Gait & Posture 57 (2017) 211–216

Contents lists available at ScienceDirect

Gait & Posture

journal homepage: www.elsevier.com/locate/gaitpost

Full length article

Cognitive-motor interference in multiple sclerosis: What happens when the gait speed is fixed?

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ARTICLE INFO

Keywords:
Cognition
Dual task cost
Gait
Multiple sclerosis
Walking

ABSTRACT

During the last decade, numerous studies have confirmed a coupling between walking performance and cognition in people with multiple sclerosis (PwMS). Our aim was to provide new insights into a walking-cognitive dual-task (DT) in PwMS. We tested the DT phenomenon by controlling the walking speed using an instrumented treadmill. Thirty PwMS (20 women) with a mean age 40.1 (SD = 12.0) participated in the study. Twenty-one healthy subjects served as controls. Each subject completed a sequence of tests: a) Normal walking (ST) – the participant walked on the instrumented treadmill at a comfortable walking speed for 1 min; b) Cognitive evaluation (ST) – subjects performed two cognitive tests while seated; c) DT cognitive tests performed while walking on the treadmill at the identical speed performed during normal walking. Outcome measures were spatio-temporal parameters of gait (mean and variability), the Word List Generation Test (WLG) and the Serial-3 Subtraction Test. MS participants significantly decreased their cadence while increasing their stride length during the DT condition compared to the ST condition. Non-significant differences were observed for the WLG and Serial-3 Subtraction Cognitive Tests between the ST condition and the DT condition in both the MS and healthy groups. In terms of gait variability parameters, MS subjects demonstrated a 2 to 3-fold greater gait variability compared to the healthy controls. Non-significant differences in gait variability parameters were observed between the ST and DT conditions in both the MS and control groups. This study provides new insights into the DT phenomenon in the MS population.

1. Introduction

Walking difficulties and cognitive impairments are clinical hallmarks of people with multiple sclerosis (PwMS) [1,2]. Cognitive deficits have been reported in 45%-70% of people affected by this disease [3]. As for gait deficits, numerous studies have confirmed that PwMS walk slower with decreased stride lengths [4] have reduced knee and ankle motion [5] and elevated variability [6] compared to healthy controls.

During the last decade, numerous studies confirmed a coupling between walking performance and cognition in PwMS [7]. The relationship between the two functions is generally investigated by a dual-task (DT) paradigm [8–10] where participants perform a walking test (referred to as a single task (ST) condition) followed by a second examination, where the subject is asked to repeat the walking test while performing a cognitive task (referred to as a DT condition).

Results of these testing conditions are usually presented in terms of gait changes occurring during a DT condition compared to a ST condition. These deficits are considered dual task costs (DTCs). In most studies investigating DT conditions in PwMS, the most prominent DTCs involved walking speed. PwMS automatically reduced their walking speed while engaged in a cognitive challenge [11,12].

However, a question remains – is DTCs abnormal in the MS population? In a recent meta-analysis systematic review, Learmonth et al. reported that the addition of cognitive tasks similarly reduced gait and balance function in both PwMS and healthy adults [11]. Moreover, it is unclear whether a similar performance is associated with differential neural activation.

Several possibilities may explain the inconclusive evidence regarding DTCs in PwMS. Firstly, most previous studies exclude information on DTCs with respect to cognitive performance. Moreover, in these studies, basic cognitive capabilities were not separately evaluated from the walking test. Secondly, previous investigations examining DT in PwMS did not consider patient prioritization (between walking stability to success on the cognitive test) during the DT condition. Worth noting, although it is expected that most neurological patients spontaneously prioritize gait stability over success during a cognitive task [13]

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http://dx.doi.org/10.1016/j.gaitpost.2017.06.024
Received 6 February 2017; Received in revised form 18 April 2017; Accepted 22 June 2017
0966-6362/

in some cases a "posture second" strategy was used, signifying that the cognitive task was prioritized over gait [14]. Furthermore, Yogev-Seligmann et al. reported that gait performance differed significantly during a DT condition when subjects were instructed to focus on the cognitive task compared to a directive to focus on walking stability [15].

Therefore, the primary aim of the present study was to further explore the walking-cognitive DT in PwMS. We tested the DT phenomenon by controlling the walking speed using an instrumented treadmill. Usually, the subject is free to change his walking speed during the DT. In our study, we prevented the participant from reducing his/her walking speed while performing the cognitive task.

We assumed that in a scenario where the patient cannot reduce his walking speed during a DT condition, the DTCs would indicate a poorer cognitive performance (during walking compared to sitting) and/or greater gait variability (during a DT condition compared to normal walking), thus, confirming or reducing, whether a walking-cognitive coupling exists in the MS population.

2. Methods

2.1. Study participants

The study was a case-control study comprising 51 participants. Thirty PwMS, 20 women and 10 men, aged 40.1 (S.D = 12.0) were recruited from the Multiple Sclerosis Center, Sheba Medical Center, Tel-Hashomer, Israel. Twenty-one apparently healthy subjects (15 women and 6 men), aged 38.1 (S.D = 6.8), with no history of walking and/or cognitive impairments served as controls.

Inclusion criteria for the MS participants included: (1) a neurologist-confirmed diagnosis of definite MS according to the revised McDonald criteria [16]; (2) between 2.0 to 5.5 on the Expanded Disability Status Scale (EDSS) [17], comparable to walking at least 100 m without a walking aid; (3) age range from 25 to 55 years; (4) ability to ambulate on a treadmill for at least 5-min; and (4) relapse-free for at least 90 days prior to testing.

Exclusion criteria included: (1) orthopedic disorders that could negatively affect mobility; (2) major depression or cognitive decline hindering walking on a treadmill; (3) pregnancy; (4) blurred vision; (5) cardiovascular disorders; (6) respiratory disorders; (7) or ingestion of steroids or fampridine. All participating subjects signed an informed consent. The study was approved by the Sheba Institutional Review Board.

2.2. Gait analysis

Gait parameters were obtained using the Zebris FDM-T Treadmill fitted with an electronic mat of 10,240 miniature pressure sensors, embedded underneath the belt. The treadmill's speed can be adjusted from 0.2 and 22 km/h at intervals of 0.1 km/h. When the subject stands/walks on the treadmill, the pressure exerted by his feet is recorded by the sensors at a sampling rate of 120 Hz. Dedicated software integrates the pressure signals and provides the major spatiotemporal parameters during gait. The use of a Zebris instrumented treadmill is a well- established tool for computing gait analysis in PwMS [18,19].

2.3. Experimental protocol

Gait and cognitive assessments were performed by a physical therapist experienced in neurological rehabilitation, at the Center of Advanced Technologies in Rehabilitation, Sheba Medical Center, Israel. Each subject completed a sequence of 4 consecutive tests with a 1-min rest break between tests:

1. Defining comfort walking speed − Subjects were requested to walk on the instrumented treadmill with their casual footwear at a starting speed of 0.5 km/h. While walking, the belt speed was increased by 0.3 km/h every 15 s in a stepwise manner. Once the participant informed the tester that the walking speed best characterized his/her normal walking pace, the specific velocity was defined as the comfort walking speed.
2. Normal walking − Based on the defined comfort walking speed, the participant walked on the instrumented treadmill for 1 min, recording major spatio-temporal parameters of gait. In addition, gait variability was expressed by the coefficient of variation (CV) (CV = SD/mean). The CV (%) was operationalized as a measure of relative gait variability [20].
3. Cognitive evaluation − Subjects performed two cognitive tests while **seated:** the Word List Generation (WLG) and the Serial-3 Subtraction Tests. The order of tests was random (a flipped coin). Both cognitive tests were audio recorded and subsequently examined by the assessor to prevent scoring miscalculations.
   - the WLG test − the test is part of the brief repeatable battery of neuropsychological tests for MS [21]. Specifically it is a test of verbal fluency. Subjects were instructed to say out loud as many words as possible beginning with the Hebrew letters "Bet" or "Gimmel" within a defined period of 1-min [22]. According to the test guidelines, names of people and places were excluded from the count. Furthermore, the plurality of a word was counted as a single word. The final score was calculated as the number of correct items expressed in the 1-min period.
   - Serial-3 Subtraction Test − the test is used to assess mental tracking and has been used in various investigations relating to the DT phenomenon in PwMS [7,9]. Starting from a 3-digit number (e.g. 350 or 400), the subjects were instructed to subtract 3 and articulate the calculated number out loud (e.g. 400, 397, 394, etc). The task was repeated continuously for 1-min. Scores were recorded for the correct numbers. The accuracy rate was calculated as correct scores divided by total attempts.
4. Walking-cognitive dual task − subjects were instructed to perform two DT walking-cognitive trials:
   - walking on the instrumented treadmill while performing the WLG test, expressing a different letter not used while in a sitting position;
   - walking on the instrumented treadmill while performing the Serial-3 Subtraction Test, starting with a different number than articulated in the sitting position.

Cognitive tests performed while walking, were identically scored as in the seating position (Phase 3).

Importantly, the speed of the treadmill's belt in both DT trials, was set according to the comfort walking speed defined in phase 1. Subjects were not allowed to reduce the belt speed during the DT examination. Specific prioritization instructions were not given to the subjects prior or during the test. To prevent a situation where the sequence of the experimental tests affected the cognitive performance, the order of the third and fourth phases were randomized (a flipped coin).

2.4. Statistical analysis

Data analysis was performed using IBM SPSS statistics software (Version 23.0 for Windows, SPSS Inc. NY, USA). Data were initially examined for normality violations, outliers, errors and missing values. Descriptive statistics determined the demographic and clinical characteristics of the study participants. All outcome variables showed a normal distribution.

In addition to the standard spatio-temporal parameters of gait, the walk ratio was calculated according to the following formula: walk ratio = mean step length (mm)/cadence (steps/min). The walk ratio is a valid simple index for co-ordination during gait. The main advantage of the walk ratio is its independence from walking speed. A decreased walk ratio due to a walking pattern of shorter and more frequent steps,