females (r = 0.606).

The analysis of correlation between voice characteristics and disease severity (H&Y, UPDRS-III) failed to show any link between voice and UPDRS-III. However, some of the voice features such as f0 (r = 0.456), min f0 (r = 0.509), and max f0 (r = 0.433) showed statistically significant relationship with H&Y in patients as general, but this correlation was lost when the test was applied to two sexes separately (Table 3).

Relationship between voice and motor disabilities

Table 4 shows significant correlations between some of the motor features (UPDRS-III subscales) and the patients' voice. The "speech" subscale had a correlation with jitter ($P = 0.048$) and shimmer of voice ($P = 0.020$). Facial expression had a statistical relationship with SDf0 ($P = 0013$) and shimmer ($P = 0.013$). There was also a positive correlation between kinetic tremor of the hands with f0 ($P = 0.008$) and max f0 ($P = 0.006$).

Gender-specific relationship between voice and motor disabilities

A summary of voice features that show gender-specific relationships with UPDRS-III subscales is shown in Table 5.

DISCUSSION

Lack of statistically significant differences between the voice of the IPD patients during the "on" state and the voice of the control group may suggest that dopaminergic medications have positive effects on the voice in PD.[24] It is generally believed that voice is an axial feature of IPD, but none of the axial subscales of UPDRS-III such as gait and postural stability had a relationship with voice. On the other hand, most of the nonaxial features (like tremor) had a positive correlation with voice. Therefore, we still need more studies to find out whether voice is an axial or a peripheral (nonaxial) feature of PD.

The duration of PD showed a positive correlation with f0 and its variation but had no correlation with the disease severity (UPDRS-III). The mean f0 refers to vocal folds' movements during time and UPDRS-III evaluates some nonspeech movements. Fineness and super subtlety of the laryngeal muscle functions make them more vulnerable to motor disorders, so vocal fold movement shows earlier and more advanced alternations due to PD compared with other motor abnormalities. Therefore, "voice" might be a more sensitive indicator of disease progression than other motor features of PD.

Like other research, only a limited relationship was observed between voice and motor disabilities.[15,18] It may be suggested that the motor speech control system is basically different from peripheral motor control mechanisms. Meanwhile, by analyzing both sexes, more relationship was observed between voice and motor disabilities; almost half of them were between different types of tremor and voice. It indicates that tremor is an important main feature of PD that affects phonation characteristics of the patients significantly.

In the present study, the relationship between the duration of disease, voice, and disease severity, especially the "speech" part

TABLE 5.
***P* Values of Significant Correlation Between UPDRS-III and Subscales (Motor Disabilities) With Voice of PD Patients by Sex Segregation**

	f0	SDf0	Min f0	Max f0	Jitter	Shimmer	HNR
Speech		0.041*			0.048*		
Facial expression		0.034*				0.042†	
Postural stability			0.04†				
Posture						0.04†	
Spontaneity of mov		0.021*			0.045*		
Kinetic tremor of the hands	0.002†			0.002†			
Rest tremor amplitude	0.013*		0.013*	0.018*			
Constancy of rest tremor	0.022*		0.022*	0.03*			

* Male.
† Female.
Abbreviations: f0, average fundamental frequency; HNR, harmonic to noise ratio; max, maximum; min, minimum; PD, Parkinson's disease; SDf0, standard deviation of fundamental frequency; spontaneity of mov, spontaneity of movement (body bradykinesia); UPDRS-III, third part of the Unified Parkinson's Disease Rating Scale.

of UPDRS-III, was expected. Although UPDRS-III is a very common tool for evaluating PD motor disabilities, all subscales including "speech" were evaluated subjectively by a 0–4 scoring system. Speech is a sophisticated multidimensional system that requires a very high level of coordination between respiration, phonation, and articulation. Therefore, it seems that more detailed and accurate measures are needed for speech assessment in PD, and UPDRS-III is not an effective and sufficient tool for its evaluation.

Although other studies have reported some differences between sexes, such as lower age at onset, better motor abilities,[25] and higher tremor and dyskinesia in women,[26,27] we realized that Iranian patients showed a different pattern. Here, females had an older age at onset, more prolonged disease, and more severe motor disabilities (not statistically significant), but phonation abnormalities were more frequent in males and showed more correlations with severity of motor disabilities (11 items *vs* five items). It may suggest that PD has more influence on the voice of males than on the voice of females.[28]

CONCLUSION

In this study, we tried to find any relation between voice and motor disabilities of IPD, and to discover any link between voice characteristics and the disease duration and severity of Iranian IPD patients.

Although more studies warranted finding the relationship between motor function and voice in IPD, it seems that the phonation system and voice are more sensitive to IPD duration and severity than other motor subsystems, and speech has a separate motor control mechanism. PD affects the voice of the males more than females. Tremor is the most effective cardinal feature of IPD that negatively influences voice.

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REFERENCES

1. Skodda S. Aspects of speech rate and regularity in Parkinson's disease. *J Neurol Sci*. 2011;310:231–236.
2. Fahn S, Jankovic J. *Principles and Practice of Movement Disorders*. Philadelphia: Churchill Livingstone Elsevier; 2007.
3. Mate MA, Cobeta I, Jimenez-Jimenez FJ, et al. Digital voice analysis in patients with advanced Parkinson's disease undergoing deep brain stimulation therapy. *J Voice*. 2012;26:496–501. [Epub 2011/06/28. eng]; PubMed PMID: 21704492.
4. Muller J, Wenning GK, Verny M, et al. Progression of dysarthria and dysphagia in postmortem-confirmed parkinsonian disorders. *Arch Neurol*. 2001;58:259–264. [Epub 2001/02/15. eng]; PubMed PMID: 11176964.
5. Hartelius L, Svensson P. Speech and swallowing symptoms associated with Parkinson's disease and multiple sclerosis: a survey. *Folia Phoniatr Logop*. 1994;46:9–17. [Epub 1994/01/01. eng]; PubMed PMID: 8162135.
6. Logemann JA, Fisher HB, Boshes B, et al. Frequency and cooccurrence of vocal tract dysfunctions in the speech of a large sample of Parkinson patients. *J Speech Hear Disord*. 1978;43:47–57. [Epub 1978/02/01. eng]; PubMed PMID: 633872.
7. Holmes RJ, Oates JM, Phyland DJ, et al. Voice characteristics in the progression of Parkinson's disease. *Int J Lang Commun Disord*. 2000;35:407–418. [Epub 2000/08/30. eng]; PubMed PMID: 10963022.
8. Blanchet PG, Snyder GJ. Speech rate treatments for individuals with dysarthria: a tutorial. *Percept Mot Skills*. 2010;110(3 pt 1):965–982. [Epub 2010/08/05. eng]; PubMed PMID: 20681347.
9. Yorkston KM. Treatment efficacy: dysarthria. *J Speech Hear Res*. 1996;39:S46–S57. [Epub 1996/10/01. eng]; PubMed PMID: 8898266.
10. Asgari M, Shafran I. Predicting severity of Parkinson's disease from speech. *Conference proceedings: Annual International Conference of the IEEE Engineering in Medicine and Biology Society IEEE Engineering in Medicine and Biology Society Annual Conference*. 2010;2010:5201–5204.
11. Bayestehtashk A, Asgari M, Shafran I, et al. Fully automated assessment of the severity of Parkinson's disease from speech. *Comput Speech Lang*. 2015;29:172–185. [Epub 2014/11/11. Eng]; PubMed PMID: 25382935. Pubmed Central PMCID: PMC4222054.
12. Tsanas A, Little MA, McSharry PE, et al. Accurate telemonitoring of Parkinson's disease progression by noninvasive speech tests. *IEEE Trans Biomed Eng*. 2010;57:884–893. [Epub 2009/11/26. eng]; PubMed PMID: 19932995.
13. Tsanas A, Little MA, McSharry PE, et al. Novel speech signal processing algorithms for high-accuracy classification of Parkinson's disease. *IEEE Trans Biomed Eng*. 2012;59:1264–1271. [Epub 2012/01/18. eng]; PubMed PMID: 22249592.
14. Gamboa J, Jiménez-Jiménez FJ, Nieto A, et al. Acoustic voice analysis in patients with Parkinson's disease treated with dopaminergic drugs. *J Voice*. 1997;11:314–320.

15. Midi I, Dogan M, Koseoglu M, et al. Voice abnormalities and their relation with motor dysfunction in Parkinson's disease. *Acta Neurol Scand*. 2008;117:26–34. [Epub 2007/11/23. eng]; PubMed PMID: 18031561.
16. Miller N, Allcock L, Jones D, et al. Prevalence and pattern of perceived intelligibility changes in Parkinson's disease. *J Neurol Neurosurg Psychiatry*. 2007;78:1188–1190. [Epub 2007/04/03. eng]; PubMed PMID: 17400592. Pubmed Central PMCID: PMC2117612.
17. Martinez-Sanchez F, Meilan JJ, Carro J, et al. Speech rate in Parkinson's disease: a controlled study. *Neurologia*. 2015;doi: 10.1016/j.nrl.2014.12.002; [Epub 2015/02/11]; PubMed PMID: 25660139. Estudio controlado del ritmo del habla en la enfermedad de Parkinson. Eng Spa.
18. Goberman AM. Correlation between acoustic speech characteristics and non-speech motor performance in Parkinson Disease. *Med Sci Monit*. 2005;11:CR109–CR116. [Epub 2005/03/01. eng]; PubMed PMID: 15735562.
19. Ho AK, Iansek R, Marigliani C, et al. Speech impairment in a large sample of patients with Parkinson's disease. *Behav Neurol*. 1998;11:131–137. [Epub 2001/09/25. Eng]; PubMed PMID: 11568413.
20. Skodda S, Rinsche H, Schlegel U. Progression of dysprosody in Parkinson's disease over time—a longitudinal study. *Mov Disord*. 2009;24:716–722. [Epub 2009/01/02. eng]; PubMed PMID: 19117364.
21. Skodda S, Gronheit W, Schlegel U. Impairment of vowel articulation as a possible marker of disease progression in Parkinson's disease. *PLoS ONE*. 2012;7:e32132. [Epub 2012/03/06. eng]; PubMed PMID: 22389682. Pubmed Central PMCID: PMC3289640.
22. Brabo NC, Minett TS, Ortiz KZ. Fluency in Parkinson's disease: disease duration, cognitive status and age. *Arq Neuropsiquiatr*. 2014;72:349–355. [Epub 2014/05/28. eng]; PubMed PMID: 24863510.
23. Skodda S, Visser W, Schlegel U. Vowel articulation in Parkinson's disease. *J Voice*. 2010;25:467–472.
24. Bejjani BP, Gervais D, Arnulf I, et al. Axial parkinsonian symptoms can be improved: the role of levodopa and bilateral subthalamic stimulation. *J Neurol Neurosurg Psychiatry*. 2000;68:595–600. [Epub 2000/04/15. eng]; PubMed PMID: 10766889. Pubmed Central PMCID: 1736917.
25. Lyons KE, Hubble JP, Troster AI, et al. Gender differences in Parkinson's disease. *Clin Neuropharmacol*. 1998;21:118–121. [Epub 1998/05/14. eng]; PubMed PMID: 9579298.
26. Haaxma CA, Bloem BR, Borm GF, et al. Gender differences in Parkinson's disease. *J Neurol Neurosurg Psychiatry*. 2007;78:819–824. [Epub 2006/11/14. eng]; PubMed PMID: 17098842. Pubmed Central PMCID: PMC2117736.
27. Zappia M, Annesi G, Nicoletti G, et al. Sex differences in clinical and genetic determinants of levodopa peak-dose dyskinesias in Parkinson disease: an exploratory study. *Arch Neurol*. 2005;62:601–605. [Epub 2005/04/13. eng]; PubMed PMID: 15824260.
28. Majdinasa F, Moradi N, Karkheiran S, et al. Voice Handicap Index (VHI) in Persian speaking Parkinson's disease patients. *Salmand*. 2014;9.