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Relative Changes in Ankle and Hip Control during Bilateral Joint Movements in Persons with Multiple Sclerosis

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Abstract

Objective—The purpose of this study was to quantify hip and ankle impairments contributing to movement dysfunction in multiple sclerosis (MS).

Methods—Volitional phasing of bilateral hip and ankle torques was assessed using a load-cell-instrumented servomotor drive system in 10 participants with MS and 10 age-matched healthy participants. The hips and ankles were separately bilaterally oscillated 180° out of phase (40° range of motion) at a frequency of 0.75 Hz while the other joints were held stationary. Participants were instructed to assist in the same direction as the robot-imposed movement. The hip and ankle torques were measured and work was calculated for each movement.

Results—Total negative work at the ankle was significantly different between groups ($p=0.040$). The participants with MS produced larger negative work during hip flexion ($p=0.042$) and ankle flexion ($p=0.037$). Negative work at the hip was significantly correlated with the Berg Balance Scores and Timed 25 Feet Walk Test, and trends demonstrated increasing negative work with increasing clinical impairment in MS.

Conclusions—These results suggest an increased importance of the hip in functional balance and gait in MS.

Significance—Rehabilitation strategies targeting ankle recovery or compensation using the hip might improve movement function in MS.

Keywords

joint moment; negative work; robot; coordination

Introduction

A better understanding of the deficits in coordination of the ankles and hips in people with multiple sclerosis (MS) could help direct the rehabilitation of functional movements. In people with MS, altered coordination (Sosnoff et al., 2011), lower extremity weakness (Kent-Braun et al., 1997; Thoumie et al., 2005) and abnormal stretch reflexes (Knutsson & Richards, 1979; Sinkjaer et al., 1993; Toft et al., 1993) often contribute to limitations in functional movements such as gait (Mueller et al., 1995; Nadeau et al., 1999; Milot et al., 2008). While motor impairments likely occur in both the ankle and the hip, there is increasing evidence of a compensatory strategy that includes a redistribution of torques from the ankle to the hip in people with neurological impairments (Nadeau et al., 1999; Lewis & Ferris, 2008; Jonkers et al., 2009). Thus, identifying the relative impairments of the ankles and hips and the subsequent effects on function might shed light on the underlying mechanisms of dysfunction in MS.

Measurement of negative work during bilateral movements is one technique that captures a combination of impairments in the generation of coordinated muscle activity. In neurologically impaired populations, cyclic bilateral leg movements elicit abnormal reflex responses (Steldt & Schmit, 2004; Knikou et al., 2007; Lewek et al., 2007), resulting in inappropriate muscle activity (Onushko & Schmit, 2008; Onushko et al., 2010) and poor coordination that is correlated to reduced walking function (Hyngstrom et al., 2010). This altered coordination translates to inefficient work production, manifested as an increase in negative work during bilateral movements (Kautz & Brown, 1998; Ting et al., 1998). Hence, measurement of negative work during active bilateral leg movements is a viable technique for characterizing the ability to produce concentric muscle contractions that are coordinated with movement – a key feature of the control of muscle activity.

The measurement of negative work during cyclical movements, like other measurements of impairment, would be expected to correlate with sensorimotor function. Deficits such as muscle fatigue, reduced joint torque, asymmetries in joint torque, gait asymmetry, and altered gait parameters can be detected in early stages of MS (Kalron et al., 2011a) and correlate with clinical measures of function, such as the EDSS (Huisinga et al., 2012). However, the relative impairment of the ankles and hips, and the contribution of impairments at each joint to functional movements involving control of the legs in people with MS are unknown.

In the current study, we measured coordination patterns during active bilateral movements of the hips or ankles in people with MS. Participants with MS and age-matched healthy participants were asked to assist an imposed, bilateral, sinusoidal oscillation of the hips or ankles. We hypothesized that the participants with MS would have an increase in negative work in the lower limbs compared to the healthy participants. We anticipated that the impairment would be greater at the ankle, reflected by larger negative work at the ankle than the hip. Further, we postulated that larger ankle impairments would cause compensation by the hip during functional tasks in participants with MS.

Methods

Study Participants

Ten participants with MS (2 males 8 females, age range: 38–57 yrs, mean age: 50.6 yrs) participated in this study. All participants with MS were ambulators that tended to be active in the community. At the time of the study, five of ten participants were taking disease modifying medications and three were taking medication to improve their walking (Ampyra; Acorda Therapeutics, Inc., Ardsley NY) and/or antispastic medication to reduce the frequency and intensity of spasms (baclofen). The clinical features of each participant are described in Table 1. Additionally, ten participants (2 males 8 females, age range: 43–57 yrs, mean age: 51.8 yrs) with no reported neurological damage were recruited into the study as healthy participants. Exclusion criteria included: significant cardiovascular problems, respiratory failure, major orthopedic problems including contracture of limbs, joint replacements, significant medical co-morbidity, concurrent illnesses limiting the capacity to conform to study requirements, or the inability to give informed consent. Written informed consent was obtained prior to study participation and all procedures were conducted in accordance with the Helsinki Declaration of 1975 and approved by the Institutional Review Boards of Marquette University and the Medical College of Wisconsin.

Clinical Assessment

A variety of clinical tests were used to evaluate each participant's function and ability to participate in the study. The Modified Ashworth Scale (MAS) was used to measure the muscle hypertonia in the knee and ankle of the participants with MS (Bohannon & Smith, 1987). The Berg Balance Scale (BBS) was used to evaluate the balance function in people with MS (Berg et al., 1992). The 25 feet walk test (25FWT) was used to evaluate the walking ability of the participants with MS (Kaufman et al., 2000). The Fatigue Severity Scale (FSS) was used to determine whether fatigue was a significant factor of the participant's daily activities (Krupp et al., 1989). The Symbol Digit Modalities Test (SDMT) was used to evaluate the cognitive function of the participants with MS (Lewandowski, 1984). All clinical tests were completed by a licensed physical therapist prior to beginning the experiment. Participant specific information is provided in Table 1.

Experimental Setup

Bilateral hip and ankle isokinetic flexion and extension were imposed on the study participants using a novel leg robot (Figure 1). Study participants lay supine with both legs secured in custom, adjustable leg braces. The leg joints were held at 20° knee flexion and 10° ankle plantarflexion during the imposed hip movements and at 20° hip flexion and 20° knee flexion during the imposed ankle movements. The leg braces were attached to the leg robot which used servomotor drive systems (Kollmorgen, Northampton, MA) to impose oscillations at the aligned leg joints. For hip movements, torque transducers (S. Himmelstein and Company, Hoffman Estates, IL) attached to the leg braces provided measurements of sagittal plane hip, knee, and ankle torques during the imposed movement. Torque transducers (JR3, Woodland, CA) attached to the ankle braces provided measurements of ankle forces and torques during imposed ankle movements. A knee brace was used to

restrict medial-lateral movement of the legs during imposed ankle oscillations. Joint position was monitored using optical encoders (US Digital, Vancouver, WA).

Surface electromyograms (EMGs) were recorded bilaterally from the vastus medialis, rectus femoris, vastus lateralis, medial hamstrings, medial head of the gastrocnemius, soleus, and the tibialis anterior from all participants. Recording electrodes (Delsys Inc, Boston, MA) were placed on the cleansed, lightly abraded skin over each muscle belly. EMG signals were bandpass filtered (25–450 Hz) prior to sampling. Custom LabVIEW software (National Instruments Corp., Austin TX) was used to control joint trajectory and acquire torque and position signals. All signals were low-pass filtered (500 Hz) prior to data acquisition and sampled at 1000 Hz using a data acquisition card (National Instruments Corp., Austin TX) and a PC.

Experimental Protocol

Hip Oscillation—The participants lay supine with custom leg braces securing their legs to the leg robot. The hip joints were aligned to the servomotor axes of the robot. Oscillations of the legs about the hips were applied using the servomotor. For calibration of the load cells before the experiment, two hip movements were performed to approximate the biomechanical properties of the leg and leg brace. The torque due to gravity, passive joint resistance, and mass moment of inertia were estimated (further described later). First, slow, unilateral incremental movements (5° steps) were imposed about the left and right hip to estimate the torque contribution due to gravity and passive joint resistance throughout the range of motion. Second, fast 1.5 Hz leg oscillations were imposed to each leg, moving through a 30° range of motion (25° hip flexion to 5° hip extension) to determine the combined inertial constant of the leg and leg brace. Participants were instructed to remain as relaxed as possible during these movements.

For the hip oscillation protocol, the participant's legs were moved at 180° out of phase through a 40° range of motion (30° hip flexion to 10° hip extension) for twenty cycles. The knee and ankles were held isometrically in the leg braces at 20° knee flexion, 10° ankle plantarflexion. The leg movements were performed at 0.75 Hz, and study participants were instructed to either assist the imposed motions (active movement), or to remain inactive during the imposed motions (passive movement). Participants were not provided with any feedback on their performance during the trials. The trials started with two passive trials, followed by two active trials, and then another two active trials. Maximal voluntary contraction (MVC) measures were performed before and after the hip oscillation trials. Flexion and extension MVCs on each hip were tested separately, with rest time in between each test.

Ankle Oscillation—After the hip oscillation protocol concluded, the participant was unsecured from the hip setup of the leg robot and allowed to take up to a 10 minute break. When ready, the participant again lay supine in the leg robot, with custom ankle braces securing the feet and ankles to the leg robot. The ankle joints were aligned to the servomotor axes of the leg robot and bilateral oscillations about the ankles were applied using the servomotor. Similar to the hip oscillation protocol, two ankle movements were performed to

approximate the biomechanical properties of the feet and ankle brace prior to the ankle protocol. The torque due to gravity, passive joint resistance and mass moment of inertia were estimated in a manner similar to the hip testing. Slow, unilateral incremental movements (5° steps) were imposed about the ankle to estimate the torque contribution due to gravity and passive joint resistance. Fast 1.5 Hz leg oscillation movements were imposed to each foot, moving through a 20° range of motion (15° ankle dorsiflexion to 5° ankle plantarflexion) to determine the combined inertia of the feet and ankle braces. Participants were instructed to remain as relaxed as possible during these movements

For the ankle oscillation protocol, the participant's feet were moved 180° out of phase through a 40° range of motion (20° ankle dorsiflexion to 20° ankle plantarflexion) for twenty cycles. The hip and knee were held isometric in the knee braces (20° hip flexion, 20° knee flexion). Movement of the ankles was performed using the same protocol used for the hips.

Data Analysis

The biomechanical properties of the leg and leg brace were measured to calculate the torque due to active muscle contraction. The measured torque had to be corrected for gravitational torque, torque due to passive joint resistance, and inertial torque. The general equation used to calculate the active torque τ_{joint} for each joint was:

$$\tau_{\text{joint}} = \tau_{\text{measured}} - \tau_{\text{passive/gravity}} - \tau_{\text{inertia}}$$

where τ_{measured} was the raw, measured torque for a specific joint, $\tau_{\text{passive/gravity}}$ was an approximated torque produced by the passive joint resistance and gravity, and τ_{inertia} was the calculated torque based on the inertial properties of the leg and leg brace.

The technique used to calculate the torque due to active muscle contraction is the same as previous studies (Steldt and Schmit 2004, Onushko and Schmit 2007). Briefly, the $\tau_{\text{passive/gravity}}$ was estimated by fitting a polynomial curve (torque vs. hip angle) to the trials in which the leg was moved in slow incremental steps through the range of motion. Torque data from the hold periods were used to estimate the combined gravitational and passive joint resistance. A polynomial function was then used to estimate the $\tau_{\text{passive/gravity}}$ during the movement trials and subtracted from the measured torque. Similarly, the inertial coefficient was estimated from the trials with rapid oscillations in midrange. The $\tau_{\text{passive/gravity}}$ was first subtracted from the measured torque. The hip angular acceleration was calculated from the movement trajectory and the inertial coefficient was identified using a regression. This inertial coefficient was then applied to the test trial acceleration data to calculate τ_{inertia} , which was subtracted from the measured torque.

After subtraction of $\tau_{\text{passive/gravity}}$ and τ_{inertia} , the remaining torque signal was the active joint torque produced by the participant. All torque signals were then low-pass filtered (5Hz) using a second order zero phase delay Butterworth filter.

Phase Analysis—A phase analysis was performed on the active torques to determine the timing of activity with respect to the hip and ankle position during the imposed movements.

The timing of responses was tested using circular statistics (Batschelet 1981) as described previously (Onushko and Schmit 2007). Briefly, torque signals were separated into flexion and extension components, and the cycle period was normalized to a 360° polar plot, with 0° being full flexion and 180° defined as full extension. The peak torques for each oscillation cycle were calculated and averaged, allowing each data point on the polar plot to represent each participant's peak torque and corresponding phasing during oscillation.

To analyze the phasing of the torques independent from their magnitude, the peak torques from each cycle were normalized to a unit vector, and averaged across trials. The resulting mean vector was defined by its magnitude (0–1 range) and phase angle. If the phasing of the vectors was identical for all cycles, the magnitude would be 1; whereas if the phasing was random, the mean vector amplitude would be close to 0. To examine the phasing across participants, the mean vector for each participant was again normalized to a unit vector and a mean vector across participants within a group was calculated. The Rayleigh Test was first used to determine if the torques generated had significantly similar phasing within groups ($p < 0.05$). The significance of the mean angle from the peak torques generated across groups (MS vs. Healthy) was statistically tested using the Watson-Williams Test ($p < 0.05$).

Torque Amplitude Analysis—The peak flexion and extension torques for the hip and ankle were determined in order to identify differences in volitional effort between the groups. The left and right leg joint torque signals were separated into flexion and extension components, and the peak torque was identified for each cycle of movement. These values were then averaged between both legs of each participant, averaged within each participant, and across groups for analysis.

MVC Analysis—The joint torque produced during flexion and extension MVCs at the hip and ankle of each leg were first determined separately to estimate the participant's volitional strength and for comparison between groups. Second, the flexion and extension MVC torques were separately averaged across each joint (e.g. averaged right and left hip flexion) to obtain a measure of the participant's flexion strength and extension strength at the hip and ankle. Third, the flexion and extension MVC torques were averaged together at the hip and at the ankle to obtain an overall measure of volitional strength at each joint. All MVCs were normalized by the participant's body weight.

Negative Work Ratio Analysis—The amount of positive and negative hip and ankle work done during active leg oscillations was calculated to determine the efficiency of active movement at the hip and ankle. The joint torque signals were separated into flexion and extension components, and the area under the temporal torque signal was calculated as work. The amount of work was then further identified as being either positive or negative work, where positive work would correspond to joint torque in the same direction as the movement of the leg robot (e.g. flexion torque during the flexion phase of movement), and negative work was associated with torque countering the movement of the leg robot (e.g. extension torque during the flexion phase of movement).

The analysis of negative work ratio parameters was similar to that of the MVC analysis. The flexion and extension negative work ratios at the hip and ankle of each leg were first

determined separately to estimate the participant's coordination and for comparison between groups. Then the flexion and extension negative work ratios were separately averaged across each joint (e.g. averaged right and left hip flexion) to obtain a measure of the participant's flexion negative work ratio and extension negative work ratio at the hip and ankle.

EMG Analysis—EMG activity was measured and compared between groups to determine if differences in functional movement could be explained by deficits in muscle activity. Group EMG profiles for each participant were calculated by averaging EMG activity from each movement cycle for all active movement trials, then averaging the participants' EMG profiles within each group. To compare the amount of inappropriate muscle activity during movement, the root mean square (RMS) EMG value of the antagonist muscle at the hip and ankle was calculated for the first 50% of the movement cycle. For example, during the ankle extension movement, RMS EMG of the ankle flexors (tibialis anterior) was calculated for the first 50% of the extension movement (25% of the entire movement cycle). These RMS values for each participant were then averaged within groups.

Statistical Analysis

For the analysis of phasing of torques, the Rayleigh Test was used to determine if the torques had significant phasing within groups ($p < 0.05$). The significance of the mean angle from the peak torques generated across participant groups was statistically tested using the Watson-Williams Test ($p < 0.05$).

A three-way ANOVA with group (MS/healthy participants), age (young/old), and sex (male/female) as fixed factors was used to identify possible confounding factors. The Shapiro-Wilk test was first used to determine if the data was normally distributed. Fixed factors with non-significant interactions were removed and the ANOVA was rerun to compare the between-group differences in MVC torque and peak torque during active bilateral leg movement (normal distribution). The Mann-Whitney U (MWU) test was used to determine the between-group differences in negative work ratios and RMS EMG at the hip and at the ankle (non-normal distribution). All tests were conducted using SPSS software (SPSS Inc., Chicago IL) with significance accepted at $p < 0.05$. A linear regression was used for statistical analysis of the relation between the joint parameters and clinical scores of BBS and 25FWT.

Results

Peak Torque Phasing and Amplitude

In this study, we tested whether strength and coordination during active bilateral leg movements were significantly different between participants with MS and healthy participants. In participants with MS, we also tested correlations between measurements and impairment. Specifically, we analyzed flexion and extension MVC torques, as well as peak torques and negative work produced during active bilateral leg movement at the hip and ankle.

Peak flexion and extension torque amplitudes and phasing during assisted movement were used to compare the overall coordination patterns between the MS and healthy participants (Figure 2). The patterns of peak torque production were similar between the MS and healthy

participants. Normalized torques and their corresponding polar angles were calculated from peak torque values. Angles of peak torque phasing were used to determine if the torques were similarly phased within groups using Rayleigh's Test and the phasing of torques between groups was compared using the Watson-Williams Test (Table 2). Peak torque phasing was not significantly different between the groups ($p>0.05$), indicating similar phasing performance during the active bilateral movement.

Peak hip and ankle torque and phasing parameters were averaged between both legs for each participant and within groups to get an estimate of the overall torque and phasing. For the healthy participants, peak hip flexion and extension torque occurred at a polar angle of approximately 50° , corresponding to an anatomical angle of 18° hip flexion. For the participants with MS, peak hip flexion and extension torque occurred at a polar angle of approximately 35° , corresponding to an anatomical angle of 22° hip flexion. At the ankles, the healthy participants' peak ankle extension and flexion torque occurred at a polar angle of approximately 84° , corresponding to an anatomical angle of 1° ankle dorsiflexion which is close to the neutral position, while the participants with MS showed peak ankle extension and flexion torque occurring at a polar angle of approximately 65° , corresponding to an anatomical angle of 5° ankle dorsiflexion. Overall, peak torque production occurred slightly earlier in the participants with MS compared to the healthy participants, but the differences were not significant ($p>0.05$).

Peak torque amplitudes during active bilateral leg movement were slightly higher at both the hip and ankle in the healthy participants compared to the participants with MS, but the differences were not significant between groups (Table 3), indicating a similar self-selected sub-maximal effort level for both groups.

Strength and Coordination Impairments

MVC torques were measured to estimate of the participant's strength and impairment at the hip and ankle. Flexion and extension MVC torques for the hip and ankle were calculated and found to be not significantly different between groups ($p>0.05$) (Table 4).

Negative work ratios at the hip and ankle were calculated to describe the efficiency of coordination during bilateral leg movement. Single participant ensemble torque traces of a typical participant with MS and healthy participant demonstrated that the negative work produced during extension and flexion phases of movement in the participant with MS were larger than the healthy participant (Figure 3). Hip and ankle flexion negative work ratios (Figure 4) were found to be significantly different between groups (MWU, hip $p=0.002$, ankle $p=0.019$). This difference in work production between both groups might be associated with differences in muscle activity during leg movement (Figure 5). The participants with MS demonstrated increased antagonistic muscle activity during hip movement compared to the healthy participants. Rectus femoris activity increased at the end of hip extension, while medial hamstrings activity was elevated during hip flexion. Similarly at the ankle, medial gastrocnemius activity increased at the end of ankle dorsiflexion, and tibialis anterior activity was elevated during ankle plantarflexion in the participants with MS. However, analysis of antagonistic muscle RMS EMG during movement showed that only the RF activity was significantly higher in participants with MS (MWU, $p=0.029$).

Regression analyses of MVC and negative work ratio to clinical measures of BBS and 25FWT were used to determine the relationship between strength and coordination dysfunction and clinical measures of impairment. Regression analyses of MVC torque to BBS and 25FWT showed no significant trends (Table 4). Regression analyses of flexion and extension negative work ratio at the hip and ankle to clinical measures of BBS and 25FWT showed consistent trends of increasing negative work ratio with increasing clinical measures of impairment (Figure 6). The regressions between negative work ratio and clinical measures were consistently stronger at the hip than the ankle, with hip flexion and extension ratios showing stronger and significant ($p<0.05$) Spearman's correlation coefficients compared to ratios at the ankle (Table 5).

Discussion

Results from this study showed a reduced ability to coordinate bilateral movement at the hips and ankles in people with MS. Despite producing similar peak torque amplitudes and phasing during active movement, participants with MS had a higher negative work ratio than the healthy participants, particularly during hip and ankle flexion. This effect was more pronounced at the ankle when both flexion and extension negative work ratios were averaged. Furthermore, the negative work ratio at the hip was strongly correlated to clinical measures of balance and gait.

Deficits in Reflexes and Work Production

During bilateral joint movements, overall patterns of active torque were similar between groups, denoted by peak torque amplitudes and phasing that were not significantly different between groups. Although each participant was instructed to exert a strong but sub maximal level of effort when assisting the movement, the self-selected effort in both groups resulted in similar peak torque amplitudes and phasing. This indicates that the participants with MS were able to utilize a strategy that allowed them to perform the task despite physical impairments. This similarity in general performance between both groups might be attributed to two main factors - comparable group MVC strength and the simplicity of the movement task. Although the participant movement ability ranged from low (BBS=29, 25FWT=18.4s) to high function (BBS=56, 25FWT=7.30s), group MVCs as a whole were not significantly different. Thus, the ability of participants with MS to generate joint torque was not significantly compromised compared to the healthy participants. Furthermore, the bilateral leg movement task was a simple, controlled, single degree of freedom motion, where the effect of gravity and balance was eliminated, likely allowing the participants with MS to perform similarly to the healthy participants.

Although participants with MS were able to produce similar peak torque amplitudes and phasing during bilateral movement, the pattern of work produced during the movement was different from the healthy participants. Generally, the participants with MS had a higher negative work ratio than the healthy participants, particularly during the flexion phase. Furthermore, when considering the total negative work ratio (consisting of the average of flexion and extension negative work ratio per joint), the negative work ratio at the ankle was significantly higher in the participants with MS. As the phasing of peak torque was similar

between groups, this negative work reflected errors in the early and late parts of the movement cycle, particularly around the transitions between flexion and extension.

Spasticity may have played a role in the increased negative work ratio in participants with MS. Although the participants with MS did not have high levels of spasticity during clinical examination (total average spasticity from Modified Ashworth Score=0.425) or during passive bilateral movement at the hip and ankle, we cannot eliminate the possibility of spastic reflexes influencing active, out-of-phase, bilateral movement. Imposed sinusoidal leg movements reveal abnormalities in reflex modulation in human spinal cord injury (Steldt & Schmit, 2004) and other neurologically impaired populations (Knikou et al., 2007; Lewek et al., 2007). The effect of abnormal reflex modulation is exaggerated during flexion (Knikou et al., 2006), end of range of movement (Schmit et al., 2000), and extended muscle lengths (Schmit et al., 2002; Knikou et al., 2006). This is consistent with participants with MS in this study having a larger negative work ratio during flexion, with negative work being produced near flexion-extension transitions and at the ends of range of motion. At the ankle, greater torque asymmetries (Kalron et al., 2011b) and impaired modulation of the stretch reflex along with increased ankle joint stiffness (Sinkjaer et al., 1996) might contribute to an increase in negative work during ankle flexion. The effects during ankle extension are likely to be muted due to an absence of reflex-mediated responses in the ankle flexors in MS (Toft et al., 1993). It is probable that the bilateral nature of the movement enhanced spastic reflex excitability (Onushko & Schmit, 2007) in the participants with MS, which resulted in co-contraction of antagonistic muscles during movement, similar to people with stroke (Hidler et al., 2007). In people with neurological impairment and high spasticity, the reflex responses might trump volitional effort and disrupt motor control (Onushko & Schmit, 2008; Onushko et al., 2010). Interestingly, spasticity (based on the Modified Ashworth Score) was not a strong predictor of high negative work ratio in the current study, suggesting that the combination of volitional effort and reflex feedback might be critical.

Deficits in Coordination and Functional Movement

In the current study, the participants with MS demonstrated a difference in ability to coordinate muscle activity at the transition points of bilateral movement, pointing towards a neurological deficit in simultaneously controlling the timing of activity in multiple muscles. These deficits could be related to timing of flexors and extensors at a single joint, or in the interlimb coordination of muscle activity. Interlimb control mechanisms are important for unilateral tasks (Ting et al., 1998) as well as for coordinating activity between muscles that perform antagonistic functions on opposite sides of the body (Ting et al., 2000). Similarly, the coordination of muscle timing across joints and across limbs is important for the generation of power (Wakeling et al., 2010) and movement efficiency (Blake et al., 2012). In people with neurological injury, these coordination patterns can become disrupted. Interlimb coupling between the arm and leg is altered after stroke (Kline et al., 2007), and intralimb coordination is substantially compromised. In the current study, the compromise to timing of muscle activity in participants with MS during transition points whilst maintaining peak torque output and timing is consistent with altered coordination in people with MS.

Features of the bilateral motor task used in the current study might be altered to increase sensitivity of measurements of motor deficits in people with MS. The deficits in coordination in people with MS appeared to be direction-specific, as a larger negative work ratio during joint flexion was observed. The role of muscles as an extensor or flexor depends on movement rate (Neptune et al., 1997) and the effective work production in muscles is differently affected in stroke survivors, depending on function (Kautz & Brown, 1998). Thus, altering the movement trajectory to examine differences in flexor and extensor coordination might be warranted. In the current study, the bilateral leg movement was done at a fairly low frequency which was likely within the comfortable speed of movement for participants with MS, allowing them to produce torques comparable to the healthy participants. As effective work production diminishes at higher rates in healthy participants (Neptune & Herzog, 1999) and elderly (Clark et al., 2010), further studies using the same experimental paradigm with higher movement rates might exacerbate the neurological deficits and highlight effects of movement frequency on coordination in people with MS.

Relationship between Inefficient Work Production and Impairment

Although the participants with MS showed a higher negative work ratio at both the hip and ankle compared to the healthy participants, a strong relationship between negative work ratio and clinical measures of walking and balance was manifested only at the hip. This observation indicates that the hip might play the more important role in determining functional ability and would suggest that the ankle has become dissociated from functional importance. An increased dependence on the hip might be related to the greater impairment at the ankle, reflected by the larger negative work ratio at the ankle, compared to the hip in participants with MS. This would suggest that people with MS change their motor control strategy to increase the contributions from the hip, compared to the ankle. Alternately, compensatory actions by the hip might become critical for functional tasks. This notion is consistent with evidence that impaired hip coordination is correlated with poor walking function in stroke (Hyngstrom et al., 2010), and an increased reliance on the hip in MS (Thoumie, 2002), stroke survivors (Jonkers et al., 2009), and the elderly (DeVita & Hortobagyi, 2000; Savelberg et al., 2007) to maintain gait function. Additional testing of the relative roles of the hip and ankle in functional movements is needed to assess whether there is a fundamental change in motor control in people with MS.

Limitations of the Study

In this study, the disease subtype and EDSS score of the participants with MS were not available; however, a comprehensive testing of function was performed. To ensure a baseline level of function and consistency in disease state of the participants with MS, the inclusion criteria included the ability to walk independently and perform the experimental task, and that the disease was in a state of remission during the time of testing. Furthermore, several clinical tests that are part of the Multiple Sclerosis Functional Composite were performed to quantify the functional characteristics of the participants with MS. Medications that acted on the disease progression or improved function were not part of the exclusion criteria, as they were common to people with MS. The only exclusion criteria for medication was that botulinum toxin was not administered within a three month window as it could significantly alter muscle tone and movement function.

Another limiting factor in the experimental protocol was that the type of leg movement (hip or ankle) was not randomized, and the results might reflect order effects when comparing performance between both joints within each group. Between group comparisons were not affected by the fixed order, as both groups underwent the same order of leg movement.

The parameters quantified in this study such as MVC torque and negative work ratio represent the impairments measured in a very controlled setting and within an isolated joint movement (in the leg robot). These controlled measurements suggest that these impairments might also affect daily function in people with MS, but it is important to make these measurements in an ecological task such as during overground walking or standing balance, to ensure that these findings are directly clinically relevant.

This study included only ten participants with MS, which limits generalization of the results. In particular, the linear regression analysis indicating significant correlations between negative work ratio at the hip and clinical measures of balance and walking was conducted with only ten samples. This small sample size can make it difficult to identify violations of model assumptions and spurious data points; however, the data appeared to be well distributed along the line and there was some consistency across hip measures. There might be value in confirming the observed trends in future studies.

In conclusion, we found that participants with MS had a reduced ability to coordinate bilateral movement at the hips and ankles, despite being able to produce similar peak torque amplitude and phasing as compared to the healthy participants. This reduced ability to coordinate movement was reflected by the negative work ratio. The negative work ratio at the hip was more strongly correlated to clinical measures of function than the ankle, indicating that there is a shift in motor control towards the hip in people with MS.

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Highlights

1. Impairments in coordination of the hips and ankles in people with MS were documented by negative work during imposed bilateral leg movements.
2. Measurements of negative work at the hip, but not the ankle, were correlated to clinical measures of balance and gait speed in people with MS.
3. These results suggest that people with MS rely more strongly on hip control than ankle control for functional balance and walking.

Figure 1. Experimental setup

Leg robot used to impose bilateral hip oscillations and record sagittal plane torques during hip movements (A) and ankle movements (B). Two servomotor systems were used to impose movements about the hip and ankle joints. The hip joint was moved between 30° flexion and 10° extension, while the ankle joint was moved from 20° dorsiflexion to 20° plantarflexion.

Figure 2. Group Averaged Polar Plots of Peak Torque

Average right hip and ankle peak flexion (○) and extension torques (△) for two active assist trials per participant. Full joint flexion corresponds to 0° and full extension corresponds to 180°. The direction of movement is counterclockwise on the polar plot. Torque magnitudes (Nm) are represented radially on the polar plots. No significant differences were found between participants with MS and healthy participants during right and left leg assisted movements for peak torque phase and amplitude data ($p > 0.05$).

Figure 3. Single Trial Ensemble Average Torque

Single participant (MS: S03 and healthy participant: C01) torque traces showing negative work (shaded area under the curve) produced during active bilateral movement at the hip and ankle. For hip movement, extension torque is positive and flexion torque is negative. For ankle movement, plantarflexion torque is negative and dorsiflexion torque is positive. The participant with MS was observed to produce more negative work than the healthy participant.

Figure 4. Group Hip and Ankle Negative Work Ratio

The participants with MS had a significantly larger negative work ratio during hip and ankle flexion than the healthy participants (MWU hip flexion $p=0.002$, ankle flexion $p=0.019$). Significance was accepted at $p<0.05$. Standard deviation bars are indicated.

Figure 5.

Group Average EMG. Group averaged EMG traces showed increased antagonistic muscle activity during movement transition periods in the participants with MS. Rectus femoris (RF) activity increased at the end of hip extension, while medial hamstrings (MH) activity was elevated during hip flexion in the participants with MS, compared to the healthy participants. Similarly at the ankle, medial gastrocnemius (MG) activity increased at the end of ankle dorsiflexion, and tibialis anterior (TA) activity was elevated during ankle plantarflexion in the MS group.

Group Hip and Ankle Negative Work Ratio. The participants with MS had a significantly larger negative work ratio during hip and ankle flexion than the healthy participants (MWU hip flexion $p=0.002$, ankle flexion $p=0.019$). Significance was accepted at $p<0.05$. Standard deviation bars are indicated.

Figure 6. Negative Work and Clinical Measures Regressions

Flexion and extension negative work ratios and regression lines at the hip and ankle were plotted against the BBS and 25FWT. The MS negative work ratios generally increased with increasing impairment, with the hip negative work ratios being stronger predictors of clinical measures than the ankle negative work ratios. * indicates a significant Spearman's correlation coefficient $p < 0.05$.

Table 1

Clinical Features of MS Subjects

Subject	Age (yrs)	Years with MS	9HPT (s)	SDMT	FSS (of 7)	BBS (of 56)	25FWT (s)	Modified Ashworth Score *	Medications
S01	49	27	22.77	30	6.56	40	11.17	2	Ampyra, Copaxone
S02	52	15	28.65	40	6.00	46	9.32	2	Tysabri
S03	56	30	24.98	39	5.11	29	14.71	8	Baclofen, Ampyra, Interferon Beta, Amantadine
S04	48	8	17.64	50	4.50	55	6.94	4	Interferon Beta
S05	47	11	24.35	33	5.11	40	12.79	5	
S06	59	10	18.73	53	4.11	56	7.33	0	Tysabri
S07	50	5	21.65	48	4.44	47	6.51	0	Baclofen
S08	38	2	21.30	46	4.67	56	6.52	6	Baclofen, Ampyra
S09	57	6	27.35	37	4.78	35	18.40	6	
S10	50	3	20.52	44	4.67	52	7.62	1	

Clinical tests include the Nine Hole Peg Test (9HPT), Symbol Digit Modalities Test (SDMT), Fatigue Severity Scale (FSS), Berg Balance Scale (BBS), and 25 Feet Walk Test (25FWT).

* Modified Ashworth Score is calculated by summing the individual Modified Ashworth Scale muscle scores (0–4) from the left and right knee extensors, knee flexors, ankle plantarflexors, ankle dorsiflexors (total of 8 muscles), to obtain a scoring range of 0 (low muscle tone) to 32 (high muscle tone).

Table 2

Rayleigh and Watson-Williams Test Significance

		Rayleigh p values		Watson-Williams p value	
		Control	MS		
Hip	Right	Flexion	.000171	.000017	.425
		Extension	.0000361	.0000203	.346
	Left	Flexion	.000627	.000691	.278
		Extension	.000214	.000247	.265
Ankle	Right	Flexion	.00150	.00260	.263
		Extension	.000377	.000481	.521
	Left	Flexion	.000349	.0368	.505
		Extension	.0000369	.00240	.238

All parameters were significant for the Rayleigh Test ($p < 0.05$), indicating that there was a directedness in the phasing of torques in each group. All parameters were not significant for the Watson-Williams Test ($p > 0.05$), indicating that the phasing of torques between groups was similar.

Table 3

Group Peak Torques

	Control		MS		ANOVA	
	τ	s.d.	τ	s.d.	F	p
Hip	Flex	35.91	16.91	29.14	13.23	.993 .332
	Ext	36.88	16.82	37.33	21.46	.003 .959
Ankle	Flex	10.70	3.21	10.13	5.43	.082 .777
	Ext	16.00	6.25	14.50	10.46	.154 .699

Torques (τ) and standard deviations (s.d.) are in Nm. All parameters were not significant (ANOVA, degrees of freedom=1, $p>0.05$).

Table 4

MVC Group Significance and Regression Parameters

	ANOVA		Regression	
	F	p	BBS	25FWT
Hip	Ext	.112	.742	.515
	Flex	.588	.453	.592
Ankle	Ext	2.705	.117	.441
	Flex	1.631	.218	.294

Separate flexion and extension MVCs were not significantly different between groups (ANOVA, degrees of freedom = 1, $p > 0.05$). Regressions between MVCs and clinical measures (Pearson's correlation coefficient, r) were generally weak ($p > 0.05$).

Table 5

Negative Work Ratio Regression Parameters

		Mann-Whitney U		Regression	
		U	p	BBS	25FWT
Hip	Flex	11.00	0.002	-0.829	0.745
	Ext	46.00	0.796	-0.848	0.855
Ankle	Flex	19.00	0.019	-0.134	-0.067
	Ext	25.00	0.063	-0.323	0.503

The negative work ratio (Mann-Whitney U test, degree of freedom= 18) was significantly different between groups during hip and ankle flexion. Hip flexion and extension negative work ratio showed the strongest regression (Spearman's correlation coefficient.) to the BBS and 25FWT (highlighted in bold, p<0.05).