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Fatigue induced changes to kinematic and kinetic gait parameters following six minutes of walking in people with Multiple Sclerosis

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Purpose

The aim of this study was to examine the effect of six minutes of walking on fatigue, exertion and spatiotemporal, kinematic and kinetic gait parameters in people with Multiple Sclerosis (MS).

Methods

Thirty-four people with MS with moderate levels of disability completed measures of fatigue, exertion and instrumented gait analysis before and after six-minute trials of rest and walking (using a modified six-minute walk test, m6MWT). Ten age and gender matched healthy controls completed analysis before and after the m6MWT.

Results

The MS group had a significant increase in self-reported fatigue following the m6MWT, however there was no effect on spatiotemporal gait parameters. During stance on the more affected side ankle dorsiflexion at initial contact decreased, while knee and hip flexor moments and hip power absorption increased. On the less affected side ankle and knee power absorption, and hip extensor

moment all increased. Healthy controls showed increases in joint kinetics likely due to increased walking speeds following m6MWT.

Conclusion

For people with MS, ankle dorsiflexion angle reduces at initial contact following walking induced fatigue, while increased power absorption at the hip, knee and ankle indicate gait inefficiencies that may contribute to higher levels of fatigue and exertion.

Introduction

Difficulty walking is often rated as the most challenging aspect of living with Multiple Sclerosis (MS) and is associated with reduced quality of life and increased financial burden [1, 2]. Weakness [3], sensory loss [4], ataxia [5] and spasticity [6] may impair walking ability in people with MS, while reduced speed [7] and increased energy cost [8] can reduce the capacity to walk long distances. Fatigue, another common symptom reported by people with MS [9], may also contribute to reduced walking capacity [10]. Muscle fatigue is known to worsen with physical activity [11] and is related to perceived fatigue levels in people with MS [12] .

To date, research into muscle fatigue in people with MS has focussed on the neurophysiological aspects of activity-dependent fatigue induced by controlled muscle contractions [13]. These studies have found muscle fatigue is caused by deterioration in both central and peripheral neuromuscular function and is associated with slower gait speed and reduced cadence [14]. Other studies have reported that the energy cost of walking is positively associated with perceived fatigue and double limb support time, and inversely associated with gait speed and stride length [8]. Presently there has been limited research into the direct effects of muscle fatigue on daily activities such as walking in people with MS. Higher levels of fatigue are reported in the afternoon by people with MS, however previous work has reported no significant differences in spatiotemporal characteristics of gait

measured in the afternoon of a day compared to the morning [15]. A more detailed study of gait mechanics in people with MS found reduced ankle power at push-off, reduced knee power absorption and reduced peak knee extensor moments to be associated with increased levels of self-reported fatigue [16], suggesting that fatigue is associated with gait changes in people with MS.

A few studies have investigated the effects of walking-induced fatigue on the variability of gait kinematics in people with MS. Crenshaw et al. found no change in kinematic or kinetic variability following a fatiguing walk in 20 people with MS [17], while a pilot study by Sehle et al. reported some increased kinematic variability in individual patients following walking at preferred speed to the point of exhaustion on a treadmill [18]. It is unclear whether these inconsistent findings in kinematic variability might be due to differences in the distance walked, as these were not documented in either study. The amount of walking that is likely to induce changes in gait mechanics in people with MS requires clarification.

Walking distance is often used to classify disability and disease progression in people with MS [19, 20]. The six-minute walk test (6MWT) is recognised as a measure of functional mobility in people with MS [21] and leads to increased levels of perceived fatigue [10, 22], reduced cadence in slower walkers [23] and poorer balance after walking [24]. In addition, we have recently reported that a modified 6MWT (m6MWT) using a 10-metre walkway can cause a deterioration in lower limb muscle strength and standing balance in people with MS, however the effects on gait mechanics are unknown [22]. While there is no standardised 6MWT protocol to assess mobility in people with MS, modified protocols that involve frequent 180-degree turns have been shown to be more physically demanding when compared to using square walkways [25].

Identifying changes in gait kinematics and kinetics due to walking-related fatigue would assist in designing gait re-training interventions that aim to increase walking capacity. The aim of this study

was to investigate the effect of six minutes of walking on perceived fatigue, exertion, and spatiotemporal, kinematic and kinetic gait parameters in people with MS with moderate levels of disability, and to compare these effects with those induced in healthy control participants. We hypothesized that in people with MS with moderate disability, the m6MWT would induce increased levels of perceived fatigue and exertion, with an associated deterioration in gait mechanics, not seen in healthy control participants.

Methods

Participants

Thirty-four people with MS were recruited from the MS Society of South Australia, a multidisciplinary hospital clinic and private physiotherapy clinics in South Australia via email and newsletter advertisements. Eligible participants were required to have a confirmed diagnosis of MS from a neurologist and an Expanded Disability Status Scale (EDSS) score of 3.0-6.0 indicative of moderate disability (people who can ambulate, yet have a number of mild to moderate neurological impairments.) [26]. Participants were excluded if they: (i) had an exacerbation or relapse of MS within the past 3 months; (ii) used medication prescribed for fatigue or mobility such as Amantadine, Modafinil or Fampridine; (iii) had significant cardiac or respiratory disease; (iv) suffered from severe depression; or (v) had arthritis, fibromyalgia, pain or other illness that severely limited their walking. Ten healthy controls well matched in terms of age, sex, height and weight were recruited from the hospital and university staff. All participants provided informed written consent prior to involvement in the study, which was approved by the Repatriation General Hospital Research and Ethics Committee (EC00191).

Protocol

Participants in the MS group were initially screened for disease severity with the EDSS by a certified Neurostatus investigator (www.neurostatus.net). Participants were then randomised using sealed,

opaque envelopes to either a six minute walk or a six minute rest trial, and returned within 2 weeks to complete the other trial at the same time of day. Measures of acute fatigue and gait mechanics were collected immediately before and after the 6-minute walk/rest trials.

For the walking trial we used a m6MWT version with the aim to induce fatigue [22]. Participants were instructed to walk back and forth along a 10-metre walkway as fast as possible for six-minutes following the instructions "walk as fast as you comfortably can, bearing in mind that you will be walking for six minutes". Participants were permitted to use assistive devices (i.e. canes) if required. Distance walked was recorded at each minute. For the rest trial, participants were instructed to sit comfortably in a chair and relax for six minutes. Healthy control participants completed the m6MWT trial only.

Self-reported fatigue and perceived exertion

Participants indicated their fatigue levels using the Visual Analogue Scale for Fatigue (VAS-F) immediately before and after each six-minute trial. [27] Perceived exertion was recorded at each minute for both rest and walking trials using the 10-point Modified Borg Rating of Perceived Exertion (RPE) scale [28].

Gait analysis

Gait analyses were performed using an eight-camera Vicon MX3 system (Vicon, Oxford, UK). The camera system recorded the trajectories of reflective markers attached to the body according to the Helen Hayes lower limb marker set [29] as participants walked along a level floor walkway. External ground reaction forces were also measured from clean foot strikes onto one of four AMTI force plates (AMTI, Watertown, MA) embedded in the floor. Repeated walking trials were undertaken until at least three trials with satisfactory marker data and force data from each leg were recorded.

Vicon Nexus software (v1.4) was used to process the acquired data and calculate spatiotemporal parameters and joint kinematics (joint angles) and kinetics (internal joint moments and powers) of the hip, knee and ankle for both left and right limbs. Customised LabView software (v7.1, National Instruments, Texas, USA) was used to extract spatiotemporal, kinematic and kinetic parameters of interest from a gait cycle of each walking trial. Appendix A includes the list of parameters extracted for analysis.

Mean spatiotemporal, kinematic and kinetic data for both limbs were calculated from three walking trials for each participant. The 'more affected' and 'less affected' limbs of the MS participants were determined by the level of muscle power within the pyramidal score of the EDSS examination. There was no significant difference between gait data of left and right legs for the healthy controls so the left leg was analysed as the majority of MS participants exhibited a 'more affected' left side.

Statistical analysis

Data were analysed using SPSS version 19 (IBM, Chicago, USA). An initial inspection of the data for normal distribution revealed VAS-F to be positively skewed, so this variable was log transformed to permit parametric analysis. In the MS group, within-subject pairwise comparisons were used to determine minute-by-minute change in distance walked during the m6MWT. Independent samples t-tests were used to compare RPE scores and distance walked for each minute of the m6MWT between the healthy controls and people with MS. For the MS group a repeated measures 2 factor General Linear Model Analysis of Variance was used to investigate the effect of six minutes of walking on perceived fatigue and gait parameters with condition (rest versus walking) and time (pre or post 6 minute condition) as factors. For healthy controls a paired t-test was used to compare perceived fatigue and all gait parameters before and after the m6MWT. For all tests, the level of statistical significance was set to 0.01 to account for multiple comparisons and minimise the chance of type I errors.

Results

Thirty-four participants (26 female) with MS, mean age 49.1 ± 10.4 years, 8.2 ± 7.9 years since diagnosis, completed the study without incident. At the initial assessment, participants had EDSS scores (mean ± SD) of 3.7 ± 0.7, median (range) 3.5 (3-6). Gait data for two MS participants were unusable due to data corruption, leaving data for 32 people with MS (24 female), mean age 50.3 ± 9.9 years, EDSS 3.6 ± 0.6, median 3.5 (3-6), height 167.0 (1.0) cm, weight 77.2 (17.7) kg for inclusion in the analyses. All data were successfully obtained from the 10 healthy controls (7 females) with a mean age 45.1 ± 14.0 years, height 169.2 ± 8.7 cm, weight 78.7 ± 13.7 kg.

Self-reported fatigue and perceived exertion

In the MS group there was a significant effect of condition, $F(1,33)=18.93$, $p<0.001$, time $F(1,33)=9.66$, $p<0.001$ and interaction $F(1,33)=66.78$, $p<0.001$ on self-reported fatigue, demonstrating an increase of fatigue following the m6MWT compared with rest (Figure 1). Paired t-test showed a significant increase in exertion level in MS compared with healthy controls in only the last minute of the m6MWT ($p<0.01$) (Figure 2). In the healthy controls, self-reported fatigue increased following the m6MWT, although this was not statistically significant ($p=0.05$).

Insert Figure 1 about here

Distance walked

The total distance walked during the m6MWT was significantly less in the MS group ($p<0.001$), compared with the healthy control group, as was the distance walked in each minute of the test (all $p<0.001$) (Figure 2). Within group pairwise comparisons showed no differences in the distance walked between each minute for the healthy control group. In the MS group, there was a trend

towards a reduced distance walked in the final three minutes compared to the first minute (minute 4, p=0.02, minute 5, p= 0.02, minute 6, p= 0.01).

Insert Figure 2 about here

Gait parameters – healthy control group

Table 1 shows that the healthy controls significantly increased their walking speed and cadence following the m6MWT ($p<0.01$), and that joint kinematic parameters did not change significantly. Table 2 shows significant increases in joint kinetic parameters following the m6MWT in the healthy control group, including maximum hip flexor moment, maximum knee extensor moment, maximum knee flexor moment during stance, maximum ankle dorsiflexor moment and maximum ankle plantar flexor moment (all $p < 0.01$). There was also a significant increase in maximum hip power absorption in mid stance, maximum hip power generation in stance and ankle push-off power generation following the m6MWT (all $p < 0.01$).

Gait parameters – MS group

The gait data for people with MS presented in table 1 shows that there was no significant condition*time interaction effects on spatiotemporal parameters, indicating a similar change in speed, cadence, double support, stride and step length following the walking and rest periods. There was only one condition*time interaction effect for kinematic parameters, which showed a decrease in ankle dorsiflexion angle at initial contact in the more affected leg following the m6MWT, relative to the rest condition ($F_{1,31} = 7.95$, $p < 0.01$) (Table 1).

Insert Table 1 about here

On the more affected side there was a number of significant condition*time interaction effects for gait kinetics. These results showed that following the m6MWT relative to the rest condition, there was an increased maximum hip flexor moment in swing ($F_{1,31} = 11.90$, $P < 0.01$), increased knee flexor moment in early stance ($F_{1,31} = 11.01$, $p < 0.01$) and increased hip power absorption in late stance ($F_{1,31} = 11.33$, $p < 0.01$) (Table 2).

On the less affected side there were significant condition*time interaction effect for gait kinetics showing that following the m6MWT relative to the rest condition, there was an increased maximum hip extensor moment ($F_{1,31} = 16.71$, $p < 0.01$), increased knee power absorption in early stance ($F_{1,31} = 15.08$, $p < 0.01$) and increased ankle power absorption ($F_{1,31} = 12.36$, $p < 0.01$) (Table 2).

Insert Table 2 about here

Discussion

Healthy control participants

The healthy control participants walked with significantly increased speed and cadence following the m6MWT. While the instruction for the instrumented gait analysis was to walk at comfortable speed, healthy controls appeared to carry over some speed from the m6MWT for which they were instructed to walk 'as fast as you comfortable can'. While there were no changes in gait kinematics, kinetic changes revealed significant increases in positive work, which correspond to the increased speed and cadence. In particular, the increases in maximum hip flexor moment and power generation, and ankle plantar flexion moment and power generation evident post m6MWT demonstrate key speed related gait kinetic increases [30].

People with MS

Self-reported fatigue and perceived exertion

The study findings indicate that six minutes of walking elicited acute changes in self-reported fatigue and perceived exertion and demonstrable changes in gait mechanics in people with MS with moderate levels of disability. The m6MWT, therefore appears to be a challenging task for people with MS that requires significant effort (Figure 2) and increases self-reported fatigue (Figure 1), changes that were less evident in healthy controls. Previous work examining the energy cost of walking in people with mild MS during the 6MWT has not shown any association with self-reported fatigue [31] with cardiorespiratory demands or exertion dyspnoea [32]. However, associations between self-reported fatigue and reduced distance and velocity have been reported [33, 34], which likely relate more directly to the motor impairments observed in gait [16].

Walking speed during m6MWT

The MS group also walked significantly shorter m6MWT distances compared to healthy controls with a trend towards reduced gait speed in the second half of the m6MWT (Figure 2). This finding is supported by other studies that have found reduced speed in the last one to five minutes of the 6MWT in people with MS [35, 36]. Gait slowing appears to coincide with steady state aerobic metabolism, as Motl et al. demonstrated with physiological measurements during the final three minutes of the 6MWT [37]. A 'deceleration index' may be a useful measure of walking behaviour in MS [7], as a recent study showed 'decline' in walking speed , rather than 'mean' walking speed over the 6MWT to have a stronger association with self-reported fatigue [34]. While there has been some support for a shortened two-minute walk test to assess walking ability in people with MS [36], our findings suggests six minutes may be required to gain important clinical information on walking-induced fatigue.

Spatiotemporal parameters

The lack of change in spatiotemporal parameters is consistent with a previous study, which found no changes in spatiotemporal parameters other than reduced cadence following a 6MWT in a slower and more disabled group of people with MS [23]. While our group of people with MS with moderate disability levels were able to maintain similar spatiotemporal features, instrumented gait analysis identified some key kinematic and kinetic changes indicative of movement compensations and poor movement control following the m6MWT.

Kinematics

The only kinematic changes detected following the m6MWT was the reduced ankle dorsiflexion at initial contact. This may indicate increased motor fatigue in the tibialis anterior muscle, which is susceptible to activity-induced fatigue in people with MS [11, 14, 38]. A delayed activation of the tibialis anterior muscle after initial contact in people with MS has also been previously measured [39], with reduced dorsiflexion angles observed in more mildly disabled groups of people with MS [40, 41]. The less dorsiflexed position following the m6MWT may indicate a further delay of tibialis anterior activity upon loading [39]. Assisting dorsiflexion is therefore a target for orthotic intervention with functional electrical stimulation shown to increase dorsiflexion angle [42,43], with a twelve-week training program shown to reduce perceived exertion over a two-minute walk test [43]. Both functional electrical stimulation [44,45] and a dynamic dorsiflexion orthosis [46] have also demonstrated an ability to improve walking efficiency in people with MS. Assisting toe-clearance in swing is an important objective, since trips are the most frequent type of falls experienced by people with MS [47]. This compensation may be aided by progressive resistance training since this has previously been shown to lead to improved toe clearance during gait in people with MS [48].

Kinetics

There were a number of kinetic changes that suggest fatigue-induced increases in internal moments and power absorption in stance for both the more and less affected legs in the MS group. In the

more affected leg, the increase in knee flexor moment at initial contact indicates poor neuromuscular control at the knee. During early stance the knee extensor moment, used as a shock absorber, which has previously been shown to be reduced in people with MS when compared to healthy controls [49], showed no further reduction following the m6MWT. The increase in hip power absorption on the more affected side may indicate a useful compensation for reduced neuromuscular control at the hip, as a previous study as shown that reduced hip power absorption is associated with increased disability levels in people with MS [49].

In the less affected leg there was an increase in knee power absorption at loading response, which has been previously shown to correlate with fatigue impact using the modified fatigue impact scale [16]. The increased ankle power absorption on the less affected leg in stance phase may also indicate poor eccentric control in the ankle plantarflexors due to muscle fatigue. A recent study has shown that plantarflexor strength has been shown to be a predictor of walking capacity as measured by the 6MWT [50]. All of the observed increases in 'negative work' during stance following the m6MWT are likely to contribute to energy-absorbing and inefficient movement strategies [51]. This negative work may indicate walking-induced muscle fatigue, supported by previous findings of walking-induced reductions in lower limb strength and balance control in people with MS [22]. Furthermore, another recent study also demonstrated that reduced 6MWT walking distance is associated with reduced muscle oxidative capacity in people with MS [52].

There were also some compensatory kinetic changes that indicate increased positive work in both the more and less affected legs of the MS group. The large increase in hip extension moment in the less affected leg demonstrates some capacity to work harder as a compensation to maintain speed. Increased hip flexor moment at 'pull-off' is also likely to assist forward momentum to compensate for reduced ankle power at push-off which has been reported in people with MS compared with heathy controls [39, 49]. The observed increases in positive work may also contribute to the

reported increase in effort and fatigue in people with MS, compared to healthy controls. People with MS are likely to increase the underlying central corticomotor activity needed to increase or maintain muscle power during walking, which could contribute further to walking-induced fatigue [38, 53-55].

Study Limitations

Our study used a modified version of the 6MWT with a 10m walkway and frequent 180 degree turns, instead of a more standardised 6MWT protocol with longer walking paths. Therefore, the distances, fatigue and effort cannot be compared to other studies. It has been demonstrated that a 6MWT involving walking in a corridor with 180 degree turns is significantly more demanding in terms of physiological energy cost, when compared to square walking using 90 degree turns [25]. Our method however, was consistent throughout the study and did result in a 'fatiguing walk'. Our gait analysis was also limited to the sagittal plane, therefore any movement compensations in other planes were not characterised in the present study. In addition, our results may only be inferred to people with moderate levels of disability as we did not include people with MS with more severe disability, who are likely to demonstrate more pronounced changes in gait following six-minutes of walking [23]. Finally, it is acknowledged that the sample of healthy normal participants included for comparison purposes was small (n=10) and was therefore not an ideal control group for the larger sample of MS participants (n=34).

Conclusion

This study provides important information about walking behaviour over extended distances in people with MS. In particular, joint kinetics revealed increases in moments and power absorption at the hip, knee and ankle during stance phase, which are likely to increase the energy cost of walking [43]. The large increase in hip extensor moment in the less affected side and hip flexor moment in the more affected side may indicate some capacity for positive compensatory output to maintain speed. These walking induced gait changes should be monitored and targeted within therapeutic

interventions that aim to increase walking capacity and reduce walking-induced fatigue in people with moderately disabled MS.

Declaration of interest

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