JRRD
Volume 50, Number 8, 2013
Pages 1139–1148

Body composition and physical function in women with multiple sclerosis

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Abstract—Persons with multiple sclerosis (MS) have reduced physical activity (PA) and lower-limb physical function and potentially disordered body composition compared with their peers without MS. The aim of this study was to determine whether PA and body composition were differentially associated with lower-limb physical function in persons with MS compared with controls. Females with MS and age- and body mass index-matched female controls (n = 51; average age 48.1 +/– 9.7 yr) were measured for PA with daily step counts, relative fat mass (%Fat), and leg lean mass (LM-LEG) via dual energy X-ray absorptiometry and for lower-limb physical function with objective performance tests. Persons with MS had 12.5% to 53% poorer lower-limb physical function than controls (all $p < 0.05$). PA, %Fat, and LM-LEG to body mass ratio (LM-LEG/BM) were associated with lower-limb physical function in both persons with MS and controls (all $p < 0.05$). Based on median splits, higher %Fat, lower LM-LEG/BM, and MS conferred poorer lower-limb physical function (all $p < 0.05$). PA, %Fat, and LM-LEG/BM were associated with lower-limb physical function, suggesting that body composition, specifically reducing adiposity and increasing lean mass and/or increasing PA levels, may be a potential target for MS interventions.

Key words: 6-minute walk, adiposity, body composition, lean mass, multiple sclerosis, pedometer step counts, physical activity, physical function, weight status, women.

INTRODUCTION

As a result of demyelination of the axons within the central nervous system and neuronal loss, persons with multiple sclerosis (MS) commonly exhibit decreased balance and coordination, which can result in reduced physical function. Loss of motor function in the lower limbs, in addition to the leg weakness and spasticity associated with the pathology of MS, may lead to difficulties with ambulation. These factors combine to potentially contribute to reductions in the performance of activities of daily living and tasks that are commonly used to assess physical

Abbreviations: %Fat = relative fat mass, ANT = anterior, BM = body mass, BMI = BM index, CON = controls, DXA = dual energy X-ray absorptiometry, GLETQ = Godin Leisure Time Exercise Questionnaire, IRB = institutional review board, LLPF = lower-limb physical function, LM-LEG = leg lean mass, LM-LEG/BM = LM-LEG to BM ratio, MED = medial, MS = multiple sclerosis, PA = physical activity, PDDS = Patient Determined Disease Steps, POST = posterior, SD = standard deviation, SEBT = Star Excursion Balance Test, UPGO = timed up-and-go test, WALK = 6-minute walk test.

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http://dx.doi.org/10.1682/JRRD.2012.08.0144

functioning [1]. When compared with individuals without MS, persons with MS have poorer performance on lower-limb physical function assessments [2].

Identifying the elements most related to physical functioning for persons with MS, unrelated to disease status, may allow optimization of lifestyle choices that prolong independence. Body composition, primarily adiposity and lean mass, plays a role in physical functioning among older adults, because those older adults with more optimal body composition demonstrate better performance than those with increased levels of body fat and decreased levels of lean muscle mass [3]. For example, Valentine et al. found that measures of lower-limb physical function (LLPF) in older women were significantly affected by body composition, because performance on gait and balance tasks was related to adiposity, leg lean mass (LM-LEG), and LM-LEG to body mass (BM) ratio (LM-LEG/BM) [4]. This latter outcome, LM-LEG/BM, is emerging as an important determinant of functional ability, especially in females who have higher levels of adiposity and lower levels of lean mass. This ratio explores the interaction between the individual's ability to carry the load (LM-LEG) and the load to be carried (BM).

There is some evidence to suggest that ambulatory persons with MS may have poorer lower-limb body composition, specifically increased lower-limb percent fat and decreased percent lean mass, than controls (CON) [5]. In contrast, others have found that whereas no significant body composition differences exist between ambulatory persons with MS and ambulatory CON, nonambulatory persons with MS demonstrate significant decreases in fat-free mass when compared with ambulatory age-matched CON, not surprising due to greater disuse [6]. Because the prevalence of MS is higher in women, this relationship may be one of importance for persons with MS, but the relationships among body composition, physical activity (PA) level, and physical function in persons with MS are not currently well characterized and could lend insight into novel intervention targets.

The evidence that ambulation status may affect body composition in persons with MS highlights the importance of PA for persons with MS who still have the ability to ambulate regularly. Persons with MS have decreased PA levels compared with healthy counterparts [7–8]. Lower levels of PA in the MS population have been associated with increased disability progression, as well as an increased number of comorbidities, including hypertension, hyperlipidemia, and arthritis, which are all associated with decreased health-related quality of life [9–10]. Correlates that have been identified with lower PA levels in persons with MS include advancing disease progression, use of a device with ambulation, increasing age, and unemployment [11]. Lower levels of PA combined with poorer body composition may contribute to greater declines in physical function for persons with MS.

Thus, in this context, the primary objective of the present study was to evaluate the relation among PA and body composition outcomes and LLPF in women with MS and controls. We hypothesized that (1) persons with MS would have similar adiposity but a less favorable lean mass to BM ratio, lower levels of PA, and poorer LLPF compared with CON matched in age and BM index (BMI); (2) lower PA, higher adiposity, and lower LM-LEG/BM would be related to poorer LLPF in both groups but the associations would be stronger in persons with MS.

METHODS

Subjects

Community dwelling Caucasian women with MS (n = 25) and CON (n = 26) matched in age and BMI were recruited for this study. Descriptive characteristics are included in **Table 1**. Patients with MS were recruited from the surrounding area (i.e., within a 60 min drive to the campus) through advertisements delivered among our laboratory database of persons with MS, National MS Society support groups, and contacts with local neurologists. CON were recruited through email advertisement delivered among faculty and staff of a major university.

MS disease modifying therapies were reported by 82 percent of the participants with MS. Regarding education, 83 percent of those with MS and 97 percent of CON received a college education. Regarding income as another metric of socioeconomic status, 76 percent of those with MS and 88 percent of CON had an annual income exceeding $40,000.

The diagnosis of MS based on McDonald criteria was confirmed in writing (i.e., form letter) by each patient's neurologist. Five persons with MS used a cane or walker during ambulation. Twenty-one persons with MS had a relapsing-remitting clinical course, three had a secondary progressive clinical course, and one had a primary progressive clinical course. Severity of neurological

Table 1.
Characteristics (mean ± standard deviation) of female participants with multiple sclerosis (MS) and controls (CON).

Characteristic	MS (n = 25)	CON (n = 26)	p-Value
Age (yr)	48.1 ± 9.7	48.2 ± 10.1	0.98
PDDS (arbitrary units)	1.9 ± 1.6	—	—
Disease Duration (yr)	9.8 ± 7.2	—	—
BM (kg)	70.7 ± 11.4	71.3 ± 14.2	0.85
Height (cm)	162.1 ± 6.8	163.8 ± 6.5	0.36
BMI (kg/m^2)	27.5 ± 5.0	26.6 ± 5.3	0.77
Pedometer Count (steps/d)*	7,321.2 ± 3,222.6	11,389.7 ± 4,668.4	0.001
GLTEQ			
Vigorous†	0.6 ± 1.4	2.5 ± 2.4	0.001
Moderate†	2.1 ± 2.4	3.9 ± 3.0	0.03
Light†	3.0 ± 2.7	3.1 ± 2.9	0.89
Total Score†	24.9 ± 23.2	50.9 ± 30.6	0.002
Body Fat (%)	37.2 ± 4.5	34.0 ± 8.1	0.09
LM-LEG (kg)	14.3 ± 2.2	15.5 ± 1.9	0.03
LM-LEG/BM	0.20 ± 0.02	0.20 ± 0.03	0.01

*Persons with MS n = 23.
†Persons with MS n = 24.
BM = body mass, BMI = BM index, GLETQ = Godin Leisure Time Exercise Questionnaire, LM-LEG = leg lean mass, LM-LEG/BM = LM-LEG to BM ratio, PDDS = Patient Determined Disease Steps.

disability for persons with MS was determined by the Patient Determined Disease Steps (PDDS) scale [12]. The median PDDS score was 2.0 (interquartile range 0.5–3.0), indicating moderate disability.

Participants with MS met the eligibility criteria if they were ambulatory with or without single-point assistance, had abstained from smoking for 6 or more months, and were willing to wear an activity monitor for a 7 d period. Persons with MS were relapse free over the previous 30 d period.

Body Composition

Whole body soft tissue was measured using dual energy X-ray absorptiometry (DXA) (Hologic QDR 4500A, software version 12.7.3; Waltham, Massachusetts), and relative fat mass (%Fat) was the outcome of interest for this study. Additionally, a regional analysis was performed per manufacturer guidelines and involved bisecting the femoral neck to determine mineral-free LM-LEG. Precision for DXA measurements of interest is 1–1.5 percent in our laboratory.

Lower-Limb Physical Function

Physical function was assessed using the 6-minute walk test (WALK), the timed up-and-go test (UPGO), and the Star Excursion Balance Test (SEBT). The WALK consisted of 6 min of timed walking in a circular path, with persons with MS using their assistive device if applicable. A WALK script was read before beginning the WALK assessment and included instructions that emphasized that subjects should safely cover as much distance as possible by walking as fast as possible over the course of the assessment. For those who chose to complete the assessment, total distance walked over the course during the 6 min was recorded using a calibrated measurement wheel (Stanley MS50; New Briton, Connecticut). The WALK has been found to be a reliable measure in persons with MS [13].

For the UPGO, participants began the assessment seated in a chair without arms. They were asked to place their arms across their chest, feet flat on the floor; on the command "go," participants were instructed to volitionally stand and walk as quickly as possible around a cone placed 2.5 m in front of the chair and then return to a seated position [14]. Participants who were able to complete this assessment performed two timed UPGO trials, and the fastest trial was used for analysis.

Unilateral dynamic balance was assessed using the SEBT for both the right and left legs in the anterior (ANT), medial (MED), and posterior (POST) directions [15]. The SEBT requires participants to stand with their hands on their hips while establishing the single leg stance, and then reaching maximally in the direction of interest with the opposite leg. To perform each reach, the participant's stance heel was placed at the center of a grid marked on the floor. The grid consisted of eight lines extending at 45° increments from the center of the grid; each line was labeled according to the direction of excursion relative to the standing leg. Following familiarization trials, a maximum of five reaches in reference to the stance leg were completed in the ANT, MED, and POST directions. Reach distance was recorded as the distance from the heel of the stance foot to the distal touch point of the reach leg. Reach distances were normalized for leg length of the reach leg [15]. For each participant able to complete the assessment, SEBT composite score was calculated by summing all normalized reach lengths.

Physical Activity

Objective PA, as defined by step count per day, was determined using the pedometer feature of the ActiGraph single-axis model 7164 (Manufacturing Technology Inc; Fort Walton Beach, Florida). Participants were instructed to wear the monitor on the nondominant hip, fastened to a belt worn around the waist, for a 7 d period during all waking hours, except when bathing and swimming. Participants recorded the time spent wearing the activity monitor on a written log, which was verified by inspecting the recorded data, and step counts were calculated as the average from that 7 d period. The Godin Leisure Time Exercise Questionnaire (GLTEQ) was also used to determine the participants' number of self-reported exercise bouts and their strenuous, moderate, and mild intensity activity over the 7 d period [16]. Both measures have evidence of validity when used with persons with MS [12,17].

Statistics

Data were analyzed with PASW for Windows version 18.0 (IBM Corp; Armonk, New York). Mean and standard deviation (SD) values were calculated for all participant characteristics and primary outcome variables, and distribution statistics were computed to ensure data were normally distributed. PA data as measured by steps per day were nonnormally distributed and were log-transformed, using log base 10, which normalized the data; however, non-log-transformed values are displayed in tables to aid reader interpretation. Independent samples *t*-tests were conducted to determine group differences. Bivariate correlations were conducted to determine the associations between measures of body composition, PA, and measures of LLPF within each group. To further evaluate the influence of group and body composition on LLPF, primary variables of interest were median split and 2 × 2 analyses of variance were conducted.

All data are presented as mean ± SD, except the figure, which express variability using standard error bars. Statistical significance was set at the $p \leq 0.05$ level.

RESULTS

By design, persons with MS and CON were similar in age, height, weight, and BMI (**Table 1**). Persons with MS had significantly lower step counts than CON: 7,321.2 ± 3,222.6 steps/d and 11,389.7 ± 4,668.4 steps/d, respectively. Our participants were classified as low active for persons with MS and active for CON, as categorized by pedometer cut points for healthy adults [18]. Persons with MS also reported fewer moderate and vigorous activity bouts, in addition to lower total leisure time exercise scores via the GLTEQ, than CON (all $p < 0.05$). The median value for %Fat was 37.6 percent for persons with MS and 34.7 percent for CON. The body composition data are displayed in **Table 1**, indicating that although not significant, persons with MS had higher %Fat ($p = 0.09$, Cohen $d = 0.54$), lower LM-LEG, and less favorable LM-LEG/BM ratio than CON (both $p < 0.05$). Compared with CON, persons with MS had significantly poorer performance on all measures of LLPF: 27 percent shorter WALK distance, 53 percent slower UPGO speed, and reduced reach lengths in the ANT, MED, and POST directions (right: 8.0%, 9.3%, 21.6%; left: 6.2%, 16.5%, 22.0%, respectively), as shown in **Table 2**.

Relationships among body composition, PA, and LLPF overall and by group are shown in **Table 3**. In persons with MS, PDDS was significantly related to all measures of LLPF but was not related to any components of body composition (data not shown; $r = –0.15$ to 0.27). PA (step count) was not related to %Fat and LM-LEG/BM in persons with MS but was moderately related in CON ($p = 0.01$). Step count was strongly associated with all tasks of physical function, including WALK, UPGO, and SEBT, in persons with MS ($r = 0.84, –0.71, 0.56$, respectively; all $p < 0.05$), while only significantly associated with WALK in CON ($r = 0.53$, $p < 0.05$). Bouts of moderate intensity activity, as identified by the GLTEQ, were not significantly related to any measures of physical performance in either group, while GLTEQ light bouts were related to SEBT composite score ($r = –0.57$) in persons

Table 2.
Lower-limb physical function performance (mean ± standard deviation) in female participants with multiple sclerosis (MS) and controls (CON).

Measure	MS	CON	*p*-Value
6-Minute Walk (m)*	1,557.4 ± 475.0	2,136.8 ± 310.3	<0.001
Timed Up and Go (s)†	6.1 ± 1.1	4.0 ± 0.8	<0.001
SEBT Composite Score‡	4.2 ± 0.8	4.8 ± 0.6	0.002

Note: Participants who were unable or unwilling to complete any of above functional assessments were excluded from analysis.
*Persons with MS $n = 21$, CON $n = 26$.
†Persons with MS $n = 25$, CON $n = 25$.
‡Persons with MS $n = 21$, CON $n = 26$.
SEBT = Star Excursion Balance Test.

Table 3.
Relationships between relative fat mass, lean mass, physical activity, and lower-limb physical function in female participants with multiple sclerosis (MS) and controls (CON).

Measure	WALK	UPGO	SEBT Composite
MS			
PDDS	–0.70*	0.45†	–0.54*
%Fat	–0.10	0.51†	–0.22
LM-LEG	0.45†	0.06	0.31
LM-LEG/BM	0.53*	–0.53†	0.35
Step Count	0.84†	–0.52†	0.56†
GLTEQ			
Vigorous	0.17	–0.14	0.07
Moderate	0.01	0.03	–0.21
Light	–0.36	0.18	–0.57*
Total	–0.03	0.15	–0.27
CON			
%Fat	–0.74*	0.52*	–0.49†
LM-LEG	–0.22	–0.05	0.14
LM-LEG/BM	0.72†	–0.49†	0.63*
Step Count	0.53†	–0.34	0.21
GLTEQ			
Vigorous	0.65*	–0.25	0.32
Moderate	0.10	–0.05	–0.07
Light	–0.05	–0.06	0.12
Total	0.49†	–0.19	0.22

*Significant correlation at $p < 0.01$.
†Significant correlation at $p < 0.05$.
%Fat = relative fat mass, BM = body mass, GLTEQ = Godin Leisure Time Exercise Questionnaire, LM-LEG = leg lean mass, LM-LEG/BM = LM-LEG to BM ratio, PDDS = Patient Determined Disease Steps, SEBT = Star Excursion Balance Test, UPGO = timed up and go test, WALK = 6-minute walk test.

with MS only. GLTEQ vigorous bouts were moderately strongly associated with WALK performance in CON (r = 0.65). LM-LEG was significantly associated with WALK performance in persons with MS only (r = 0.45). Relative adiposity, %Fat, was associated with gait and balance measures of LLPF in CON, while %Fat was associated with UPGO performance only in persons with MS. LM-LEG/BM mass ratio was associated with all measures of LLPF in CON and only gait-related tasks in persons with MS.

Evaluating median splits for %Fat and LM-LEG/BM (**Table 4** and **Figure (a)-(f)**), in the absence of any interactions, main effects (all $p < 0.05$) were determined for (1) %Fat and group, such that higher %Fat and MS were associated with slower UPGO time; and (2) LM-LEG/BM and group, with a lower ratio and MS being associated with shorter WALK distance, slower UPGO time, and lower SEBT composite score. Regarding the WALK measure of LLPF, there was a significant main effect for group, with CON performing better. Alternatively, %Fat did not influence WALK in persons with MS, resulting in no main effect for %Fat in the presence of a significant interaction. MS was associated with poorer SEBT performance compared with CON, in the absence of an interaction; %Fat did not influence SEBT.

Table 4.
Descriptive characteristics of median split variables (mean ± standard deviation) in female participants with multiple sclerosis (MS) and controls (CON).

Measure	MS		CON	
	Low	High	Low	High
%Fat	33.9 ± 3.2	40.3 ± 3.1	27.6 ± 4.6	40.4 ± 5.0
LM-LEG/BM	0.19 ± 0.008	0.22 ± 0.01	0.20 ± 0.02	0.25 ± 0.02

%Fat = relative fat mass, LM-LEG/BM = leg lean mass to body mass ratio.

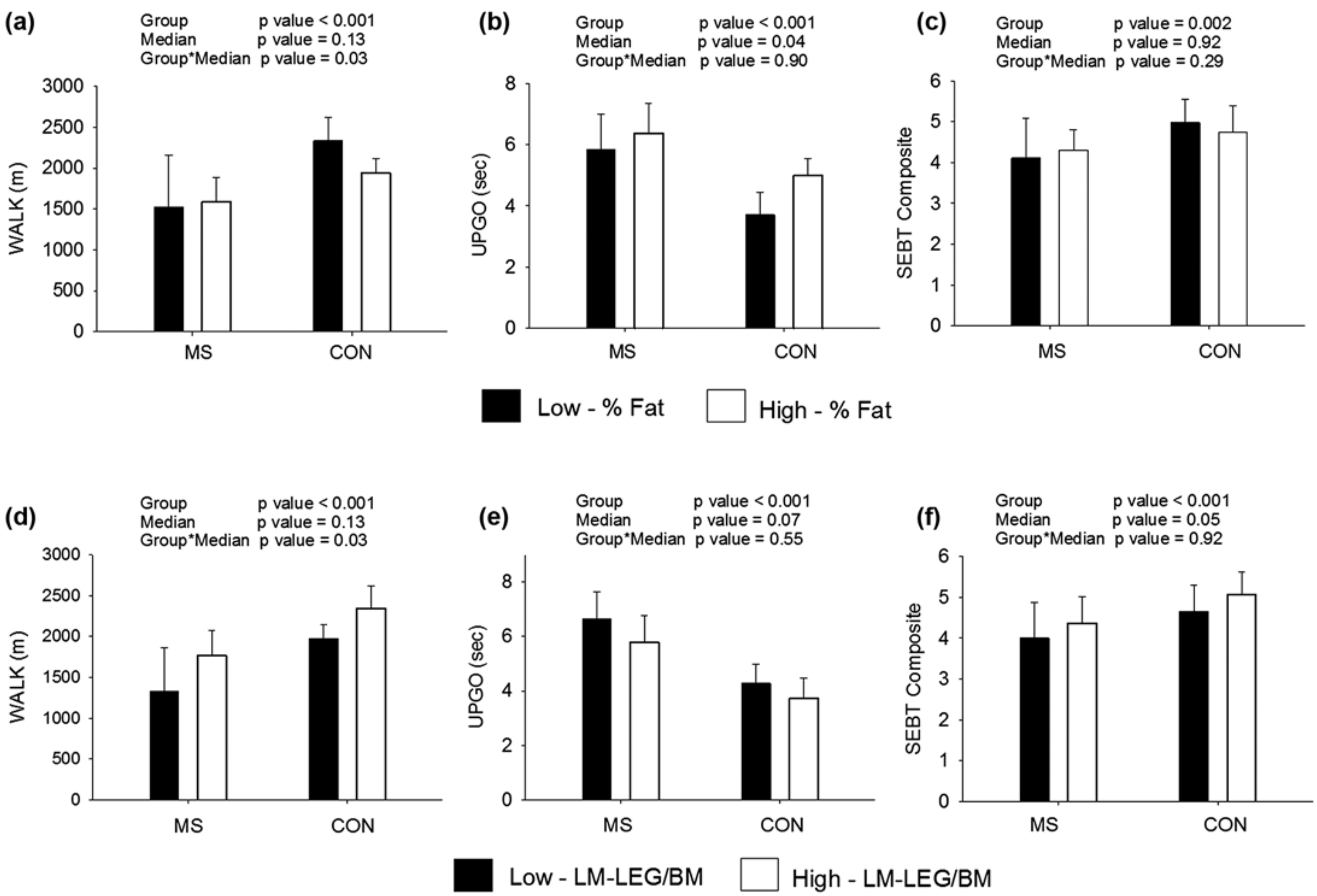

Figure.
Median splits of relative fat mass (%Fat) in relation to **(a)** 6-minute walk test (WALK), **(b)** timed up and go test (UPGO), and **(c)** Star Excursion Balance Test (SEBT) composite and median splits of leg lean mass (LM-LEG) to body mass (BM) test ratio (LM-LEG/BM) in relation to **(d)** WALK, **(e)** UPGO, and **(f)** SEBT composite for female participants with multiple sclerosis (MS) and controls (CON).

DISCUSSION

The potential influence of body composition on physical function in persons with MS has not been well characterized. The novel results from the present study indicate that body composition, specifically, adiposity and the ratio between LM-LEG and BM, are associated with LLPF in persons with MS. Importantly, because MS already invokes reductions in LLPF, the negative implications of body composition are potentially additive such that the person with MS who has higher adiposity or a reduced lean mass to BM ratio has the greatest decrements in LLPF (compared with CON or persons with MS who have a healthier body composition). This is especially true for tasks that mimic activities of daily living that require moving the BM in an ambulatory fashion, such as UPGO and WALK. The novelty of our findings suggests that, as with older obese women, strategies to reduce BM or enhance LM-LEG may be critical intervention targets to preserve physical function for women with MS.

Because our participants were intentionally matched for sex, age, and BMI, the absence of significant differences in adiposity and lean mass was not unexpected. The present findings are consistent with other research, indicating that there are no significant differences in levels of whole body adiposity between ambulatory persons with MS and control subjects matched for BMI [5–6,19]. Findings by Formica et al. indicate that there are no significant differences in regional measures of body composition, specifically lean mass in the lower limbs, between persons with MS and CON [6]. Sioka et al. reported similar results when using a sample of both men and women, but when examining regional composition separately by sex, there was a difference among females with MS and CON [5]. Ambulatory females with MS had less favorable composition in both the right and left lower limbs, as indicated by an increased percentage of fat mass and a lower percentage of LM-LEG compared with female CON [5]. Our data show a small but significant difference in LM-LEG between persons with MS and CON, leading to a less favorable ratio of LM-LEG/BM in persons with MS, which may have implications for physical function. This relationship requires further examination.

Persons with MS engaged in less PA, measured objectively and by self-report, than healthy CON. These findings are in accordance with current research examining PA patterns in persons with MS [7–8]. Persons with MS reported engaging in light intensity bouts primarily, indicating that they may avoid more intense leisure time activity, perhaps as a result of increased difficulty engaging in more intense forms of activity because of MS-related symptoms.

When evaluating LLPF, persons with MS demonstrated, as expected, poorer performance in both gait- and balance-related tasks than CON subjects. Our battery of LLPF assessments examined three types of functional abilities dependent on the lower limbs, ambulatory endurance (WALK), the ability to move one's mass from a seated position and ambulate as quickly as possible (UPGO), and dynamic balance (SEBT). While disease status was the strongest predictor of all measures of LLPF, objectively measured PA was independently related to gait-related LLPF assessments, WALK and UPGO, in both groups, providing further evidence that PA is an important modifiable risk factor to prevent physical disability related to ambulatory activities of daily living. The protective role that increasing levels of PA plays in improving gait-related function has been well established [20].

When evaluating body composition contributions to LLPF, as both lean and fat components play a role in physical function ability, assessing LM-LEG/BM is critical because it evaluates the portion of the body used to move the entire BM compared with the total load to be moved. The current study supports the relationship between LM-LEG/BM and gait-related tasks of LLPF. A similar relationship has been demonstrated in older women, but not in men [3], and as the prevalence of MS is greater in women, aging females with MS may be at higher risk for body-composition-mediated changes in physical function.

Increased levels of adiposity may negatively influence gait-related LLPF, because those persons with MS and CON with higher adiposity had poorer measures of LLPF, consistently of note for the UPGO task in persons with MS. This relationship is supported by data from samples of older adults [4,21]. For example, Chalé-Rush et al. found that BMI, age, sex, minutes of vigorous PA, and number of medications were associated with 400 m walk time, supporting the relationship that increased adiposity, as measured by BMI, is detrimental to gait-related functional measures in women [21]. Data from our own laboratory determined that women with increased adiposity, %Fat as measured by DXA, had poorer performance on gait-related tasks, including the UPGO and the 7 m walk, than their leaner counterparts [4]. The reason that %Fat influenced UPGO and not WALK in persons with MS is unclear, but could be related to the age of our cohort or the interplay between leg muscle strength and BM in our sample.

It has been suggested that to prevent disability in older adults, interventions targeting a reduction in weight, specifically adiposity, and improving ambulatory physical function are vital and may be of more importance than interventions that focus solely on improvements in lean mass or muscle strength [22]. Due to the similarities in the relationships between PA, body composition, and LLPF in both older adults and persons with MS, these targets may also be instrumental in intervention development for persons with MS.

Further elucidation of the roles that PA and salient elements of body composition (i.e., adiposity, lean mass) play in determining LLPF in persons with MS is warranted. Our results should be interpreted within the recognized limitations of our study. Certainly, our cross-sectional design does not allow inference of causality between variables of interest. Because we did not collect data regarding comorbid conditions or aspects of psychological health (i.e., fatigue, pain, depression), we are unable to examine how these factors may affect PA level and/or body composition. The ability to generalize our findings to the entire MS population is limited, because our sample was restricted to ambulatory persons with MS. In addition, our sample consisted primarily of women with relapsing-remitting MS, limiting the generalizability of these finding to those persons with primary and secondary progressive MS.

CONCLUSIONS

In summary, these data suggest that mediating factors, including disease status, PA, and the capacity to move one's BM, are associated with the reductions in physical function experienced by persons with MS. PA and body composition are both modifiable variables that could be important avenues for improving physical function. Interventions targeted at increasing and maintaining PA levels and weight management, specifically reducing adiposity and preserving lean mass, in persons with MS should continue to be developed and delivered to the MS community.

ACKNOWLEDGMENTS

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Manuscript editing: B. Fernhall, R. W. Motl, E. M. Evans.
Financial Disclosures: The authors have declared that no competing interests exist.
Funding/Support: This material was based on work partially funded by the University of Illinois Urbana-Champaign Research Board (B. Fernhall).
Institutional Review: The institutional review board (IRB) of the University of Illinois, Urbana-Champaign approved all procedures used in the study, and all participants signed an IRB-approved informed consent before enrollment.
Participant Follow-Up: The authors do not plan to inform participants of the publication of this study because contact information is unavailable.

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Submitted for publication August 8, 2012. Accepted in revised form March 7, 2013.

This article and any supplementary material should be cited as follows:
Ward CL, Suh Y, Lane AD, Yan H, Ranadive SM, Fernhall B, Motl RW, Evans EM. Body composition and physical function in women with multiple sclerosis. J Rehabil Res Dev. 2013;50(8):1139–48.
http://dx.doi.org/10.1682/JRRD.2012.08.0144