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Research Article

Comparison of Dysphonia Severity Index and its Parameters Among Individuals with Multiple Sclerosis and Healthy Subjects

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Abstract

Background: Concerning demyelination's process in multiple sclerosis (MS), speech changes often occur earlier than other symptoms; thus early diagnosis of these changes is necessary. According to recent studies, phonation subsystem appears with the most symptoms compared with other subsystems, especially in the initial stages. In this study, the researchers aimed at comparing these symptoms in MS patients with healthy people using dysphonia severity index (DSI) and its parameters.
Methods: This study was conducted on 40 MS patients and 20 healthy individuals in Ahvaz city. The subjects were asked to phonate vowel /a/ for calculating maximum phonation time (MPT), maximum F0, jitter, minimum intensity, and DSI score with the Praat software. For statistical analysis of data, Kolmogorov-Smirnov and independent t-test were used.
Results: The mean scores of DSI in MS patients (1.07 ± 1.51) was significantly lower than the control group (3.603 ± 1.13) (P value < 0.001). Maximum phonation time and maximum frequency values in MS patients were lower than the control group (MPT, P value = 0.005; maxF0, P value = 0.003). Jitter and minimum intensity values in MS patients were higher than the control group ($jitter_{ppq5}$, P value < 0.001; min intensity, P value = 0.040).
Conclusions: The findings of this study indicated that the MS group had worse vocal quality than the healthy group, which means they were at risk of voice and speech problems; therefore, acoustic assessments can determine the vocal impairments of the disease at the early stages and prevent progression of vocal impairments with an appropriate treatment plan. Also, dysphonia severity index, as a reliable tool, can detect vocal quality impairments in multiple sclerosis and can be a supplementary assessment tool for early detection of degenerative diseases.

Keywords: Multiple Sclerosis, Voice Quality, Phonation, Speech

1. Background

Speech production is the functional result of a collection of speech subsystems, including respiratory, phonation, articulation, resonatory, and prosody (1). The proper functioning of these subsystems is the result of the integration of uncountable neuro-cognition, neuromuscular, and musculoskeletal activities that results in the transmission of a communication message through intelligible speech; any disturbance in this integration make problems for the function of speech subsystems and, consequently, speech intelligibility (2). One of the most common causes of speech impairment is multiple sclerosis (MS). Multiple Sclerosis is a progressive autoimmune disease that affects the central nervous system (1, 2). Central nervous system involvement in the progression of MS, in addition to the development of motor disorders in organs, leads to speech problems by weakening the speech muscles, including palate, larynx, and tongue muscles (3). A variety of speech problems are reported in 40% of people with MS (1, 3). According to studies on speech features in progressive neurological diseases, each of the speech subsystems is affected by varying degrees from mild to severe (3, 4). Among the speech subsystems, the phonation subsystem shows more damage, especially in the early stages of the disease, than other subsystems (1, 4-6). This subsystem, in the process of multiple sclerosis, by damages, such as loudness control, breathiness, harsh vocal quality, and pitch control affects the vocal quality and speech intelligibility (1, 7). Consequently, problems in speech intelligibility and disturbance in the transmission of communication messages result in serious damage to verbal communication skills and the quality of life of an individual, including social, educational, and occupational life (1, 8). Therefore, evaluation and investigation of this subsystem can be important in terms of early diagnosis and timely treatment of speech disorders in this progressive disease.

Different methods, such as perceptual, acoustic, as well as aerodynamic and physiological evaluations, using computer and laboratory developed equipment, are used to evaluate phonation subsystem disorders (9). Of these, acoustic evaluations are widely used in non-invasive methods in clinical and research departments. These accurate and sensitive instruments quantitatively and objectively report changes in the vocal tract and the articulatory organs in the early stages of neurological disorders (5, 8); hence, acoustic analysis can be applied to detect changes in the phonation subsystem and the vocal quality caused by neurological disorders (10).

One of the acoustic assessments of vocal quality to determine impairments to this subsystem is dysphonia severity index (DSI). The DSI quantitatively measures acoustic parameters, such as maximum phonation time, jitter, maximum frequency and minimum intensity that determine vocal quality, and by means of a normalized formula, a score is reported as the general status of the vocal quality (11). As commonly accepted, evaluating several parameters is more reliable than evaluating only one parameter, such as fundamental frequency, shimmer, or jitter (11, 12). This index has two versions of alpha and beta (11, 13). The alpha version was designed in 2000 by Wuyts and colleagues; in this version, the examiner requires a software such as multi-dimensional voice program and voice range profile to execute and calculate each parameter (11). Maryn et al., in 2017, designed the beta version for this formula; the beta version's feature is the possibility of using the Praat software. One of the benefits of this version for the dysphonia severity index, given the easy access to this software in comparison with other software, is that speech and language pathologists can easily investigate these parameters in everyday clinical practice (13). In general, this index is a valuable clinical tool for quantitative description of voice disorders and determining damage severity that has been used in researches in different countries and languages (12, 14, 15). Based on studies conducted using this index, the DSI, as well as other vocal acoustic assessments are able to determine the severity of voice disorders, changes made before and after the treatment of vocal damage, and differentiate between individuals with and without voice problems (12, 14, 16). Another advantage of this index is the strong correlation with perceptual valid tools, such as VHI, GRBAS, CAPE-V, and instrumental evaluations, such as Video Laryngostroboscopy (12, 16, 17). Wuyts et al. also believed that the DSI is not influenced by gender, since the maximum phonation time in males is compensated by the highest frequency in the female population and the average score of the DSI in females and males are relatively similar (11, 18).

Regarding the diagnostic significance of the damage to the mentioned subsystem, especially in the early stages of the disease, to prevent the development of speech impairments and vocal quality, conducting research to evaluate the vocal impairments in MS patients and identification of an appropriate tool for rapid and convenient diagnosis of these impairments in the early stages of the disease is necessary. So far, only a few studies have focused on evaluation of phonation subsystem impairments in this disease by means of valid acoustic tools; therefore, this study examined changes of this subsystem and the vocal quality using the DSI (Beta version) and the acoustic parameters that determine this index in individuals with MS compared to healthy subjects.

2. Methods

This descriptive-analytical and cross-sectional study was performed from October to December 2016, on 40 patients with multiple sclerosis (13 males and 27 females), at the MS association of Khuzestan and 20 healthy (9 males and 11 females) individuals. The sample size was calculated based on the standard deviation of jitter (SD = 0.546) obtained from a study by Dogan et al. (19) with $\alpha = 0.05$ (type 1 error rate) and $\beta = 0.2$ (type 2 error rate). Twenty healthy individuals were matched for age with the patient group. The subjects were aged 18 to 60 years old. Study entry requirements included a definitive diagnosis of multiple sclerosis, the absence of infection in upper respiratory system or a cold for three weeks before the test and entering the assessment, having no voice problems before entering the study, being monolingual (Persian), not having severe problems in understanding and not having a history of tracheostomy and head and neck surgery, no use of tobacco and alcohol, lack of anatomical problems of speech organs (lips, tongues, etc.), no history of hormonal disorders, or the use of hormonal drugs. In this study, only patients with MS in the relapsing-remitting phenotype were included. The patient was excluded if she/he had a recurrence period within a month before the study.

Initially, subjects were approved for MS by a neurologist. Then, people were investigated for inclusion and exclusion criteria in the Khuzestan MS Association; subjects that had the criteria were selected and referred to a speech and language pathologist with clinical experience in the treatment of speech disorders in progressive diseases. In the next stage, a consent form and individual information recording were completed by the subjects; then tasks related to the acoustic assessment were taken from individuals by a speech and language pathologist. The study protocol was approved by the ethics committee of the Jundishapur University of Ahvaz (IR.AJUMS.REC.1395.545).

Tasks related to acoustic assessments and recording of voice samples were performed in an acoustic room (noise level < 20 dB). To record voice samples, an unidirectional dynamic cardioids AKG, C1000S microphone was connected to a portable computer at a distance of 10 cm, 45 degrees from the subject's mouth (13). Before recording the voice samples, the examiner described each task for the subjects and performed it practically. In case of any problem, the items were explained for the person. Acoustic analysis of data was performed using the Praat software version 5. 1. 44. The test items were run as follows:

2.1. Maximum Phonation Time

Subjects were asked to take a deep breath by sitting and lying on the seat and with the examiner's cue the vowel /a/ be expressed in the comfortable loudness and pitch and as long as possible continuing the phonation. The duration of the vowel phonation was measured three times for each subject, and the maximum number (maximum phonation time) was plotted in the equation (12).

2.2. Jitter

The participants were asked to produce a sustained /a/ at their comfortable loudness and pitch for three seconds and repeated this task three times. Each vowel attempt was recorded in 44 /1 KHZ and 16 bit resolution. Then, to determine the jitter, the Praat software was used. To analyze this parameter, 0.5 seconds after the start of the vowel, one central second of produced vowel, using this software, was selected and from 'voice report' option number related to jitter (ppq5) (13) for each of three vowels were extracted and the least of all three trials was reported (12).

2.3. Maximum Frequency

After providing the necessary training and demonstrating the correct pattern to the subjects in relation to the pitch of voice, with the examiner's cue, they were asked to begin to sustain the vowel /a/ with habitual pitch and then going up to the highest frequency in their frequency range. Then, using the Praat software, the maximum frequency number was extracted and entered in the equation (12).

Table 1. Demographic Information of MS Patients and Healthy Group

Variables	Multiple Sclerosis (N = 40)	Control Group (N = 20)
Age, mean ± SD	35.17 ± 9.05	34.40 ± 14.24
Gender, Male/ Female	13/ 27	9/ 11

2.4. Minimum Intensity

The subjects were asked to produce the vowel /a / at their habitual pitch and reduce the intensity before the level of whispering for 5 seconds. The value of the minimum intensity was measured (12).

After computing each of the four acoustic parameters, the value of each parameter, using the Praat software, was given in the following equation (13):

1) $DSI_{beta} = 1.127 + 0.164 \times MPT + 0.0053 \times F0\ max - 0.038 \times I\ min - 5.30 \times Jitter_{PPQ}$

Statistical analysis of data was performed using the SPSS 21 software and significant level $\alpha = 0.05$. Normality of the data was evaluated using the Kolmogorov-Smirnov test. Based on the results of this test, the distribution of data in this study was normal and independent t-test was used for comparison between healthy and patient groups.

3. Results

3.1. Demographic Data

The sample consisted of 40 MS patients with mean age of 35.17 ± 9.05 years and 20 healthy subjects with an average age of 34.40 ± 14.24 years (Table 1).

3.2. Comparison of Acoustic Parameters in Multiple Sclerosis Patients with Healthy Individuals

Regarding the normal distribution of data in both patient and healthy groups, independent t-test was used to compare the mean of the acoustic parameters between the two groups of patients and healthy controls; the results of the statistical test showed a significant difference between the two study groups. The mean score of maximum phonation time in subjects with MS (16.76 ± 6.36) was significantly lower than the healthy group (21.83 ± 6.88) (P value = 0.005). The mean score of jitter in the patients group (0.38 ± 0.17) was significantly higher than the normal group (0.15 ± 0.06) (P value = 0.000). The mean score of highest frequency in the patient group (298 ± 72.46) was significantly lower than the control group (366 ± 95.78) (P value = 0.003). Also, the mean score of the minimum intensity in the patient group (61.17 ± 4.25) was significantly higher than the control group (58.75 ± 4.11) (P value = 0.040). The mean, standard deviation, and the coefficient of significance of these parameters are given in Table 2.

Table 2. Comparison of Acoustic Parameters and Dysphonia Severity Index Between MS and Control Groups[a]

Variables	Multiple Sclerosis	Control Group	P Value	95% CI
Maximum phonation time	16.76 ± 6.36	21.83 ± 6.88	0.005	-8.65, -1.48
Jitter	0.38 ± 0.17	0.15 ± 0.06	< 0.001	0.15, 0.31
Maximum frequency	298 ± 72.46	366 ± 95.78	0.003	-30.13, -23.49
Minimum intensity	61.17 ± 4.25	58.75 ± 4.11	0.040	0.11, 4.73
Dysphonia severity index (beta version)	1.07 ± 1.51	3.603 ± 1.13	< 0.001	-3.29, -1.75

[a]Values are expressed as mean ± SD.

3.3. Comparison of Dysphonia Severity Index in Multiple Sclerosis and Healthy People

In order to compare the score of DSI between the two groups of MS and healthy participants, according to the normal distribution of data, independent t-test was used, which showed a significant difference between the mean score of MS patients (1.07 ± 1.51) and healthy group (3.603 ± 1.13) (P value = 0.000). The average score for statistical details is given in Table 2.

4. Discussion

The present study was conducted with the aim of evaluating quantitative changes of phonation subsystem and vocal quality in progressive multiple sclerosis, on 40 patients with multiple sclerosis, compared with 20 healthy subjects without any voice complaints. In this regard, the acoustic parameters, including maximum phonation time, jitter, maximum frequency, and minimum intensity were acoustically studied; also, the DSI (beta version) was used to provide a quantitative report of the voice quality for comparison between the two target groups.

4.1. Comparison of Acoustic Parameters Among People with Multiple Sclerosis and Healthy People

Maximum phonation time: The results of this study indicated a significant decrease in the mean maximum phonation time compared with healthy Persian speakers. Many studies reported a reduction in the maximum phonation time (19-21). The reduction of this vocal parameter may be indicative of a reduction in respiratory volume, as reported by Gosselink (2000); the reduction of respiratory capacity in patients with MS is due to respiratory muscle weakness and impairment of autonomic regulation of respiration (22). Yamout also reported a reduction in the maximum phonation time due to reduced respiratory volume in more severe stages of the disease, due to the posterior chink of vocal cords during the phonation in data obtained from patient laryngoscopy; He also stated that, concerning vocalization needs, coordination between laryngeal and respiratory muscle function, the changes in the vocal quality and the reduction of the maximum phonation time may be due to weakness of the respiratory and laryngeal muscles and be the first symptoms of motor degeneration (20).

Jitter: The jitter in the present study indicated a significant increase in people with MS compared to healthy subjects. Also, most studies on the acoustic features of speech in MS reported an increase in jitter in patients with MS than in healthy subjects (19, 21, 23, 24). Yamout (2008) also reported an increase in perturbation parameters and stated that an increase in these parameters could indicate the variability and inconsistency of muscle contractions involved in the phonation in this progressive disease (20).

Maximum fundamental frequency: The results of this study indicated a reduction in the maximum fundamental frequency in people with MS compared to healthy subjects. This decrease could be attributed to a reduction in the ability to control phonation and phonatory instability (25). So far, a few studies have been performed with regards to changes in the maximum fundamental frequency in this population.

Minimum intensity: The statistical analysis of the present study data showed the increase of minimum intensity in patients with MS compared to healthy subjects. The ability to reduce the intensity in the progressive disease of multiple sclerosis, under the influence of phonatory instability, is limited to varying degrees in the affected population. The damage to this ability and the extent of that damage, due to the different neuropathologies in each individual or different regions of demyelinated in individuals, is different; however, the weakness of the respiratory muscles and, consequently, the appreciable decrease in respiratory capacity in these patients clearly affects the ability to change and controls the intensity (25). Also, instability and inconsistency in the movements of the vocal folds can be attributed to the inability to reduce the intensity (26).

4.2. Comparison of Dysphonia Severity Index Among People with Multiple Sclerosis and Healthy People

In the present study, the mean score of DSI in healthy subjects was higher than those with MS and the statistical analysis showed a significant difference between the two groups in terms of the score of this index. The DSI using a standardized formula examines changes in acoustic parameters of vocal quality (maximum phonation time, jitter, minimum intensity, and maximum fundamental frequency); therefore, the significant difference of these parameters among the two groups in the present study resulted in a significant difference in the scores of the index between these groups. Previous studies have shown that this index has the ability to differentiate healthy people from people with voice problems (12, 15, 17, 27). Based on the results of the present study, which is in line with previous studies (4, 6), individuals with multiple sclerosis, including those at high risk of phonation impairments, and the DSI as a sensitive tool to these impairments in this group, can be used in daily clinical evaluations for diagnostic purposes of patients with multiple sclerosis. It has been suggested that in future studies, other speech subsystems should be investigated with appropriate clinical tools in this progressive disease.

4.3. Conclusion

The phonation subsystem and vocal quality in MS disease due to central nervous system involvement is damaged and impacts speech intelligibility. Diagnosing these problems in the early stages of the disease and preventing further progress in the problems of this subsystem and speech intelligibility through early treatment programs are of particular importance. In this regard, the use of appropriate assessment tools for timely detection of these problems plays an important role. Furthermore, DSI (Beta version) is capable of detecting voice problems in degenerative MS disease, and is able to differentiate people with these problems from healthy people; this index is also appropriate for daily clinical practice.

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References

1. Hartelius L, Nord L, Buder EH. Acoustic analysis of dysarthria associated with multiple sclerosis. *Clin Linguist Phon*. 2009;**9**(2):95–120. doi: 10.3109/02699209508985327.
2. Duffy J. *Motor Speech Disorders: Substrates. Differential Diagnosis and Management*. 2nd ed. New York: Mosby; 2005. 592 p.
3. LaDuke KM. *Speech characteristics in multiple sclerosis*. University of Wyoming; 2001.
4. Rong P, Yunusova Y, Wang J, Green JR. Predicting Early Bulbar Decline in Amyotrophic Lateral Sclerosis: A Speech Subsystem Approach. *Behav Neurol*. 2015;**2015**:183027. doi: 10.1155/2015/183027. [PubMed: 26136624]. [PubMed Central: PMC4468279].
5. Sapir S, Ramig LO, Spielman JL, Fox C. Formant centralization ratio: a proposal for a new acoustic measure of dysarthric speech. *J Speech Lang Hear Res*. 2010;**53**(1):114–25. doi: 10.1044/1092-4388(2009/08-0184). [PubMed: 19948755]. [PubMed Central: PMC2821466].
6. Darley FL, Brown JR, Goldstein NP. Dysarthria in multiple sclerosis. *J Speech Hear Res*. 1972;**15**(2):229–45. doi: 10.1044/jshr.1502.229. [PubMed: 5047862].
7. Hartelius L, Theodoros D, Cahill L, Lillvik M. Comparability of perceptual analysis of speech characteristics in Australian and Swedish speakers with multiple sclerosis. *Folia Phoniatr Logop*. 2003;**55**(4):177–88. doi: 10.1159/000071017. [PubMed: 12802090].
8. 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**(2). e32132. doi: 10.1371/journal.pone.0032132. [PubMed: 22389682]. [PubMed Central: PMC3289640].
9. Ziethe A, Patel R, Kunduk M, Eysholdt U, Graf S. Clinical analysis methods of voice disorders. *Curr Bioinform*. 2011;**6**(3):270–85. doi: 10.2174/157489311796904682.
10. Kent RD, Weismer G, Kent JF, Vorperian HK, Duffy JR. Acoustic studies of dysarthric speech: methods, progress, and potential. *J Commun Disord*. 1999;**32**(3):141-80. quiz 181-3, 187-9. doi: 10.1016/S0021-9924(99)00004-0. [PubMed: 10382143].
11. Wuyts FL, De Bodt MS, Molenberghs G, Remacle M, Heylen L, Millet B, et al. The dysphonia severity index: an objective measure of vocal quality based on a multiparameter approach. *J Speech Lang Hear Res*. 2000;**43**(3):796–809. doi: 10.1044/jslhr.4303.796. [PubMed: 10877446].
12. Hakkesteegt MM, Brocaar MP, Wieringa MH, Feenstra L. The relationship between perceptual evaluation and objective multiparametric evaluation of dysphonia severity. *J Voice*. 2008;**22**(2):138–45. doi: 10.1016/j.jvoice.2006.09.010. [PubMed: 17570633].
13. Maryn Y, Morsomme D, De Bodt M. Measuring the Dysphonia Severity Index (DSI) in the Program Praat. *J Voice*. 2017;**31**(5):644 e29–40. doi: 10.1016/j.jvoice.2017.01.002. [PubMed: 28187924].
14. Zhou Z, Ge P, Liu Q, Liu M, Zhang W. [Observation of the dysphonia severity index in evaluating curative effect of vocal cord polyp surgery]. *Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi*. 2015;**50**(8):673–6. Chinese. [PubMed: 26696208].
15. Aghadoost O, Amiri-Shavaki Y, Moradi N, Jalai S. A Comparison of Dysphonia Severity Index in Female Teachers With and Without Voice Complaints in Elementary Schools of Tehran, Iran. *Nursing and Midwifery Studies*. 2013;**1**(3):133–8. doi: 10.5812/nms.9904.
16. Hakkesteegt MM, Brocaar MP, Wieringa MH. The applicability of the dysphonia severity index and the voice handicap index in evaluating effects of voice therapy and phonosurgery. *J Voice*. 2010;**24**(2):199–205. doi: 10.1016/j.jvoice.2008.06.007. [PubMed: 19185461].
17. Nemr K, Simoes-Zenari M, de Souza GS, Hachiya A, Tsuji DH. Correlation of the Dysphonia Severity Index (DSI), Consensus Auditory-Perceptual Evaluation of Voice (CAPE-V), and Gender in Brazilians With and Without Voice Disorders. *J Voice*. 2016;**30**(6):765 e7–765 e11. doi: 10.1016/j.jvoice.2015.10.013. [PubMed: 26627119].
18. Hakkesteegt MM, Brocaar MP, Wieringa MH, Feenstra L. Influence of age and gender on the dysphonia severity index. A study of normative values. *Folia Phoniatr Logop*. 2006;**58**(4):264–73. doi: 10.1159/000093183. [PubMed: 16825779].
19. Dogan M, Midi I, Yazici MA, Kocak I, Gunal D, Sehitoglu MA. Objective and subjective evaluation of voice quality in multiple sclerosis. *J Voice*. 2007;**21**(6):735–40. doi: 10.1016/j.jvoice.2006.05.006. [PubMed: 16815671].

20. Yamout B, Fuleihan N, Hajj T, Sibai A, Sabra O, Rifai H, et al. Vocal symptoms and acoustic changes in relation to the expanded disability status scale, duration and stage of disease in patients with multiple sclerosis. *Eur Arch Otorhinolaryngol*. 2009;**266**(11):1759–65. doi: 10.1007/s00405-009-1003-y. [PubMed: 19513739].
21. Khorramshahi H, Heidari S, Goharpey S. [Comparison of jitter, shimmer and S/Z ratio in multiple sclerosis patients]. *Jundishapur Sci Med J*. 2013;**6**(11). Persian.
22. Gosselink R, Kovacs L, Ketelaer P, Carton H, Decramer M. Respiratory muscle weakness and respiratory muscle training in severely disabled multiple sclerosis patients. *Arch Phys Med Rehabil*. 2000;**81**(6):747–51. [PubMed: 10857518].
23. Feijo AV, Parente MA, Behlau M, Haussen S, de Veccino MC, Martignago BC. Acoustic analysis of voice in multiple sclerosis patients. *J Voice*. 2004;**18**(3):341–7. doi: 10.1016/j.jvoice.2003.05.004. [PubMed: 15331106].
24. Konstantopoulos K, Vikelis M, Seikel JA, Mitsikostas DD. The existence of phonatory instability in multiple sclerosis: an acoustic and electroglottographic study. *Neurol Sci*. 2010;**31**(3):259–68. doi: 10.1007/s10072-009-0170-3. [PubMed: 19876591].
25. Hartelius L, Buder EH, Strand EA. Long-term phonatory instability in individuals with multiple sclerosis. *J Speech Lang Hear Res*. 1997;**40**(5):1056–72. doi: 10.1044/jslhr.4005.1056. [PubMed: 9328877].
26. Gerald FJF, Murdoch BE, Chenery HJ. Multiple sclerosis: Associated speech and language disorders. *Aust J Hum Commun Disord*. 2014;**15**(2):15–35. doi: 10.3109/asl2.1987.15.issue-2.02.
27. Van Lierde KM, De Ley S, Clement G, De Bodt M, Van Cauwenberge P. Outcome of laryngeal manual therapy in four Dutch adults with persistent moderate-to-severe vocal hyperfunction: a pilot study. *J Voice*. 2004;**18**(4):467–74. doi: 10.1016/j.jvoice.2004.02.003. [PubMed: 15567048].