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Detection of Different Levels of Multiple Sclerosis by Assessing Nonlinear Characteristics of Posture

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Abstract

Background: Multiple sclerosis (MS) is a chronic disorder of the central nervous system that affects various parts of the brain and the spinal cord, leading to interruptions of the nervous, defense and movement systems, which usually affect balance and gait. Considering that the diagnosis of MS and its classification is a function of the expertise of the physician, the use of creative methods can help physicians to diagnose and classify different levels of the disease.

Methods: The primary objective of the present study was to detect different levels of MS disease based on the nonlinear evaluation of body features. To do so, we studied eight MS patients and posture information of these patients such as the center of pressure (COP) were recorded at different levels with various degrees of Expanded Disability Status Scale (EDSS) by a motion analyzer device, while subjects were standing on the force plate in the eyes-opened and eyes-closed modes. After extracting and validating features that are used to assess posture disorders and explain the balancing behavior, the support vector machine (SVM) was employed to classify different levels of disease. Using the Spearman correlation test, each feature evaluated by the EDSS test.

Results: The features obtained from Higuchi's fractal dimensional algorithm in both anterior-posterior and mediolateral directions of the COP, which were significant ($P<0.05$) were selected and provided to SVM and neural network for classification of different levels. It found that SVM outperformed neural network and was able to carry out the classification with the accuracy of 90.7%.

Conclusion: As an intelligent method, the non-linear evaluation of body features such as dimensional fractal analysis of the COP can help physicians diagnose different levels of MS with greater precision.

Keywords: Multiple sclerosis; Posture; Nonlinear systems; Diagnosis of disease; Support vector machine.

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Introduction

In the normal state of standing, the mediolateral oscillation controlled, and the human body acts as an inverse pendulum so that in the event of any disturbance, it keeps itself from falling. Multiple sclerosis (MS) is a progressive disease[1] that ultimately leads to the death of a patient.[2] It caused by the autoimmune system of the body[3] in which defense cells of the body (white cells), after destroying a pathogen in the central nervous system; begin to attack astrocytes.[4] Astrocyte cells are in charge of producing the myelin sheath, which is required to increase the speed and quality of transferring action potential.[5] With the demolition of the myelin sheath, information does not properly transmit to the central nervous system, and the person suffers from impaired functioning in various systems, such as the motor system. A small disorder in the balance system results in loss of stability increased body oscillations and change of motor pattern.[6] MS and schizophrenia are that both develop during early adulthood.[7-9] Therefore, an intelligent method, in addition to aiding physicians in examining posture disorders, diagnosing MS disease and categorizing it into different levels, paves the way for accurate and precise diagnosis. Given the progressive nature of this disease, the Expanded Disability Status Scale (EDSS)[10] is used to measure the progression of the disease. The Kurtzke's EDSS is a method for quantifying and measuring the degree of disability in MS patients. In fact, by assigning a score to 8 functional systems (FSs) and the ability of a person to walk a certain distance (the movement ability), EDSS measures the severity of MS disease on a scale of 0 to 10, with zero indicating absence of any impairment in the FSs and 10 signifying the death of the MS patient. In the literature on posture assessment, Corradini et al in their research on early diagnosis of postural disorders in MS patients through movement analysis, proposed a controlling model for maintaining balance and posture of MS patients using the reverse pendulum model and Arma controller. This model was able to distinguish MS patients from other patients.[11] Chagdes et al in a 2016 paper on limited oscillations in the standing position of human body used Pitchfork and Hopf algorithms with reverse pendulum model (representing body muscles), together with a reinforcing gain in the feedback loop of the human control model, presenting a mathematical model that could demonstrate stable and unstable areas of human posture. In general, they revealed that learning about the limited cycle of posture oscillations could aid the diagnosis of musculoskeletal disorders, and considering that the cycle of oscillations associated with specific parameters of the musculoskeletal system, it can be effective for the treatment of this disease.[12] One common problem of MS patients is lack of balance in performing voluntary and routine tasks. In this regard, Chagdes et al in 2013 proposed a dynamic stability model of a person standing on a balance board. The analysis of this system is crucial for balance improvement and early diagnosis of musculoskeletal disorders. They used Pitchfork and Hopf algorithms to linearly determine critical and supercritical areas of muscle stability performance on the balance platform, providing a general description of posture status, which could aid physicians in timely diagnosis and treatment of the disease.[13] Krishnan et al in a 2012 paper on controlling posture in performing voluntary actions in MS patients with the goal of studying organs involved in adjusting posture during voluntary actions and other associated disorders found that it enabled physicians to diagnose and improve the patient's balance.[14] The body of most people oscillates in the anterior-posterior and mediolateral directions. Considering that center of pressure (COP) displacement signifies body oscillation and neuromechanics required to maintain vertical position, serving as the most common variable for examining body stability, it was used to describe the structure of posture. This study aims to evaluate the nonlinear features of the posture to identify various levels of MS disease. Therefore, the movement pathways of COP in patients recorded at 3 different levels in 2 anterior-posterior and mediolateral directions using a standard test approved by the MS Society of the United States to assess body balance.[15] In the following, the characteristics describing person's ability to assess balance in MS patients extracted and the validity of each characteristic checked by Spearman correlation and EDSS test to provide the classifier with effective features for distinguishing different levels of the disease.

Materials and Methods

The general research process is as follows in Figure 1.

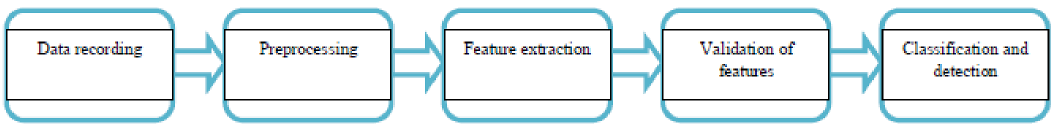

Figure 1. General Research Process.

Data Recording

Eight patients with a definite diagnosis of MS participated in this test. Also, the progression of disease was measured and labeled by a specialist. The study procedure explained to all subjects, and they signed a written consent form. The patients who assigned to good, moderate and poor levels regarding the severity of their disability included in the study. The average age, weight, and height of subjects were in the range of 23-45 years, 50 to 73 kg and 1.55 to 1.76 cm, respectively. In this study, the posture of patients was examined by a motion analyzer device called AMTI Accu Gait, which was equipped with a force plate and measured COP. The data could access by Vicon-Nexus software. The force plate, the force of Fz applied at a distance of X and Y from the center of coordinate as shown in Figure 2 and the momentums of Mx and My generated by force in the range of X and Y-axes of force plates were measured. With this information known, the X and Y position of the COP can calculate according to the following formulas.

$$y_{cp} = \frac{M_y}{F_z} \quad (1)$$

$$x_{cp} = \frac{-M_y}{F_z} \quad (2)$$

To assess the accuracy of the data recorded by the

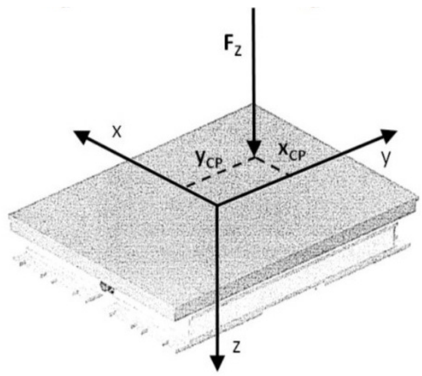

Figure 2. Determine the Center of Pressure Using Measured Forces and Moments.[13]

device, a 1-kg dumbbell considered as the benchmark and the benchmark data was chosen as the standard. The displacement chart of COP (stabilogram) for healthy subjects and the benchmark were drawn (Figure 3), and with stabilogram reported in articles were compared. The similarity of these indices confirmed the accuracy of the data. 37 light reflecting markers with a diameter of 14 mm were placed directly on the skin at the specified areas using a two-sided adhesive with an approximate thickness of 0.5 mm, as shown in Figure 4. The markers were attached to the body in the standing position. For data recording, 6 cameras with light transmitter diodes and a frequency of 100 Hz used. The data of all participants were recorded once to 3 times by the device and 6 cameras in a dark room with 10-minute time intervals. The subjects were in the standing position while their eyes were open and closed.

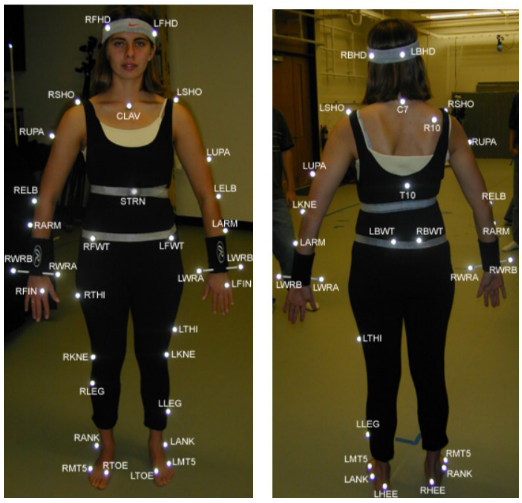

Figure 4. Place of Markers.

Preprocessing

The processing steps of data consisted of preprocessing, which helps the extraction of final results. Data preprocessing usually involves the discovery of outlier and identification of missing data. Table 1 reports data specification and the number of usable data.

Feature Extraction

In this study, 4 statistical characteristics including mean and standard deviation[16] together with nonlinear characteristics such as correlation dimension[17,18] and Higuchi fractal dimension (FD) extracted from COP variable in both AP and ML directions (Table 2). Since there are 15 and 14 COPs recorded in the eyes-open and eyes-closed modes, respectively, 2 feature matrices with the following dimensions were obtained for both modes.

Dimensions of the feature matrix in the eyes-open mode: 15 × 9

Dimensions of the feature matrix in the eyes-closed mode: 14 × 9

The ninth column of feature matrices dedicated to the classification of MS patients into 3 levels of good (0), moderate (1), and weak (2) regarding the severity of the disability. Since each computational characteristic expanded in a particular range, in this research, a normalization method based on the maximum and minimum span in the range of 0 to 1 was used.

$$D_{normal} = \frac{D - D_{min}}{D_{max} - D_{min}} (D_{New-max} - D_{New-min}) + D_{New-min} \quad (3)$$

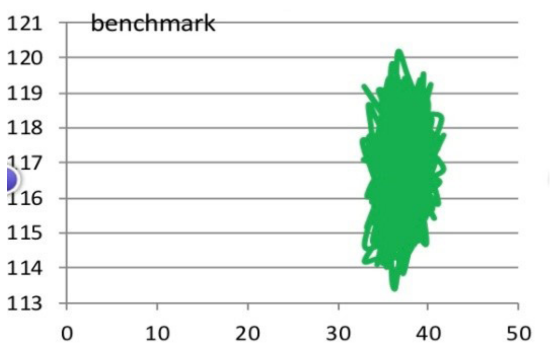

Figure 3. Stabilogram of Benchmark.

Validation of Features

In this study, the Spearman correlation test was used to

Table 1. Data Specification of Patients in the Open Eye and Close Eye

Name of Patient	Number of All Data		Number Missing of Data	Number Usable of Data	EDSS	Classification
	OE	CE				
AA	2	2	-	4	1	Good
FK	2	2	-	4	1	Good
MN	2	2	-	4	1	Good
SA	1	1	2	2	1	Good
SM	2	2	-	4	5	Poor
ZM	1	1	2	2	6	Poor
ZN	2	2	-	4	3	Moderate
MKH	3	2	1	5	3	Moderate

Table 2. Extracted Features

Direction		Feature
AP	ML	Higuchi fractal dimension
AP	ML	Correlation dimension
AP	ML	Standard deviation
AP	ML	Mean

measure each feature with the EDSS test. Features with $P < 0.05$ allocated to support vector machine (SVM)[19] and neural network[20,21] for classification. According to P values of extracted properties, Higuchi's features of fractal dimensional selected in anterior-posterior and mediolateral directions.

Classification and Detection

The problem in the question has three classes. According to one against all strategy, each time an SVM with RBF kernel function is trained to separate a class from the rest of the data. Since there are three classes, three separate SVMs trained. In the SVM[22] output, the confusion matrix was created, which was then used to calculate the accuracy criterion.[23] To report the efficiency of the classifier, in addition to the classification accuracy, sensitivity, specificity, and precision were also examined according to the following formulas and parameters in Table 3. Table 4 reports the results of classifiers.

$$\text{Precision (\%)} = \frac{TP}{TP+FP} \times 100 \tag{4}$$

$$\text{Sensitivity (\%)} = \frac{TP}{TP+FN} \times 100 \tag{5}$$

$$\text{Specificity (\%)} = \frac{TN}{TP+FP} \times 100 \tag{6}$$

$$\text{Accuracy (\%)} = \frac{TP+TN}{TP+FP+FN+TP} \times 100 \tag{7}$$

Discussion

The partial oscillations of the body provide valuable information about changes in the control status engendered by age, disease, skill and practice [24]. Therefore, a suitable variable to assess the stability of posture and balance is COP. It is measured by the force plate when a person is in the standing position and examined from 2 different perspectives. According to the first view, some studies utilize a set of COP parameters, which provide a more exhaustive explanation of the balance, as an appropriate feature for assessing posture disorders. In 2014, Saripalle et al conducted a study on the classification of body movements based on posturographic data. Based on the analysis of COP parameters, they managed to categorize 11 body movements in the standing position using SVM with a Gaussian kernel and an accuracy of 88%.[25] Since time series of COP have chaotic[26] and fractal properties[27] and the control system is a definitive nonlinear system,[28] according to the second view, various studies have investigated the stability of posture and balance using nonlinear dynamics and chaos theory. In 2014, Khayat et al investigated the effect of age on static balance. Based on the COP analysis in the frequency and chaos domains, Lyapunov exponent features, low-frequency power ratio, and standard deviation, they were able to classify the control signal of the body posture for different age groups using a multilayer perceptron neural network with an accuracy of 79.1%.[29] In 2004, Golz et al analyzed the differences between various postural sway trajectories. With the purpose of identifying the effect of alcohol on the body control system and distinguishing alcohol users from non-alcoholics, they studied COP time series in the

Table 3. List of Parameters Used in the Formulas

Summary	Full Name	Explanation
TP	True positive	The total number of patients that correctly classified into the relevant classes.
TN	True negative	
FP	False positive	The number of patients that do not belong to the class, but the classifier has mistakenly identified them as belonging to that class
FN	False negative	The number of patients that belong to the class, but the classifier has mistakenly not identified them as belonging to that class

Table 4. The Performance Results of 3 Classifiers

Classifier	Mode	Precision	Accuracy	Sensitivity	Specificity
SVM	Open eye	86.7%±1.7	90.7%±1.8	86.6%±1.8	94.4%±1.9
	Close eye	85%±1.7	90.1%±1.8	90.5%±1.8	92.9%±1.8
MLP	Open eye	55.5%±1.1	88.8%±1.7	96%±1.9	91.6%±1.8
	Close eye	75%±1.5	86.7%±1.7	96%±1.9	91.6%±1.8
RBF	Open eye	75%±1.5	83.3%±1.6	83.3%±1.6	88.8%±1.7
	Close eye	87.5%±1.7	88.8%±1.7	96%±1.9	88.8%±1.7

frequency domain, reporting higher accuracy in detecting small changes in the body control system by the SVM classifier compared to K-means and neural networks.[30] Lamoth et al used entropy sample of non-linear dynamic criteria, as an indicator of the chaos and complexity of the system, to compare three groups of students with different characteristic. The 3 groups consisted of ordinary students, students of physical education and gymnast students. They studied acceleration of partial body sway as the main variable, with their results suggesting that the complexity of the acceleration time series in gymnast students was higher than that of physical education and ordinary students. Further, the Lyapunov exponent, who indicates the extent of system instability,[31] was highest for ordinary students, followed by Physical Education students and gymnasts. In other words, the stability of gymnast students was greater than that of the other 2 groups, and the stability of physical education students excelled that of ordinary students. Therefore, with an enhanced ability to maintaining balance and stability, the complexity of the system and its stability is also increased.[14] In this study, FD analysis, which is a nonlinear method, was used as a measure of complexity for balance control system of MS patients at three different levels of disease. In the standing and static position, higher FD values obtained from the Higuchi algorithm (in the range of 1 and 2) indicates greater freedom of movement while FD values close to one indicates lower freedom of movement.[32] The FD value of the balance control system at the good level was higher than the moderate and weak levels, and the FD value of the moderate level was more than that of the weak level. Considering the progression of the disease, increased FD for patients assigned to the good level could attribute to the greater flexibility and compatibility of this group of patients with diverse conditions (standing with eyes closed in darkness). Further, greater complexity reveals that the control system at the good level is more automatic than it is in other levels and this group of patients requires lower attention to maintain balance. On the other hand, lower complexity at moderate and weak levels of the disease could be due to the progression of the disease and the inability to exploit total freedom in maintaining balance. This study showed that the FD value, as a criterion for the complexity of the balance control system, could be significantly different between three different levels of the disease in both AP and ML directions, indicating that FD analysis allows the detection of a person's ability in maintaining balance and stability. Moreover, SVM classifier with RBF kernel had desirable performance in the classification of three different levels of the disease with the non-linear feature of Higuchi's FD algorithm in 2 AP and ML directions, and its accuracy in the eyes-open and eyes-closed modes was higher than that of the neural network. The following suggestions can help improve the results of this study. First, increasing the number of participants to collect more training examples for classifiers. Second, incorporating the analysis of dynamic balance and gait in the tests. Third, using other features and classifiers to improve the results. Fourth, considering the effect of depression as an independent intervention factor in tests and undertaking a study on this subject.

Acknowledgment

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Conflict of Interest Disclosures

The authors declare that they have no conflict of interests.

Ethical Statement

The present study was approved by Islamic Azad University of Central Tehran Branch. In addition, informed consent was signed by the patients.

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