Research Report

Variability in Postural Control With and Without Balance-Based Torso Weighting in People With Multiple Sclerosis and Healthy Controls

Charlotte M. Hunt, Gail Widener, Diane D. Allen

C.M. Hunt, BS, Graduate Program in Physical Therapy, University of California San Francisco/San Francisco State University, 1600 Holloway Ave, HSS 112, San Francisco, CA 94132 (USA). Address all correspondences to Ms Hunt at: charlottemaryhunt@gmail.com.

G. Widener, PT, PhD, Doctor of Physical Therapy Program, Samuel Merritt University, Oakland, California.

D.D. Allen, PT, PhD, Graduate Program in Physical Therapy, University of California San Francisco/San Francisco State University.

© 2014 American Physical Therapy Association

Publish Ahead of Print: xxxx

Accepted: May 18, 2014

Submitted: July 15, 2013
Abstract

Background: People with multiple sclerosis (MS) have diminished postural control; center of pressure (COP) displacement varies more than in healthy controls. Balance-based torso-weighting (BBTW) can improve clinical balance and mobility in MS; exploration using both linear and nonlinear measures of COP may help determine if BBTW optimizes movement variability.

Objective: Investigate effects of BBTW on people with MS and healthy controls during quiet standing.

Design: Quasi-experimental, comparing COP variability between groups, eye closure, and weighting conditions in the anterior-posterior and medial-lateral directions.

Methods: 20 participants with MS and 18 healthy controls stood on a forceplate during four conditions: eyes open and closed, without and with BBTW. Linear measures of COP displacement included range and root mean square (RMS); nonlinear measures included approximate entropy (ApEn) and Lyapunov exponent (LyE). Three-way repeated-measure ANOVAs compared measures across groups and conditions. Association between weighting response and baseline nonlinear variables was examined. When significant, MS subgroups were created and compared.

Results: MS and control groups had significantly different range, RMS, and ApEn values (range and RMS: p<.01; ApEn: p<.05); eyes open or closed conditions had significantly different range and RMS (range and RMS: p<.01). Change with weighting correlated with LyE (r=-.70) and ApEn (r=-.59). Two MS subgroups, with low and high baseline LyE, responded to BBTW in...
opposite directions (p<.003), with a significant main effect for weighting condition (p<.05), LyE medial-lateral direction only.

Limitations: Small samples, no identification of impairments related to LyE at baseline.

Conclusions: LyE may help differentiate subgroups that respond differently to BBTW. In both subgroups LyE values moved towards the average of healthy controls, suggesting that BBTW may help optimize movement variability in people with MS.
Introduction

Multiple sclerosis (MS) is the leading progressive neurologic disease in young adults, affecting 2.5 million people worldwide. In the United States, an estimated 10,000 people are diagnosed with MS every year. Over 90% of those living with MS report decreased mobility, frequently concurrent with a decrease in postural control.\(^1\),\(^2\) Even early in the course of the disease, people with MS develop differences in mobility compared to healthy individuals.\(^3\),\(^4\) Rehabilitation that addresses postural control potentially prolongs higher levels of mobility over the 20 years most people remain ambulatory post diagnosis.\(^2\) One rehabilitative intervention in which small weights are strategically applied to the torso based on the direction of balance loss, balance-based torso-weighting, has resulted in immediate improvements in clinical measures of balance and mobility in people with MS.\(^5\)-\(^7\) These improvements, however, have varied across individuals, perhaps because of heterogeneous characteristics in samples.

Heterogeneity in MS occurs because patients develop different areas of demyelination, many that affect postural control. Postural control, the act of maintaining, achieving, or restoring upright posture during standing and walking, requires sensory and motor systems to work together in a complex interaction.\(^8\)-\(^11\) Impairment of commonly affected neural pathways associated with sensation, vision, vestibular input, sensory integration, motor control, and muscle activation\(^12\)-\(^16\) makes dysfunction in postural control strategies and subsequent loss of balance more likely, increasing the risk for falls.\(^13\),\(^15\),\(^17\),\(^18\) More than 50% of younger and middle-aged people with MS report having fallen recently and over 50% of older people with MS report having injurious falls.\(^19\)-\(^21\) The majority of people with MS report fear of falling and many report curtailing their activity because of this fear.\(^22\)
Assessing the component of postural control involved in maintaining the body’s center of mass within the boundaries of the base of support frequently involves examining postural sway, where larger sway correlates with higher fall incidence.\(^{23}\) Center of pressure (COP) displacement, an indicator of postural sway, has consistently diverged between people with and without MS. Karst et al.\(^{3}\) reported decreased COP displacement during reaching tasks for people with minimal impairments from MS compared to healthy controls. Huisinga et al.\(^{24}\) noted increased COP displacement in quiet standing in people with moderate impairments from MS compared to healthy controls. Daley and Swank\(^{17}\) assessed anterior-posterior postural sway with eyes open and eyes closed, noting that, with eyes closed, 8% of their 13 minimally impaired patients but 100% of the 16 patients with severe impairments exhibited sway more than three standard deviations greater than the mean of age-matched controls (\(p<.03\) for differences among 4 groups with MS, \(n=113\)).

Traditional reports of postural sway have noted the amount of COP displacement using \textit{linear} measures like range and root-mean-square (RMS). Recent literature has advocated the addition of \textit{nonlinear} measures to the assessment of movement over time, with proposed advantages in assessing deficits post-injury or with dysfunction.\(^{25,26}\) Human movement occurs dynamically based on the state of the system and environment at prior moments and the most efficient trajectory to meet the goal in succeeding moments. For example, COP displacement should indicate that the person sways back and forward, right and left depending on the immediately preceding position towards the center or edge of the base of support, rather than swaying at random, or with the same pattern regardless of the starting position. Meeting goals efficiently means incorporating sufficient complexity in the variability of movement to adapt to environmental changes while the movement occurs. Nonlinear measures can provide insight into
each individual’s capability to meet movement goals in multiple environments under different conditions.\textsuperscript{25}

Nonlinear measures of pattern structure include approximate entropy (ApEn, a measure of unpredictability) and Lyapunov exponent (LyE, a measure of divergence).\textsuperscript{26} Invariable patterns show exact repetition with no divergence, resulting in low values on both ApEn and LyE. Highly variable movement shows randomness, lack of patterns, and highly divergent variation, resulting in higher values of ApEn and LyE. In describing the \textit{optimal movement variability} theoretical perspective, Stergiou et al\textsuperscript{26} posit that normal movement requires the right level of complexity, with structured variability but not exact repetition. Differences in nonlinear measures in people with MS compared to healthy controls may underlie observed movement dysfunction in MS. Lower values of ApEn in MS have indicated more repetitive movement compared to healthy controls for COP displacement during quiet standing\textsuperscript{24} and for stride length and width during steady gait.\textsuperscript{27} The authors interpreted these differences as reduced capacity to adapt and respond to perturbations.\textsuperscript{24,27} Higher values of LyE in MS have indicated more divergence in trunk acceleration during gait compared to healthy controls.\textsuperscript{28} Huisinga et al\textsuperscript{28} interpreted greater divergence as lack of control from one gait cycle to the next, with disturbances in one gait cycle potentially impacting the next and subsequent gait cycles.

In addition to distinguishing between normal and disordered movement, nonlinear measures can show change with intervention.\textsuperscript{26,29,30} Theoretically, interventions that optimize movement variability should result in an increase when baseline values are lower than optimal, and a decrease when baseline values are higher than optimal.\textsuperscript{26} However, studies have not yet reported differences in direction of change in nonlinear measures based on differences in pre-intervention values. Examining the association between pre-intervention variable values and the change in
these variables with intervention may help discern different movement characteristics of people that respond differently to an intervention like balance-based torso-weighting (BBTW).

Strategic application of small weights using BBTW typically results in immediate improvement in the ability to resist or respond to a balance perturbation,\textsuperscript{31} and, on average, results in faster gait.\textsuperscript{5,6} For patients, wearing the weights daily during exercise or activity has improved function (holding a Romberg position eyes open and closed, holding a single-leg stance, decreased dizziness and assistance needed during gait, reading while walking) both with and without weights, with better function while weighted.\textsuperscript{7} The mechanism for improved function with BBTW is under investigation. Location of the weights does not directly correlate with direction of change in COP.\textsuperscript{31} Further, immediate BBTW results remain significant when assessors are blinded\textsuperscript{5} or patients are randomized to a BBTW or placebo (standardized weight placement with 1.5\% body weight) group.\textsuperscript{6} Investigating nonlinear measures of COP variability with BBTW may help unmask differences in individual response and enhance future research into its mechanism.

In a previous study without an intervention, Huisinga et al,\textsuperscript{24} has reported measures of variability of COP displacement in eyes open and closed conditions in MS and healthy controls, with higher range and RMS but lower ApEn and LyE values for people with MS compared to controls. In their protocol, participants stood with feet apart for 3.5 minutes for each condition. Our protocol differs from theirs because our primary purpose was to examine the effects of a specific intervention, BBTW, on the variability of COP in people with MS.

We examined ApEn, LyE, range, and root mean square (RMS) of COP displacement during quiet standing, eyes open and eyes closed, in people with MS and healthy controls. We
hypothesized that range, RMS, ApEn, and LyE values would differ in the medial-lateral and anterior-posterior directions, between: 1) people with MS and healthy controls, 2) eyes open and eyes closed conditions, and 3) no-weight and weighted conditions. To test our premise that effective BBTW results in optimization of movement variability, we also examined the relationship between BBTW_change and baseline variability. We hypothesized that: 4) ApEn and LyE measures would go up with BBTW if baseline values were low, and go down with BBTW if baseline values were high.

Methods

Eligibility for participants with MS included diagnosis of MS, ability to communicate in English, exceeding 17 years of age, ability to ambulate 30 feet or more (with or without a cane), self-reported balance or mobility difficulties caused by MS, and capability of tolerating up to three hours of testing with rest breaks. Exclusion criteria included exacerbation of MS within the past two months, diagnosis of a concurrent neurological disorder, or any pain that could be exacerbated by external perturbations during standing or multiple trials of walking. Participants with MS were recruited through newsletter ads for the [masked] Chapter of the National Multiple Sclerosis Society and local neurology clinics. Eligibility criteria for control participants included the ability to communicate in English, absence of any known diagnoses or current pain that would affect balance or gait, and physical criteria that matched each participant with MS. Physical criteria to match included age (within 7 years), height (within 5 inches), weight (within 20 pounds), and sex (Table 1). Control participants were recruited through personal contacts and online postings on Craigslist.org. All participants provided informed consent for their participation. This study met the requirements for ethical research according to the institutional review board of [masked] University.
Participants completed a medical questionnaire about symptoms and fall history. Responses to the medical questionnaire were used to determine approximate levels of disability, represented as equivalence scores on the Expanded Disability Status Scale (EDSS; where 0=normal neurological function, and 10=death due to MS). Clinical measures for each participant included height, weight, foot length, leg length, heart rate and blood pressure. A BBTW garment without weights was applied and adjusted to fit the trunk. All participants wore the garment throughout testing.

Static balance without weighting was assessed while participants stood quietly with feet together, touching at heels and forefeet, and aligned with markings on a forceplate. Participants were instructed to stand as still as possible for 10 seconds for one trial with eyes open (EO) and a second with eyes closed (EC). We chose the 10-second time period for each trial to imitate part of the BBTW procedure for determining weight placement. Although clinically relevant, the abbreviated time period restricted the number of times COP displacement might repeat any patterns of movement, potentially limiting accurate calculation of nonlinear measures.

**BBTW Protocol**

Following the baseline static standing without weights, standing balance was assessed with the BBTW protocol and assessment kit (Motion Therapeutics, Inc., Oxnard, CA). Assessment of balance included observation of relative amount and direction of sway during static standing with EO and EC. To control for possible inter-rater differences, one physical therapist performed all assessments and weight application. Another physical therapist guarded participants during
balance testing. The tester perturbed standing balance of each participant with anterior, posterior, and lateral nudges to the shoulders and pelvis and observed amount and latency of recovery and amount and direction of balance loss. Balance loss was defined as tilt or lean of the trunk requiring opposing parachute reaction, stepping response, or manual contact by the tester or guard to regain center of mass over the base of support. The tester also applied rotational force towards the right and left through the shoulders and then pelvis to determine asymmetry in ability to resist rotational force. Weights were strategically placed on the BBTW garment in 0.25 to 0.5 pound increments via Velcro attachment. The tester confirmed the location of weights with additional perturbations and weight adjustments until the participant showed minimal loss of balance or sway latency when perturbed and showed greater symmetry of force production when rotational resistance was applied.

Once location of weights was confirmed, participants had a mandatory rest period prior to retesting static standing. Participants aligned feet again with lines marked on the forceplate. Weighted static standing trials EO and EC were then performed for 10 seconds each on the forceplate.

*Data Analysis*

The forceplate recorded COP displacement at 600 Hz by default (BioWare software, Kistler Instrument Corp, Amherst, NY). To determine an appropriate sampling frequency, we examined the power spectrum produced from a representative sample of the COP time series. The power spectrum showed that 99.9% of the sample frequency was contained below 3.4 Hz, indicating
that the subsampling frequency should be set between 6.8 Hz and 34 Hz (2-10 times the highest frequency present in the signal). We down sampled all of the data to 25 Hz.

Each condition was examined separately for the medial-lateral (ML) and anterior-posterior (AP) directions.

Data were processed through Cortex software (Motion Analysis Corp, version 1.1.4.368, Santa Rosa, CA), and then exported to Excel (Microsoft, version 2010, Redmond, WA). Nonlinear measures were calculated using a custom program in MatLab (The Mathworks Inc., Natick, MA). ApEn was calculated using the algorithm developed by Pincus\textsuperscript{33, 34} \((m=2, r=0.2, \text{lag}=1, N=250)\). LyE was calculated using the algorithms Global False Nearest Neighbor for embedding dimension,\textsuperscript{35} and Average Mutual Information for time delay. To determine the parameters for LyE for comparison across all participants, we calculated embedded dimension and time delay for each time series and found the average values (embedding dimension=4, time delay=4), then used these to obtain LyE for all participants.

Analyses of Range, RMS, ApEn, and LyE were performed in two directions (ML and AP, as in Huisinga et al.\textsuperscript{24}) using mixed design repeated measure analyses of variance (2x2x2):

1) HC and MS (GROUP);

2) EO and EC (EOEC CONDITION);

3) No-weight and weighted (WEIGHT CONDITION).

Examination of the association between change with BBTW intervention and pre-intervention values of LyE and ApEn used correlation:

4) BBTW\_change (weighted minus no-weight values) versus Baseline (no-weight values).
When examining correlations, we focused on the EO condition as most applicable to normal activities for most individuals. We expected that if BBTW changed variability towards an optimal movement pattern, then people who had baseline values below the optimum would increase those values (with a positive number for BBTW_change) and people with baseline values above optimum would decrease those values (with a negative number for BBTW_change). Where correlation was significant, the MS group was subdivided into two groups according to lower and higher baseline values; a three-way analysis of variance was repeated using the new subgroups (3x2x2). When the main effect for SUBGROUP was significant, pairwise analyses determined which subgroups were different. When interactions between SUBGROUP and WEIGHT CONDITION were significant, t-tests revealed potential differences in effect of weighting in subgroups. Analyses were performed in Excel and SPSS (version 20.0) with level of significance set at $\alpha=0.05$.

**Results**

Twenty people with MS (EDSS$^{32}$ range equivalent 2-6) and twenty healthy controls participated. All participants were female (prevalence in MS is generally 2-3 women: 1 man); the few men who expressed interest did not meet study criteria regarding timing of exacerbations and confirmed diagnosis. For two healthy controls, technical difficulties with the forceplate and software made their data unusable, leaving 18 healthy controls for most measures (MS: N=20, HC: N=18) (see Table 1). For two of the remaining healthy controls, a LyE value could not be calculated for one of the EC conditions; thus, for LyE, only 16 healthy controls were analyzed in the ANOVAs (MS: N=20, HC: N=16).

1) **MS vs. HC GROUP**
For the variables Range, RMS, and ApEn, but not LyE, a significant main effect of GROUP was found in both the ML and AP directions (Table 2). People with MS had higher Range and RMS values but lower ApEn values in both ML and AP directions compared to healthy controls.

2) **EOEC CONDITION**

For Range and RMS, the main effect of EOEC CONDITION was significant (Table 2); Range and RMS values were higher in the EC condition than in the EO condition for both ML and AP directions. For ApEn and LyE, the main effect of EOEC CONDITION was not significant in either direction. A GROUP by EOEC CONDITION interaction was significant for ApEn (F\(_{1,36}\): 4.77; p = .036) in the ML direction, with lower ApEn values for healthy controls when the eyes were closed, but higher values with eyes closed for people with MS.

3) **WEIGHT CONDITION**

For all variables, the main effect of WEIGHT CONDITION was not significant in either ML or AP direction (Table 2). No interaction effects were significant between WEIGHT CONDITION and other factors.

4) **BBTW_change vs. Baseline**

The correlation between BBTW_change and value of LyE at baseline, EO, was r = -.70 (p<.001) in the ML direction (Figure 1) and r = -.75 (p<.001) in the AP direction. The correlation between BBTW_change and value of ApEn at baseline, EO, was r = -.59 (p<.005) in the ML direction and not significant (r = -.19) in the AP direction.

*Sub-grouping*
Because the correlation between BBTW_change and baseline was moderately strong for LyE, and both LyE and ApEn correlated with BBTW_change in the ML direction, we subdivided the group with MS based on the median LyE (2.07) for healthy controls in the EO condition, ML direction. The resulting subgroups had higher and lower values of LyE, respectively (MS HiLyE N=6: LyE average 2.22; MS LoLyE N=14: LyE average 1.54), compared to controls (HC N=18: LyE average 2.07). Although we focused on the ML direction, we noted that, in the MS HiLyE subgroup, five of the six people had LyE values greater than the HC average for both ML and AP directions.

For LyE, a significant main effect of SUBGROUP was found in the ML direction (three-way ANOVA, 3x2x2, F_{2, 33}: 7.56; p=0.002), with a pairwise difference between the MS subgroups (p=.002), where MS LoLyE values were lower than MS HiLyE values. Also, the main effect for WEIGHT CONDITION was significant (F_{1, 33}: 4.26, p = .047), where LyE values generally decreased with BBTW. No interaction effects were significant.

ANOVA (2x2x2) were repeated for each variable in the ML direction with just the MS subgroups. The interaction was significant between SUBGROUP and WEIGHT CONDITION in the ML direction for LyE (F_{1, 18}: 7.153, p = .015), with LyE values moving up with BBTW for MS LoLyE and down with BBTW for MS HiLyE. The interaction tended toward significance for Range (F_{1, 18}: 3.168, p = .092) and RMS (F_{1, 18}: 2.975, p = .102), with linear variability tending to decrease with BBTW for MS LoLyE and increase with BBTW for MS HiLyE. For ApEn in the ML direction, the interaction was significant between SUBGROUP, WEIGHT CONDITION, and EOEC CONDITION (F_{1, 18}: 8.184, p = .010). For MS LoLyE, ApEn values increased in the EO condition and decreased in the EC condition with BBTW. ApEn values changed in the opposite direction for MS HiLyE with BBTW.
T-tests revealed significant differences between subgroups in response to BBTW in the ML direction but not the AP direction for LyE, ApEn and RMS (Table 3). The two MS subgroups tended to respond to BBTW in opposite ways (increasing or decreasing depicted in Table 4) for LyE, ApEn, and RMS, with differences significant for LyE (p<.003).

Range and RMS data were highly correlated across participants for all conditions (r = .94 to .99) so only RMS is depicted in the tables.

Discussion

We postulated that, if effective, BBTW would optimize movement variability. In these samples, weighting showed a significant effect in LyE in the ML direction when people with MS were grouped by pre-intervention LyE values. Further, values on LyE, ApEn, and RMS in the MS subgroups changed or tended to change in opposite ways with weighting, possibly toward a more optimal pattern. MS subgroup differences were masked when analyzing average responses to BBTW.

Analyzing data for the total groups prior to subgroup analyses tested the utility of our protocol despite the limited time series (10 seconds) for nonlinear measures. Huisinga et al24 performed a similar study of linear and nonlinear variability in COP displacement for healthy controls and people with MS but used a much longer time series (3.5 minutes). Despite differences in length of time series, main effects for our first two hypotheses paralleled theirs for Range, RMS, and ApEn; LyE results differed between these two studies.

1) MS and HC: our data showed differences in Range, RMS, and ApEn in both ML and AP directions. The two groups did not differ on LyE in either direction. Huisinga et al24 reported the same group effects for Range and RMS. In their study, ApEn differed
between groups only in the ML direction, and LyE differed between groups (lower in MS) for both ML and AP directions.

2) EO and EC: our data showed differences in Range and RMS in both ML and AP directions. The eye conditions did not differ on ApEn or LyE, although we noted an interaction between group and eye condition in the ML direction for ApEn. Huisinga et al.\textsuperscript{24} reported significant differences for RMS but not for ApEn and LyE, no interaction effect for ApEn, and presence of interaction effects for LyE in both ML and AP directions.

Unlike Huisinga et al.\textsuperscript{24} our analyses included a third factor to address the intervention, and we examined the correlation between BBTW\_change and baseline COP variability.

3) No-weight and weighted: Weighting was not significant for any measure in ML or AP directions when examining controls and total MS group. Weighting condition was significant for LyE in the ML direction after we subdivided the MS group based on pre-intervention LyE values.

4) BBTW\_change and baseline: Change in LyE with weighting showed a moderately strong negative correlation with LyE at baseline in both the ML and AP directions. People with lower values and higher values tended to change in opposite ways with this intervention, potentially converging on more optimal movement variability. The subgroups responded differently from each other on nonlinear and linear variables.

If BBTW optimizes movement variability,\textsuperscript{26} it may help reduce the risk of falls while providing patients with greater freedom when encountering changes in their environment. However, analyzing the effectiveness of any intervention requires accurate categorization of patients.
according to the type of response projected. Nonlinear variables may help to distinguish between motor control that is so random that people are unable to accomplish target tasks consistently, or so rigid and predictable that they can only accomplish target tasks when the conditions stay the same. People with MS could have more random and divergent variability than normal, or more rigid and repetitive patterns than normal, depending on an individual’s specific symptoms, disease subtype, lesion volume or location of lesions. For example, people with ataxia may respond differently than people with spasticity. This study supports the possibility of movement optimization with BBTW. First, both LyE ($r = -0.70$, $p<0.001$) and ApEn ($r = -0.59$, $p<0.005$) show a negative but moderate to strong correlation between baseline values and change that occurred with weighting. Second, BBTW resulted in changes in opposite ways (increasing versus decreasing) for the two MS subgroups, a significant difference for LyE, and a tendency for ApEn and RMS. If BBTW results in changes in COP variability, whether too repetitive or too random, to move the pattern toward optimal variability, then application of the intervention to both groups is supported.

Although MS subgroups changed towards the mean of controls on LyE with weighting, optimization of movement variability remains uncertain. The healthy controls had a large between-subject variance, with LyE values completely overlapping values in the two MS subgroups at baseline. This overlap hinders targeting a single value of LyE as the goal for “optimal” divergence. Despite the overlap in LyE values, the two groups had distinctly different linear measures of variability, with larger Range and RMS values for people with MS compared to healthy controls. Optimizing the amount of movement variability would imply that both subgroups should decrease in linear measures with weighting. However, only the MS LoLyE subgroup decreased RMS with BBTW, while the MS HiLyE subgroup appeared to increase
RMS. Perhaps hypermetria in the MS HiLyE subgroup becomes exaggerated with the small additional inertial mass of BBTW, resulting in increased Range and RMS.\textsuperscript{36} The observed changes were small and only in the ML direction for either subgroup, but the MS LoLyE subgroup seemed to have the more recognizable optimization of the amount of movement variability with BBTW.

Limitations to our study include the small sample sizes and the short monitoring time (10 seconds). Sample size was further decreased for assessing LyE because for two of the healthy controls, LyE could not be calculated in one of eight conditions. However, these were the only two trials that did not yield a LyE value out of the 304 time series examined. In addition to the small sample, multiple procedures were performed without correction of alpha levels, increasing the possibility of finding spurious results in our exploratory study. Similarities between our results and those of Huisinga et al\textsuperscript{24} support the conclusions of both studies, however, and support our protocol for examining differences with and without BBTW.

Another limitation was that the baseline and intervention conditions were assessed during the same session, restricting practice of alternative postural control strategies with BBTW. Previous studies indicating changes in nonlinear measures with intervention have employed longer time periods. Two infants (1 year old) with cerebral palsy underwent a two-month program of therapy of different types; one infant showed increased complexity of behavior as indicated by a higher ApEn.\textsuperscript{26} Six individuals post-stroke underwent constraint-induced movement therapy for 2 weeks, but the higher ApEn post-intervention did not reach statistical significance.\textsuperscript{37} Individuals with hemiparesis and cerebral palsy participated in perturbation training for 12 weeks with a resulting increase in gait complexity (higher ApEn).\textsuperscript{29} Our data indicate that variability can change with intervention in this short time period, but further changes with potentially important
functional effects likely require additional experience with the weighted condition, such as wearing the weights for 30 minutes twice daily for several weeks during exercise and function.\textsuperscript{7}

We collected no clinical measures of dysmetria, spasticity, or sensory loss in this study and thus can make no definitive associations of impairments with LyE subgroup membership; we noted that EDSS scores ranged from 2 to 6 in both MS LyE subgroups. Future studies will examine possible associations like amount of sensory dysfunction in the lower extremities. Previous studies examining the effects of restricting one sensory modality have shown that the remaining postural system compensates with a higher reliance on fewer sensory modalities to maintain balance.\textsuperscript{38, 39} When sensory systems have deficits, delayed postural control may manifest in larger Range and RMS before catching postural sway and moving back towards an equilibrium point. Our data showed the expected increase in COP Range and RMS in the EC condition in both AP and ML directions but did not show concomitant significant decreases in ApEn or LyE that might indicate more repetitive postural sway with eye closure. On the other hand, we expected that BBTW, as a form of sensory augmentation, should decrease Range and RMS; this occurred in the MS LoLyE subgroup. Our medical questionnaires did not reveal any patterns of self-reported sensory deficits but more precise assessment could clarify any association. The fact that the MS subgroups showed opposing results with BBTW provides helpful guidance for future studies in identifying categories of patients showing optimized linear and nonlinear variability with weighting.

Augmented sensory signals associated with BBTW may result in greater attention to body position. Cavanaugh et al\textsuperscript{40} provided evidence refuting this contention by examining the effects of a secondary cognitive task on ApEn of COP displacement in standing for healthy individuals. ApEn significantly increased during dual tasking. If weighting captures attention of participants,
ApEn should have increased, at least in the healthy controls. The only group that tended to increase with ApEn was MS LoLyE, implying that participants in the current study were not expending attentional resources on sensory stimuli provided by BBTW. Confirmatory studies with dual tasks could help to disprove increased cognitive attention as the mechanism underlying BBTW.

Conclusion

Nonlinear measures can complement traditional measures of variability. Determining whether patients have more random or more repetitive structure to movement variability can help guide expectations regarding response to an intervention. In this study, people with MS differed from healthy controls on Range, RMS, and ApEn but not LyE measures of COP displacement in the ML and AP directions while standing for 10 seconds. EO and EC conditions differed on Range and RMS but not ApEn or LyE. Weighting the torso using the BBTW method produced no difference in measures when analyzed in total MS and control groups. However, change with weighting correlated moderately strongly with baseline LyE and ApEn. With the MS group divided into participants with more and less divergent COP displacement (HiLyE and LoLyE), the effect of weighting was significant for LyE in the ML direction. Future analysis of postural sway variability along with sensorimotor impairments may reveal more information about the characteristics of those who respond best to BBTW and the mechanism underlying its effects.
Dr Widnener and Dr Allen provided concept/idea/research design, fund procurement, and institutional liaisons. All authors provided writing and data collection and analysis. Ms Hunt and Dr Allen provided project management and study participants. Dr Allen provided facilities/equipment and consultation (including review of manuscript before submission). The authors express their gratitude to Ms. Cynthia Gibson-Horn, who performed the balance-based torso-weighting assessment and weighting protocol on all study participants.

This study was approved by the Institutional Review Board of San Francisco State University.

The data, in part, were presented at the Second International Symposium on Gait & Balance in Multiple Sclerosis: Interventions for Gait & Balance in Multiple Sclerosis (before recruitment of final healthy participants); October 19–20, 2012; Portland, Oregon, and as a platform presentation at the 3rd International Symposium on Gait and Balance in Multiple Sclerosis; October 18-19, 2013; St Louis, Missouri.

This study was supported by Award Number R15HD066397 from the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Eunice Kennedy Shriver National Institute of Child Health and Human Development or the National Institutes of Health.

References


<table>
<thead>
<tr>
<th>Variable</th>
<th>Participants with MS</th>
<th>Healthy Controls</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Participants in Category</td>
<td>20</td>
<td>18</td>
<td>-</td>
</tr>
<tr>
<td>Age in years, mean (SD), range</td>
<td>49.4 (13.4), 24-68</td>
<td>47.3 (11.2), 29-69</td>
<td>0.615</td>
</tr>
<tr>
<td>Years since diagnosis, mean (SD)</td>
<td>12.8 (8.2)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>EDSS score equivalent, mean (SD), range</td>
<td>4.1 (1.6), 2-6</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Number of falls in last 12 months</td>
<td>2.0 (3.4)</td>
<td>0.3 (0.5)</td>
<td>0.008</td>
</tr>
<tr>
<td>Height, mean (SD) cm</td>
<td>166.2 (6.0)</td>
<td>165.5 (7.2)</td>
<td>0.754</td>
</tr>
<tr>
<td>Weight, mean (SD) kg</td>
<td>73.2 (15.7)</td>
<td>72.4 (14.8)</td>
<td>0.868</td>
</tr>
<tr>
<td>% body weight BBTW, mean (SD)</td>
<td>1.0 (0.4)</td>
<td>0.8 (0.3)</td>
<td>0.026</td>
</tr>
<tr>
<td>Type of MS (number of people)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary Progressive (PP)</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Secondary Progressive (SP)</td>
<td>4</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Relapsing Remitting (RR)</td>
<td>11</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Unknown (UN)</td>
<td>4</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Vision impairment (number of people)</td>
<td>10</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Dysesthesia (number of people)</td>
<td>16</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Vestibular impairment (number of people)</td>
<td>11</td>
<td>0</td>
<td>-</td>
</tr>
</tbody>
</table>

MS = Participants with Multiple Sclerosis; HS = Healthy Controls; SD = Standard deviation; kg = kilograms; EDSS = Expanded Disability Status Scale; BBTW = Balance-Based Torso Weighting. *Two-tailed t-test, α=.05
Table 2: Main Effects of Mixed Design Repeated Measures Analyses of Variance for Four Measures in Two Directions of Center of Pressure Displacement

<table>
<thead>
<tr>
<th></th>
<th>Medial-lateral Direction</th>
<th></th>
<th></th>
<th>Anterior-posterior Direction</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F *</td>
<td>P</td>
<td>F *</td>
<td>P</td>
<td>F **</td>
<td>P</td>
</tr>
<tr>
<td>MS, HS</td>
<td>10.73</td>
<td>0.002</td>
<td>10.84</td>
<td>0.002</td>
<td>8.53</td>
<td>0.006</td>
</tr>
<tr>
<td>EO, EC</td>
<td>10.20</td>
<td>0.003</td>
<td>9.86</td>
<td>0.003</td>
<td>0.34</td>
<td>0.561</td>
</tr>
<tr>
<td>NW, W</td>
<td>0.01</td>
<td>0.928</td>
<td>0.11</td>
<td>0.738</td>
<td>0.01</td>
<td>0.91</td>
</tr>
</tbody>
</table>

*degrees of freedom = 1, 36

**degrees of freedom = 1, 34

RMS = root mean square linear variable; ApEn = approximate entropy nonlinear variable; LyE = Lyapunov exponent nonlinear variable

MS= people with multiple sclerosis; HS = healthy controls

EO = eyes open condition; EC = Eyes closed condition

NW= no-weight condition; W = weighted condition
Table 3: Mean (SD) Change in LyE, ApEn, and RMS with Weights in Each Eye Closure Condition

<table>
<thead>
<tr>
<th>Variable and group</th>
<th>EO ML</th>
<th>EC ML</th>
<th>EO AP</th>
<th>EC AP</th>
</tr>
</thead>
<tbody>
<tr>
<td>LyE</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HC</td>
<td>-0.119 (.85)</td>
<td>-0.126 (.41)</td>
<td>0.0005 (.64)</td>
<td>-0.165 (.65)</td>
</tr>
<tr>
<td>MS LoLyE</td>
<td>0.199 (.55)</td>
<td>-0.087 (.50)</td>
<td>-0.172 (.63)</td>
<td>-0.025 (.59)</td>
</tr>
<tr>
<td>MS HiLyE</td>
<td>-0.196 (.46)</td>
<td>-0.532 (.38)</td>
<td>*-0.070 (.72)</td>
<td>-0.246 (1.2)</td>
</tr>
<tr>
<td>ApEn</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HC</td>
<td>0.002 (.16)</td>
<td>-0.030 (.15)</td>
<td>-0.050 (.17)</td>
<td>0.002 (.17)</td>
</tr>
<tr>
<td>MS LoLyE</td>
<td>0.068 (.14)</td>
<td>-0.021 (.08)</td>
<td>-0.021 (.13)</td>
<td>-0.034 (.10)</td>
</tr>
<tr>
<td>MS HiLyE</td>
<td>-0.058 (.07)</td>
<td>*0.020 (.07)</td>
<td>*-0.035 (.09)</td>
<td>0.043 (.15)</td>
</tr>
<tr>
<td>RMS (cm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HC</td>
<td>-.017 (.18)</td>
<td>.040 (.21)</td>
<td>.032 (.21)</td>
<td>-.022 (.21)</td>
</tr>
<tr>
<td>MS LoLyE</td>
<td>-.045 (.28)</td>
<td>-.048 (.40)</td>
<td>-.019 (.36)</td>
<td>-.065 (.35)</td>
</tr>
<tr>
<td>MS HiLyE</td>
<td>.190 (.19)</td>
<td>*0.093 (.40)</td>
<td>.035 (.14)</td>
<td>-.021 (.22)</td>
</tr>
</tbody>
</table>

A negative change means that the value goes down with balance-based torso-weighting.

LyE = Lyapunov exponent nonlinear variable; ApEn = approximate entropy nonlinear variable; RMS = root mean square linear variable

EO = eyes open condition; EC = eyes closed condition; ML = center of pressure movement in the medial-lateral direction; AP = center of pressure movement in the anterior-posterior direction

HC = healthy controls, n=18; MS LoLyE = people with multiple sclerosis having LyE values lower than the healthy median LyE value (2.07) recorded with eyes open in ML direction, n=14; MS HiLyE = people with multiple sclerosis having LyE values higher than healthy median LyE value when recorded with eyes open in ML direction, n=6.

*t-test for difference between groups: p< .05; LyE, t = 2.17; ApEn, t=2.75; RMS, t=-2.19.
Table 4: Variables Averaged Over Eyes Open and Closed Conditions in the Medial-Lateral Direction to Depict Directional Change Tendencies with Weighting

<table>
<thead>
<tr>
<th>Variable and group</th>
<th>No Weight</th>
<th>Weighted</th>
<th>Change with Weights</th>
</tr>
</thead>
<tbody>
<tr>
<td>LyE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HC</td>
<td>2.03 (.31)</td>
<td>1.91 (.33)</td>
<td>↓</td>
</tr>
<tr>
<td>MS LoLyE</td>
<td>1.73 (.16)</td>
<td>1.79 (.38)</td>
<td>↑  ††</td>
</tr>
<tr>
<td>MS HiLyE</td>
<td>2.42 (.35)</td>
<td>2.06 (.49)</td>
<td>↓</td>
</tr>
<tr>
<td>ApEn</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HC</td>
<td>0.56 (.17)*</td>
<td>0.55 (.12)*</td>
<td>↓</td>
</tr>
<tr>
<td>MS LoLyE</td>
<td>0.44 (.10)</td>
<td>0.46 (.11)</td>
<td>↑</td>
</tr>
<tr>
<td>MS HiLyE</td>
<td>0.47 (.07)</td>
<td>0.45 (.04)</td>
<td>↓</td>
</tr>
<tr>
<td>RMS (cm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HC</td>
<td>0.47 (.19)**</td>
<td>0.48 (.15)**</td>
<td>↑</td>
</tr>
<tr>
<td>MS LoLyE</td>
<td>0.90 (.61)</td>
<td>0.85 (.43)</td>
<td>↓</td>
</tr>
<tr>
<td>MS HiLyE</td>
<td>0.81 (.41)</td>
<td>0.95 (.54)</td>
<td>↑</td>
</tr>
</tbody>
</table>

LyE = Lyapunov exponent nonlinear variable; ApEn = approximate entropy nonlinear variable; RMS = root mean square linear variable.

HC = healthy controls, n=18; MS LoLyE = people with multiple sclerosis having LyE values lower than the healthy median LyE value (2.07) recorded with eyes open in ML direction, n=14; MS HiLyE = people with multiple sclerosis having LyE values higher than healthy median LyE value when recorded with eyes open in ML direction, n=6.

†t-test for difference between MS groups: **LyE No-weight, t= -4.59, p<.004.**

†† difference between MS groups: **LyE Change with Weights, t=-3.51, p<.003.**

*t-test for difference between HC and MS groups: p< .05; **ApEn No-weight, t=2.55; Weighted, t=2.54.**

**difference between HC and MS groups: p< .01; RMS No-weight, t=-3.05; Weighted, t=-3.68.
Figure 1

Change in LyE in Response to BBTW

LyE in Quiet Standing Pre-BBTW