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Gait Variability and Energy Cost of Oveground Walking in Persons With Multiple Sclerosis: A Cross-Sectional Study

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Abstract

Objective: This study examined the associations between gait variability based on common spatiotemporal parameters and energetic cost of walking in persons with multiple sclerosis.

Design: Eighty-six persons with multiple sclerosis underwent the 6-min walk while wearing a portable metabolic unit. The cost of walking was generated by dividing the net steady-state VO_2 (milliliter per kilogram per minute) by walking speed during the 6-min walk. Participants further completed two trials of walking on the GAITRite mat at a self-selected pace for measuring spatiotemporal parameters. Variability of step length, step time, stride length, swing time, stance time, stride velocity, and single- and double-support time was indexed by the coefficient of variation.

Results: Variability in the spatiotemporal variables and Expanded Disability Status Scale scores were significantly correlated with cost of walking (i.e., [rho] = 0.25-0.36). Multivariate analysis revealed that disability (Expanded Disability Status Scale: [beta] = 0.186), stance time variability ([beta] = 1.446), and step length variability ([beta] = -1.216) explained significant variance ($R^2 = 0.38$, $P < 0.001$) in cost of walking.

Conclusions: We provide evidence of the positive association between gait variability and cost of walking during overground walking in persons with multiple sclerosis. The findings highlight the need for interventions aiming to reduce gait variability, thereby reducing the energetic demands of walking in this population.

There is evidence that the energetic cost of walking (C_w), defined as the amount of oxygen consumed per kilogram of body weight per unit distance traveled,[1] is higher in persons with multiple sclerosis (MS) compared with healthy controls.[2] The higher C_w may be associated with gait impairment in MS.[3] We are aware of one study that reported significant inverse correlations between gait speed and stride length with C_w and a positive correlation between double-limb support and C_w in persons with MS.[4] Persons who walked with slower velocity, had shorter strides, and spent more time with both feet on the ground (i.e., double-limb support) spent more energy when walking.

Previous studies examining the associations between gait parameters and C_w in MS have focused on mean values of gait parameters but have not considered measures of gait variability (i.e., the stride-to-stride fluctuations in walking).[4] This is important because individual variability in kinematic variables is considered an index of movement consistency or stability.[5] Gait variability further offers a complementary way of quantifying walking and its changes with the disease. Gait variability represents a way of monitoring the impact of interventions and rehabilitation and the effects on other physiological systems (i.e., cardiovascular). Of note, one study using treadmill walking suggested that increased step variability may contribute to increased C_w in young, healthy individuals without MS or other disease.[6] Another study compared the gait mechanics and metabolic cost in 10 healthy adults during treadmill walking with and without external stabilization.[7] This study demonstrated that lower foot placement variability associated with external stabilization was accompanied by modest but significant decreases in metabolic C_w. We believe that exploring gait variability and its association with C_w may identify potential intervention targets of rehabilitation programs focusing on reducing energy expenditure during walking in persons with MS. If successful, targeting gait variability may improve walking efficiency, which may have a positive impact on participation and fatigue in MS.

The present study examines the associations between variability in common spatiotemporal gait parameters (i.e., step time, step length, stride length, stride time, swing time, stance time, single- and double-support time) and C_w in persons with MS. Based on results from previous work,[6] we hypothesized that metrics of spatiotemporal gait variability would be associated with C_w in persons with MS such that larger amounts of variability during gait would yield higher C_w.

METHODS

Participants

This cross-sectional study used secondary outcomes from a baseline testing session of a behavioral intervention for increasing physical activity in persons with MS.[8] Participants were contacted (*a*) by mail through a flyer that was sent to patients in North American Research Committee on Multiple Sclerosis registry or (*b*) by e-mail through a flyer that was sent to participants in a database from previous studies conducted in the laboratory for the past 5 yrs. There were 511 participants who initially expressed interest and who were contacted via phone by the project coordinator. After explaining the study protocol, the project coordinator undertook screening for inclusion with 230 individuals who remained interested. The inclusion criteria involved (*a*) having a definite diagnosis of MS (i.e., physician's verification of MS diagnosis), (*b*) being relapse free for the past 30 days, (*c*) being able to walk with or without an assistive device (i.e., cane, crutch, or walker) for collection of oxygen C_w and gait outcomes, (*d*) between 18 and 64 yrs of age, (*e*) willing and able to travel to the laboratory to complete the walking assessments, (*f*) participating in less than 3 days per week of physical activity behavior, (*g*) having a low risk for contraindications of physical activity based on no more than a single "yes" response on the Physical Activity Readiness Questionnaire; and (*h*) able to provide a physician's approval for participation in the study. Of the 230 persons screened, 102 did not meet inclusion criteria, with the primary reasons being too physically active (53.7%) or unwilling to travel to our laboratory (21.7%); 39 additional persons did not provide physician's approval; and 3 cancelled the testing session because of scheduling conflicts. This resulted in a final analyzed usable data of 86 persons with MS who enrolled in the study.

Measures

Energetic C_w

A commercially available portable metabolic unit, K4b2 (Cosmed, Rome, Italy), was used to measure breath-by-breath oxygen consumption (VO_2) during a standard 6-min walk test (6MW).[9] The 6MW was performed overground in a well-lit and safe hallway with two 180-degree turns marked by cones separated 75 feet apart. The O_2 and CO_2 analyzers of the portable metabolic unit were calibrated using known concentrations of gases, and the flowmeter was calibrated using a 3-l syringe (Hans Rudolph, Kansas City, MO). VO_2 (milliliter per kilogram per minute) was measured as 30-sec averages for 1 min both before the 6MW (i.e., resting VO_2) and over the entire test. The total distance traveled (meter) was also measured using a measuring wheel (Stanley MW50, New Briton, CT). Net steady-state VO_2 was calculated by (*a*) calculating steady-state VO_2 as the average VO_2 value across the final 3 mins of the 6MW (i.e., mins 4-6)[10] and (*b*) subtracting resting-state VO_2 values for the 1 min before the 6MW. The C_w was then computed by dividing net steady-state VO_2 (milliliter per kilogram per minute) by walking speed during the 6MW (meter per minute).[1] This resulted in C_w expressed as milliliter per kilogram per minute.

Gait Variability

Gait variability was determined using a 16-foot electronic walkway (GAITRite, CIR Systems, Inc, Haverton, PA). Participants completed two trials of walking on the GAITRite mat at a self-selected pace for measuring spatiotemporal parameters. Variability of step length (centimeter), step time (second), stride length (centimeter), swing time (second), stance time (second), stride velocity (centimeter per second), and single- and double-support time (second) was expressed as the coefficient of variation (CV), which is calculated as follows: CV = standard deviation/mean. Coefficient of variation is operationalized as a relative measure of variability.[11] The recorded variables were averaged across both trials. A detailed description of each variable can be located in the technical reference manual available athttp://www.gaitrite.com.

Procedure

The protocol was approved by a university institutional review board, and all participants provided written informed consent before data collection. The protocol included a single session for collecting all data in a university laboratory setting. Data were collected either during the morning or in the afternoon, which best accommodated participants' availability. Of note, previous studies conducted with persons with MS have demonstrated no or very small effect of time of the day in gait parameters/variability.[12,13] All participants initially completed a questionnaire to provide clinical and sociodemographic information. Participants then underwent neurological examination by a neurostatus-certified researcher for the generation of an Expanded Disability Status Scale (EDSS) score.[14] Participants completed two trials on the GAITRite, followed by 10 mins of seated rest. Participants were fitted with the K4b2 portable metabolic system during the seated rest. Once wearing the system and after ensuring normal, resting metabolic functioning, participants were given standardized instructions for undertaking the 6MW and then completed the test. Participants were compensated US $50 for completing the session. This study conforms to all STROBE guidelines and reports the required information accordingly (see Checklist, Supplemental Digital Content 1,http://links.lww.com/PHM/A596).

Data Analysis

All analyses were carried out using SPSS Version 22 (SPSS Inc; IBM Corp, Armonk, NY) and significance level was set at a *P* value of less than 0.05. Kolmogorov Smirnov revealed that the variables included in this study did not present a normal distribution. Descriptive statistics are presented as median (interquartile range), minimum and maximum. We further decided to present the data as means (SD) to better compare our results with previous work. Missing data were replaced by a sample mean using the expectation-maximization approach, after the missing completely at random test revealed that the missing data occurred at random.[15] Bivariate Spearman's correlation was performed between metrics of gait variability, disability level (i.e., EDSS), and C_w. Values for correlation coefficients of 0.1, 0.3, and 0.5 were interpreted as small, moderate, and large, respectively. We further used liner regression analysis with stepwise entry to identify significant predictors of C_w, by including only variables significantly associated in the bivariate correlation analysis plus age and disease duration. Age and disease duration were included because of the large variance in the sample and because of its logical relationship with oxygen consumption capacity.

RESULTS

Demographic Characteristics

The sample included 86 persons with MS. The majority of the sample was female (*n* = 66/76.7%), with an average age of 49.2 (SD = 8.9) yrs, and average body mass index was 28.4 (SD = 7.89) kg/m^2. Nearly 78% of the participants presented with relapsing-remitting MS, approximately 12 (SD = 8.1) yrs of disease, and moderate levels of disability ($EDSS_{median}$ = 3.5, IQR = 3.25).

Energetic C_w and Gait Variability

The average steady-state VO_2 for the sample was 13.8 (SD = 3.8) mL[middle dot]kg^{-1}[middle dot]min^{-1} and the average VO_2 resting state was 3.4 (SD = 1.07) mL[middle dot]kg^{-1}[middle dot]min^{-1}. The net steady-state VO_2 was 10.3 (SD = 3.7) mL[middle dot]kg^{-1}[middle dot]min^{-1}. During the 6MW, participants traveled an average of 418.6 (SD = 154.1) meters. This resulted in participants performing the test at an average speed of 69.7 (SD = 25.6) m/min. Using the calculations described in the methods section, the net C_w was 0.16 (SD = 0.09) mL[middle dot]kg^{-1}[middle dot]min^{-1}. Descriptive data of the metrics of gait and gait variability are presented in Table 1. Briefly, the mean step length was 58 (SD = 12.9) cm and step time of 0.73 (SD = 0.65) secs. On average, participants presented with a swing time of 0.46 (SD = 0.30) secs and stride velocity of 99.6 (SD = 31.7) cm/sec. These values are similar to those observed in other sample of ambulatory persons with MS.[16]

TABLE 1. Descriptive values of spatiotemporal metrics of gait and gait variability indexed by the coefficient of variability

Parameter	Mean (SD)	Median (IQR)	Minimum	Maximum
Means				
Step length, cm	58.1 (12.9)	58.2 (17.5)	25.1	89.2
Step time, sec	0.73 (0.65)	0.58 (0.11)	0.48	5.86
Stride length, cm	116.9 (25.5)	118.1 (33.4)	50.8	178.8
Swing time, sec	0.46 (0.30)	0.40 (0.05)	0.30	2.94
Stance time, sec	0.87 (0.51)	0.75 (0.19)	0.61	4.69
Stride velocity, cm/sec	99.6 (31.7)	104.0 (43.8)	9.86	160.04
Single-support time, sec	0.46 (0.30)	0.40 (0.05)	0.30	2.94
Double-support time, sec	0.57 (0.92)	0.36 (0.15)	0.22	7.48

Coefficient of variability*				
Step length	0.09 (0.28)	0.04 (0.05)	0.01	2.66
Step time	0.10 (0.29)	0.04 (0.04)	0.01	2.05
Stride length	0.05 (0.05)	0.03 (0.03)	0.01	0.44
Swing time	0.11 (0.30)	0.04 (0.03)	0.01	2.11
Stance time	0.05 (0.06)	0.04 (0.03)	0.01	0.62
Stride velocity	0.07 (0.11)	0.05 (0.05)	0.01	0.99
Single-support time	0.11 (0.30)	0.04 (0.03)	0.01	2.11
Double-support time	0.13 (0.31)	0.08 (0.06)	0.02	2.23

*Coefficient of variability (CV = standard deviation/mean).

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TABLE 2. Spearman rank-order correlations (ρ) between metrics of ariability (i.e., CV), disability, and energetic Cw in 86 persons ith MS

	C_w	
Metrics of Gait Variability	Correlation Coefficient	95% CI
Step length CV	0.25*	0.04–0.43
Step time CV	0.25*	0.04–0.43
Stride length CV	0.25*	0.04–0.43
Swing time CV	0.30*	0.09–0.48
Stance time CV	0.32*	0.11–0.49
Stride velocity CV	0.30*	0.09–0.48
Single support CV	0.30*	0.09–0.48
Double support CV	0.36*	0.16–0.53
EDSS (score)	0.29*	0.08–0.47

*Statistical significance at P < 0.05.

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Step time CV	0.25*	0.04–0.43
Stride length CV	0.25*	0.04–0.43
Swing time CV	0.30*	0.09–0.48
Stance time CV	0.32*	0.11–0.49
Stride velocity CV	0.30*	0.09–0.48
Single support CV	0.30*	0.09–0.48
Double support CV	0.36*	0.16–0.53
EDSS (score)	0.29*	0.08–0.47

*Statistical significance at $P < 0.05$.

TABLE 3. Significant predictors of the energetic Cw in persons with MS

Model	Variable	Unstandardized *B*	SE *B*	β
1	EDSS	0.17	0.005	0.387
2	EDSS	0.013	0.005	0.291
	Stance time CV	0.356	0.138	0.269
3	EDSS	0.008	0.004	0.186
	Stance time CV	1.911	0.349	1.446
	Step length CV	−0.380	0.080	−1.216

Regression model was adjusted by age and years of disease.
Model 1: R2 = 0.15; ΔR2 = 0.15; P < 0.001.
Model 2: R2 = 0.23; ΔR2 = 0.06; P = 0.011.
Model 3: R2 = 0.38; ΔR2 = 0.17; P < 0.001.

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Model 1: $R^2 = 0.15$; $\Delta R^2 = 0.15$; $P < 0.001$.
Model 2: $R^2 = 0.23$; $\Delta R^2 = 0.06$; $P = 0.011$.
Model 3: $R^2 = 0.38$; $\Delta R^2 = 0.17$; $P < 0.001$.

Bivariate correlations between metrics of gait variability, disability, and C_w are given in Table 2. Briefly, Spearman's rank-order *rho* correlations indicated that relative variability (i.e., CV) in step length, step time, stride length, swing-time, stance time, stride time, single- and double-support, as well as EDSS scores were significantly and weakly-to-moderately associated with C_w (i.e., [rho] = 0.25-0.36) (Table 2).

The correlations conducted for the C_w and spatiotemporal metrics of gait variability were followed by linear regression analysis with stepwise entry to determine whether significant gait variability metrics correlates of C_w observed in Table 2 predicted C_w. Because age and disease duration had high variability in the sample, we opted to include these variables into the analysis as controlling variables. Findings from the stepwise linear regression analysis are given in Table 3. Briefly, disability (i.e., EDSS), stance time variability, and step length variability entered into the equation and explained significant variance in C_w. This indicated that disability level and variability in stance time and step length emerged as independent predictors of C_w in persons with MS (Table 3).

DISCUSSION

This study examined the associations between variability in metrics of spatiotemporal gait parameters (indexed by the coefficient of variability) and C_w in 86 persons with MS. All metrics of gait variability (i.e., step length, step time, stride length, swing time, stance time, stride velocity, and single- and double-support time) examined in the present study were positively associated with C_w, such that those presenting with higher variability had greater C_w. In addition, EDSS scores (i.e., disability level) were positively associated with C_w, such that those with greater disability severity (i.e., higher EDSS scores) presented with greater C_w. Further analysis revealed that disability severity and variability in stance time and step length emerged as significant predictors of C_w, explaining approximately 36% of the variance in C_w. This suggests that disability severity and increased variability in stance time and step length significantly contribute toward the energetic penalty of overground walking in persons with MS. Our results support previous research that has demonstrated the association between disability severity and C_w involving persons with MS.10 We are unaware of previous work examining gait variability and C_w in persons with MS. However, our findings that different metrics of gait variability are associated with C_w corroborates the results of a previous study in different populations. Of note, one study conducted in ambulatory persons with stroke observed that reduction in energetic cost of overground walking with support was accompanied by changes in temporal gait parameters such as decrease in stride time variability.17 Researches have further investigated the extent to which gait characteristics explain differences in metabolic (i.e., O_2) C_w in adults with Down syndrome. The authors observed that step length, step width, and step time variability uniquely explain about 22% of the variance in the C_w in this population, with step length variability presenting with the greatest unique contribution to the variance. According to the authors, 75% of the excess C_w in adults with Down syndrome is due to underlying factors that increase center of mass mediolateral motion and the variability in their center of mass anteroposterior velocity, step length, and step width.18 Investigators have further observed that increased step variability was associated with significantly higher energy expenditure during treadmill walking in a small sample (n = 11) of healthy young adults.6 Similarly, investigators have observed that healthy adults walking with asymmetric steps time require substantial metabolic cost above those imposed by nonpreferred step times.19 Taken together, the findings of the present study and previous works highlight the potential key role of gait variability in the C_w not only in persons with MS but also in different clinical populations.

There is evidence suggesting that stance phase dominates the C_w. For instance, researchers investigating the C_w using a modeling approach that allowed them to measure instantaneous energy consumption rates in individual muscles over the full gait cycle observed that the stance phase represented 71% of the total muscle energy consumption during preferred stride rate walking.20 This is consistent with our findings such that stance time variability moderately correlated with C_w and was a significant independent predictor of C_w in our sample. It is possible persons with MS who have increased gait variability spend energy not only to drive the center of mass during walking but also to further on movements to correct for irregular foot placement, requiring an extra effort (i.e., energy demand) of stability control during walking.6 This is supported by evidence demonstrating that persons with MS have higher energetic C_w.21

It is believed that persons with MS have increased gait variability compared with healthy controls during walking and that such increased variability occurs early on in the disease and apparently worsens with increasing disability.22 Greater C_w during walking can have a significant impact on energy reserves of persons with MS, and this can have an impact on fatigue, a common symptom in persons with MS.23 Gait variability has been further suggested to be a more sensitive fall predictor in persons with MS with low disability than a disability assessment (i.e., EDSS).24 Collectively, this suggests gait variability as an important and critical aspect of disease to be considered in rehabilitation programs in this population. Interventions focusing on reducing gait variability may potentially benefit multiple aspects associated with the disease (e.g., fatigue) that have been associated with reduced quality of life in this population.25 Research has demonstrated that exercise training is effective in improving metrics of gait (such as those investigated in the present study) in older adults of the general population. For instance, investigators conducted a 6-mo study using a music-based multitask exercise program requiring participants to walk in time with music or to walk while simultaneously handling objects or instruments. Compared with the control group, the training program led to improvements in outcomes such as gait velocity, stride length, stance time, and mediolateral angular velocity.[26] Although not conducted in persons with MS, the previous provides evidence that improvements in gait variables such as those addressed in the present study (e.g., stride length, stance time) are possible. However, it is unclear whether improvements in those parameters translate to reduced variability during gait. Future studies should investigate whether an intervention focusing on improving aspects of gait translates into reduced gait variability in persons with MS and potential outcomes such as mobility.

To our knowledge, this is the first study to examine metrics of spatiotemporal gait variability as variables associated with C_w in persons with MS. Previous studies have reported important and significant associations between mean spatiotemporal gait parameters, fatigue, daily activity, and disability status with C_w in persons with MS in both treadmill and overground walking.[4,10,27] The novelty of the current study was the focus on metrics of spatiotemporal gait variability as potential correlates of C_w during overground walking in persons with MS to have a better understanding of whether individual gait variability affects C_w. This is important because there is some evidence of the clinical relevance of gait variability in persons with MS.[11,24,28]

This study provided preliminary evidence of the associations between metrics of gait variability and the energy cost of overground walking in persons with MS, and along with the relatively large sample size (*n* = 86), these could be regarded as strengths of the study. This study has some limitations. Because of the cross-sectional nature of the study, causality cannot be established. Another limitation is the demographic and clinical composition of our sample, which was composed mostly by women with the relapsing-remitting course of the disease. Despite the sample being similar to other studies with MS,[4,11,28] it is important that future studies investigate similar purposes in a more diverse sample with involvement of a control group. Future studies should further examine the effects of rehabilitation interventions addressing gait variability on C_w and its potential relations with activity and perception of fatigue in persons with MS. Another point to be considered when interpreting the findings of this study lies in the fact that we did not have data on spasticity. There is evidence suggesting that spasticity is associated with walking performance and gait variability.[29,30] For instance, researchers examined the association between alterations of the motor system metrics and C_w in 33 persons with MS with an average age of 41 yrs. The authors observed that C_w was significantly associated to spasticity of the lower limbs, whereas in lower limb and truncal weakness, it did not contribute to higher C_w.[29] More recently, Phadke et al.[30] examined the effect of spasticity and cognitive dual task on gait variability and gait asymmetry in 43 adults with neurological disorders (7/43 with MS) with an average age of 52 (SD = 19) yrs. The authors observed that step length asymmetry was higher in those with high ankle spasticity compared with those with low ankle spasticity.[30]

We demonstrated that variability in step length, step time, stride time, swing time, stance time, single-support time, and double-support time positively correlated with C_w in the bivariate analysis. We further demonstrated that in the multivariate analysis, disability (i.e., EDSS scores) and variability in stance time and step length emerged as significant predictors of C_w in this sample. Such findings highlight the need for interventions targeting specific aspects of gait variability for reducing the energetic demands of walking in this population. Nonetheless, further studies addressing gait variability and C_w in persons with MS are needed to improve our understanding on this matter, which may translate to better recommendations for rehabilitation interventions in this population.

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