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Vocal signal analysis in patients affected by Multiple Sclerosis

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Abstract

Multiple Sclerosis (MS) is one of the most common neurodegenerative disorder that presents specific manifestations among which the impaired speech (known also as dysarthria). The evaluation of the speech plays a crucial role in the diagnosis and follow-up since the identification of anomalous patterns in vocal signal may represent a valid support to physician in diagnosis and monitoring of these neurological diseases.

In this contribution, we present a method to perform voice analysis of neurologically impaired patients affected by MS aiming to early detection, differential diagnosis, and monitoring of disease progression. This method integrates two well-known methodologies to support the health structure in MS diagnosis in clinical practice. Acoustic analysis and vowel metric methodologies have been considered to implement this procedure to better define the pathological voices compared to healthy voices. Specifically, the method acquires and analyzes vocal signals performing features extraction and identifying possible important patterns useful to associate impaired speech with this neurological disease. The contribution consists in furnishing to physician a guide method to support MS trend. As result, this method furnishes patterns that could be valid indicators for physician in monitoring of patients affected by MS. Moreover, the procedure is appropriate to be used in early diagnosis that is critical in order to improve the patient's quality of life.

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Keywords: Multiple Sclerosis, vocal signal analysis, vowel metric, acoustic analysis

1 Introduction

Neurodegenerative diseases are conditions primarily affecting the neurons and causing the disruption of the information flow within the brain and between the brain and rest of the body

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[23]. Multiple Sclerosis (MS) is one of the most common among the neurodegenerative disorders. Multiple Sclerosis (MS) is a chronic demyelinating disease that affects the central nervous system interfering with nerve impulses within the brain, the spinal cord and the optic nerves [2]. Even though the temporal evolution of MS is different for each patient, four disease courses have been identified in MS: (*i*) Clinically Isolated Syndrome (CIS), (*ii*) Primary Progressive MS (PPMS), (*iii*) Relapsing-Remitting MS (RRMS), and (*iv*) Secondary Progressive MS (SPMS) (the last two being the most common ones) [11]. Approximately 85% of the population affected by MS is initially diagnosed with RRMS, with an observed increase in patient's disability produced by clearly defined attacks or neurological symptoms, alternated with recovery phases which worsen until his total inactivity. The 30-50% of patients affected by RRMS, develop SPMS within 10 years. SPMS is characterized by a progressive worsening of the neurological function and a consequent increase of the disability over time.

MS is a degenerative disorder which presents specific symptomatologies, among which speech impairment (also known as *dysarthria*) [15]. Dysarthria is a motor speech disorder resulting from neurological injury due to damages in the central or peripheral nervous system. The evaluation of dysarthria, by using a noninvasive acoustic analysis of vocal signal, represents a valid clinical support to the otolaryngologist, neurologist and speech pathologist for early and differential diagnosis and for documenting the disease progression. Clinical assessment of dysarthria in patients affected by MS have been studied and reported in literature, with statistically significant differences with respect to normal subjects [25] [18]. In the last few years, new acoustic measures of dysarthric speech have been proposed as alternative methods to more effectively differentiate dysarthric from healthy speech [27] [20]. Authors in [9] propose a study to determine the extent to which vowel metrics are capable of distinguishing healthy from dysarthric speech and among different forms of dysarthria, testing the Discriminant Function Analysis (DFA).

Acoustic analysis has been reported in literature as a tool to evaluate and characterize vocal pathological signals [24] [1]. Authors in [26] analyze the acoustic parameters commonly used in applications of acoustic analysis as well as the fundamental frequency, jitter, shimmer and Harmonic to Noise Ratio (HNR) to define a procedure for automatic diagnosis of larynx pathologies. Several signal processing algorithms have been implemented to perform vocal signal analysis with the aim to identify pathological voices in voice datasets [16] [17]. Moreover, software tools have been produced to extract vocal feature for signal analysis; for example, in [12] jitter measurements have been evaluated by comparing the results of four tools. Multi Dimensional Voice Program (MDVP) and PRAAT are the most common tools used for voice analysis in clinical practice [7] [13]. To better define the results of acoustic analysis algorithms and tools the vowel metric is often used [19] [22] [6]. To this end, the contribution proposed in [14] regards relevant data acquisition and analysis methods to define the speech parameters as the Vowel Space Area (VSA) and the Formant Centralization Ratio (FCR).

All of these contributions highlight significant differences between patients with MS and normal subjects, justifying the assumption that speech analysis may become a helpful tool for the diagnosis and monitoring of the disease progression. Additionally, sharing data and information for increasing knowledge can be performed in a distributed laboratory as in [28] [29] [3].

In this paper, the evaluation of vocal signals in patients with MS has been performed by using an acoustic analysis and a vowel metric analysis on the acquired samples. In particular: (*i*) the PRAAT tool has been used to execute acoustic analysis, (*ii*) a software written in Matlab has been coded to calculate the vowel metrics and (*iii*) statistical analyses have been performed to evaluate significant results.

2 Methods

Speech alterations can be studied by analyzing several parameters obtained from vocal signals with the aim to describe the voice objectively and identify specific patterns. The parameters extracted to perform the analysis reported in this contribution are described in the following sections. In particular, two types of methods have been used to extract these parameters to furnish a more detailed analysis for the evaluation and identification of possible correlations between vocal signal and MS disease. The two methods are: acoustic vocal analysis (i) and (ii) vowel metric analysis. The first extracts the principal acoustic parameters in term of frequency content; the second, instead, extracts parameters describing the vowel articulation.

2.1 Acoustic Analysis

Vocal signal is produced by the pulsing of the vocal folds that creates a pattern of amplitude modulation in the waveform and harmonicity in the spectrum. The produced vocal signal is a complex periodic wave made up of several simple periodic waves. The acoustic analysis of this signal produces a set of acoustic parameters [31]. Currently, the most common parameters generally used by physician and referenced in literature are [26]:

- Fundamental frequency (F_0);
- Jitter;
- Shimmer;
- Harmonic to Noise Ratio (HNR).

Fundamental frequency (F_0) is a robust feature of the speech signal. It is measured in Hertz (Hz, cycles per second) and it is defined as the number of times in which a sound wave produced by vocal cords is repeated during a specific time period [26]. The fundamental frequency is determined by the rate of modulation of the vocal folds during voiced speech **and it decreases in pathological voices**. Vocal fold vibration produces many harmonics above F_0 that decrease in amplitude as the frequency increases. Synthetically, the Pitch is the fundamental frequency of the vocal cords vibration followed by four/five Formants (F_1, F_2, F_3, F_4, F_5) at higher frequencies. The formants are the bands of energy that correspond to the resonances of the vocal tract for particular shapes.

Jitter and shimmer are measurements of F_0 disturbance and they are essential in the description of vocal characteristics. Jitter parameter is defined as the frequency variation of the sound wave periodically (cycle to cycle) and it is especially affected by the lack of control of cords vibration. Generally, a pathological voice presents a higher percentage of jitter compared to healthy voice: a variation between 0.5% and 1% is considered a significant value. Typically, two types of jitter parameters are considered: absolute and relative [5]. Absolute jitter, J_A, represents the average absolute difference between two consecutive periods and it is calculated as:

$$J_A = \frac{1}{N-1} \sum_{i=1}^{N-1} |T_i - T_{i+1}| \tag{1}$$

Relative jitter, J_R, is the average absolute difference between two consecutive periods divided by the average period and it is evaluated as:

$$J_R = \frac{\frac{1}{N-1}\sum_{i=1}^{N-1}|T_i - T_{i+1}|}{\frac{1}{N}\sum_{i=1}^{N} T_i} \tag{2}$$

In both equations, T_i are the extracted F_0 period lengths and N is the number of extracted F_0 periods.

Shimmer parameters, instead, is defined as the amplitude variation of the sound wave and its changes are related to mass lesions on the vocal cords. Shimmer values less than 3% for adults and around 0.4% and 1% for children are considered in pathological voice. As for jitter, also for shimmer two types of parameters are evaluated: relative, S_R and dB, S_{dB} [5]. The first is defined as the average absolute difference between the amplitudes of two consecutive periods, divided by the average amplitude and it is expressed as:

$$S_R = \frac{\frac{1}{N-1}\sum_{i=1}^{N-1}|A_i - A_{i+1}|}{\frac{1}{N}\sum_{i=1}^{N} A_i} \tag{3}$$

The second is the average absolute difference of the base 10 logarithm of the difference between two consecutive periods multiplied by 20 and it is calculated as:

$$S_{dB} = \frac{1}{N-1}\sum_{i=1}^{N-1}|20log(A_{i+1}/A_i)| \tag{4}$$

In both equations, A_i are the extracted peak-to-peak amplitude data and N is the number of extracted F_0 periods.

The Harmonic to Noise Ratio (HNR) is a measurement of the voice pureness and it is expressed in decibel (dB) as the ratio between the energy of periodic components (harmonics) and the energy of non periodic component (noise) in a voice segment [4]. HNR is the mean amplitude (i.e., energy) of the average wave divided by the mean amplitude of the isolated noise components and can be calculated as follows:

$$HNR = 10x\log_{10}(\frac{HarmonicEnergy}{NoiseEnergy})dB \tag{5}$$

By using this equation, if 99 of the energy of the signal is in the periodic part, and 1 is noise, the HNR is 20 dB. A HNR of 0 dB means that there is equal energy in the harmonics and in the noise. HNR reflects the speech efficiency: an healthy voice is characterized by a high HNR, instead values less than 7 dB indicate pathological voices.

2.2 Vowel Metric

Speech samples associated with dysarthria are often characterized by vowels centralization due to undershooting of articulatory targets. The Vowel Space Area (VSA) is an acoustic index commonly used in clinical research to evaluate the vowel articulation [30]. In particular, for voice with dysarthria, VSA is expected to be compressed as a result of vowel centralization [21]; instead, for both healthy patient's speeches and hyperarticulated vowels, VSA is expected to be expanded [8]. In general, dysarthric vowel production is characterized by centralization of formant frequencies and reduction in static vowel space area [9]. This indication is very useful in voice monitoring and analysis, where VSA can be applied to vocal signals in order to perform a more accurate investigation. The vowel space illustration is a graphical method able to show where a speech signal, generated by the pronunciation of a vowel, is located in both the

acoustic and the articulatory spaces, based on the first two formants for vowels. The horizontal axis shows the frequency of the first formant (F_1) and the vertical axis represents the frequency of the second formant (F_2). This 2-dimensional representation corresponds to an articulatory space. VSA is generally constructed by the Euclidean distances between the first formant (F_1) and second formant (F_2) coordinates of the corner vowels /i/, /u/, and /a/ (triangular VSA or tVSA), or the corner vowels /i/, /u/, /a/, and /e/ (quadrilateral VSA, or qVSA) in the $F_1 - F_2$ plane. tVSA and qVSA computations are reported following according to [21]:

$$tVSA = |((F_{1_i} * (F_{2_a} - F_{2_u}) + F_{1_a} * (F_{2_u} - F_{2_i}) + F_{1_u} * (F_{2_i} - F_{2_a}))/2)| \tag{6}$$

$$\begin{aligned} qVSA = \frac{1}{2}(((F_{1_e} * F_{2_i}) + (F_{1_a} * F_{2_e}) + (F_{1_u} * F_{2_a}) + (F_{1_i} * F_{2_u})) - \\ ((F_{1_i} * F_{2_e}) + (F_{1_e} * F_{2_a}) + (F_{1_a} * F_{2_u}) + (F_{1_u} * F_{2_i}))) \end{aligned} \tag{7}$$

F_1 and F_2 represent the first and the second formant respectively related to each vowel.

Moreover, another parameter has been evaluated to enhance the sensibility of the analysis: the Formant Centralization Ratio (FCR) reduces the individual variability within measurements allowing to better identify dysarthria than the only use of tVSA and qVSA. FCR has been proposed to maximize sensitivity to vowel centralization and minimize sensitivity to interspeaker variability and it is calculated as:

$$FCR = (F_{2_u} + F_{2_a} + F_{1_i} + F_{1_a})/(F_{2_i} + F_{1_a}) \tag{8}$$

The centralization of formants and/or the compression of VSA in dysarthric speakers have been reported in several contributions [10] [21]. These studies report a significant positive correlation between VSA and speech intelligibility, demonstrating a correlation between VSA and speech capability in different neurodegenerative diseases. Modifications of intelligibility of speech can be associated with MS, so the presented paper proposes the analysis of these parameters for patients affected by MS with the aim of try to define a range of possible values correlated to speech alterations.

3 Experimental Results

The aim of the proposed contribution is to study the vocal signals acquired from patiens affected by MS, in order to evaluate them and to identify relevant patterns. Voice data from patients affected by MS has been compared with data from healthy subjects. For the study, 53 pathological patients affected by SM between 25 and 74 years of age have been enrolled at the Neurological Operative Unit, Center of Multiple Sclerosis, in Cosenza (Italy), divided as follows:

- 18 patients affected by SMSP (7 men and 11 women);
- 35 patients affected by SMRR (11 men and 24 women).

A set of voices between 24 and 68 years has been acquired among healthy subjects.

The acquisition protocol, which has been defined with clinicians, as a first step calls for the acquisition of an informed consent signed by each patient who participates to the study. The acquisition of a continuous and sustained pronunciation of the five vowels /a/, /e/, /i/, /o/,

/u/ is performed for 5 seconds. The acquisition has been made inside a clinical laboratory with optimal acoustic setup and with the subjects sitting comfortably. The vocal signal has been recorded with an omnidirectional microphone placed near the mouth of subject, by using a sampling frequency of $22.05kHz$ and a resolution of 16 bits. All signals have been recorded in .wav format and analyzed with PRAAT.

Two methodologies of acoustic analysis and vowels metric have been applied to acquired vocal signals of patients affected by MS and healthy subjects to evaluate the behavior of speech and identify possible significant patterns for this neurodegenerative disease. The results of both methodologies have been reported below. Moreover, a statistical analysis has been performed to find the most significant results.

3.1 Results by Acoustical Analysis

Acoustic analysis has been performed by using PRAAT on vocal signal of subjects enrolled and the results have been reported in the following tables. The following parameters have been extracted for healthy subjects (HS) and for patients affected by Secondary Progressive Multiple Sclerosis (SPMS) and by Relapsing-Remitting Multiple Sclerosis (RRMS): fundamental frequency, jitter (absolute and relative), shimmer (relative and dB) and HNR. For all of these parameters, a discrimination between men and women has been made, taking into account their different vocal characteristics in terms of frequency.

Table 1 reports the values of fundamental frequency F_0 both for healthy and pathological subjects. Values are expressed in Hz and maximum, minimum and mean are reported. The general tendency is a reduction of F_0 according to Section 2. The results show an increase of the F_0 average in men for SPMS; instead, F_0 average decreases in women both for SPMS and RRMS.

	HS			SPMS			RRMS		
F_0 (Hz)	max	avg	min	max	avg	min	max	avg	min
Men	121,79	116,02	110,84	192,3	125,26	97,05	134,17	109,29	90,73
Women	206,03	199,64	187,61	198,04	168,01	138,46	270,26	169,63	84,57

Table 1: Results of the Fundamental Frequency for healthy subjects (HS) and patients affected by SPMS and RRMS

In table 2, relative jitter values are reported for healthy and pathological subjects. Values are expressed in percentage and maximum, minimum and average are also reported. In this case, jitter presents an average value of less than 0.5% both for male and female healthy subjects, in accordance with the standard values reported in section 2. Moreover, the average values of jitter for male and female pathological subjects are greater than 0.5%, associated to a possible lack of control in cord vibration for MS disease according to the indication reported in Section 2.

	HS			SPMS			RRMS		
Jitter	max	avg	min	max	avg	min	max	avg	min
Men	0,42	0,36	0,29	1,83	0,7	0,19	4,57	0,79	0,21
Women	0,4	0,32	0,21	3,83	0,82	0,12	2,99	0,5	0,08

Table 2: Results of local jitter expressed in percentage for healthy subjects (HS) and patients affected by RRMS and SPSM

The results for relative shimmer values are reported in Table 3. Values are expressed in percentage and maximum, minimum and average values are also reported. For shimmer, the mean values increase in presence of SPMS disease for both men and women; it increases also for RRMS disease in female patients. An increase of shimmer value in pathological patients could be associated to mass lesions on vocal cords (see Section 2).

	HS			SPMS			RRMS		
Shimmer	max	avg	min	max	avg	min	max	avg	min
Men	15,16	8,46	3,98	13,54	8,7	4,67	22,06	8,13	2,31
Women	8,06	5,81	4,63	16	8	2	16,51	6,73	2,94

Table 3: Results of local Shimmer in % for healthy subjects (HS) and patients affected by SPMS and RRMS

The last results about HNR are shown in Table 4. As for the other parameters, the values of maximum, minimum and average are reported and they are expressed in dB. The results show an increase of the average value in MS patients confirming a reduction of speech efficiency and pureness.

	HS			SPMS			RRMS		
HNR	max	avg	min	max	avg	min	max	avg	min
Men	20,25	13,44	9,6	18,15	14,29	11,23	21,01	14,39	4,25
Women	18,26	16,71	13,09	27,64	17,42	7,31	26,16	16,98	6,71

Table 4: Results of HNR in dB for healthy subjects (HS) and patients affected by SPMS and RRMS

The tables show a different behavior of acoustical parameters in patients affected by MS compared to healthy subjects according to values reported in literature. This result could be a valid indicator in diagnosis and monitoring of MS disease.

3.2 Results by vowel metric analysis

Praat has been used to automatically extract all F_1/F_2 pairs corresponding to voiced frames and vowel metric analysis has been performed by using Matlab. In Matlab, a module has been defined to load F_1 and F_2 values extracted by PRAAT software and calculate tVSA, qVSA and FCR according to the equations 6, 7, 8 reported in section 2. Then, the Matlab module maps F_1/F_2 pairs for each vowel in two plots (one for tVSA and one for qVSA respectively) to compare the different behavior between pathological and health subjects.

Table 5 reports the results of the vowel metric analysis both for healthy subjects and patients affected by SPMS and RRMS. Generally, the vowel area decreases for pathological subjects. There is a remarkable reduction of the area for patients with RRMS, even though a tVSA increases can be notified in SPMS. Moreover, a light increase of the FCR values can be noted in patients with MS.

To better underline the difference of vowel areas for healthy and pathological subjects, Figure 1 reports a graphical representation of the qVSA values. The qVSA is calculated as the area within the irregular quadrilateral formed by the first and second formants (F_1 and F_2) of the corner vowels /i/, /e/, /a/, and /u/.

Metric	HS	SPMS	RRMS
tVSA	579,8	673,45	97,45
qVSA	674,23	525,89	108,56
FCR	1,95	1,96	1,98

Table 5: Results expressed as average values for tVSA, qVSA and FCR for healthy subjects (HS) and patients affected by SPMS and RRMS

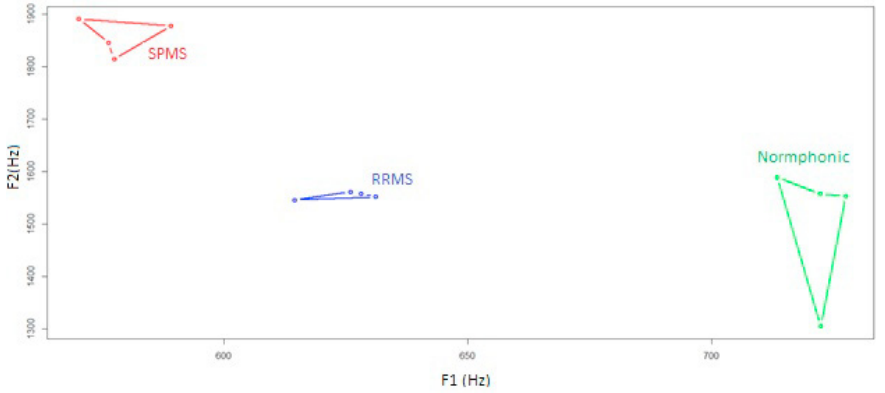

Figure 1: qVSA for healthy (green), RRMS (blue) and SPMS (red) subjects

The patients affected by RRMS present a lower area. The reduction of the vowel space area represents a centralization of formant frequencies appearing in dysarthria cases, as indicated in section 2.

3.3 Statistical results

Statistical analysis has been performed to evaluate the obtained results by using the online tool SISA (Simple Interactive Statistical Analysis). T-test with a confidence interval of 95% has been used to compare the mean of healthy (HS) and pathological subjects (MS) for the features showing the highest difference: relative jitter and relative shimmer. Table 6 shows the results of the statistical test. Mean and standard deviation (SD) values are also reported because they are necessary to calculate p-value.

Parameter	Subjects	Number	Mean	SD	p-value
Jitter	HS	7	0,341	0,0007	0,0001
	MS	55	0,65	0,0085	
Shimmer	HS	7	6,9	03	0,0001
	MS	55	8,07	0,04	

Table 6: Results of t-test for jitter and shimmer for healthy subjects (HS) and patients affected by SPMS and RRMS

The obtained p-value is less than 0.05, which confirms that the observed differences between healthy and pathological subjects means are statistically significant, with a confidence level of 95%. These values are the results obtained after six months of work; they are preliminary but

they have been discussed and validated from the clinical component.

4 Conclusions

The aim of the contribution is to propose a method for the evaluation and identification of significant patterns in voice samples acquired from patients affected by Multiple Sclerosis. The obtained results show different values for all parameters, distinguishing normal and pathological subjects as indicated in literature. Future works include enrolling new patients and perform additional tests.

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