



Contrasting relationship between depression, quantitative gait characteristics and self-report walking difficulties in people with multiple sclerosis

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ABSTRACT

The purpose of this study was to examine the relationship between depression and walking in the multiple sclerosis (MS) community. This study included 132 people with MS (PwMS) (80 women), mean EDSS 2.9 (S.D. = 1.7). Depression was assessed by the Hospital Anxiety and Depression Scale questionnaire. Spatio-temporal parameters of gait were studied using an electronic walkway. Participants filled out a valid self-rated measure of walking ability, the Multiple Sclerosis Walking Scale (MSWS-12) questionnaire. Computerized cognitive scores were included in the analysis in a multivariable analysis. Forty PwMS (30.3%) were classified as suffering from depression. Individuals in the depressed group walked slower than those in the non-depressed group; 92.2 (S.D. = 30.5) vs. 107.9 (S.D. = 29.4) cm/s, respectively. However, after controlling for age, gender and EDSS, the difference between the groups was considered non-significant; $p = 0.986$. As for the MSWS-12 self-report questionnaire, regardless of the controlling factors (age, gender, EDSS), scores for participants in the depressed group were significantly elevated, indicating poor walking abilities, compared to scores in the non-depressed group; 40.8 (S.D. = 15.9) vs. 26.6 (S.D. = 13.7); $p = 0.002$, respectively. Furthermore, according to the linear regression model, by utilizing the self-rated measure of walking ability, we were able to explain ~20% of the variance related to depression, while spatio-temporal parameters of gait were excluded from the model. In PwMS, depressive symptoms are related to self-perception of walking, but not to quantitative gait parameters.

1. Introduction

Depression is one of the most common symptoms in people with multiple sclerosis (PwMS) (Feinstein et al., 2014). According to a recent systematic review and meta-analysis based on 87,756 PwMS, the mean prevalence for depression was 30.5% (Boeschoten et al., 2017), which is much higher when compared with the general population where the annual prevalence has been reported between 2% and 10% (Bromet et al., 2011).

Typical depressive symptoms include apathy, social withdrawal, feelings of worthlessness, guilt and poor self-esteem (Feinstein, 2004). Symptoms which may more accurately indicate a comorbid depressive episode include a pervasive low mood, anhedonia, diurnal mood variation, suicidal ideation, pessimistic or negative patterns of thinking and impaired functionality unrelated to or out of proportion to one's physical disability (Murphy et al., 2017). The relationship of PwMS with depression, including the impact of MS disease activity, severity

and duration, remains complicated with some studies reporting no relationship at all (Möller et al., 1994; Minden et al., 1987). Others have demonstrated an association between depression and MS disease progression (McIvor et al., 1984; Chwastiak and Edhe, 2007).

Although various studies have examined the association between depressive related constructs and walking in MS (Kalron, 2016; Motl et al., 2012, 2017), only a few studies have focused on the specific contribution of depression on walking in PwMS (Ensari et al., 2015; Garg et al., 2016; Gottberg et al., 2007). Ensari et al. (2015) explored the relationship between depressive symptoms and walking impairment in a cohort of 269 PwMS discovering a significant positive relationship between depression and a self-report walking questionnaire, the MS walking scale-12 (MSWS-12). In contrast, non-significant differences between depressed and non-depressed PwMS ($n = 166$) were noted in walking speed (Gottberg et al., 2007). Moreover, depressive symptoms were found unrelated to disease severity in a group of 83 PwMS (Pronvinciali et al., 1999).

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Several explanations may illuminate the inconsistencies found in previous studies researching depression and walking in PwMS. Several reports evaluated walking solely by employing the self-report questionnaire (Ensari et al., 2015; Garg et al., 2016), others measured walking speed according to a ten-meter walk test (Gottberg et al., 2007). Although these walking tests are common and have been validated in PwMS, they are limited in their ability to detect in-depth gait characteristics. Previous studies did not consider the patient's cognitive status. It is well known that cognition is related to walking performance (Downer et al., 2016) and depression symptoms in PwMS (Patel et al., 2017), therefore, logically all three components (cognition, gait and depression) should be analyzed concurrently in order to fully address the relationship between walking and depression in the MS population. An association between depression, walking disabilities and cognitive performance has been demonstrated in the elderly (Hajjar et al., 2009) and in those afflicted with Parkinson's disease (Lord et al., 2013), however, not in PwMS.

Our primary goal, therefore, was to examine the relationship between depression and walking in PwMS. Cognitive performance, subjective (i.e self-reported walking difficulties) and objective (i.e quantitative gait parameters) walking components, were taken into account. The study was motivated by the awareness that new information might improve future intervention programs directed at reducing symptoms of depression and/or improving walking capabilities in the MS population.

2. Methods

2.1. Study design and participants

This observational retrospective cross-sectional study included 132 patients with MS (80 women and 52 men) recruited from the Multiple Sclerosis Center, Sheba Medical Center, Tel Hashomer, Israel. Inclusion criteria included: (1) a neurologist-confirmed diagnosis of definite MS according to the revised McDonald criteria (Polman et al., 2011); (2) an Expanded Disability Status Scale (EDSS) score of < 7.0 (Kurtzke, 1983) a consistent ability to walk at least 20 m without resting; (3) subject had performed a quantitative gait assessment; (4) subject had performed a computerized cognitive test; (5) subject had completed the Hospital Anxiety and Depression Scale (HADS) scale; (6) gait trials, cognitive tests and the HADS questionnaire were completed within 6 months of each other; (7) the patient was relapse-free for at least 90 days prior to testing.

Exclusion criteria included: (1) orthopedic disorders that could negatively affect balance; (2) pregnancy; (3) blurred vision; and (4) cardiovascular and/or respiratory disorders. All participating subjects gave written informed consent for use of their data in the research project. The study was approved by the Sheba Institute Ethics Committee.

2.2. Hospital Anxiety and Depression Scale (HADS)

The HADS is a validated self-report screening scale used to investigate the prevalence of emotional distress among patients at general medical clinics (Zigmond and Snaith, 1983). The scale rates two components: anxiety and depression, each consisting of 7 items. Each question is scored in a simple Likert fashion (0 through 3), yielding a range of scores from 0 to 21 for each item (Crawford et al., 2001). The questionnaire includes three cut-off scores indicating different levels of clinically relevant distress: a score between 0 and 7 is considered normal and 8–21 - an abnormal depression rate (Zigmond and Snaith, 1983). The HADS is widely used in clinical practice and has been validated in the MS population (Honarmand and Feinstein, 2009). In the present study, scores were extracted solely for the depression scale.

2.3. Gait analysis

Spatio-temporal parameters of gait were studied using the

GAITRite™ system (CIR Systems, Inc. Haverton, PA, USA), which consists of a 4.6 m long electronic walkway containing 2304 compression-sensitive sensors arranged in a grid pattern. As the subject ambulates across the walkway, pressure is exerted by his feet, thus activating the sensors. Simultaneously, targeted software utilizes special algorithms to automatically group the activated sensors and form footprints.

The system integrates all footprints and provides the following spatio-temporal parameters: velocity, cadence, step/stride length, step/stride time, heel to heel base of support, swing/stance time, single/double time and percentage according to the gait cycle. We also extracted the variability of step length, step time and single support expressed by the coefficient of variation (CV) ($CV = SD/mean$). The CV (%) is operationalized as a measure of relative gait variability.

All participants were instructed to walk across the mat at a self-selected speed in one direction without stopping. Participants started walking 2 m before the mat and 2 m after the mat. Each participant performed six consecutive walking trials. The values from all trials were subsequently averaged to produce the final results. Gait measures were collected by a physical therapist specialized in neurological rehabilitation. Data collected by the GAITRite system are well established in the MS population (Comber et al., 2017).

In addition, all participants filled out a Multiple Sclerosis Walking Scale (MSWS-12) questionnaire. The MSWS-12 is a valid self-rated measure of walking ability in PwMS. The questions were based on the patient's walking limitations (due to MS) during the past 2 weeks. Each item was scored on a 1–5 scale; the higher the score, the more perceived walking difficulties. The MSWS-12 has good evidence for its internal consistency, test-retest reliability and validity of scores as a measure of walking impairment in MS (Hobart et al., 2003).

2.4. Cognitive assessment

We extracted data from the computerized cognitive battery of tests completed by the participants (Mindstreams; NeuroTrax Corp., Medina, New York, USA). Outcome measurements encompassed the following cognitive domains: verbal and nonverbal memory, executive function, visual spatial processing, verbal function, attention, information processing speed and motor skills. Each cognitive domain score was normalized and equivalent to an IQ scale (mean: 100, SD: 15) in age and education-specific domains. Cognitive scores from the tests have been found to have good test-retest reliability and construct validity relative to paper-based tests in the MS population (Achiron et al., 2007).

2.5. Statistical analysis

MS subjects were divided into two groups: depressed and non-depressed with allocation determined according to the HADS scores. The cut-off point for distribution was set at 8. PwMS with scores ≥ 8 were assigned to the depressed group and those with < 8 were assigned to the non-depressed group. The selected cut-off point was based on Honarmand and Feinstein's (2009) study that validated the HADS with the Structured Clinical Interview for DSM-IV Disorders and its defined scores for depressed and non-depressed (Honarmand and Feinstein, 2009).

Descriptive statistics determined the demographic and clinical characteristics of the study participants according to their group allocation. Group differences in age and gender distribution were determined using an independent sample-t and chi-square test, respectively. All spatio-temporal parameters of gait and cognitive data were normally distributed according to the Kolmogorov-Smirnov test. Differences in gait and cognitive parameters between the depressed and non-depressed groups were determined using the multivariate analysis of variance (MANOVA) test controlling for age, gender and the EDSS score.

The evaluation of potential predictors for depression status (dependent variable) was calculated by a stepwise linear regression

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