



Multiscale entropy identifies differences in complexity in postural control in women with multiple sclerosis



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ARTICLE INFO

Article history:

Received 29 April 2015

Received in revised form 28 October 2015

Accepted 3 December 2015

Keywords:

Multiple sclerosis
Posture
Complexity
Entropy
Sensory loss
Balance control

ABSTRACT

Loss of postural center-of-pressure complexity (COP complexity) has been associated with reduced adaptability that accompanies disease and aging. The aim of this study was to identify if COP complexity is reduced: (1) in those with Multiple Sclerosis (MS) compared to controls; (2) when vision is limited compared to remaining intact; and (3) during more demanding postural conditions compared to quiet standing. Additionally, we explored the relationship between the COP complexity and disease severity, fatigue, cutaneous sensation and central motor drive. Twelve women with MS and 12 age-matched controls were tested under quiet standing and postural maximal lean conditions with normal and limited vision. The key dependent variable was the complexity index (C_1) of the center of pressure. We observed a lower C_1 in the MS group compared to controls in both anterior–posterior (AP) and medio-lateral (ML) directions (p 's < 0.002), during the performance of maximal self-regulated leans (AP: p < 0.001; ML: p = 0.018), and under limited vision (AP: p = 0.001; ML: p = 0.006). No group-by-vision interaction (p > 0.05) was observed, indicating that limiting vision did not impact COP complexity differently in the two groups. Decreased cutaneous sensitivity was associated with lower C_1 values in the AP direction among those with MS (r^2 = 0.57); all other measures did not exhibit significant relationships. The findings reported here suggest that (1) MS is associated with diminished COP complexity under both normal and challenging postures, and (2) complexity is strongly correlated with cutaneous sensitivity, suggesting the unique contribution of impaired somatosensation on postural control deficits in persons with MS.

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1. Introduction

Multiple Sclerosis (MS) is an auto-immune disorder impacting ~1.3 million people worldwide [1] and is brought on by degradation of T-cell myelin surrounding the neurons of the central nervous system (CNS). This degeneration of the myelin sheath impairs cutaneous sensation and motor signaling resulting in postural instability [2] and increased fall rates [3–5]. Previous research has demonstrated altered postural control in MS; specifically, reduced temporal margins of the center-of-pressure (COP) to the boundaries of stability [2,6] and increased postural sway [2,7], both of which may be related to increased risk and rates of falls [3].

Goldberger and Lipsitz developed the ‘loss of complexity hypothesis’ [8,9] as a way to describe how a breakdown in the number of functional degrees of freedom in the body leads to frailty and an increased risk for disability or injury. It has been suggested that the reduction of complexity may be indicative of a reduced ability to adapt and respond to challenges, such as during postural perturbations [8]. Reductions in the complexity of postural fluctuations have been associated with aging [10,11] and disease [7,12]. How task demands and constraints impact the complexity of postural fluctuations is currently unknown. Earlier research, however, has suggested that different task constraints can either increase or decrease complexity as a function of aging [13].

Huisinga et al. [7] reported reductions in postural COP complexity in people with MS using an approximate entropy technique. These results, however, may be confounded by two well established shortcomings of this technique: (1) it fails to capture the nature of COP fluctuations across the range of time scales in which sensorimotor processes contribute to the control of upright standing [16], and (2) it suffers from a self-matching bias that may underestimate the degree of complexity in the signal

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[17]. Therefore, identifying how MS impacts the control of posture across multiple time scales may help elucidate how various underlying sensorimotor mechanisms contribute to changes in postural control in this population.

Multi-scale entropy (MSE), based on the sample entropy algorithm, eliminates the self-matching bias and evaluates fluctuations over a range of time scales, quantified by the complexity index. MSE has previously identified differences in COP complexity among older individuals with somatosensory [10,11] and visual impairments [11], in those exhibiting frailty due to aging [18], and in adolescent idiopathic scoliosis [12].

Individuals with MS are thought to rely more heavily on vision for the control of posture compared to non-MS controls in order to overcome cutaneous sensory loss [2,4]. To evaluate this claim we systematically manipulated vision in order to evaluate if limiting vision (a) reduces the complexity of postural fluctuations, and (b) impacts those with and without MS differently. If individuals with MS do indeed place greater reliance on visual information to control posture then a greater reduction in the COP complexity among this group would be expected under visually challenged conditions.

In addition to impaired postural control, individuals with MS consistently exhibit increased acute and chronic fatigue [14,19], reduced cutaneous sensation [2,20], and decreased central motor drive [15]. These changes likely contribute to impaired function in MS [8]; however, it remains unclear if any of these factors are associated with changes in COP complexity. Therefore, it is of clinical relevance to relate these changes in function to changes in COP complexity.

The purpose of the current study was to identify if the complexity of COP fluctuations are impacted by the presence of MS as well as the effect of limiting vision and the performance of an internally regulated postural perturbation. We hypothesized that: (1) compared to controls, the COP fluctuations of individuals with MS will exhibit lower values of the complexity index; (2) limiting vision will result in reductions in the complexity index of the COP in both groups, with the MS group exhibiting a greater reduction in the complexity index when vision is limited; (3) Increased postural demand under self-generated postural perturbations (i.e., maximal leans) will reduce the complexity index in both the MS and control groups compared to upright quiet standing; and (4) the complexity index of COP fluctuations during quiet standing will be negatively correlated with disease severity, age, acute and chronic fatigue, and positively correlated with cutaneous sensitivity and central motor drive, indicating that the changes in sensorimotor function and fatigue associated with MS are related to decreases in the complexity of COP fluctuations.

2. Methods

2.1. Participants

Twelve women with MS (52.9 ± 9.3 years, 1.61 ± 0.06 m, and 70.8 ± 10.0 kg) and twelve age and sex matched controls (54.9 ± 8.5 years, 1.63 ± 0.09 m, and 71.2 ± 14.4 kg) volunteered for this study. Prior to testing, participants provided written informed consent in accordance with University policy. This cohort included individuals with all the MS subtypes: one primary progressive, six relapse remitting, four secondary progressive and one participant for whom the study neurologist could not identify the MS subtype. All MS participants were free of MS related exacerbations or symptoms for at least six-months prior to testing, had no oculomotor or cerebellar disorders, had visual acuity better than 20/200, and were ambulatory.

2.2. Procedures

Participants with MS completed testing procedures over the course of two laboratory visits to minimize fatigue; the first visit consisted of functional assessment and the second visit consisted of postural testing. Both sessions were held in the morning to ensure participants were in their most rested state. Individuals without MS (CON) participated in one visit during which they completed both functional and postural testing.

For the MS group only, the functional assessment included evaluation of disease severity by the study neurologist using the Expanded Disease Status Scale (EDSS) [21]. All participants self reported chronic and acute fatigue by the fatigue severity scale (FSS) [22] and visual analog fatigue scale (VAFS) [23], respectively. Additionally, cutaneous sensory thresholds were quantified by measuring the time it took for the vibration from a 128 Hz tuning fork to decay to a level where it could no longer be identified, with longer times indicating greater cutaneous sensitivity. Finally, central motor drive was assessed by counting the number of toe taps completed in 10 s [15].

Postural testing included quiet standing and maximal forward, backward, left and right leans. All postures were performed for 25 s with both normal (eyes open) and limited vision (eyes closed for quiet standing and lights off for the challenging postures with dim equipment lighting only for safety). Rest periods between trials were approximately 2 min. The quiet standing trial was performed first and then the maximal lean conditions were randomized. The order of the visual conditions was counterbalanced between participants for each postural condition. Stance width was standardized such that 33 cm separated the lateral borders of the feet.

2.3. Data analysis

3D kinetics were collected at 100 Hz from two adjacent strain gauge force platforms (AMTI, Newton, MA) using Qualisys Track Manager software (Qualisys Medical-AB, Gothenburg, Sweden) and were used to compute the COP time series. These data were filtered using a fourth-order zero-lag band-pass Butterworth filter with cutoffs of 2 and 20 Hz to ensure the removal of postural drifts while maintaining postural dynamics. Sample entropy was calculated at 11 time scales (0.03–0.33 s) from the time series of both the anterior-posterior (AP) and medial-lateral (ML) COP positions for all five postures. The use of 11 time scales allowed for 227 samples at the longest time scale, which is more than the minimum number of samples (200) necessary for reliable calculation of sample entropy [24].

2.4. Multiscale entropy

The complexity index (C_1) was used as the primary dependent variable for analyzing the differences in postural fluctuations between group (MS and CON), posture (quiet standing and maximal leans) and vision (normal and limited). The C_1 of the COP positions in both the AP and ML orthogonal directions were analyzed in accordance with the methods outlined in Costa et al. [25] and Goldberger et al. [26]. First, sample entropy (S_E) [17] was calculated (Eq. (1)):

$$S_E(m, r, N) = -\ln \frac{U_{m+1}(r)}{U_m(r)} \quad (1)$$

where S_E is the sample entropy value, m is the number of samples being compared ($m=2$), r is the radius of similarity (15% of standard deviation), N is the number of samples and U is the probability of the samples falling within r .

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