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Gait and six-minute walk performance in persons with multiple sclerosis

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ABSTRACT

The six-minute walk (6MW) has been established as a clinic-based, performance measure of walking endurance that reflects community ambulation in multiple sclerosis (MS). Consequently, identifying the contribution of variables to 6MW performance may provide targets for improving real-life walking in MS, and these variables may differ as a function of disability. This study examined cadence and stride length as gait variables that explain differences in 6MW performance between persons with MS and controls, and by level of disability. 256 community-residing persons with MS and 49 non-MS controls performed a standard 6MW test and completed 2 trials of comfortable walking on an electronic walkway for quantifying gait. Regression analyses indicated that cadence and stride length explain differences in 6MW performance between MS and controls, and by level of disability in MS. The contribution of cadence and stride length to walking endurance differed as a function of disability, such that cadence and to a greater extent stride length explained variance in 6MW performance in mild MS, whereas cadence and stride length explained approximately an equivalent amount of variance in 6MW performance in moderate-to-severe MS. We provide evidence for intervention strategies that are specific to disability level to improve walking endurance in MS.

1. Introduction

Walking is one of the most valued physical functions across levels of disability among persons with multiple sclerosis (MS) [1], and limitations in walking are both prevalent and challenging in this population [2]. The prevalence and impact of walking limitations in MS typically worsens across levels of accumulating disability [3–5]. Walking limitations have negative consequences for participatory outcomes such as activities of daily living, quality of life, and employment [2]. The management of walking limitations has been identified as an important, but unmet need in persons with MS [6]. This underscores the importance of identifying variables that can become targets for maintaining and improving important walking domains across levels of disability in MS.

Walking endurance, in particular, might represent a domain of walking that is particularly important in MS. Walking endurance is commonly assessed in the clinical setting using the six-minute walk (6MW) and the 6MW has been identified as a feasible, reliable, and reproducible measure of walking endurance in MS [3]. Performance on the 6MW test has been reduced among persons with MS compared with healthy controls [3,7,8], and across levels of disability among persons with MS [3,5,9]. 6MW performance has been associated (range of $r = .52–.68$) with objectively-measured, ambulatory physical activity outcomes (i.e., real world walking) in persons with MS [10–12]. Performance on the 6MW has further been associated with symptomatic fatigue ($r = .31–.66$) [3,13,14], quality of life ($r = .69$) [3], and activities of daily living ($r = .81$) [13] in MS. Collectively, such observations highlight the importance of identifying variables that can become targets of rehabilitation interventions that improve and maintain walking endurance across levels of disability in persons with MS.

Cadence and stride length are temporal and spatial components of gait that describe walking velocity, and therefore might represent targets of therapeutic and rehabilitative interventions for improving walking endurance in MS. Indeed, cadence and stride length provide information on specific features of the gait cycle that are associated with walking limitations beyond velocity alone. There are data indicating that persons with MS have slower cadence and shorter stride length than healthy controls [15–17], and that cadence and stride length change as a function of disability status [4]. Researchers have further adopted rehabilitation approaches such as rhythmic auditory stimulation (RAS) for improving cadence and stride length in 10 persons with MS who had gait disturbance [18], and this might translate into improved daily walking, as well as other functional, symptomatic, and participatory outcomes – if these spatial and temporal parameters of gait contribute to walking endurance performance. We further note that the contribution of gait parameters for walking endurance, in particular, might differ between MS and controls and between levels of disability in MS.

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This study examined cadence and stride length as gait parameters that explain differences in 6MW performance between persons with MS and non-MS controls as well as between levels of disability in MS (i.e., mild vs. moderate-to-severe MS). We expected that stride length would explain differences in 6MW performance between persons with MS and healthy controls to a greater extent than cadence. This is based on previous research indicating that stride length is compromised in persons with mild MS compared to healthy controls, whereas cadence is somewhat preserved in mild MS [7]. We further predicted that both cadence and stride length would explain differences in 6MW performance between persons with mild and moderate-to-severe MS based on results indicating that both factors differ across disability levels in MS [4]. The results from this study may inform the design of interventions to improve walking endurance in MS by identifying specific spatiotemporal gait parameters that can be targeted, possibly depending on level of disability.

2. Method

2.1. Participants

This study was an extension of previous research designed to validate Multiple Sclerosis Walking Scale-12 scores as a measure of walking quality based on spatiotemporal gait parameters [19]. The sample in this cross-sectional, comparative study included 256 community-dwelling participants with MS, and an additional 49 non-MS controls who were recruited for the present study. The inclusion criteria for all participants were: age 18–65 years; ambulatory with or without an assistive device; and absence of risk factors for undertaking exercise testing based on the Physical Activity Readiness Questionnaire (PAR-Q) [20]. Additional criteria for participants with MS were a clinically definite diagnosis of MS and relapse-free during the past 30 days prior to completing testing. We recruited 500 individuals with MS and 81 controls that were assessed for study eligibility. Of these individuals, 244 persons with MS and 32 controls did not meet the criteria for inclusion or were unable to be scheduled for testing.

2.2. Procedure and outcome measures

This study was approved by an Institutional Review Board. All participants provided written informed consent. Assessments were conducted at two testing sites (the University of Illinois at Urbana-Champaign and the Illinois Neurologic Institute in Peroia, IL) by the same group of researchers who were trained to administer the outcomes according to standardized protocols. Participants completed the 6MW in an accessible hallway according to standardized instructions [3]. To quantify the distance traveled during the 6MW, a member of the research team followed 3–5 feet behind the participant with a measuring wheel (Stanley MS50, New Briton, CT). Participants completed two walking trials wearing footwear on a GaitRite™ (CIR systems, Inc) electronic walkway to collect cadence (steps/min) and stride length (cm) data. Participants were asked to walk at a comfortable speed for both trials. Importantly, we differentiated instructions between the GaitRite™ and 6MW trials to emphasize the difference in walking behaviors. An average value from the two trials was generated for each gait parameter. Demographic and clinical characteristics were obtained using a self-report questionnaire. The Patient Determined Disease Steps (PDDS) [21] scale was used to characterize the extent of neurological disability of the MS sample. The PDDS is an inexpensive surrogate for the Expanded Disability Status Scale (EDSS) and scores on the PDDS are strongly related with scores on the EDSS [21]. Participants with MS were grouped by disability level as mild (i.e., PDDS score 0–2) or moderate-to-severe (i.e., PDDS score 3–6).

2.3. Statistics

The data were analyzed using PASW Statistics, Version 18.0 (SPSS Inc., Chicago, IL). Descriptive statistics were used to summarize demographic and clinical characteristics of the samples. Values in the text are mean (SD), unless otherwise noted. Independent samples *t*-tests and chi-square tests were conducted to determine differences between groups on demographic characteristics. Walking performance outcomes (i.e., 6MW distance, cadence and stride length) were compared between groups (i.e., control, mild MS and moderate-to-severe MS) using a series of one-way analyses of covariance (ANCOVA) controlling for covariates, if necessary. Follow-up comparisons were conducted to identify specific differences in walking performance outcomes between groups. We performed multiple hierarchical linear regression analyses to explain differences in 6MW performance between persons with MS and controls, and between persons with mild and moderate-to-severe MS. The first regression analysis examined the contribution of cadence and stride length to 6MW between participants with MS overall and controls. The first step of the model controlled for age, followed by group (i.e., MS vs. control) in the second step. Stride length and cadence were entered in the final step to determine the contribution of each variable independently to 6MW performance. The second regression analysis examined the contribution of cadence and stride length to 6MW performance between participants mild MS and participants with moderate-to-severe MS. Age, disease duration, and clinical course of MS were entered in the first step of the model, followed by disability group (i.e., mild vs. moderate-to-severe MS) in the second step. Both gait variables of interest were entered in the final step. The final regression was performed to identify differences in the contribution of cadence and stride length to 6MW performance within each group. Age was entered in the first step of the model, followed by cadence and stride length in the second step. Statistical significance was $p < .05$.

Table 1
Demographic and clinical characteristics in non-MS controls, overall MS sample, and MS groups by level of disability.

	Control		MS					
			Overall MS sample		Mild disability		Moderate-to-severe disability	
Characteristic	Mean (*SD*)	Range	Mean (*SD*)	Range	Mean (*SD*)	Range	Mean (*SD*)	Range
Age, years*,#	40.3 (9.3)	22–58	48.6 (9.4)	21–65	46.5 (10.2)	21–64	50.7 (8.08)	23–65
Sex, female/male	38/11		205/51		106/22		99/29	
Height, cm	170.9 (9.7)	155–194	169.1 (8.6)	154–197	168.4 (8.3)	154–197	169.8 (8.8)	155–195
Weight, kg	75.6 (14.2)	53–114	79.6 (20.5)	45–165.7	77.7 (17.5)	49.8–138	81.7 (23.2)	45–165.7
Disease duration, years#	N/A	N/A	10.9 (8.1)	1–39	9.7 (8.1)	1–39	12.1 (8.0)	1–39
Disease course# (RRMS/SPMS/PPMS/NR)	N/A	N/A	215/25/14/2		122/1/5/0		93/24/9/2	
PDDS, median (IQR)#	N/A	N/A	2.5 (3.0)	0–6.0	1.0 (1.0)	0–2.0	4.0 (1.0)	3.0–6.0

RRMS = relapsing-remitting MS; SPMS = secondary progressive MS; PPMS = primary progressive MS; PDDS = patients determined disease steps; NR = not reported; IQR = interquartile range. *Significant difference between control and overall MS sample; #Significant different between mild and moderate-to-severe MS; $p < .05$.