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Cognitive processing speed has minimal influence on the construct validity of Multiple Sclerosis Walking Scale-12 scores

Robert W. Motl [a,*], Diego Cadavid [b], Brian M. Sandroff [a], Lara A. Pilutti [a], John H. Pula [c], Ralph H.B. Benedict [d]

[a] Department of Kinesiology and Community Health, University of Illinois at Urbana–Champaign, United States
[b] Biogen Idec, United States
[c] College of Medicine, University of Illinois at Peoria, United States
[d] Department of Neurology, SUNY Buffalo School of Medicine, United States

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ABSTRACT

Background: The Multiple Sclerosis Walking Scale-12 (MSWS-12) has been a commonly used patient reported outcome for measuring walking impairment in research involving multiple sclerosis (MS).
Objective: We examined the possibility that cognitive processing speed (CPS) influences the association between MSWS-12 scores and other measures of ambulation (i.e., construct validity).
Methods: 96 MS patients completed the MSWS-12, underwent a neurological examination for generating an Expanded Disability Status Scale (EDSS) score, and completed the Symbol Digit Modalities Test (SDMT), Timed 25-Foot Walk (T25FW), 4 trials on the GAITRite™ for generating the functional ambulatory profile (FAP) score, and Six-minute Walk (6MW).
Results: The SDMT was significantly correlated with MSWS-12 scores ($r = -.428$) and T25FW ($r = -.459$), 6MW ($r = .512$), FAP ($r = .275$), and EDSS ($r = -.404$) scores. There were statistically significant correlations between MSWS-12 and T25FW ($r = .568$), 6MW ($r = -.680$), FAP ($r = -.595$), and EDSS ($r = .737$) scores. Lastly, four separate hierarchical linear regression analyses indicated that, after controlling for age, gender, disease duration, and clinical course, T25FW, 6MW, FAP, and EDSS scores individually were significant correlates of MSWS-12 scores, and the associations (i.e., standardized beta-coefficients) were still statistically significant with minimal attenuation when controlling for SDMT scores.
Conclusion: There was minimal evidence that CPS influenced the construct validity of MSWS-12 scores.

1. Introduction

Walking impairment is a common consequence of multiple sclerosis (MS) [1,2] and walking represents one of the most valued functions in this population [3,4]. Such observations have underscored the adoption of walking outcomes in clinical research and practice involving MS patients [1] with increasing emphasis placed on inclusion of a patient-reported outcome (PRO) [5]. The Multiple Sclerosis Walking Scale-12 (MSWS-12) [6] has been a commonly used PRO based on the strength and breadth of evidence for the construct validity of its scores. The evidence for its construct validity is largely based on associations with other ambulatory-based outcomes such as timed 25-foot walking (T25FW), six-minute walk (6MW), functional ambulatory profile (FAP) (i.e., an integrative measure of gait parameters), and Expanded Disability Status Scale (EDSS) [6–11]. Nevertheless, the construct validity of scores from a PRO, such as the MSWS-12, might be compromised by a range of cognitive impairments [12,13].

One of the most common cognitive impairments documented based on neuropsychological testing in MS involves cognitive processing speed (CPS) [14,15]. CPS reflects the amount of information that can be processed within a given unit of time [16], and deficits in CPS may underlie other cognitive impairments [17] in MS [16] including long-term and working memory [18–20]. Performance on measures of CPS, particularly the Symbol Digit Modalities Test (SDMT) [21], has been associated with walking outcomes in MS patients [22,23]. We are unaware of research that has examined the possibility that CPS might influence the construct validity of a PRO of walking impairment in MS.

This study examined the possible influence of CPS on the construct validity of MSWS-12 scores in persons with MS. To do this, we initially examined the associations among SDMT, MSWS-12, T25FW, 6MW, FAP, and EDSS scores as well as demographic (i.e., age and gender) and clinical (i.e., disease duration and MS clinical course) variables. We further examined the associations between MSWS-12 scores and T25FW, 6MW, FAP, and EDSS scores individually while controlling for demographic and clinical variables and then examining the influence of SDMT scores.

* Corresponding author at: University of Illinois at Urbana–Champaign, Department of Kinesiology and Community Health, 233 Freer Hall, 906 South Goodwin Ave., Urbana, IL 61801, United States. Tel.: +1 217 265 0886; fax: +1 217 244 7322.
E-mail address: robmotl@illinois.edu (R.W. Motl).

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2. Method

2.1. Participants

The participants were recruited through three local neurology practices in central Illinois, USA. There were 96 patients meeting diagnostic criteria for clinically-definite MS [24]. Two additional inclusion criteria were (a) capacity for independent ambulation or ambulation with an assistive device and (b) willingness to voluntarily complete ambulatory and cognitive testing. Participants who had a relapse in the past 30 days were excluded from the study. There were no inclusion or exclusion criteria based on cognitive functioning. All participants satisfying inclusion criteria provided written informed consent.

2.2. Measures

2.2.1. Cognitive processing speed

We used the SDMT as a measure of CPS. This test is a relatively quick assessment and valid in MS [25,26] and scores have been associated with walking outcomes in previous research [22,23]. The SDMT captures visual/spatial processing speed and working memory. The main outcome measure of the SDMT was the total number of correctly provided numbers (maximum of 110) in the 90 second period [21] with higher scores reflecting better CPS. This test loads on the mental speed factor of the Minimal Assessment of Cognitive Function in MS (MACFIMS) [26], has been included in the Brief International Cognitive Assessment for MS [27], and has been correlated with whole-brain and deep gray matter atrophy in MS [28]. The SDMT further has been considered for inclusion in the Multiple Sclerosis Functional Composite, a composite clinical outcome measure in MS [29,30].

2.2.2. PRO, Multiple Sclerosis Walking Scale-12

The MSWS-12 is a 12-item PRO of the impact of MS on walking [6]. Example items are "In the past two weeks, how much has MS limited your ability to walk?" and "In the past two weeks, how much has MS slowed down your walking?". The 12-items on the MSWS-12 are rated on a scale ranging between 1 (*Not at all*) and 5 (*Extremely*). The total MSWS-12 score is computed by summing the individual item scores, subtracting 12 (i.e., the minimum possible score for the summed items), dividing by 48 (i.e., the maximal score of the summed items after subtracting 12), and then multiplying the result by 100 [6–11]. The total MSWS-12 score ranges between 0 and 100 and higher scores indicate greater perceived walking impairment.

2.2.3. Timed 25-foot walk

The T25FW was administered as a measure of walking speed. The T25FW consisted of the participant walking 25 ft as quickly and safely as possible in a hallway clear of obstacles. Two trials were performed, and the main outcome measure was the mean time (seconds) taken to complete the T25FW [30]; shorter times reflect faster walking speed.

2.2.4. Six-minute walk

The 6MW was included as a measure of walking endurance. The 6MW was performed in a rectangular, carpeted corridor with hallways that exceeded 50 m in length and that were clear of obstructions and foot traffic. We provided standardized instructions and emphasized walking as far and as fast as possible for 6 min and performed the test on a surface consistent with the original validation work in MS [31]. One researcher followed alongside the participant for safety, while another researcher followed 1 m behind the participant and recorded the distance traveled (meters) using a measuring wheel (Stanley MW50, New Briton, CT) [11,32]; longer distances reflect better walking endurance.

2.2.5. GAITRite

The GAITRite™ (CIR systems, Inc.) is a 26-foot, electronic walkway with embedded sensors arranged in a grid-like pattern for identifying footfall contacts during normal walking and provided an integrative metric of gait dysfunction based on the FAP score. The FAP score is an integration of selected temporal and spatial parameters into a single, numerical representation of gait (i.e., FAP score is based on the linear association of the step length/leg length ratio with step time when velocity is "normalized" based on leg length). The FAP score ranges between 0 and 100 [33] with higher scores reflecting less gait impairment.

2.2.6. Expanded Disability Status Scale

Participants underwent a neurological exam for the generation of an Expanded Disability Status Scale (EDSS) score [34]. The EDSS score is based on an evaluation of functional systems (FS), including visual, brainstem, pyramidal, cerebellar, sensory, bowel/bladder, cerebral, and other as well as ambulatory function (i.e., 500 meter walk). The FS scores receive 'step' scores, and the 'step' scores are combined with ambulatory function into an overall EDSS score. The EDSS score can range between 0 (no disability) and 10 (death from MS) [34].

2.3. Procedure

The procedure was approved by a local Institutional Review Board. The data were collected during a single session in a clinical setting by the same group of researchers. The researchers who collected data were doctoral level graduate students, post-doctoral fellows, professors of kinesiology, and a neurologist. The participants provided demographic information, completed the MSWS-12, and underwent a neurological examination for generating an EDSS score [34] and an interview for classification of MS clinical course [35]. The neurological examination and interview were conducted by a board certified neurologist who is a Neurostatus certified EDSS examiner. This was accompanied by completion of the SDMT, T25FW, GAITRite™, and 6MW tests. The tests were not conducted in the same order per participant as we had upwards of 4 participants per data collection session. We provided 15 or more minutes of rest between the ambulatory assessments for minimizing motor fatigue. All participants received $20 remuneration.

2.4. Data analysis

The data were analyzed using IBM SPSS statistics version 19.0. Descriptive statistics were provided as mean ± standard deviation, unless otherwise noted. We examined the associations among SDMT, MSWS-12, T25FW, 6MW, FAP, EDSS scores, as well as demographic and clinical variables, using Pearson product–moment correlation coefficients (r). We then regressed MSWS-12 scores individually on T25FW, 6MW, FAP, and EDSS scores using separate hierarchical linear regression models. We entered demographic and clinical variables as covariates in Step 1, T25FW, 6MW, FAP, or EDSS scores in Step 2, and SDMT scores in Step 3.

3. Results

3.1. Participant characteristics

The mean age of the participants ($N = 96$) was 52.7 ± 11.1 years (range = 30–78 years), the gender distribution was predominantly female (77 women/19 men), and the sample was mostly Caucasian ($n = 91$, 94.8% of cases). The participants primarily had a relapsing-remitting clinical course ($n = 79$, 82.3% of cases); there were 13 persons with primary or secondary progressive MS and 4 persons with a clinical course that was unclassified. The mean disease duration of the participants was 11.8 ± 10.0 years (range = 1–43 years). Of the 96 persons, 81 or 84.4% were on a disease-modifying therapy and 62 or 66.6% were on a symptomatic therapy. There were no participants