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Correlation between Acoustic Parameters and Disease Severity and Duration in Patients with Multiple Sclerosis

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Abstract

Background: Since in multiple sclerosis (MS), changes in speech and voice quality often precede other signs and symptoms; early diagnosis of these changes is necessary. In this study, an acoustic examination of phonation subsystem was performed. Due to the progressive nature of multiple sclerosis, the aim of this study was to examine the correlation between acoustic parameters of voice quality and disease severity and duration.

Methods: This descriptive-analytic study was performed on 43 patients with multiple sclerosis. The disease severity was detected by a neurologist based on the Expanded Disability Status Scale (EDSS) for each patient. Acoustic analysis was performed during the production of sustained vowel /a/ and accordingly, the maximum phonation time (MPT), perturbation of the frequency (jitter), perturbation of amplitude (shimmer), the maximum and minimum frequency, and the highest and lowest intensity were evaluated. All the acoustic analyses were performed using PRAAT software. Data were statistically analyzed using Spearman's correlation coefficient by SPSS version 21.

Results: The lowest intensity showed a significant correlation with disease severity (P=0.00). Also, the highest and lowest intensity showed a significant correlation with disease duration (P=0.022 and P=0.002).

Conclusion: One of the earlier symptoms of central nervous system impairment resulting from multiple sclerosis is changes in phonation subsystem and voice quality. These changes may appear at any clinical stages; however, the symptoms might get worse over time, with the progression of the disease. Therefore, immediate acoustic assessments and interventions can prevent more degradation of voice quality.

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Introduction

Speech production system consists of an interconnected and complex set of speech subsystems including respiration, phonation, articulation, resonance, and prosody (1). The proper function of these subsystems results from the integration of uncountable neurocognitive, neuromuscular, and musculoskeletal activities which make speech production intelligible and understandable. Any disturbance in the integration results in speech problems and, thus, in speech intelligibility disorders, which directly affects verbal communication and also the individuals' social, educational and occupational positions (2). Hence, assessment, diagnosis, and treatment of speech disorders and voice quality are of great importance.

Neurological disorders, including progressive multiple sclerosis (MS), can affect speech and voice quality and finally may lead to speech disorders and speech intelligibility disturbance (3). Multiple sclerosis is a progressive autoimmune disease that affects the central nervous system (3). The type and severity of its symptoms vary depending on which part of the nervous system is involved (4). In general, five clinical phenotypes of MS include CIS (Clinically isolated syndrome), relapsing-remitting MS (RRMS), primary progressive MS (PPMS), secondary progressive MS (SPMS), and progressive relapsing MS (PRMS) (5). In addition to motor disorders in the organs, involvement of the central nervous system in MS affects speech function. Also, it is observed that throughout the course of the disease progression, the processes of demyelination in 40% of the patients lead to the weakness of the speech production muscles, including palatal muscle, laryngeal muscle and tongue muscle (4). The weakness of these speech muscles result in voice quality disorders including harshness (86%), deficit in loudness (68%) and pitch (69%) variations (6, 7). The degeneration of speech production muscles in MS affects each subsystem to varying degrees from mild to severe (4).

Since changes in speech and individual voice quality often occur earlier than motor signs and symptoms in neurological disorders, such as multiple sclerosis (8, 9), early diagnosis of these changes is of great importance. Acoustic evaluation with high accuracy and sensitivity can reveal any changes in the vocal tract and speech articulators in the early stages of neurological disorders (9, 10). Hence, as a complementary instrument along with other medical diagnostic procedures, acoustic assessments of speech and voice quality for diagnosing and implementing timely therapeutic interventions is essential in these disorders (11).

Acoustic assessments in MS, like other neurological disorders, have the capacity to detect any deviations or disturbances in speech abnormalities. Therefore, acoustic assessments can be used for differential diagnosis of multiple sclerosis against other neurological disorders (1), and also for assessment of the speech changes, such as its deterioration in the process of this progressive disease or its improvement as a result of treatment. Also, such an assessment is applicable in determining the severity of impairment (1). Thus, the need for acoustic assessments especially in the early stages of the disease as well as during the process of treatment in order to explore the effects of medical and behavioral therapies, is intensely inspired.

Based on the studies conducted on MS, alterations in periaqueductal gray matter, as a common finding in MS, affect phonation subsystem (12), which consequently cause more damages, especially in the early stages of the disease (3, 10, 13). In the process of the disease progression, some changes and deviations result in perceptual vocal symptoms-such as deficit of loudness control, impaired pitch control, harsh voice quality, and breathiness, which consequently affect voice quality (1, 14). One of the methods in investigating these impairments is acoustic assessments, which are objective and sensitive to any changes in the vocal tract as well as to speech abnormalities in motor speech disorders caused by neurological diseases (10).

There are few studies on the relationship between phonation parameters and neurological status in MS, therefore, it is critical to shed light over this relationship and the way the parameters are correlated. To investigate the impairment of the phonation subsystem in patients with MS, the present study focused on phonation parameters including maximum phonation time (MPT), frequency perturbation (jitter), amplitude perturbation (shimmer), the maximum and minimum frequency, the highest and lowest intensity. Concerning the progressive nature of the disease and the fact that voice quality and consequently acoustic features of speech might be affected (15), in this study it was attempted to examine the relationship between acoustic parameters and the disease severity and duration. This study also aimed to investigate the changes in the parameters associated with the phonation subsystem caused by MS, and to analyze the correlation between these changes and the characteristics of the disease, as well as the way the above-mentioned acoustic changes were affected.

Materials and Methods

In this analytical-descriptive study, 43 MS patients with a mean age of 35.3±9.23 years, were included. The sample size of the study was calculated according to Bauer et al (16) and using the correlation sample size formula ($\alpha = 0.05$, $\beta = 0.02$). The inclusion criteria for this study were as follow: age range between 18-60 years, the definite diagnosis of the disease by a neurologist, absence of any infections in the upper respiratory tract within three weeks before recording the audio samples or on the assessment day, no history of voice problems, tracheostomy, head and neck surgery, no history of smoking or drug abuse, no history of hormonal disorders prior the study, being monolingual (Persian language), no history of perceptual or cognitive problems, no history of anatomical problems of articulatory system (lip, tongue, etc.), not being in relapse phase; also concerning the high prevalence of the relapsing-remitting phenotype in Iran (17), only MS patients belonging to this category were eligible to take part in the study.

To collect data, first, diagnosis of MS was confirmed by a neurologist, and the severity of disease was determined based on the Expanded Disability Status Scale (EDSS) for each individual. The scale ranges from a score of 0 (normal neurological examination) to 10 (death from MS complication) (18). Then, the participants were selected based on the inclusion and the exclusion criteria from those visiting MS Society of Ahwaz, Khuzestan, before referring to a certified speech-language pathologist (SLP) (19). Next, all the subjects signed a written consent form and filled out personal information sheets. Thereafter, they underwent acoustic assessments by an SLP. It should be noted that this study was approved by the Ethics Committee of the Ahvaz Jundishapur University of Medical Sciences (IR.AJUMS.REC.1395.545).

These tasks and recording of acoustic samples were done in a soundproof room via a microphone (the *unidirectional dynamic cardioids AKG, C1000S)* attached to a portable computer at a distance of 10 cm and 45-degree angle to the subject's mouth (8, 20, 21). Before recording the audio samples, the tasks were explained and demonstrated to the patients by the examiner. Then each task was performed by the patients before the recording started. The test items were conducted as following:

Measurement of maximum phonation time

The participants were asked to take a deep breath while reclining and sitting on a seat, and after receiving a cue, sustain the vowel /a/ for as long as they could at the most comfortable loudness and pitch. After obtaining the beginning and the end of sustained vowels, the phonation time was measured three times for each patient using PRAAT software; the greatest number was recorded as the maximum phonation time (22).

Measurement of Jitter and Shimmer

The participants were asked to phonate the vowel /a/ at their comfortable loudness and pitch during three seconds for three times. Each attempt was recorded at 44.1 KHZ and 16-bit resolution. Then, PRAAT software was used to determine the percentage of jitter and shimmer. To analyze these parameters, the central 1 second of the vowel was examined using this software(22). Next, according to the voice report part, the number of jitter (ppq5) (23) and the number of shimmer (apq5) were extracted for all three vowels and the lowest of all three attempts was reported (22).

Measurement of the maximum and minimum frequency

After instructing and demonstrating the participants how to produce the highest and the lowest pitch by the SLP, they were asked to start phonating the vowel /a/ at their habitual pitch, going up to the highest pitch, and down to the lowest pitch of their voice. At each step, with the examiner’s hand cue, the participants started to vocalize; they would stop sustaining the vowel with the examiner’s hand cue. Then, the maximum and minimum frequencies were measured using PRAAT software (22).

Measurement of the highest and the lowest intensity

The participants were asked to phonate the vowel /a/ with the lowest loudness at a comfortable pitch, and then with the highest loudness each time for 5 seconds. The intensity was determined after voice recording (21). PRAAT software was used to extract this parameter.

Acoustic analysis of the data was performed using PRAAT software version 44.1.5. Data were then analyzed statistically using SPSS version 21. The significant level was considered at P= 0.05. To assess the normality of the data, Kolmogorov-Smirnov test was used. Subsequently, Spearman's Correlation Coefficient for non-normal variables was calculated to verify the correlation between variables.

Results

Demographic data

This study was conducted on 43 patients (28 women, 15 men) with multiple sclerosis. The age range of the patients was between 18 and 57 years with a mean age of 35.3±9.23 years. The disease duration was between 5 and 276 months. EDSS score was between 0 (no disability) and 6 (more sever disability). Demographic characteristics of the patients are presented in Table 1.

Table 1. Demographic characteristics of MS patients (n=43)

Feature	Numerical Data
Age (mean ± SD)	35.3±9.23
Male/female	15/28
EDSS score (mean ± SD)	2±1.5
Duration of disease (mean ± SD)	60±56.30

Correlation between acoustic parameters and expanded disability status scale

The results of the study showed no significant correlation between acoustic parameters and disease severity, except for the lowest intensity, which had an inverse relationship with disease severity (P<0.01) (Table 2). The correlation between these two parameters is shown in Figure 1.

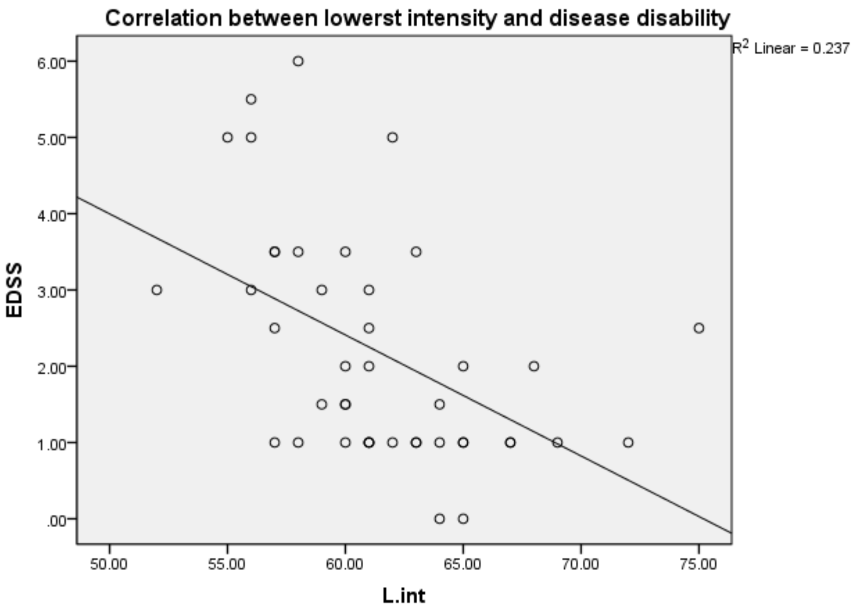

Fig.1 The lowest intensity and EDSS scatter plot. The lowest intensity (L.int) had an inverse significant correlation with disease disability. The solid line is smooth.

Correlation between acoustic parameters and disease duration

The results of the study showed that there was no significant correlation between the maximum phonation time, jitter, shimmer, fundamental frequency, the lowest and highest frequencies, and disease duration; however, the lowest and highest intensities showed a significant inverse correlation with disease duration (P<0.05) (Table 2). The correlation between the lowest and highest intensities and disease duration are shown in Figure 2.

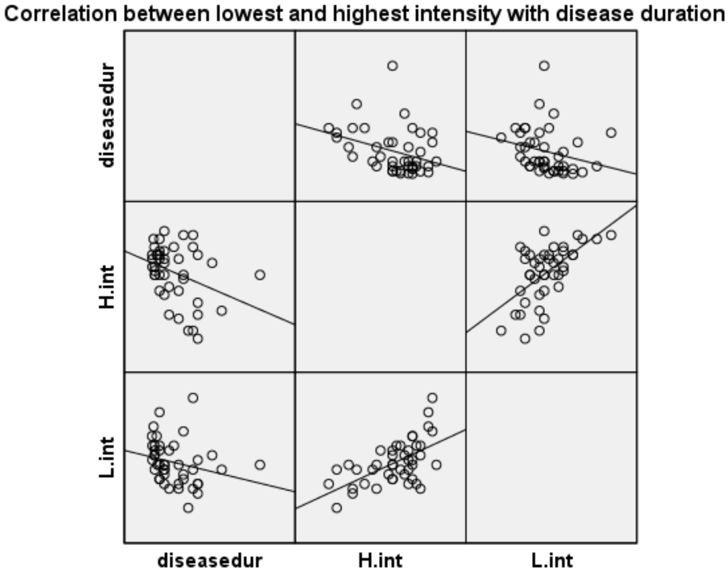

Fig.2 The lowest intensity (L.int) and highest intensity (H.int) and disease duration matrix scatter plot. The lowest and highest intensity intensity had an inverse significant correlation with disease duration. The solid lines are smooth.

Table 2. Correlation between acoustic parameters and EDSS and disease duration.

Acoustic Parameters	EDSS		Duration of Disease	
	Correlation Coefficient	P-value	Correlation Coefficient	P-value
MPT	-0.216	0.164	-0.166	0.287
Jitter	0.285	0.064	0.288	0.061
Shimmer	0.289	0.060	0.277	0.072
F0	0.020	0.897	-0.042	0.787
Maximum frequency	-0.134	0.392	-0.152	0.331
Minimum frequency	0.033	0.835	-0.042	0.791
Highest intensity	-0.227	0.144	-0.349	0.022*
Lowest intensity	-0.572	0.000*	-0.452	0.002*

Abbreviations: F0: fundamental frequency, EDSS: expanded disability status scale, *: significant ($p<0.05$)

Details of the acoustic parameters are presented in Table 3.

Table 3. Mean and standard deviation of acoustic parameters.

Acoustic Parameters	Mean	Standard Deviation
MPT	16.43	6.36
Jitter	0.39	0.19
Shimmer	2.154	1.03
F0	186.11	48.30
Maximum frequency	297	71.99
Minimum frequency	172	50.48
Highest intensity	78.60	7.01
Lowest intensity	61.48	4.61

Discussion

In this study, 43 patients with multiple sclerosis who referred to MS Society of Ahwaz, Khuzestan, were included and the acoustic changes of their voice quality with respect to the determinant acoustic parameters including maximum phonation time (MPT), frequency disturbance (jitter), amplitude disturbance (shimmer), the maximum and minimum frequencies, the highest and lowest intensities, was evaluated. These acoustic parameters were chosen to investigate the changes in the phonation subsystems. Also, for each patient, the neurological characteristics associated with multiple sclerosis, i.e. the disease severity and duration, which all reflect the degree of disease progression, were determined; furthermore, the correlation between the acoustic parameters and these characteristics was investigated.

The aim of this study was to evaluate the acoustic changes of the voice quality and the phonation subsystem in the process of MS progression and also to investigate the correlation between these changes and the disease severity and duration.

Correlation between acoustic parameters and the disease severity

The statistical analysis of the obtained data indicatedlimited intensity variations, an inverse relationship between these variations, and the disease severity. As shown in other studies, the ability to increase and decrease the intensity of voice in MS is influenced and limited by varying degrees of phonatory instability in the MS patients. The intensity impairment and its degree depend on different neuronal pathologies in each individual or different demyelinated regions in different individuals (3, 24). However, in general, weaknesses of the respiratory muscles, and consequently, a significant decrease in the respiratory capacity clearly affect the ability to increase intensity in these patients (1, 25). Also, instability and inconsistency in the vocal cord movements can be attributed to the inability to reduce the voice intensity. The inability to change the voice intensity and the limited intensity range lead to a perceptual sign of "monoloudness" in MS patients, which clearly affects the prosody (25). In the present study, the lowest level of voice intensity was significantly correlated with disease severity. Similarly, Hartelius (2000) found loudness variation impairments positively are correlated with disease disability (6). Also, Darley et al. (1972) stated more severe neurologic involvement related to more sever voice quality involvement including loudness variation (3). However, Yamout et al. (2009) reported no significant correlation between acoustic parameters and disease severity. It must be noted that Yamout et al. (2009) didn’t investigate the voice intensity variations in their study (15).

Regarding the significant correlation between the lowest intensity and disease severity observed in the present study, an increase in the disease severity in patients with multiple sclerosis can lead to more instability and inconsistency in the vocal cord movements. Therefore, the intensity range can become limited, which, in higher degrees of disability, results in monoloudness, inability to change the voice intensity as well as the loudness variations in speech emphasis, and whispering (1, 3, 6). As far as the intensity changes in patients with multiple sclerosis are concerned, limited studies have been conducted to check how intensity changes are correlated with the disease severity, so further studies on this issue are still required.

Correlation between acoustic parameters and disease duration

According to the results of the present study, there is a significant correlation between the highest and lowest loudness and disease duration. Similarly, Hartelius et al. (1995 & 2000) reported a positive correlation between speech deviations including tremor and intensity variations with the number of years in progression (1, 6). Concerning being sensitive to respiratory capacity and emerging as one of the first vocal symptoms, this parameter is better to be taken into account in the initial evaluations (25). Few studies have been conducted to investigate the relationship between intensity variations and disease duration in MS patients.

Overall, vocal symptoms can be expected at any stages of the disease, but with increased severity in this progressive disease, voice quality is more affected. Similarly, Yorkston et al. (2003), evaluated speech problems in MS patients using self-evaluation tools, and reported that patients with no speech problem showed less disability than those with severe speech problems. Yorkston et al. (2003) reported a strong relationship between speech problems and disease severity and the progressive stages of the disease (26). Therefore, the determinants of voice quality should be evaluated in the early stages of the disease. Further studies on this issue are of interest to consider other acoustic parameters and variations of other speech subsystems.

Conclusion

Speech and voice quality are affected during the development of multiple sclerosis. In this research, phonation subsystem, as one of the speech subsystems, was affected by the neurological impairments in multiple sclerosis. This susceptibility can be developed at any clinical stages, however, over time and with the disease progression, the symptoms might get worsen and negatively affect communication skills. Therefore, early acoustic assessments and timely health interventions can help prevent a further decline in the voice quality.

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