Nonlinear dynamical structure of sway path during standing in patients with multiple sclerosis and in healthy controls is affected by changes in sensory input and cognitive load

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HIGHLIGHTS

• Similar dynamical structure of sway path was seen between patients and healthy.
• Decreased regularity and complexity were seen by increased postural difficulty.
• Decreased regularity and complexity were seen by increased cognitive difficulty.

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ABSTRACT

Although several studies have applied traditional linear measures to evaluate postural control of patients with multiple sclerosis (MS), little is known about the nonlinear dynamics of this patient group. In this study, recurrence quantification analysis (RQA), a well documented nonlinear method, was used to compare the nonlinear dynamical structure of postural sway in two groups consisting of MS patients (n = 23) and healthy matched controls (n = 23). The study focuses on three levels of postural difficulty consisting of (1) standing on a rigid surface (force platform) with eyes open, (2) standing on a rigid surface with eyes closed, and (3) standing on a foam surface with eyes closed. The two levels of cognitive difficulty measured, consisted of a single postural task and a dual postural–cognitive task. It was observed that as the postural conditions became more difficult, the center of pressure (COP) time series of both groups became less regular as recorded in lower recurrence rate, less complex in deterministic structure as reflected in lower RQA entropy, and less nonstationary as reflected in the recording of lower Trend. Moreover, as cognitive conditions became more difficult, COP time series became less regular (lower %Rec in the anteroposterior direction and lower %Det in both directions), less complex in deterministic structure (lower RQA Ent in the anteroposterior direction), and less nonstationary (lower trend in the anteroposterior direction). The analytical results of the research show that there is a similar dynamical structure for both the MS patients and the control group; however, the nonlinear behavior of both groups was different under various experimental conditions.

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1. Introduction

Balance deficits are one of the most frequently reported problems of patients with multiple sclerosis (MS) [16]. Impairment in neuromuscular and musculoskeletal components of postural control such as muscle weakness and spasticity is one of the major contributing factors of postural control deficit in patients with MS [14,29]. While several studies have used traditional linear measures for evaluating the postural control of MS patients [16,19,34], little is known about the nonlinear dynamical structure of postural sway in these patients. Results extracted from nonlinear analysis can provide important insights regarding the regularity and complexity of human postural system that may not be attainable through the traditional linear measures [3,20].
Variability in the postural control of patients with MS using a nonlinear approach has been investigated in two recent studies [12,13]. In one study, Huisinga et al. used LyE and ApEnt to investigate upright postural control and found that MS patients had significantly lower values of LyE and ApEnt compared to healthy controls [13]. In another study, Huisinga et al. used LyE to investigate the effects of supervised training on standing postural control and found that pretraining LyE values of MS patients were significantly lower than those of healthy controls [12].

To date, several nonlinear methods have been employed to examine the dynamical structure of postural sway in quiet standing (e.g. recurrence quantification analysis (RQA), Lyapunov exponent (LyE), approximate entropy (ApEnt), and sample entropy (SampEnt)) [30]. It is believed that among these nonlinear methods, the RQA has better merits due to the fact that in contrast to the others, RQA does not require any prerequisites of data stationary, known statistical distribution, or the particular size of data time series [22,32]. In addition, RQA is not affected by transients, outliers, or noise [32]. RQA variables provide useful information about the regularity of COP time series based on the recurrence rate (Rec) and deterministic behavior (%Det). RQA also provides information on the complexity of recurrence plot based on Shannon entropy and on stationarity based on Trend [22]. It is necessary to note that unlike ApEnt and SampEnt, RQA Entropy (RQA Ent) does not provide information regarding “the complexity of the original signal” but is defined as a measure of “the complexity of the deterministic structure in the recurrence plot of center of pressure (COP) time series” [20,22]. The complexity in deterministic structure of COP time series could be translated into the “structured variation” within the “smooth/predictable” behavior of postural control [9]. The amount of variations within regular pattern of postural sway could determine the extent of adaptability (flexibility) of the postural control system to overcome the perturbations imposed on the human body while maintaining standing balance [9].

Riley et al. [22] first applied RQA to quantify the dynamical structure of postural sway in healthy young adults. Since then, investigators have used RQA for different neurological (e.g. Parkinson’s disease [26]) and musculoskeletal (e.g. anterior cruciate ligament (ACL) injury [17]) disorders, and studies on elderly populations [28], and ballet dancers [25]. Based on the results obtained from these studies, the postural control of pathologic conditions (i.e. Parkinson’s and ACL patients) and elderly populations is characterized by the COP time series that are more regular, more complex in deterministic structure and relatively more stationary than those of healthy populations and young adults, respectively. To the researchers’ knowledge, no study has yet investigated the deterministic structure of postural sway in patients with MS. Thus, the primary objective of the study was to characterize the nonlinear dynamical structure of postural sway obtained from the RQA in MS patients as compared to healthy, age matched controls. The researchers hypothesized that MS patients will demonstrate COP time series that are more regular, more complex in deterministic structure, and relatively more stationary than those of healthy controls.

In addition, in recent years the issue of posture–cognition interaction using nonlinear methods has received considerable attention in related literatures [9,21,26]. Postural control is the result of interaction between sensorimotor and cognitive components [16]. Cognitive impairment as working memory deficit has been documented in MS patients [5]. The consequences of sensorimotor deprivation on standing balance control of MS patients have been investigated in several studies (e.g. [2]). However, little is known for the effects of cognitive loading on postural control in this patient population [16]. For this purpose, a dual task methodology in which postural control is assessed during concurrent execution of a cognitive task was used in the present study. The researchers hypothesized different effects of cognitive loading on the dynamical structure of COP time series between persons with MS and healthy controls.

2. Materials and methods

2.1. Participants

The sample population consisted of twenty-three patients with a definite diagnosis of relapsing-remitting type of MS (mean age, height and body mass index: 32.7 ± 7.9 yr, 1.6 ± 10.4 m and 24.1 ± 3.8 kg/m², respectively; 8 males and 15 females) and 23 healthy participants (mean age, height and body mass index: 31.4 ± 7.9 yr, 1.6 ± 9.6 m and 24.6 ± 3.8 kg/m², respectively; 8 males and 15 females). Inclusion criteria of the MS patients consisted of ability to independently stand for at least 30 s [2] and ability to independently walk for 100 m with and without assistive devices [24]. Exclusion criteria consisted of (1) Expanded Disability Status Scale (EDSS) greater than 5, (2) Mini-Mental State Examination (MMSE) lower than 24 as cognitive impairments could interfere with execution of cognitive task [16] and (3) visual impairment, severe pain and vertigo on the day of assessment [19]. The mean EDSS score of the patients was 2.51 ± 1.1 points. All participants in the study signed an informed consent form which had been approved by the Local Ethics Committee.

2.2. Procedure

Postural performance was assessed during double leg stance while the participants stood barefoot on the force platform, feet apart at an angle of 30°, heels separated by 3 cm, and arms hanging at their sides [16,19]. COP data were collected at a sampling frequency of 100 Hz using a strain gauge Bertec 4060-10 force platform and Bertec AM-6701 amplifier (Bertec Corporation, Columbus, OH, USA).

The three levels of postural difficulty were standing on (1) rigid surface (force platform) with open eyes (EO); (2) rigid surface with closed eyes (EC); and (3) foam surface (10 cm thick and 35 kg/m³ foam density placed on the force platform) with closed eyes (FEC). The two levels of cognitive difficulty selected were postural task without (single) and with (dual) concurrent cognitive task. The cognitive task selected was silent backward counting in steps of 3 and from a random number of 100–200. Cognitive performance was assessed by recording the final number for both the accuracy and number of subtracted items [16]. Recording the final number was performed immediately after postural data collection from force platform.

By combining three levels of postural difficulty (i.e. EO, EC, and FEC) and two levels of cognitive difficulty (i.e. single and dual tasks), each participant was exposed to six randomly ordered experimental conditions. In addition to the aforementioned standing positions; a sitting position while performing the cognitive task was considered as the cognitive control performance.

Each experimental condition was repeated three times. Due to the detrimental effects of fatigue and heat on the performance of MS patients [8], all experiments were performed in the morning when the participants were at their highest energy state [34]. Also, to minimize the effects of fatigue on postural performance, each experimental condition was generally followed by a rest period of 5 min [16].

2.3. Data analysis

Data was recorded for 30 s continuously while the subjects stood on the force platform resulting into 3000 data points. In the next step, the embedding dimension and delay parameter, as
two constant requirements of RQA, were determined. Using the false nearest neighbors algorithm [1], the most suitable embedding dimension was found to be 5 for all the time series. The delay parameter required for space reconstruction was calculated for each time series using the average mutual information algorithm [18]. Since noise in COP data collection is inevitable [20], signals were filtered using the simple nonlinear filter method described in [27], using a dimension of 15 (three times higher than the required embedding dimension) and neighborhood size of 20% of the standard deviation (SD) of the data. This type of filtering is applied to states in the reconstructed space rather than on original time series. Based on this application, dynamical behavior will be better preserved and adverse affects of time series filtering will be avoided [33]. After that, four RQA measures, %Rec, %Det, Ent, and Trend were computed using published algorithms [35]. The neighboring radius for recurrence was considered to be 10% of the maximum phase space diameter using Euclidian norm. This value kept the recurrence rate below 5% in most cases. For the quantification process, at least three consecutive states were considered a line [10].

Another important issue in COP analysis is signal filtering. While filtering may not affect linear measures, the underlying dynamical structure of attractors may dramatically change under distortions cause by filter behavior [11]. As a consequence, many researchers prefer to use unfiltered time series for nonlinear analyses [10,26]. On the other hand, COP recordings usually contain noise; therefore, some filtering might be desired [6]. Along with applying nonlinear filter [15], in the current research the unfiltered data and Butterworth low pass filter were examined and slightly different results were obtained, but the statistical inferences were the same. In this paper, only the results of the nonlinear filtering method have been reported.

Using the average of trials increases the intra-class correlation coefficient, by contrast, an average values does not imply a true measurement scale. The researchers separately analyzed the values of the first trial, and the median, and mean of the three trials. In all cases, the statistical results were the same.

### 2.4. Statistical analysis

For each RQA variable, the average of the three trials related to each experimental condition was used for statistical analysis. To examine postural performance, a separate $2 \times 2 \times 3$ (group by cognitive difficulty by postural difficulty) mixed model of analysis of variance (ANOVA) tests was used to determine the main effects and interactions of these factors for each of the RQA variables. For multiple comparisons between 3 levels of postural difficulty, the Bonferroni adjustment method was used [7]. Cognitive performance was analyzed using a $2 \times 4$ (group by postural difficulty) mixed model of ANOVA to detect the possible main effects and interactions of the two factors on the cognitive score. Alpha was set at 0.05 for all statistical analyses.

### 3. Results

Table 1 shows the mean and SD of the RQA variables for different conditions of postural and cognitive difficulties in both groups.

The obtained results in Table 2 showed that the group had no significant effect on any variable. There were no significant interactions between the group, postural difficulty, or cognitive difficulty. The main effect of postural difficulty was significant for all variables except %Det in the direction of anteroposterior (AP). The results of post hoc multiple comparisons showed that the values of %Rec, RQA Ent, and Trend (all in medilateral (ML) direction) were significantly lower in EC than EO ($p < 0.04$). Also, the values of %Rec, RQA Ent, and Trend (all in the AP direction)
were significantly lower in FEC than EC (p < 0.02). The values of all but %Det of the RQA variables were significantly lower in the FEC than EO (p < 0.03). The main effect of cognitive difficulty was also significant for %Rec, RQA Ent, Trend, all in the AP direction, and %Det (in both directions) (see Fig. 1), but not for %Rec, RQA Ent, and Trend (in the ML direction, p > 0.05).

The results of the ANOVA analysis on the cognitive score variable showed that there was no interaction of group by postural difficulty (F3,132 = 0, p = 0.99). Also, no main effects for postural difficulty (F3,132 = 1.80, p = 0.15) and group (F1,44 = 0.02, p = 0.32) were detected in this study.

4. Discussion

The results of this study showed that when evaluating RQA variables, significant differences were found between various levels of postural and cognitive difficulties yet no differences were found between MS and healthy participants. It means that as postural conditions became more difficult from EO to EC to FEC, COP time series became less regular (lower %Rec), less complex in deterministic structure (lower RQA Ent), and less nonstationary (lower Trend). Also, as cognitive conditions became more difficult from single to dual task conditions, COP time series became less regular (lower %Rec in the AP direction and lower %Det in both directions), less complex in deterministic structure (lower RQA Ent in the AP direction), and less nonstationary (lower trend in the AP direction).

Recurrence dynamics of the states using the RQA technique showed the same complexity in deterministic structure of postural sway between two groups of MS patients and healthy controls. This finding is in contrast to the results of other nonlinear measures of complexity like ApEn in which less behavioral complexity were seen in MS patients as compared to healthy controls [12,13]. The existence of similar complexity in deterministic structure in the current study could be interpreted as the similar variation within regular pattern of postural sway in both study groups. This finding may reflect similarity in the functional adaptation of the postural control system in response to changes in sensory inputs and cognitive loads. Also, it may reflect a means of behavioral adaptability (flexibility) in which transitions across different behavioral modes could be facilitated [25]. However, this is a hypothetical (theoretical) interpretation that was not tested directly. More investigations are needed to make further progress in understanding of these findings and variables.

Huisenga et al. in two recent studies on patients with MS [12,13] found that both LyE and ApEn methods of nonlinear analysis had the ability to find differences between MS patients and healthy controls. This observed discrepancy between the former studies and this study is probably explained by some differences between the methodologies of these studies. First, the length of data collection while the subject was standing on the force platform was 30 s in the current study while it was 5 min in Huisenga et al. studies [12,13]. Fatigue is a common symptom of MS patients and standing for 5 min could adversely affect the standing postural control of these patients. Second COP data were collected at a sampling frequency of 100 Hz in the current study while this was set at 10 Hz in Huisenga et al. studies [12,13]. The influence of sampling frequency on various measures of entropy including RQA Ent, SampEn, and ApEn was investigated in a recent study by Rhea et al. [20]. They found that entropy measures can be confounded by differences in sampling frequency and recommended that researchers should therefore carefully consider the sampling frequency when comparing results between studies. Therefore, we did the whole computation with down-sampling the data to 25 Hz and 50 Hz. However, in both cases, the statistical results were the same as sampling frequency of 100 Hz and no differences were found between MS and healthy participants.

In contrast to the results obtained for the main effects of postural difficulty levels in our study, some investigators reported that as postural conditions changed from open-eyes to closed-eyes and also rigid-surface to foam-surface, postural sway became more regular and more complex [4,9,21,22,25]. Furthermore, Riley and Clark [23] reported that when sensory organization test conditions became more difficult, COP regularity increased in the form of higher %Rec and %Det. Differences in the results of the dynamical structure of postural sway under postural difficulty levels in this study and other studies may be partially related to differences in the age, type of cognitive task, and different research populations of these studies on the issue of posture–cognition interaction.

With regard to the cognitive loading effects and consistent with the results obtained in the current study, previous studies found postural sway to become less regular and less complex with increasing cognitive difficulty in young healthy subjects [21] and in ACL injured patients [17]. The results of this study showed that when cognitive difficulty increased from single to dual task conditions, COP time series became less regular, less complex (i.e. decreased complexity in deterministic structure) and less nonstationary. Systems with regular patterns of behavior may require less cognitive processing [31]. Therefore, decreased COP regularity following cognitive loading can be interpreted as a reflection of higher attentional demand of postural control under dual task as compared to single task conditions. Moreover, decreased complexity in deterministic structure of postural sway followed by cognitive loading could be interpreted as insufficient adaptation of postural control system to imposed perturbation.
Conflict of interest

None.

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