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Orthotic and therapeutic effect of functional electrical stimulation on fatigue induced gait patterns in people with multiple sclerosis

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ABSTRACT

Purpose: To assess the orthotic and therapeutic effects of prolonged use of functional electrical stimulation (FES) on fatigue induced gait patterns in people with Multiple Sclerosis (MS).

Method: Thirteen people with MS completed 3D gait analysis with FES off and on, before and after a fatiguing 6-minute walk, at baseline and after 8 weeks of use of FES.

Results: Eleven participants completed all testing. An orthotic effect on gait was not evident on first use of FES. However, therapeutic effects on gait after 8 weeks use were generally positive, including increases in walking speed due to improved neuromuscular control and power generated at the hip and ankle of the more affected limb. The action of FES alone was not sufficient to overcome all fatigue related deficits in gait but there was evidence 8 weeks use of FES can ameliorate some fatigue effects on lower limb kinetics, including benefits to ankle mechanics involved in generating power around push-off during stance.

Conclusions: Eight weeks of FES can benefit the gait pattern of people with MS under non-fatigued and fatigued conditions.
Implications for rehabilitation:

In some people with MS prolonged use of FES may be necessary before observing positive orthotic effects

Improvements in the neuromuscular control of the more affected lower limb may develop with prolonged use of FES in people with MS

Only some therapeutic benefits of FES are maintained during fatigued walking in people with MS

FES may be considered as a gait retraining device as well as an orthotic intervention for people with MS
Introduction:

Difficulty walking [1] is one of the most common problems experienced by people with Multiple Sclerosis (MS). The gait of people with MS compared to healthy individuals is characterised by reduced walking speed [2-7], which may be due to decreases in cadence [4,7], stride length [2,3,7] or step length [4,5,7]. Walking speed has been shown to progressively decrease with disease severity in part due to concomitant decreases in step length [8]. Reduced walking speed is also likely a strategy to counter impaired balance, which is common in people with MS [9], by prolonging periods of double support during stance [2,3,7].

Deviations from typical kinematic patterns of the lower limbs during gait are also observed in people with MS [10]. Increased hip flexion [2], knee flexion [2,5], and ankle plantarflexion [2,3] at initial foot contact and early stance, and decreased hip extension [2,5], knee extension [2] and ankle plantarflexion [2,11] around late stance are commonly reported features, with the decreased hip extension around late stance and decreased knee extension (i.e. increased flexion) around late swing and foot contact likely contributing to decreases in step length and walking speed. Furthermore, reductions in joint kinetics, namely internal hip, knee and ankle moments and powers have also been reported [5,12], with the patterns of joint kinetics also revealing inefficiencies in the absorption and generation of power during gait which are likely related to neuromuscular factors [12], including deficits in strength of the knee extensor and ankle dorsiflexor muscles [13].

A consequence of these abnormalities in the neuromuscular control of gait is an increased metabolic cost of walking [14] which in turn can worsen activity related fatigue [15], another major problem experienced by people with MS [16]. Fatigue in people with MS typically exacerbates pre-existing deficits in gait, with fatigued individuals demonstrating slower walking speeds with associated shorter step lengths and prolonged periods of double support compared to non-fatigued individuals [17]. Moreover, signs of impaired neuromuscular control of gait mechanics have been associated with the severity of fatigue experienced by people with MS [18,19].

Perceptions of fatigue have also been associated with impaired central drive [20] contributing to a reduction in lower limb strength [21] which is a factor in gait deficits exhibited by people with MS [9,22]. The ankle dorsiflexor muscles are particularly susceptible to the effects of fatigue, with both central and peripheral factors, including impaired central drive, contributing to weakness of these muscles [23]. Weakness of the ankle dorsiflexors can result in foot drop, a common problem of gait in MS [24], which is characterised by a lack of control of ankle dorsiflexion resulting in an inability to effectively clear the foot during the swing phase of gait. This can result in poor pre-positioning of the
foot in late swing and decreased ankle dorsiflexion at initial foot contact during stance [2,3], which can worsen with fatigue [18].

Functional electrical stimulation (FES) is an increasingly common orthotic intervention used to assist weak dorsiflexor muscles and improve ankle control during gait [24]. FES acts by stimulating the common peroneal nerve thereby overcoming deficits in central drive to facilitate contraction of the muscles controlling dorsiflexion of the ankle. The immediate beneficial effects on gait of using FES, which include reported increases in walking speed [25], have been described as an ‘orthotic effect’ [26,27] and are suggested to be primarily due to improved biomechanics of walking [25,26]. When FES is used for the first time these effects have been termed an ‘initial orthotic effect’ of the stimulation [28]. Recent evidence shows the initial orthotic effects of FES on the gait of people with MS extend to improvements in the overall kinematic pattern of lower limbs during gait [27,29], including increased ankle dorsiflexion during swing [29,30], and at initial foot contact [29-31] leading to increases in stride length [29,32]. The maintenance of an orthotic effect with prolonged use of FES has been referred to as a ‘continuing orthotic effect’ [28]. This represents the difference in gait with and without FES at the same time point after prolonged use and reflects the day-to-day orthotic effect of the intervention.

There is data to suggest the use of FES can lead to enhanced cortical excitability, which may be maintained for a period after the stimulation is turned off [33]. This is proposed as a possible mechanism by which prolonged use of FES may lead to a strengthening of residual corticospinal pathways involved in muscle contraction [26]. This may contribute to observed ‘therapeutic effects’ of FES whereby improvements in gait may be achieved over time even with the stimulation off [25-27]. Terms describing the therapeutic effects of FES have recently been proposed by Taylor et al. (2013) [28]. Therapeutic effects of FES may include: (1) a ‘training effect’ which represents the difference achieved without FES at some time point after prolonged use compared to the difference without FES at the beginning of the intervention; and (2) the ‘total orthotic effect’ which represents the difference with FES at some time point after prolonged use compared to the difference without FES at the beginning of the intervention. This reflects the combined effect of the orthotic effect superimposed on the training effect over time. Positive training effects and total orthotic effects of FES on walking speed and ankle kinematics have been reported in people with MS [32].

Despite the increased interest in the effects of FES on gait in MS [29,30,32], no studies to date have investigated the initial orthotic effect of FES on fatigue induced changes in gait that occur in people with MS [18]. Additionally it remains unclear whether prolonged use of FES delivers continuing orthotic effects and therapeutic effects (i.e. training and total orthotic effects) which can mitigate
against fatigue induced changes in gait, such as worsening foot drop. Therefore the aim of this study was to assess the orthotic and therapeutic effects of 8 weeks use of FES to the ankle dorsiflexors on fatigue induced changes in gait in people with MS. The effects assessed included the baseline initial orthotic effect before 8 weeks use of FES and the continuing orthotic effect after 8 weeks use of FES under non-fatigued and fatigued conditions, and the training effect and total orthotic effect under non-fatigued and fatigued conditions after 8 weeks use of FES. As a part of the study the effect of activity related fatigue on gait in people with MS was also assessed.

**Methods:**

**Participants**

Thirteen people with MS were recruited from a hospital MS rehabilitation clinic and private physiotherapy clinics in metropolitan Adelaide, Australia, and from newsletters of the MS Society of South Australia. Participants were eligible for inclusion if they had: (1) a definite diagnosis of MS; (2) a moderate level of disability as assessed by the Expanded Disability Severity Scale (EDSS) [34] with a score of between 3 to 6; (3) difficulty clearing one foot more than the other when walking (i.e. unilateral foot drop); and (4) the ability to walk for 6 minutes unaided or with a walking stick. Participants were excluded if they: (1) reported an exacerbation/relapse of MS in the 3 months prior to consenting to the study; (2) were taking medications prescribed for fatigue (e.g. Amantadine, Modafinil) or mobility (e.g. Fampridine); (3) had contraindications for the use of FES including (a) skin lesions or cancerous cells at the site of electrode placement, and/or (b) presence of a demand-type pacemaker, defibrillator or any electrical or metallic implant; (4) regularly used an ankle foot orthosis (AFO) to assist their walking; and (5) had passive ankle flexion to less than plantargrade (i.e. 90° dorsiflexion) due to spasticity. The study protocol was approved by the local Ethics Committee and all participants provided written informed consent prior to participating in study procedures.

**Protocol**

A commercial FES system (NESS L300®, Bioness Inc., USA) was used during the study to deliver low level electrical stimulation to the common peroneal nerve of participants. The system comprised a stimulating cuff, incorporating the stimulating electrodes, which was worn on the leg just below the knee, a hand held control unit to turn on/off and adjust the stimulation, and a foot switch sensor worn in a shoe to detect when the foot was on and off the ground to control the timing of the stimulation.

Participants attended the South Australian Movement Analysis Centre (SAMAC) at the Repatriation General Hospital, South Australia, on three separate occasions: an initial assessment and system
setup session; a baseline assessment within 3-7 days of the initial assessment; and a week 8 assessment within 3-7 days of completing 8 weeks use of FES. During the initial assessment session participants were screened for disease severity by a certified Neurostatus investigator (www.neurostatus.net) and were fitted with the FES system (NESS L300®, Bioness Inc., USA) to the more affected limb, reported as having foot drop, by a qualified orthotist. The stimulation parameters were adjusted individually for each participant. A symmetric 30Hz waveform with stimulation pulse duration of 200μsec was most commonly used with each participant with the intensity of the stimulation adjusted in 1mA steps. The intensity of stimulation used ranged between 19 to 42mA. If necessary adjustments of advanced settings of the system controlling the stimulation were made during gait to further improve ankle control during early stance. These typically involved incremental adjustments of one or two steps to prolong the time taken to ramp up to and ramp down from the set intensity level, and/or the length of time from initial foot contact before the stimulation started to ramp down. Additionally, the control unit allowed the participants to increase or decrease the stimulation in 2.5mA increments if more or less assistance was required throughout the course of a day. Participants were provided with the system to use at home for the duration of the 8 week intervention which incorporated a 3 week conditioning protocol as per the manufacturer’s instructions.

At the baseline and week 8 assessments, participants completed a 3-dimensional instrumented gait analysis immediately before and after a modified version of the six minute walk test (6MWT) [35] undertaken with the assistance of FES. The 6MWT involved walking back and forth along a 10m walkway with 180° turns at each end and was used as a means of inducing activity related fatigue [15,21]. Gait analysis was conducted under four conditions at each session in the following order: (1) before the 6MWT with the FES off; (2) before the 6MWT with the FES on; (3) after the 6MWT with the FES on; and (4) after the 6MWT with the FES off. At the baseline and week 8 assessments, participants also completed a series of strength, balance, mobility, and perceived fatigue related measures the results of which are reported elsewhere [under review].

**Gait analysis**

Three dimensional instrumented gait analysis was performed using an eight-camera Vicon MX3 motion capture system (Vicon, Oxford, UK). Reflective markers (14mm diameter) were attached using double sided tape to the participants’ pelvis and legs according to the Vicon Plug-in-Gait lower limb marker set [36]. A knee alignment device (Motion Lab Systems, USA) was positioned on each knee during a static standing trial to define each knee flexion-extension axis. The trajectories of all the markers were recorded while participants walked along a level walkway. All walking tests were
undertaken in shoes to accommodate the foot switch sensor of the FES system. To ensure repeatable placement of foot markers on the shoes participants wore the same shoes at each session and a pen mark was made on each shoe to indicate the location of the heel and toe markers. The position and alignment of the heel and toe markers was then checked with a guide comprising a small sheet of clear plastic with parallel lines marked on it. 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 of the walkway. Walking trials were repeated until at least three successful trials with satisfactory marker data and force data from each limb were recorded for each condition.

Vicon Nexus software (v1.4, Vicon, Oxford, UK) was used to process the acquired data and calculate spatiotemporal parameters, lower limb joint kinematics (joint angles) and joint kinetics (internal joint moments and powers) of the hip, knee and ankle for both the more and less affected limbs. Joint kinetics were normalised to bodyweight. Customised LabView code (v7.1, National Instruments, Texas, USA) was used to extract spatiotemporal and lower limb joint kinematic and kinetic parameters from a single gait cycle of each walking trial for each condition (see appendix A). For each participant mean spatiotemporal, kinematic and kinetic parameters for both limbs were calculated from three walking trials for each condition.

**Statistical analysis**

Before performing statistical analyses normal distribution of data was checked and confirmed based on the z-scores of skewness and kurtosis, and parametric analyses were utilised. To assess the fatigue effect of the 6MWT and the initial orthotic effect of the FES on gait, an analysis of variance with factors of “walk” (pre-6MWT vs post-6MWT) and “FES” (off vs on), respectively, was conducted on the baseline gait data. The same analysis was repeated on the gait data from the week 8 assessment to assess the fatigue effect of the 6MWT and the continuing orthotic effect after prolonged use of the FES system. To assess the training effect of FES when non-fatigued, the pre-6MWT FES off condition at baseline was compared to the pre-6MWT FES off condition at week 8 using a paired t-test. Similarly, to assess the training effect of FES when fatigued the post-6MWT FES off condition at baseline was compared to the same condition at week 8 using a paired t-test. Finally, paired t-tests were also used to assess the total orthotic effect of prolonged FES use when non-fatigued by comparing the pre-6MWT FES off condition at baseline to the pre-6MWT FES on condition at week 8, and when fatigued by comparing the post-6MWT FES off condition at baseline to the post-6MWT FES on condition at week 8. Pairwise comparisons were used to assess the training and total orthotic effects as they enabled the analysis to focus on differences between specific pairs of fatigue and FES conditions which were of most interest clinically. All data were
analysed using SPSS version 22 (IBM, Chicago IL USA), with the level of statistical significance for all tests set at p<0.05. Alpha was not adjusted for multiple comparisons due to the exploratory nature of the study and the possibility of increasing type II errors [37].

Results

Twelve of the thirteen participants who enrolled in the study completed all study procedures. One subject withdrew due to an injury unrelated to the study procedures. Additionally, one subject was excluded after reporting a relapse during the course of the study. Data from the remaining 11 participants is presented here. Participants were mostly female (7/4) with a mean age of 47 years (range 34-60 years), and had moderate disability with a mean EDSS rating of 3.5 (range 3-4). There was no significant difference in the distance walked during the 6MWT at the baseline (372 ± 114m) and week 8 assessments (384 ± 128m) (p=0.618). All participants reported an increase in perceived fatigue measured on a visual analogue scale after the 6MWT, with no significant difference between the change in perceived fatigue after the 6MWT reported at the baseline and week 8 assessments.

The mean spatiotemporal and kinematic parameters for the more affected and less affected sides for each walking condition at baseline and week 8 are presented in table 1. The corresponding kinetic parameters are summarised in table 2.

Fatigue effect of 6MWT at baseline

At baseline the fatiguing 6MWT had no effect on any of the spatiotemporal parameters but differences were observed in lower limb mechanics of the more and less affected sides. Specifically, after the fatiguing 6MWT the more affected side showed decreased dorsiflexion at initial contact (F1,10=7.31, p=0.022), increased plantarflexion in early stance (F1,10=5.96 p=0.035), and decreased maximum dorsiflexion during swing (F1,10=10.63, p=0.009). Lower limb kinetics of the more affected side during stance showed an increased maximum hip extensor moment (F1,10=5.62, p=0.039), increased hip power generation during early stance (F1,10=6.10, p=0.033), increased maximum knee flexor moment toward late stance (F1,10=16.76, p=0.002), and increased knee power absorption in early stance (F1,10=9.10, p=0.013). On the less affected side there was increased knee flexion in stance (F1,10=6.08, p=0.033), increased ankle plantarflexion in early stance (F1,10=6.24, p=0.032) and increased ankle power absorption in stance (F1,10=5.61, p=0.039). There were no observed changes in lower limb mechanics of the less affected side during swing.

Fatigue effect of 6MWT at week 8
At week 8, after the fatiguing 6MWT, the participants showed a decrease in the period of single support on the more affected side ($F_{1,10}=5.25$, $p=0.045$). Changes in lower limb mechanics of the more affected side were mostly seen at the ankle with less ankle dorsiflexion at initial contact ($F_{1,10}=15.03$, $p=0.003$) and mid stance ($F_{1,10}=5.78$, $p=0.037$), greater plantarflexion in late stance around push-off ($F_{1,10}=7.65$, $p=0.020$), and less dorsiflexion in swing ($F_{1,10}=15.08$, $p=0.003$). There was an accompanying decrease of the maximum ankle dorsiflexor moment in early stance ($F_{1,10}=9.37$, $p=0.012$). On the less affected side ankle dorsiflexion in midstance decreased ($F_{1,10}=6.12$, $p=0.033$) and ankle plantarflexion in late stance increased ($F_{1,10}=9.35$, $p=0.012$).

**Initial orthotic effect of FES at baseline**

At baseline a significant initial orthotic effect of FES was only observed at the knee of the more affected side with decreased knee flexion during early stance ($F_{1,10}=10.46$, $p=0.009$) and increased knee extension in mid stance ($F_{1,10}=9.26$, $p=0.012$) accompanied by a decreased knee extensor moment in early stance ($F_{1,10}=8.46$, $p=0.016$).

**Continuing orthotic effect of FES at week 8**

At the week 8 assessment a continuing orthotic effect of the FES led to a 0.05m/s increase in walking speed ($F_{1,10}=21.46$, $p=0.001$) through concomitant increases in cadence (1.4 steps/min, $F_{1,10}=7.87$, $p=0.019$) and stride length (0.04m, $F_{1,10}=12.94$, $p=0.005$). There was an associated decrease in the period of double support on the more affected side (0.8%, $F_{1,10}=11.18$, $p=0.007$) and a similar decrease on the less affected side (0.9%, $F_{1,10}=13.26$, $p=0.005$). There was also an increase in the period of single support on the less affected side (1.6%, $F_{1,10}=5.38$, $p=0.043$).

Changes in lower limb kinematics of the more affected side due to a continuing orthotic effect of the FES included greater hip extension in stance (0.9°, $F_{1,10}=6.22$, $p=0.032$), less ankle plantarflexion in early stance (1.3°, $F_{1,10}=13.11$, $p=0.005$), and greater hip flexion in swing (0.9°, $F_{1,10}=6.08$, $p=0.033$). There was a significant interaction of fatigue due to the 6MWT and FES on maximum ankle plantarflexion of the more affected side in late stance ($F_{1,10}=5.18$, $p=0.046$) with plantarflexion increasing by 0.7° with FES when non-fatigued (i.e. before the 6MWT) and decreasing slightly by 0.7° with FES when fatigued (i.e. after the 6MWT).

The associated changes in lower limb kinetics of the more affected side were characterised by an increased hip flexor moment in stance ($F_{1,10}=16.14$, $p=0.002$), increased ankle dorsiflexor moment ($F_{1,10}=6.45$, $p=0.029$) and plantarflexor moment in stance ($F_{1,10}=8.36$, $p=0.016$). These changes
were associated with increased hip power generation in early stance ($F_{1,10}=17.94, p=0.002$), increased hip power absorption in mid-stance ($F_{1,10}=5.06, p=0.048$), and increased hip power generation ($F_{1,10}=6.36, p=0.030$) and increased ankle power generation ($F_{1,10}=6.51, p=0.029$) in late stance.

The only significant change in lower limb kinematics on the less affected side due to the continuing orthotic effect of FES at week 8 was increased hip extension in stance ($F_{1,10}=10.01, p=0.010$). Changes in lower limb kinetics included an increased hip extensor moment in stance ($F_{1,10}=11.96, p=0.006$) and increased power absorption at the knee in early stance ($F_{1,10}=7.33, p=0.022$) and late swing ($F_{1,10}=9.61, p=0.011$).

There were significant interactions of fatigue due to the 6MWT and FES on hip flexion in swing ($F_{1,10}=16.12, p=0.002$) and ankle dorsiflexion at initial contact ($F_{1,10}=14.50, p=0.003$) of the less affected side. Hip flexion decreased with FES before the 6MWT and increased slightly after the 6MWT with FES, while ankle dorsiflexion increased slightly more with FES after the 6MWT compared to before the 6MWT.

**Insert table 2 about here**

**Training effect of FES**

When non-fatigued and fatigued the training effect of 8 weeks use of FES was seen in changes of lower limb kinetics with no significant changes in spatiotemporal or lower limb kinematic parameters.

**Non-fatigued**

When non-fatigued, the training effect on gait of using FES for 8 weeks resulted in increased power absorption at the ankle in stance (0.09 W/kg, 95%CI 0.02 to 0.16, $p=0.013$) and increased power absorption at the knee in late swing (0.29 W/kg, 95%CI 0.11 to 0.47, $p=0.005$) on the less affected side.

**Fatigued**

In contrast, when fatigued, the training effect resulting from using FES was only seen in the kinetics of the more affected limb with an increased power absorbed at the knee in early stance (0.43 W/kg, 95%CI 0.1 to 0.77, $p=0.016$) and in late swing (0.39 W/kg, 95%CI 0.18 to 0.60, $p=0.002$).

**Total orthotic effect of FES**
Non-fatigued

When non-fatigued, the total orthotic effect from prolonged use of FES led to an increased walking speed (0.07 m/s, 95%CI 0.002 to 0.147, p=0.045) and cadence (3.5 steps/min, 95%CI 0.6 to 7.06, p=0.047) with an associated decrease in the period of double support on the less affected side (1.9%, 95%CI 0.2 to 3.5, p=0.028).

The associated changes in gait mechanics were primarily seen in lower limb kinetics. The total orthotic effect when non-fatigued was characterised by an increased hip flexor moment in stance (0.15 Nm/kg, 95%CI 0.01 to 0.28, p=0.040), increased hip power generation in late stance (0.30 W/kg, 95%CI 0.49 to 0.55, p=0.024) and increased knee power absorption in late swing (0.38 W/kg, 95%CI 0.02 to 0.74, p=0.042) on the more affected side. On the less affected side there was increased knee power absorption in late swing (0.56 W/kg, 95%CI 0.40 to 0.77, p<0.001).

Fatigued

The total orthotic effect on gait when fatigued produced some significant changes in lower limb kinetics whereas spatiotemporal parameters and lower limb kinematics showed no real change. Changes in gait mechanics on the more affected side included an increased hip flexor moment in stance (0.12 Nm/kg 95%CI 0.007 to 0.23, p=0.039), increased ankle power generation in late stance (0.55 W/kg, 95%CI 0.07 to 1.03, p=0.029), and increased knee power absorption in late swing (0.51 W/Kg, 95%CI 0.17 to 0.85, p=0.007). Increased power absorption at the knee in late swing (0.54 W/kg, 95%CI 0.27 to 0.80, p=0.001) was also observed on the less affected side.

Discussion

The effect of the 6MWT at baseline and week 8 assessments resulted in fatigue induced changes in gait mechanics (i.e. ankle kinematics and joint kinetics of the hip, knee and ankle) consistent with previous work, thereby providing a sound basis with which to assess the effects of prolonged use of FES on fatigue induced changes in gait in people with MS. On average the initial orthotic effect of the stimulation delivered by the FES system was minimal at the baseline assessment. A greater range of positive continuing orthotic effects, including clinically meaningful increases in walking speed and improved neuromuscular control of the more affected lower limb, were observed following 8 weeks use of FES. Comparisons of gait mechanics with the FES off at the baseline and week 8 assessments revealed some changes in knee kinetics, particularly when fatigued, which suggest positive training effects are possible with prolonged use of FES. Overall the total orthotic effect of using FES for 8
weeks contributed to enhanced gait characterised by clinically meaningful increases in walking speed and improved neuromuscular control of the more affected lower limb.

**Fatigue effect of 6MWT**

Fatigue induced changes in gait were most evident at the ankle of the more affected limb. These included some changes observed at the baseline which persisted at week 8, with dorsiflexion in swing and dorsiflexion at initial foot contact significantly decreased following the 6MWT at both assessments. At baseline, these changes led to increased plantarflexion in early stance whereas at week 8 associated changes were seen later in stance with significantly less dorsiflexion around mid-stance, which may have contributed to a shorter period of single support on the more affected limb, and greater plantarflexion around push-off. The slightly flatter foot posture in early stance accompanying fatigue resulted in a decreased dorsiflexor moment in early stance on the more affected side. These changes confirm trends in our previous work investigating fatigue induced changes in gait after 6 minutes of walking [18], and may be indicative of reduced eccentric control of the dorsiflexor muscles resulting in ‘foot slap’, or a slow progression of the shank over the foot, due to hyperextension of the knee during stance.

At baseline, the change in ankle angle and foot posture in late swing and early stance of the more affected limb, combined with slight hyperextension of the knee during stance, likely contributed to observed changes joint moments and powers due to a shift in the position and orientation of the external ground reaction force with respect to the lower limb. The slight increase of knee hyperextension in stance coupled with the increased knee flexor moment and power absorbed at the knee of the more affected limb indicate fatigue-induced weakness which are likely to contribute to gait inefficiencies [18,38]. The increased hip extensor moment and hip power generation of the more affected side in early stance may represent some positive work needed to maintain support of the trunk and forward progression. These proximal changes in hip control could compensate for the aforementioned inefficiencies at the knee, as well as small decreases in the maximum plantarflexor moment and associated power generated at the ankle. It is worth noting that after 8 weeks of use of FES the fatiguing 6MWT did not lead to significant changes in the hip extensor and knee flexor moments and power absorbed at the knee during stance of the more affected limb. This suggests that prolonged use of FES may help to enhance the neuromuscular control of the limb receiving FES thereby assisting with improving the efficiency of gait after a fatiguing walk.

**Initial orthotic effect of FES**
At baseline, the orthotic effect upon first using the FES system was only seen at the knee of the more affected limb. There was no significant orthotic effect at the ankle or on walking speed. The observed changes at the knee included a significant decrease in maximum knee flexion during early stance followed by significantly increased knee extension, moving into hyperextension, later in stance. The decreased knee flexion likely contributed to the decreased maximum knee extensor moment seen in early stance. The increased (hyper)extension during midstance resulting from first walking with the FES on may be a strategy used by the participants to counteract the action of the FES in assisting forward progression of the shank over the ankle. A possible reason for this may be to avoid increased eccentric loading of the knee extensors, indicated by the decreased knee extensor moment, which are known to be weak in people with MS [9,22] and a predictor of their walking performance [39]. The pattern of knee hyperextension was slightly greater when fatigued with the FES on which may have been done to further compensate for eccentric demands imposed on the knee extensors which are likely to have been weakened further after the fatiguing walk [21]. Poor knee control has been shown to correlate with fatigue [19] and has been shown to deteriorate with walking induced fatigue [18,40]. This avoidance pattern leads to slightly reduced power absorbed at the knee of the more affected limb. However, with this loss of negative work at the knee during stance there may be an increase in the metabolic cost of walking [19], which has been recently shown to occur in people with MS who use FES [41] and walk at faster speeds (i.e. greater than 0.8m/s) as the current participants do.

The lack of a positive initial orthotic effect of the FES on walking speed may be due to the compensatory strategy described above and also the relatively fast walking speeds displayed by the participants which, when non-fatigued and with the FES off, was a mean of 1.18m/s. Recent evidence suggests that the greatest benefits of FES on walking speed are seen in people with MS who walk at speeds less than 0.8m/s [41]. The present data suggests that for people with MS who walk faster than 0.8m/s the benefits of FES on walking speed and gait mechanics may require more time before changes occur due to the need to become conditioned to the stimulation and adapt their gait pattern to its action. The findings of van der Linden et al [29,32] lend support to this suggestion since their work showed positive orthotic effects of FES on walking speed, spatiotemporal parameters and kinematics of the hip, knee and ankle in groups of people with MS with mean walking speeds around 0.8 m/s but still less than that of the participants in the current study. Additionally, our own findings indicating that clinically meaningful increases in walking speed (i.e. increases greater than or equal to 0.05 m/s [42]), are possible as part of the continuing and total orthotic effects of using FES for 8 weeks provide further support to the suggestion that people who display fast walking speeds may require more time to accrue orthotic benefits from FES.
**Continuing orthotic effect of FES**

After 8 weeks of use, there was a more pronounced continuing orthotic effect of the FES with a range of positive changes observed including significant increases in walking speed driven by improvements in lower limb kinematics and kinetics. The increased walking speeds were a product of significant increases in cadence and stride length, with the significant decrease in the period of double support on the more and less affected sides a result of the increased walking speed. The mechanisms driving the increases in walking speed appear related to changes in the patterns of joint moments and powers of the lower limbs.

The increased hip extension of the more and less affected sides assists with increasing stride length and contributes to moving the trunk over the leg during stance, leading to an increased flexor moment at the hip which was observed for both the more and less affected sides. For the more affected side this facilitated an increased power generation at the hip in late stance which helped to accelerate the leg into swing and producing greater hip flexion in swing. More importantly this significant increase in hip power generation late in stance, combined with (non-significant) increases in power generated at the ankle at the same time, were likely key factors responsible for the increases in walking speed. The significant increases in hip power generation and absorption earlier in stance likely represent improved neuromuscular control of the hip in transitioning from controlling flexion to initiating extension through eccentric and concentric muscle activity [12].

Similarly, the significant increase in power absorbed at the knee during stance of the less affected limb may add to an overall improved efficiency of the gait pattern after 8 weeks use of FES.

The FES may act to facilitate the observed kinetic changes in the more affected limb by firstly enhancing the eccentric control of the ankle following initial contact, leading to a significantly greater ankle dorsiflexor moment generated in early stance, and secondly by better controlling the forward progression of the shank over the ankle in mid-stance through improved contraction of the dorsiflexor muscles thereby assisting with a smoother second foot rocker during stance. The combined result of these actions enables the trajectory of the centre of pressure of the external ground reaction force to migrate further under the foot during stance likely contributing to a significantly greater plantarflexor moment generated at the ankle in late stance and also other kinetic changes proximal to the ankle.

The data suggests that the benefit of FES in improving the neuromuscular control of the more affected limb may be slightly greater when fatigued based on the size of change in the kinetic
parameters with FES on, particularly for the hip powers and ankle moments and powers, although no significant interactions were found for these parameters. It is interesting to note that in some instances the values return to non-fatigued levels. The fact that at both the baseline and week 8 assessments there was no change in ankle angles at initial contact or during swing, as has been reported previously [29,32], may be due to our inclusion criteria whereby our participants had an EDSS score range of 3-4 and could reach at least a neutral ankle angle. While the stimulation did not significantly change the angle of the ankle during gait it is evident it had other beneficial effects on mechanics of the lower limb, including at the ankle.

Training effect of FES

There were fewer training effects with the FES off when comparing gait mechanics at baseline and week 8 for non-fatigued (pre-6MWT) and fatigued (post-6MWT) conditions. The most significant training effect was the increased power absorption at the knee during early stance of the more affected limb when fatigued. This may have been due to increases in knee flexion velocity as the corresponding knee extensor moment in early stance showed no real change. This suggests that compared to baseline there was a greater capacity for eccentric knee extensor activity leading to greater negative work [12] performed by the lower limb during the loading phase in early stance.

This ability to sustain greater eccentric loading may have developed as a result of the continuing orthotic effect from prolonged use of FES, exemplified at week 8 by the increase in knee power absorption in early stance when non-fatigued and with the FES on. It is possible the continued orthotic effect of increased knee power absorption over the 8 weeks of FES use may well have led to improved eccentric control of knee flexion and a capacity to absorb more power at the knee. Lending support to this suggestion is separate data collected from the participants which revealed increases in knee extensor strength and smaller decrements in strength with fatigue over the 8 week period. Interventions that preserve or increase eccentric control of the knee may therefore be beneficial in this population [43] in conjunction with prolonged use of FES.

Total orthotic effect of FES

The total orthotic effects of the FES on gait when non-fatigued were mostly seen proximally at the hip of the more affected limb with a significantly greater hip extensor moment in early stance acting to assist with forward progression of the trunk, and greater power generated at the hip in late stance helping to accelerate the leg into swing and contributing to increases in cadence and walking speed. Part of the total orthotic effect may be attributable to the continued action of the stimulation to the dorsiflexor agonist muscles facilitating more controlled lengthening of the antagonist triceps
surae muscles. This may improve with the movement of the shank over the ankle in mid-stance and the migration of the external ground force under the foot producing greater moments about the joints of the lower limb and power generation in late stance. Spasticity of the triceps surae muscles is reported to affect walking speed in people with MS [44]. It is possible that at times the stretch delivered to the triceps surae muscles by the action of the stimulation on the dorsiflexors may have cause increased spasticity in these muscles. Although spasticity of the triceps surae muscles was not assessed in this study, the possibility of this occurring during swing may partly account for the increased power absorption at the knee in late swing which was observed under non-fatigued and fatigued conditions with the FES on.

The total orthotic effect of the FES on gait when fatigued produced increased power generation at the ankle of the more affected limb in late stance which suggests that the stimulation continues to support more effective triceps surae activity at push-off. Another effect was a significantly greater hip flexor moment in late stance, however this was not associated with a significant increase in hip power generation at the same time. The fact that the effects of increased walking speed and cadence were not maintained after a fatiguing walk suggest that FES alone, and positive changes in ankle mechanics, is not sufficient enough to mitigate all the effects of walking-induced fatigue. Future studies should determine if the total orthotic benefits of FES can be optimised by using it in combination with a structured training program that improves speed and endurance [45].

The results of this study are limited by the small number of participants, and the narrow range of disease severity (EDSS 3-4), however this sample represents ambulant people with MS with mild to moderate levels of disability, with a number of functional impairments, who typically present for assistance with their gait. Overall this study provides some important information for those clinicians prescribing FES for people with MS. In the present study clinically meaningful orthotic benefits to gait were not immediately evident when first using the FES system. This may have been due to the fast walking speeds of the participants and compensatory strategies used by the participants to counteract the action of the stimulation so as to minimise demands on the impaired neuromuscular control of the more affected lower limb during stance. However, with use over the 8 weeks, the action of the FES and accompanying changes in the pattern of neuromuscular control of the more affected limb led to clinically significant continuing and total orthotic effects of increased walking speed achieved through improved power generation at the hip and ankle in late stance. Instrumented gait analysis was also able to reveal beneficial training effects of FES on lower limb gait mechanics which likely developed over the 8 week intervention. Therefore, FES systems such as the one used in this study may be considered not only orthotic devices, but also a useful gait re-training
tool for people with MS. Analysis of gait under both non-fatigued and fatigued conditions also provided a more functional clinical scenario, revealing some therapeutic benefits of FES on gait when fatigued. Future investigations should also consider the effects of a fatiguing walk without the aid of an FES device. This work highlights the need for further research into the use of FES over longer periods to provide further insight into the potential for combined therapies to limit important fatigue related deficits in gait in people with MS.

Conclusion

In a group of people with MS with a disability rating of 3-4 on the EDSS scale there was a lack of an orthotic effect on first use of a commercial FES system. Therapeutic effects on gait after 8 weeks use were generally positive, including continuing and total orthotic effects producing increases in walking speed due to improved neuromuscular control and power generated at the hip and ankle of the more affected limb. The training effects of FES appear to be mostly associated with enhanced eccentric control of knee flexion in early stance. While the action of FES alone was not sufficient to overcome all effects of activity-induced fatigue on gait in people with MS there was evidence 8 weeks use of FES can ameliorate some effects on lower limb kinetics, including benefits to ankle mechanics involved in generating power around push-off during stance. The therapeutic benefits of FES may have potential as a gait-retraining therapy, and future research should investigate whether there are further benefits from using FES for longer periods on mitigating fatigue induced gait deficits in people with MS.

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Declaration of interest statement: The authors have no conflicts of interest to disclose.

References


### Baseline Assessment

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<th>Post-6MWT</th>
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<td>Single support (%)</td>
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### Week 8 Assessment

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<td>Maximum ankle plantarflexion in early stance (°)</td>
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<td>16.4 (4.1)</td>
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<td>Maximum ankle dorsiflexion in midstance (°)</td>
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<tr>
<td>Maximum ankle plantarflexion in late stance (°)</td>
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<tr>
<td>Maximum ankle dorsiflexion in swing (°)</td>
<td>10.9 (3.7)</td>
<td>10.4 (3.7)</td>
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Table 1. Spatiotemporal and kinematic gait parameters for each FES condition (off and on) for non-fatigued (pre-6MWT) and fatigued (POST-6MWT) conditions at the baseline and week 8 assessments. Significant fatigue, orthotic, continuing orthotic, training and total orthotic effects are indicated where appropriate with symbols in the columns to the right of the baseline and week 8 data. Data for the more affected side is in bold. All values are mean (SD).

*indicates significant effect in the two factorial analysis of variance

+ indicates significant difference in pairwise comparisons when non-fatigued
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<th>Parameters</th>
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<td>Maximum hip extensor moment in early stance (Nm/kg)</td>
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<tr>
<td>Maximum hip flexor moment in late stance (Nm/kg)</td>
<td>1.23 (0.39)</td>
<td>1.23 (0.48)</td>
<td>1.33 (0.51)</td>
<td>1.23 (0.44)</td>
<td>1.27 (0.48)</td>
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<td>Maximum hip power generation in early stance (W/kg)</td>
<td>0.77 (0.44)</td>
<td>0.80 (0.43)</td>
<td>0.87 (0.56)</td>
<td>0.99 (0.48)</td>
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<td>Maximum hip power absorption in midstance (W/kg)</td>
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<td>Maximum knee power generation in midstance (W/kg)</td>
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<td>Maximum knee power absorption in late swing (W/kg)</td>
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<td>Maximum ankle dorsiflexor moment in early stance (Nm/kg)</td>
<td>-0.13 (0.09)</td>
<td>-0.14 (0.07)</td>
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<td>-0.11 (0.05)</td>
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<tr>
<td>Maximum ankle plantarflexor</td>
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<td>1.26 (0.27)</td>
<td>1.36 (0.31)</td>
<td>1.34 (0.24)</td>
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Legend: * = Significant difference, # = Significant difference from baseline, + = Significant difference from pre-6MWT.
Table 2. Kinetic gait parameters for each FES condition (off and on) for non-fatigued (pre-6MWT) and fatigued (POST-6MWT) conditions at the baseline and week 8 assessments. Significant fatigue, orthotic, continuing orthotic, training and total orthotic effects are indicated where appropriate with symbols in the columns to the right of the baseline and week 8 data. Data for the more affected side is in bold. All values are mean (SD).

*indicates significant effect in the two factorial analysis of variance

+ indicates significant difference in pairwise comparisons when non-fatigued

# indicates significant difference in pairwise comparisons when fatigued
Appendix A

Gait parameters extracted for analysis. Maximum and minimum kinetic and kinematic parameters were extracted within specific ranges of the gait cycle indicated in parentheses as percentage of gait cycle.

**Spatiotemporal**

Walking speed (m/s)
Cadence (steps/min)
Stride length (m)
Double support (%)
Single support (%)

**Kinematics (degrees)**

Maximum hip extension in stance (0-100%)
Maximum hip flexion in swing (60-100%)
Maximum knee flexion in early stance (0-30%)
Maximum knee extension in midstance (10-50%)
Maximum knee flexion in swing (50-100%)
Ankle dorsiflexion at initial contact (0-2%)
Maximum ankle plantarflexion in early stance (0-20%)
Maximum ankle dorsiflexion in midstance (10-60%)
Maximum ankle plantarflexion in late stance (50-80%)
Maximum dorsiflexion in swing (70-100%)

**Kinetics – moments (Nm/kg)**

Maximum hip extensor moment in early stance (0-40%)
Maximum hip flexor moment in late stance (30-70%)
Maximum knee extensor moment in early stance (0-40%)
Maximum knee flexor moment in midstance (10-60%)
Maximum ankle dorsiflexor moment in early stance (0-20%)
Maximum ankle plantarflexor moment in late stance (0-60%)
Kinetics – powers (Watts/kg)

Maximum hip power generation in early stance (0-40%)
Maximum hip power absorption midstance (30-70%)
Maximum hip power generation in late stance (40-80%)
Maximum knee power absorption in early stance (0-20%)
Maximum knee power generation in midstance (10-30%)
Maximum knee power absorption in late swing (80-100%)
Maximum ankle power absorption in stance (0-60%)
Maximum ankle power generation in stance (0-65%)