CHANGES IN DYNAMIC BALANCE IN MULTIPLE SCLEROSIS PATIENTS AS RELATED TO THE SEVERITY OF DISEASE AND SELF-RATED FATIGUE

by

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ABSTRACT

Impaired balance and fatigue are two common symptoms of multiple sclerosis (MS) that can impact the everyday activities of MS patients. Maintaining balance during walking, referred to as dynamic balance, requires the legs to control the motion and position of the upper body. The purpose of the study was to determine which variables of dynamic balance were the most closely related to the severity of the patients' MS and their fatigue level, and which of the significantly related variables were sensitive enough to detect differences between the MS patients and the control subjects. Ten MS patients and eight age-matched healthy control subjects were required to attend two testing sessions, one in the morning and one in the afternoon. The subjects were also required to rate their fatigue and perceived exertion (RPE) throughout the testing sessions. Kinematic data were collected from a minimum of six walking trials before and after a walking protocol designed to raise the subjects' RPE and fatigue level. The relationships between the three groups of variables (temporal-spatial variables, trunk movement variables, center of gravity variables, and the standard deviations of the variables) and fatigue and disability level were determined using Pearson's product-moment correlation coefficients ($p<0.05$) for MS patients. The variables that correlated with the severity of disease and fatigue level were then entered into a one-way ANOVA to determine if there was a statistical difference ($p < 0.05$) between the control group and the MS group. A repeated-measures ANOVA was used to determine statistical differences ($p<0.05$), between the groups and testing sessions for fatigue and walking speed. The temporal-spatial

variables and trunk movement variables were more related to the severity of disease than the fatigue level, but the change in center of gravity variables were more related to fatigue than to the severity of disease. Two variables that were significantly related to the severity of disease or fatigue level were also found to be significantly different between the control subjects and the MS subjects: variability of the lateral center of gravity displacement between strides during the afternoon fatigue session, and the change in variability of the lateral center of gravity displacement from the afternoon fresh trials to the afternoon fatigue trials were significantly different when comparing the control subjects from the MS subjects. The lack of significant differences between MS subjects and control subjects suggested that the chosen variables were not sensitive enough to detect differences in dynamic balance between MS patients and control subject.

BACKGROUND AND SIGNIFICANCE

Multiple Sclerosis

Impaired balance is one of the most common problems people with multiple sclerosis (MS) face, and it can impact their everyday activities (Freal et al. 1984). Multiple sclerosis is a neurological disease that causes the demyelination of axons in the central nervous system (Kraft and Wessman 1974). People with multiple sclerosis often have impairments of the vestibular, visual, and somatosensory systems (Jackson et al. 1995; Nelson et al. 1995), which may compromise their dynamic balance. Decreased strength (Kent-Braun et al. 1997) and increased levels of fatigue (Freal et al. 1984; Krupp et al. 1988; Sandroni et al. 1992; Bergamaschi et al. 1997; Ford et al. 1998) are prevalent in people with multiple sclerosis. Fatigue as defined by Kroencke et al. (2000) was an "abnormal sense of tiredness or lack of energy out of proportion to the degree of daily effort … which significantly interferes with the desire or ability to perform basic daily physical and intellectual functions". People with MS who suffered from fatigue reported that the level of fatigue was worse in the afternoon than in the morning, and could worsen after moderate and vigorous exercise (Freal et al. 1984; Krupp et al. 1988).

Prior research has shown that there was an altered gait when compared to healthy controls in patients with multiple sclerosis who were able to walk without walking aides. When compared to healthy controls, multiple sclerosis patients walked with shorter step lengths (Gehlsen et al. 1986; Benedetti et al. 1999; Morris et al. 2002), prolonged gait cycles (Benedetti et al. 1999), and slower speeds (Gehlsen et al. 1986; Benedetti et al. 1999). Three studies compared multiple sclerosis patients with controls. Benedetti et al. (1989) and Gehlsen et al. (1986), determined that cadence

was lower in multiple sclerosis patients than in healthy controls, while Morris et al. (2002) found no differences in step rate between multiple sclerosis patients and healthy controls. There were also discrepancies in double support time between the three studies. Benedetti et al. (1999) found an increased double support time when compared to controls, and Morris et al. (2002) found no differences between MS patients and control subjects. When comparing gait in multiple sclerosis patients between morning and a more fatigued state during the afternoon, there were no significant differences with respect to the change of step rate, stride length, double support time, and speed for the MS patients (Morris et al. 2002).

The Expanded Disability Status Scale (EDSS) measures the severity of multiple sclerosis by ranking subjects from 0 to 10. An EDSS Score of 0 represented a patient with no neurological impairment, while a person who had died from the disease would have a score of 10 (Kurtzke, 1983). The subjects in the Benedetti et al. (1999) study had only slight neurological disability, EDSS range of 0-2, with "no impaired function" (Kurtzke 1983). Morris et al. (2002) had a range of EDSS scores from 2.5 to 5.5, which represented an MS subject population more neurologically and physically affected than the subjects in the Benedetti et al. (1999) study. Subjects with a disability level of 5.5 were categorized by the inability to walk more than 100 yards or work a "full day" (Kurtze, 1983). Gehlsen et al. (1983) had a MS population with a similar disability level as Morris et al. (2002).

Balance

The ability to remain upright while walking requires the legs to control the center of gravity and the orientation of the upper body (Winter et al. 1990a). Walking involves control over a moving base, as opposed to standing still, which requires a

person to simply maintain the center of gravity over the base of support (Winter et al. 1990a). During the single support phase, a person's center of gravity does not lie directly over the base of support (Winter et al. 1990a). At the beginning of the swing phase, the center of gravity is behind and medial to the support leg (Shimba 1984; Winter et al. 1990a). As the swing foot moves forward, the center of gravity passes medially to the support foot (Shimba 1984). The anterior movement of the center of gravity during double support is caused by the transfer of weight from the support leg to the swing leg (Winter et al. 1990b). Not only do the legs help regulate the motion of the center of gravity, they must also balance the mass of the head, arms, and trunk, which comprises 2/3 of a person's body weight (Winter et al. 1990b). The accelerations of the upper body must be controlled by the lower body in order to keep the person moving in an upright position (Winter et al. 1993)

The maintenance of the head, arms, and trunk during walking is a function of the synergistic relationship between the knee and hip (Winter 1984; Winter et al. 1990b). Winter et al. (1993) determined that a moment at the hip created by the linear accelerations of the pelvis during the "weight acceptance" and "push-off" phases of gait worked to destabilize the upper body. The destabilizing moment was found to be "opposite and equal to" the hip joint moment which was derived from inverse dynamics (Winter et al. 1993). Therefore the researchers concluded that the primary task of the hip extensors and flexors during the support phase of gait was to control the orientation of the upper body (Winter et al. 1993). Poor control of the upper body could lead to increased unsteadiness while walking, making the subject more likely to trip or fall. Gehlsen et al. (1986) did not find a significant relationship between trunk movement in the anterior-posterior direction and MS.

Dynamic balance has been quantified with different methods. Elderly subjects with balance impairment had an increased range and velocity of mediolateral motion of the center of mass while walking over an obstacle as low as 5 cm when compared to healthy elderly subjects (Chou et al. 2003). However there were no differences in velocity or range of mediolateral motion when walking over a flat surface between elderly subjects with balance impairment and those without balance impairment (Chou et al. 2003). Also, temporal and spatial measures such as reduced velocity (Winter et al. 1990b; Maki 1997; Menz et al. 2003), increased step rate (Winter et al. 1990b), reduced step length (Winter et al. 1990b; Maki 1997; Menz et al. 2003), increased step width (Maki 1997; Krebs 2002), increased length of double support phase (Hausdorff et al. 1997; Maki 1997), decreased swing phase (Hausdorff et al. 1997) , and lower toe clearance (Winter et al. 1990b) have also been used to examine dynamic balance. However, researchers have found that increased variability of the temporal and spatial variables, specifically increased stride time variability (Hausdorff et al. 1997), stride length variability, walking speed variability, and double support time variability (Maki 1997) were better indicators of elderly subjects, who were more likely to fall. Decreased step length, decreased step width, decreased walking speed, and increased double support time for example may be indicators of a more cautious gait and an increased fear of falling, but not indicators of someone who was less steady or likely to fall (Maki 1997).

Morris et al. (2002) and Gehlsen et al. (1986) examined the relationship between fatigue or disability level and the temporal and spatial variables. Gehlsen et al. (1986) found that walking speed and stride length were significantly related to the severity of disease, while double support time and step rate were not related. Morris

et al. (2002) determined that fatigue level was not significantly related to the change in walking speed, stride length, step rate, and double support time from morning to afternoon. Neither study examined the variability of these variables and the relationship between fatigue and EDSS score, although Morris et al (2002) commented that the standard deviations of the variables were greater in multiple sclerosis patients than control subjects.

Summary

Multiple sclerosis patients have shorter step lengths, slower walking speeds, and depending on the study, a longer double support time and step rate, when compared to healthy controls. Decreased walking speeds, shorter step lengths, and longer double support times have been associated with a more cautious gait (Maki 1997). Past research had also shown that multiple sclerosis patients performed worse than healthy controls on static balance tasks (Frzovic et al. 2000). Due to the more cautious gait and performance on static balance tests one might suspect that it is possible that further study would show other decreases in dynamic balance in the MS population.

Discrepancies in the temporal and spatial gait variables and the lack of information on mediolateral center of mass movement and the variability of the dynamic balance variables with respect to MS patients suggest a need for further study. Since moderate to vigorous exercise has been shown to increase levels of fatigue in multiple sclerosis patients, testing after a walking protocol may present more pronounced adjustments in dynamic balance during gait from morning to afternoon. Also, the question of which variables were the most important in

determining the severity of balance, including the likelihood of falling, remained when examining dynamic balance while walking in the elderly population.

Dynamic balance "is a complex, multifaceted construct that is well-known but difficult to quantify" (Davidson et al. 2004). However, determining the correct variables to research was not only important in the elderly population, but other populations as well including the MS population. Therefore, the purpose of this study was to determine which variables of dynamic balance were strongly related to the severity of disease in multiple sclerosis patients. The secondary purpose of the study was to determine which significantly related variables were sensitive enough to distinguish the multiple sclerosis patients from healthy aged-matched control subjects.

METHODS

Participants

Ten subjects with relapsing remitting multiple sclerosis with mean and standard deviation age of 39. 10 ± 8.27 years and 8 age-matched control subjects mean age 38.5 ± 8.98 years participated in this study. The mean height and mass of the MS subjects respectively was 171.15 ±12.66 cm and 76.56 ±12.58 kg, and the mean height and mass of the control subjects was respectively 166.37 ± 10.82 cm and 73.75 ±14.49 kg. MS subjects were included in this study if they could walk 100 yards without a walking aide. Subjects were excluded if they had other neurological, orthopedic, cardiac, or respiratory problems not associated with multiple sclerosis that affected their ability to walk. Each subject participated in two testing sessions: one in the morning and one in the afternoon. All participants signed an informed consent form in accordance with the University of Delaware's Human Subjects Review Board.

Apparatus

An eight-camera Motion Analysis Eagle digital camera system with Real-time integrated software by the Motion Analysis Corporation (Santa Rosa, CA 95403) was used to collect the data. The accuracy of the camera system is 1mm in a 3m volume (Richards 1999). The cameras recorded the positions of 5 mm reflective marker cubes placed on the body at a rate of 60 frames per second.

Procedures

Reflective marker cubes were placed on the body in compliance with the Helen Hayes Marker set. The markers were placed on the skin or on securely wrapped neoprene bands over the lateral and medial femoral condyles, lateral and medial malleoli, distal thighs, shanks, between the second and third metatarsals, posterior calcanei, anterior superior iliac spines (ASIS), sacrum, acromion processes, humeri, styloid processes of radius and ulna, and on the front, back, and top of the head (Motion Analysis Corporation, 2000). Next, a static trial was performed in order to determine virtual knee and ankle centers. For the static tests, subjects stood with feet shoulder-width apart and arms away from their bodies. To determine the hip centers, two standing trials were taken. The standing trial required the subjects to swing each leg front and back and to the side with at least 45 degrees of hip flexion and extension and 20 degrees of abduction and adduction. After the standing trials, the medial malleoli markers and the medial femoral condyles markers were removed and the subjects were then required to:

1. Rate their exertion level based on Borg's Scale for Perceived Exertion (RPE) (Borg 1998) and their fatigue level on a visual analog scale (Krupp 1998). The visual analog scale asked subjects to rate their fatigue level by drawing a vertical line

on a 0-100 mm scale, with 0 representing no fatigue and 100 representing fatigue so severe that the subject was unable to move.

2. Walk a length of approximately 4.5 m at least 6 times at their comfortable pace in order to collect kinematic data.

3. Rate their level of perceived exertion.

4. Walk over ground without data collection until their RPE increased by 3 levels. However, subjects were only required to walk for a maximum of fifteen minutes even if their RPE did not increase by three levels.

5. Walk a minimum of 6 more walking trials with data collection

6. Rate their level of perceived exertion and fatigue

The multiple sclerosis subjects' disability level was rated using the EDSS by a trained neurologist within four months of testing. One study examined the changes in EDSS score in patients with relapsing remitting multiple sclerosis over a four-year period. The researchers found no significant changes in EDSS score over the four-year period (Patel et al. 1999).

Data Analysis

Orthotrak® software was used to calculate step length (cm), step width (cm), step rate (cm), double support time (s), walking speed (cm/s), and center of gravity (COG) mediolateral range of motion (cm). Step width, step length, and walking speed were normalized by the subject's height. The standard deviations (SD) of each variable were used to measure the variability between approximately 3 gait cycles.

According to Winter et al (1990a), the primary role of the legs is to maintain the orientation of the upper body. Therefore, a vector from the center of the

pelvis to the midpoint of the shoulder markers was created in order to determine the angular range of motion of the trunk. The position of the pelvis was found by averaging the two ASIS marker positions and sacrum marker position twice. Due to the position of the sacrum relative to the ASIS, the position of the sacrum was more heavily weighted in the average. The midpoint of the shoulders was calculated by finding the midpoint of the two acromium process marker positions. The position of the vector was calculated for each stride from right heel strike to the next right heel strike. The vector's x and y coordinates were then rotated into a local coordinate system relative to the room's vertical axis. The local x-axis approximated the direction of walk, and the local y–axis approximated the body's lateral axis. Theta in the sagittal plane was defined as the angle between the room's vertical axis and the vector in the local x direction, and theta in the frontal plane was defined as the angle between the room's vertical axis and the vector in the local y direction. If the person walked with their trunk parallel to the room's vertical axis then theta would be 0 degrees. The range of the thetas in the frontal and sagittal planes were calculated for each stride.

The lateral COG displacement between strides was measured in a horizontal plane about a vector created from COG positions at successive right heel strikes. The displacement of the COG was calculated for each stride on the right side.

To determine how straight the person walked, the lateral COG displacement was calculated for the entire walking trial. Lateral displacement was defined as the horizontal range of motion about the room's x-axis, which defined the direction of walk. The lateral range was not calculated for each stride, but included the

lateral COG displacement over the several strides needed to cover the whole camera volume.

The MS results of step length, step rate, double support time, step width, walking speed, lateral COG displacement between strides, lateral COG displacement, anterior-posterior trunk theta range, mediolateral trunk theta range, and the standard deviations of these variables were correlated with the EDSS and the fatigue scores using Pearson's product-moment correlation coefficients to determine if a statistically significant relationship ($p < 0.05$) existed. Also, the EDSS score and the change in fatigue score from the different trials (AM Fresh to AM Fatigue, PM Fresh to PM Fatigue, AM Fresh to PM Fresh, and AM Fresh to PM Fatigue) were correlated ($p< 0.05$) with the corresponding changes of the temporal spatial, center of gravity, and trunk movement variables for all the MS subjects. The variables that correlated with EDSS and fatigue level were then entered into a one-way ANOVA to determine if there was a statistical difference ($p < 0.05$) between the control group and the MS group. A repeated-measures ANOVA was used to determine statistical differences ($p < 0.05$), between the groups and testing sessions for fatigue and walking speed.

RESULTS

There were no statistical differences ($p < 0.05$) between the MS subjects and control subjects with respect to age ($p=0.885$), height ($p=0.410$), or mass ($p=0.665$). The mean EDSS score was 2.8 ± 1.01, and the range was 1.5-4.5. All of the MS patients in the present study were diagnosed with relapsing-remitting MS. Two subjects had an EDSS score of 1.5, therefore the two subjects were without disability, and had only minimal neurological impairment (Kurtzke 1983). One

person had an EDSS score of 4.5, which meant that the subject was ambulatory with "relatively severe disability" and obvious neurological impairment (Kurtzke 1983).

As shown in Figure 1, there was a significant difference for fatigue level between groups ($p = 0.002$), between sessions ($p = 0.000$), and there was a significant interaction effect ($p = 0.005$). Tukey's HSD test for unequal N was used to determine where the differences occurred. The fatigue level in the MS group during the AM Fresh trials (11.85 ±13.66 mm) was significantly different ($p = 0.001$) from the AM Fatigue trials (28.20 ± 16.29 mm), and the fatigue level in the MS PM Fresh trials (22.5 ± 17.69 mm) was significantly different ($p =0.009$) from the PM Fatigue trials (35.95 ± 19.74mm). The AM Fresh trials were significantly different from the PM Fatigue trials ($p =0.000$) for the MS group. The MS group AM Fresh and the PM Fresh were not significantly different ($p= 0.074$) from each other. None of the control group fatigue levels were significantly different between sessions. The MS group was not significantly different from the control group for the AM Fresh trials ($p = 0.340$). The MS group fatigue level was significantly different from the control group fatigue level for the AM Fatigue trials ($p = 0.000$), the PM Fresh trials ($p = 0.000$), and the PM Fatigue trials ($p = 0.000$).

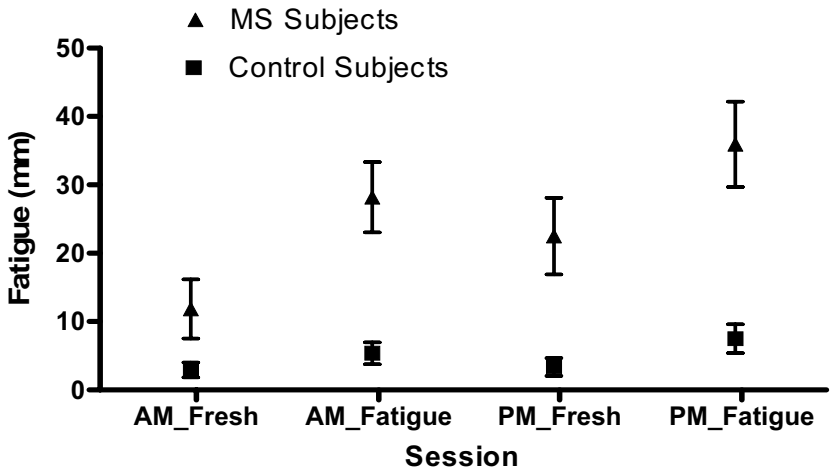

Figure 1: Differences in fatigue level between control subjects and MS subjects for each session.

Tables 1 and 2 list the r-values for the MS subjects' correlations for the different variables with the EDSS score. Fourteen variables correlated significantly with the MS subjects' EDSS scores. Tables 3 and 4 list the r-values for the MS subjects' correlations of the changes between trials for the different variables with the changes in the corresponding fatigue levels. Only two variables were significantly correlated with change in fatigue. Tables 5 and 6 list the r-values for the correlations between MS subjects' correlations with the EDSS score and the change in COG, trunk thetas, and temporal-spatial variables. Only three variables had significant relationships with the EDSS scores. Figures 2 to 19 are scatter plots of the significantly related variables. There was one MS Subject with an EDSS score of 4.5, and with the low number of subjects, having one subject more affected than the rest of the subjects may have created stronger correlations. Figures 3, 6, 9, 11, 12, 13, and 18 are examples where the one subject increased the strength of the correlations.

Table 1: The correlation coefficients between each MS subject's COG and trunk variables listed and their EDSS scores. Significant ($p<0.05$) correlations are marked with an asterisk.

VARIABLE	AM FRESH	AM FATIGUE	PM FRESH	PM FATIGUE
Lateral COG Displacement Between Strides	0.527	0.620	0.465	0.618
SD Lateral COG Displacement Between Strides	0.462	0.373	0.532	0.699*
Lateral COG Displacement	0.483	0.558	0.744*	0.777*
SD Lateral COG Displacement	0.313	0.366	0.775*	0.697*
Mediolateral Theta Range	0.231	0.330	0.342	0.463
SD Mediolateral Theta Range	0.554	0.745*	0.572	0.797*
Anterior Posterior Theta Range	0.294	0.466	0.327	0.515
SD Anterior Posterior Theta Range	0.648*	0.550	0.491	0.420

Table 2: The correlation coefficients between each MS subject's temporal-spatial variables listed and their EDSS scores. Significant ($p < 0.05$) correlations are marked with an asterisk.

VARIABLE	AM FRESH	AM FATIGUE	PM FRESH	PM FATIGUE
Step Length	-0.378	-0.430	-0.346	-0.400
SD Step Length	0.524	0.550	0.410	0.339
Step Width	0.384	0.451	0.513	0.515
SD Step Width	0.334	0.290	0.177	0.113
Double Support Time	0.378	0.622	0.464	0.572
SD Double Support Time	0.054	0.182	0.250	0.426
Step Rate	-0.438	-0.484	-0.434	-0.439
SD Step Rate	0.578	0.835*	0.450	0.701
Walking Speed	-0.496	-0.615	-0.457	-0.489
SD Walking Speed	0.370	0.668*	0.815*	0.668*

Table 3: The correlation coefficients between each of the MS subject's change in center of gravity and trunk theta variables with their change in fatigue scores. Significant correlations ($p < 0.05$) are marked with an asterisk.

VARIABLE	AM FRESH TO AM FATIGUE	PM FRESH TO PM FATIGUE	AM FRESH TO PM FRESH	AM FRESH TO PM FATIGUE
Lateral COG Displacement Between Strides	-0.315	-0.350	0.609	-0.224
SD Lateral COG Displacement Between Strides	-0.002	0.028	-0.384	-0.817*
Lateral COG Displacement	0.588	0.110	-0.590	-0.491
SD Lateral COG Displacement	0.383	0.862*	-0.501	-0.563
Mediolateral Theta Range	0.334	0.296	-0.078	-0.220
SD Mediolateral Theta Range	-0.058	0.487	0.257	-0.034
Anterior Posterior Theta Range	-0.034	0.042	-0.324	-0.368
SD Anterior Posterior Theta Range	-0.257	0.296	-0.018	0.014

Table 4: The correlation coefficients between each of the MS subject's changes of the temporal-spatial variables and their change in fatigue scores. Significant correlations ($p < 0.05$) are marked with an asterisk.

VARIABLE	AM FRESH TO AM FATIGUE	PM FRESH TO PM FATIGUE	AM FRESH TO PM FRESH	AM FRESH TO PM FATIGUE
Step Length	-0.118	0.101	-0.583	-0.397
SD Step Length	-0.432	-0.009	-0.158	-0.196
Step Width	-0.198	-0.163	-0.211	-0.456
SD Step Width	0.312	-0.040	-0.030	-0.130
Double Support Time	-0.040	0.343	0.263	-0.105
SD Double Support Time	0.195	-0.319	-0.175	-0.573
Step Rate	0.412	0.065	-0.598	-0.397
SD Step Rate	-0.078	0.374	0.112	-0.466
Walking Speed	-0.014	-0.170	-0.057	-0.513
SD Walking Speed	0.258	-0.243	-0.338	-0.113

Table 5: The correlation coefficients between each of the MS subject's change in center of gravity and trunk theta variables with their EDSS scores. Significant correlations ($p < 0.05$) are marked with an asterisk.

VARIABLE	AM FRESH TO AM FATIGUE	PM FRESH TO PM FATIGUE	AM FRESH TO PM FRESH	AM FRESH TO PM FATIGUE
Lateral COG Displacement Between Strides	0.413	0.519	-0.433	0.355
SD Lateral COG Displacement Between Strides	-0.275	-0.054	-0.039	-0.093
Lateral COG Displacement	0.520	0.430	-0.205	-0.043
SD Lateral COG Displacement	0.271	0.459	-0.037	0.365
Mediolateral Theta Range	0.409	0.608	0.219	0.528
SD Mediolateral Theta Range	0.548	0.423	0.046	0.540
Anterior Posterior Theta Range	0.481	0.683*	0.031	0.537
SD Anterior Posterior Theta Range	0.001	-0.326	-0.002	-0.566

Table 6: The correlation coefficients between each of the MS subject's change in the temporal-spatial variables and their EDSS scores. Significant correlations ($p<0.05$) are marked with an asterisk.

VARIABLE	AM FRESH TO AM FATIGUE	PM FRESH TO PM FATIGUE	AM FRESH TO PM FRESH	AM FRESH TO PM FATIGUE
Step Length	-0.402	-0.433	-0.047	-0.291
SD Step Length	-0.012	-0.057	-0.174	-0.079
Stride Width	0.062	0.065	0.042	0.056
SD Stride Width	0.019	-0.072	-0.310	-0.273
Double Support Time	0.830*	0.628	0.113	0.510
SD Double Support Time	0.156	0.037	0.196	0.313
Step Rate	-0.412	-0.345	-0.034	-0.371
SD Step Rate	0.544	0.214	-0.310	-0.087
Walking Speed	-0.765*	-0.324	0.140	-0.392
SD Walking Speed	0.424	-0.588	0.484	0.077

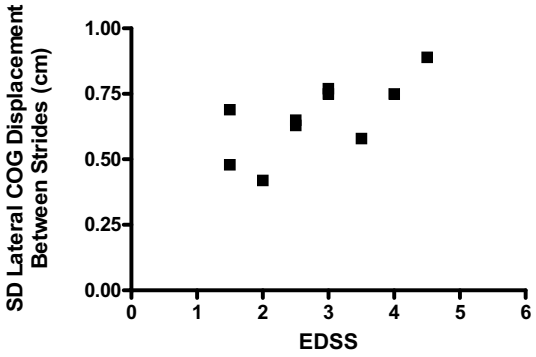

Figure 2: The relationship between SD of lateral COG displacement between strides during the PM fatigue session as related to EDSS r=0.699

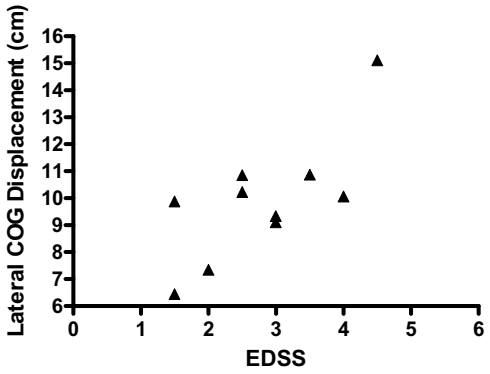

Figure 3: The relationship between EDSS and lateral COG displacement during the PM fresh session r=0.744

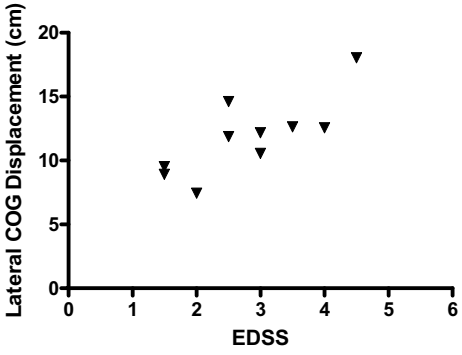

Figure 4: The relationship between EDSS and lateral COG displacement during the PM fatigue session r=0.777

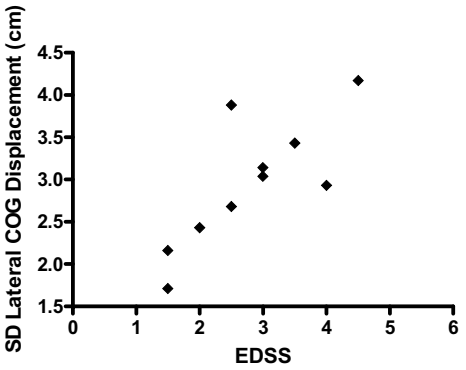

Figure 5: The relationship between EDSS and the SD of lateral COG displacement during the PM fresh session r=0.775

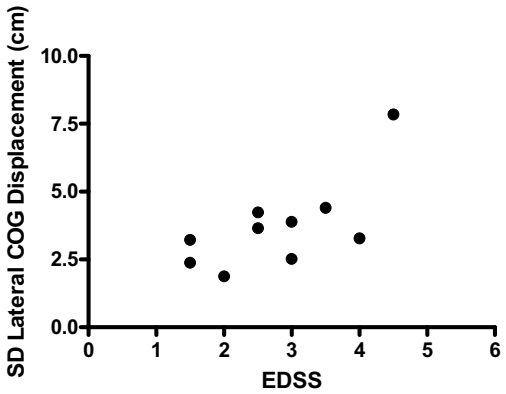

Figure 6: The relationship between EDSS and the SD of lateral COG displacement during the PM fatigue session r=0.697

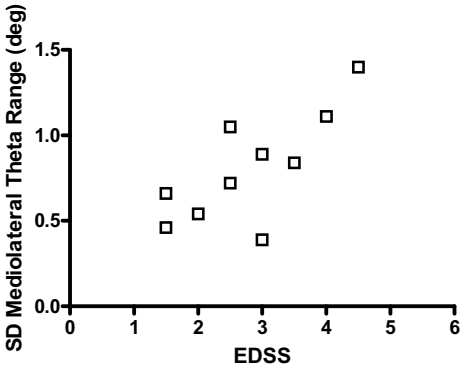

Figure 7: The relationship between EDSS and the SD of mediolateral theta range during the AM fatigue session r=0.745.

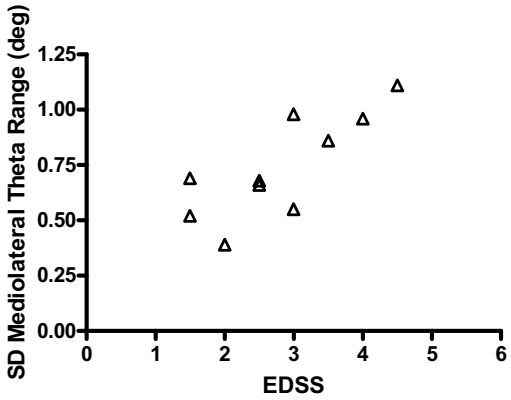

Figure 8: The relationship between EDSS and the SD of mediolateral theta range during the PM fatigue session r=0.797.

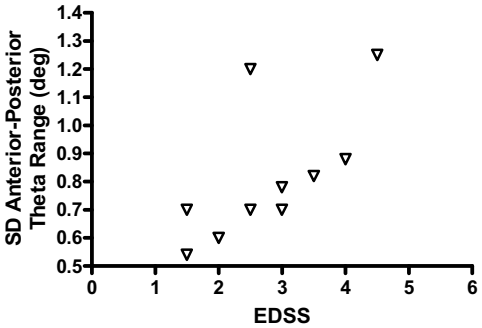

Figure 9: The relationship between EDSS and SD of anterior-posterior theta range during the AM fresh session r=0.648.

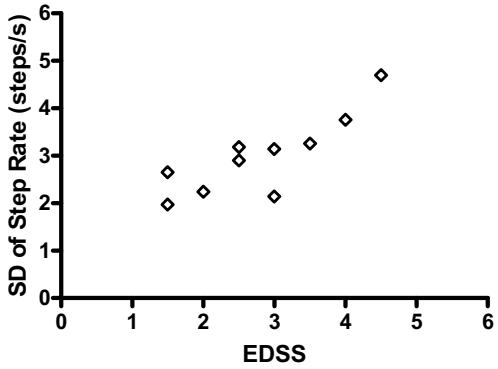

Figure 10: The relationship between EDSS and the SD of step rate during the AM fatigue session r=0.835

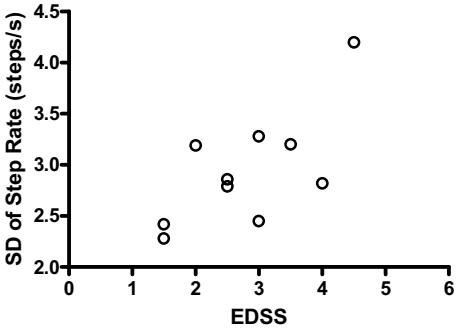

Figure 11: The relationship between EDSS and the SD of step rate during the PM fatigue session r=0.701

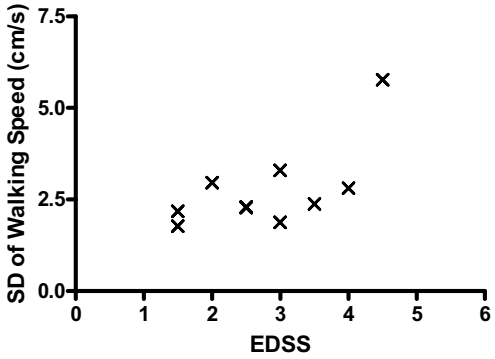

Figure 12: The relationship between EDSS and the SD of walking speed during the AM fatigue session r=0.668.

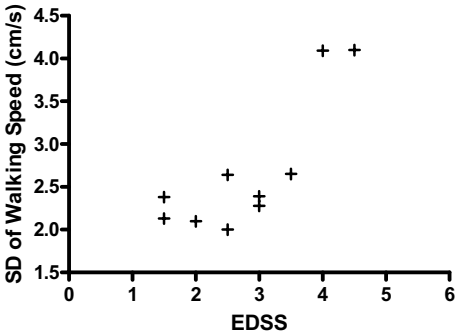

Figure 13: The relationship between EDSS and the SD of walking speed during the PM fresh session r=0.815

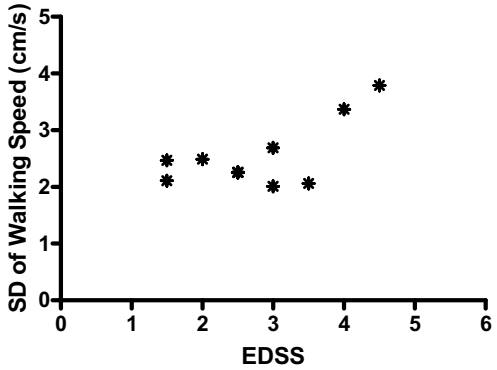

Figure 14: The relationship between EDSS and the SD of walking speed during the PM fatigue session r=0.668.

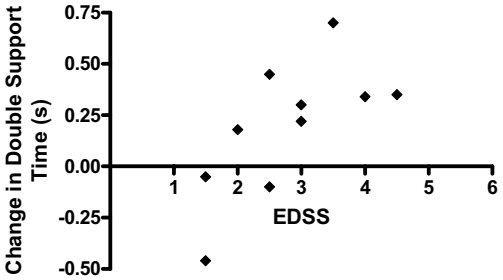

Figure 15: The relationship between EDSS and the change in double support time from the AM fresh sessions to the AM fatigue session r=0.683

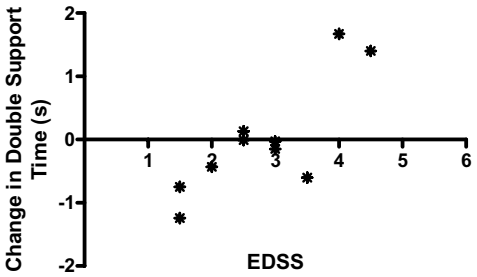

Figure 16: The relationship between EDSS and the change in double support time from the AM fresh session to the AM fatigue session r=0.830

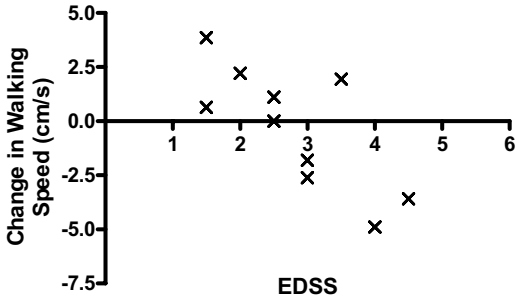

Figure 17: The relationship between EDSS and the change in walking speed from the AM fresh session to the AM fatigue session r=-0.765

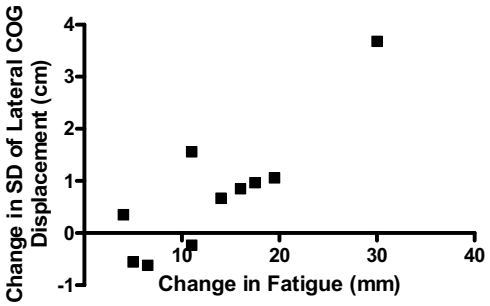

Figure 18: The relationship between the change in fatigue and the change in the SD of lateral COG displacement from the PM fresh session to PM fatigue session r=0.862

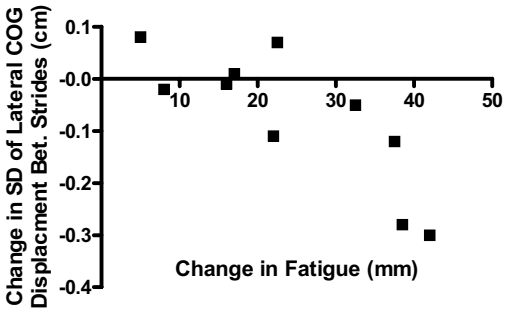

Figure 19: The relationship between the change in fatigue and the change in SD lateral COG displacement between strides from the AM Fresh to the PM Fatigue session r=-0.817

The variables that significantly correlated with EDSS scores and Fatigue levels were used to compare the MS subjects with the control subjects. Two MS groups were created for this comparison. Since the EDSS score of 1.5 represents no disability and only slight neurological impairment, a subgroup was created. The group labeled MS1 included all MS subjects, and the group labeled MS2 included all MS subjects that had an EDSS score of 2 or higher. The mean EDSS score of MS2 was 3.13 ± 0.83. Table 7 includes the p-values for all comparisons. When comparing MS1 and controls, two variables were significantly different from each other: the standard deviation of the lateral COG displacement between strides PM Fatigue (MS1 0.66 ± 0.14 cm, control 0.49 ± 0.07 cm), and the change in standard deviation of lateral COG displacement PM Fresh to PM Fatigue (MS1 0.79 ± 1.33 cm, control -0.48 ± 0.98 cm). Also, the standard deviation of the lateral COG displacement between strides PM Fatigue was significantly different when comparing MS2 and the control group (MS2 0.68 ± 0.14 cm, control 0.49 ± 0.07 cm). The change in standard deviation of lateral COG displacement from PM Fresh to PM Fatigue (MS2 0.75 ±

1.41 cm, control -0.48 ± 0.98 cm) was not significantly different when comparing the MS2 group from the controls. None of the other variables that significantly correlated with EDSS or change in fatigue level were significantly different in MS subjects or controls.

Table 7: P values of variables that significantly correlated with either the MS subjects' EDSS scores or fatigue levels. MS1 vs. control compared all MS subjects with the control subjects. MS2 vs. control compared all MS subjects except those with EDSS of 1.5 with the control subjects. Significant p values ($p < 0.05$) are marked with an asterisk.

VARIABLE	CONTROL VS. MS1	CONTROL VS. MS2
EDSS		
SD Lateral COG Displacement Between Strides PM Fatigue	0.007*	0.004*
Lateral COG Displacement PM	0.769	0.483
Lateral COG Displacement PM Fatigue	0.145	0.077
SD Lateral COG Displacement PM	0.376	0.731
SD Lateral COG Displacement PM Fatigue	0.248	0.179
SD Mediolateral Theta Range AM Fatigue	0.362	0.189
SD Mediolateral Theta Range PM Fatigue	0.163	0.115
SD Anterior Posterior Theta Range AM	0.201	0.369
SD Step Rate AM Fatigue	0.842	0.801
SD Step Rate PM Fatigue	0.986	0.612
SD Speed AM Fatigue	0.854	0.846
SD Speed PM	0.224	0.351
SD Speed PM Fatigue	0.463	0.636
Change in Fatigue		
SD Lateral COG Displacement between Strides AM Fresh to PM Fatigue	0.312	0.491
SD Lateral Range COG Displacement PM Fresh to PM Fatigue	0.034*	0.062
Relationship between EDSS scores and changes in variables		
Double support time AM Fresh to AM Fatigue	0.880	0.943
Walking Speed AM Fresh to AM Fatigue	0.892	0.550
Anterior Posterior Theta Range PM Fresh to PM Fatigue	0.683	0.822

Figure 20 shows the differences for preferred walking speed when comparing the MS1 group and the control group. There was a significant group difference between MS1 and controls ($p = 0.012$). There was no significant difference between sessions ($p = 0.418$) and no interaction effect ($p = 0.141$). Therefore, since the variables listed in Tables 1-6 may have been affected by speed and not disability level, semi-partial correlations for each of the gait variables were calculated using walking speed as the covariate. The effect of walking speed was not removed from the disability level and fatigue scores, because it was not likely that speed would impact the two measures.

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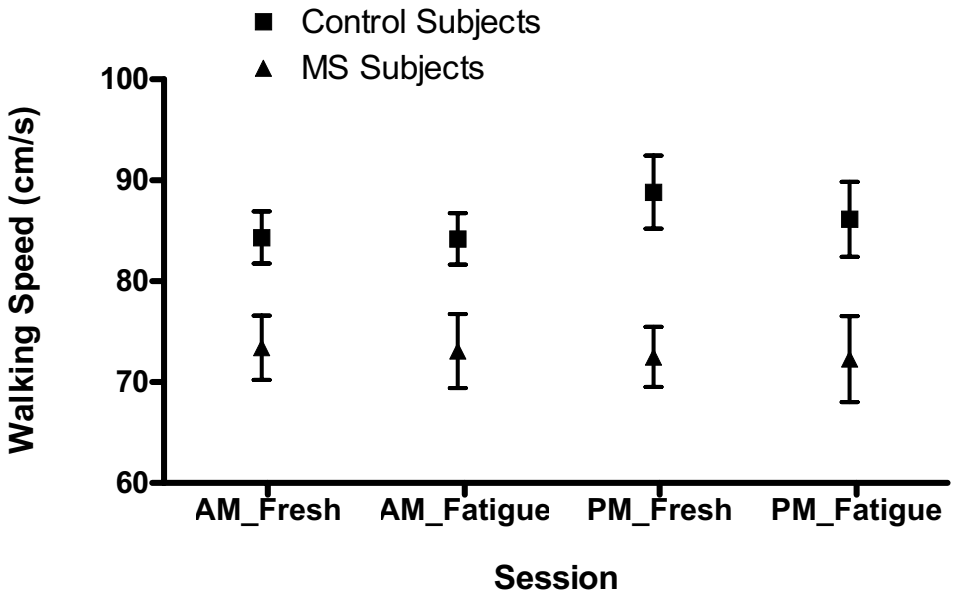

Figure 20: Differences in walking speed between the MS and control subjects for each session

Table 8 lists the significant variables and their semi-partial correlations to the MS EDSS score, and the change in fatigue level. The effects of walking speed were removed from each of the variables. Three variables during specific time periods correlated significantly with the EDSS score, however no new variables were found to correlate with the EDSS score when speed was removed from the variables. Five variables were significantly related ($p < 0.05$) with change in fatigue including three new variables: lateral COG displacement between strides AM Fresh to PM Fresh, lateral COG displacement AM Fresh to AM Fatigue, and step length AM Fresh to PM Fresh. When comparing the relationship between EDSS and the change in the COG displacement, trunk thetas, and temporal-spatial variables, only two variables were significantly related: the anterior-posterior theta range AM Fresh to AM Fatigue and the anterior-posterior theta range from PM Fresh to PM Fatigue.

Table 8: Semi-partial correlation coefficients for EDSS and fatigue with speed as a covariate for the variables that were significantly related ($p < 0.05$) to EDSS or the change fatigue. Variables that were also related when speed was not used as a covariate were marked by an asterisk.

VARIABLE	EDSS	FATIGUE
SD Lateral Range COG Displacement PM*	0.646	
SD Mediolateral Theta Range PM Fatigue*	0.651	
SD Step Rate PM Fatigue*	0.697	
Anterior Posterior Theta Range PM Fresh to PM Fatigue*	0.728	
Anterior Posterior Theta Range AM Fresh to PM Fatigue	0.641	
Lateral Range COG Displacement between strides AM Fresh to PM Fresh		0.860
SD Lateral Range COG Displacement between strides from AM Fresh to PM Fatigue*		-0.771
Lateral COG Displacement AM Fresh to AM Fatigue		0.649
SD Lateral Range COG Displacement PM Fresh to PM Fatigue*		0.858
Step Length AM Fresh to PM Fresh		-0.689

The change in standard deviation of lateral COG Displacement between PM Fresh to PM Fatigue was significantly different ($p = 0.033$) between the control subjects and the MS1 group when speed was used as a covariate. The variable was not however significantly different ($p = 0.061$) between the MS2 group and the control group. No other variables were significantly different ($p < 0.05$) when comparing the two MS groups from the control groups when the effects of speed were removed.

DISCUSSION

The purpose of this study was to determine which of the many dynamic balance variables were related to the severity of disease and fatigue when examining dynamic balance in multiple sclerosis patients. One of the main issues in dynamic balance literature, regardless of population, has been determining which variables are the most applicable in measuring dynamic balance impairment. The majority of the dynamic balance research in the elderly population, for example, has examined the relationship between temporal-spatial variables and falls. However, the role of the specific temporal-spatial variables in relation to balance impairment has also been discussed. For example, researchers have disagreed on the role of step width as a measure of balance while walking (Maki 1997; Krebs 2002). Also, previous studies have found that the variability of the selected variables was more related to balance impairment than the values of the variables alone (Hausdorff et al. 1997; Maki 1997; Menz et al. 2003). While temporal-spatial variables are relatively easy to measure, they do not tell the whole story and therefore they were not the only variables discussed in the literature. Past researchers have also examined trunk movement and COG movement when discussing differences in dynamic balance and falls (Pavol et

al. 2001; Chou et al. 2003). While there have been many studies that have examined dynamic balance in other populations, very few of these variables have been examined in the multiple sclerosis population. For the present study we have chosen to examine variables that have been prominent in the literature from three categories of dynamic balance variables: temporal-spatial, COG, and trunk movement. Also, because previous studies have examined variability as an indicator of elderly individuals who are likely to fall, we chose to examine the standard deviations of these variables (Maki, 1997; Hausdorff et al. 1997). We expected to find that the indicators of poor dynamic balance or a more cautious gait in the elderly population would indicate the same in the MS population, and that these indicators of poor dynamic balance would correlate to the severity of disease and fatigue.

The majority of MS patients have stated that fatigue was one of the main symptoms of the disease (Freal et al. 1984; Ford et al. 1998). The present study used a visual analog scale that allowed subjects to rate their fatigue subjectively. MS patients in the current study were significantly more fatigued from the morning and afternoon fresh trials to the morning and afternoon fatigue trials respectively, and these results agree with previous studies that found that fatigue may worsen after moderate or vigorous exercise (Freal et al. 1984; Krupp et al. 1988). The previous studies' measurements were obtained through questionnaires on general circumstances and not specific situations (Freal et al. 1984; Ford et al. 1998). The MS patients in the present study were not more fatigued in the afternoon fresh trials than in the morning fresh trials, in contrast to the findings of Morris et al. (2002) who found that MS patients were more fatigued in the afternoon than in the morning. Another study also found that MS subjects were more likely to be affected by fatigue in the afternoon than in the

morning; however the study examined only general impressions of overall fatigue (Freal et al. 1984). The subjects in the Morris et al (2002) study were also more neurologically involved than the subjects in the present study with a mean EDSS score of 3.8 and a range of 2.5 to 5.5. The MS subjects in the current study had a range of 1.5 to 4.5 with a mean of 2.8. The MS patients in the present study were more fatigued than the control subjects during the morning fatigued trials, and both afternoon trials.

The temporal-spatial variables were correlated to the change in fatigue and EDSS in order to determine how the severity of the disease affected variables of dynamic balance. Step length, step width, double support time, step rate, and walking speed did not correlate with disability level at any specific time period. In agreement with the present study Gehlsen et al, (1986), found no significant correlations with MS patients and disability for step rate and double support time. In contrast to the present study however, they found significant correlations between disability level and walking speed and stride length. One reason for the possible differences between step length and walking speed results in the two studies was that the subjects in Gehlsen et al. (1986) were more affected (Mean Kurtze Scale of 4 ± 1 compared to the EDSS score in the present study of 2.8 ± 1.01). The range of disability level in the MS patients who participated in the Gehlsen et al. (1986) study was 3 to 6 according to the Kurtze Scale Rating to evaluate disability level. Level 3 according to the Kurtze Scale represented people with "mild disorder not sufficient to impede normal activities" and level 6 represented patients that require "assistance when walking" (Kurtze 1983). None of the subjects in the present study used walking aides.

None of the temporal-spatial variables correlated significantly with change in fatigue when the effects of speed were not removed. Morris et al. (2002) also found that there were no significant correlations between fatigue and the temporal-spatial variables despite the MS patients in their study being more affected by the disease.

There were some significant relationships when examining the severity of disease and the changes in the temporal-spatial variables between the different sessions. The change in double support time and walking speed were significantly related to disability level. The change in double support time was significantly related to the severity of disease from the morning fresh trails to the morning fatigue trials. There was also a trend towards a significant relationship during the afternoon fresh trials to the afternoon fatigue trials, but not between the morning and afternoon fresh trials. As subjects walked for longer periods the length of double support time increased. Longer double support times have been associated with poorer balance in the elderly population (Winter et al. 1990b).

The change in walking speed from the morning fresh trials to the morning fatigued trials was also significantly related to the severity of disease. As severity of the disease increased, the subject was more likely to walk slower during the second set of trials. Decreased walking speed has been associated with fear of falling and poor balance (Maki 1997; Menz et al. 2003). However, the same trend was not seen between the afternoon trials, or between the morning and afternoon fresh trials. A possible reason for the lack of consistent results between sessions was that we did not control for speed. The only instructions were for subjects to walk at a "comfortable pace", therefore it was up to the subject to determine their own natural pace. One

subject, for example, with an EDSS score of 2 increased her speed by 18.16 cm/s from the afternoon fresh trials to the afternoon fatigued trials. The other subjects changed their speed from the afternoon fresh trials to the afternoon fatigued trials within the range of -7.37 cm/s to 1.54 cm/s.

We also examined the variability of the temporal-spatial variables to determine their relationship with the MS subject's disability level and fatigue level. The only variables that correlated significantly with EDSS during a specific time period were the standard deviation of walking speed during the morning fatigue session and the afternoon sessions and the standard deviation of step rate during both fatigue trials. Neither variable was significantly related to EDSS during the morning fresh trials, suggesting that when subjects were the most rested, the severity of disease did not have an impact on walking speed variability and step rate variability. The variability of walking speed, but not step rate, seemed to be related to the severity of disease and the time of day. Increased standard deviation of walking speed between strides has been found to be an indicator of elderly subjects more likely to fall (Maki 1997). Previous researchers have not examined the relationship of the variability of step rate as related to falls in the elderly population, however stride time variability has been found to be an be an indicator of someone more likely to fall (Hausdorff et al. 1997). Therefore, the increased variability of step rate and the variability of walking speed in relation to the severity of disease presents evidence that MS subjects may have an increased likelihood of falling the more severely the subject was affected by MS.

Neither the MS subjects nor the control subjects in the present study were significantly different from each other with respect to any of the significantly

correlated variables. Morris et al. (2002) found that changes from morning to afternoon with respect to speed, cadence, stride length, and double limb support time were more variable in MS subjects than the control subjects, however the researchers did not perform statistical analysis on these results so it is unclear whether these differences were significant.

Since the previous studies on MS and gait have all found that walking speed was significantly slower in MS subjects than control subjects (Benedetti et al, 1999 and Morris et al, 2002), and since walking speed can influence other variables, we decided to compare speed between the MS group and control group. The MS group in the present study walked significantly slower than the control group. Speed therefore was used as a covariate. With the effects of speed removed only the standard deviation of step rate during the afternoon fatigue trials remained significantly correlated to EDSS. The results suggested that the relationship with EDSS and the standard deviation of step rate was not dependent on the changes in speed and strengthens the relationship between the severity of the disease and step rate variability. Since step timing variability has been associated with falls in the elderly population (Hausdorff et al. 1997) it is feasible that increased step rate variability in the MS population might indicate increased balance impairment related to the severity of disease. Conversely, it showed that the relationship between EDSS and the change in double support time might not be related to the severity of disease but related to the change in walking speed. However, with speed as a covariate the MS group was not different from the control group with respect to the standard deviation of step rate during the afternoon fatigue trial. When speed was not used as a covariate, none of the variables correlated with the change in fatigue. However, when the effects of

speed were removed the change in step length was negatively related to the change in fatigue from morning to afternoon. Reduced step length has been associated with a more cautious gait and fear of falling in the elderly population (Maki 1997; Menz et al. 2003) suggesting MS subjects might have a more cautious gait. The change in step length was not significantly different in MS subjects than controls when speed was used as a covariate.

Other than the change in walking speed, the change in double support time, the change in step length when speed was used as a covariate, and walking speed variability, no other temporal-spatial variable that had been significantly related to balance impairment in the elderly population was related to either fatigue or disability in the multiple sclerosis subjects. Also, while there was some indication of decreased dynamic balance as the severity of disease increased, the relationship was not enough to distinguish between the control group and the MS group. Overall the results suggested that due to the lack of sensitivity of the significantly related temporal spatial variables to show differences between the MS subjects and the control subjects, this group of variables may not be useful when discussing dynamic balance in the MS population, especially in relation to self-rated fatigue.

Winter et al. (1993) determined that the primary role of the hip extensors and flexors were to control the orientation of the upper body during the support phase of gait. Therefore, we also examined the range of trunk movement in the anterior posterior and mediolateral directions to determine if there was a significant relationship with the severity of disease and fatigue level. The variability of mediolateral trunk movement during both fatigue trials was significantly related to the severity of disease, however the changes in the amount of variability of mediolateral

trunk movement between sessions was not related to severity of disease or change of fatigue. The more affected the subject the more variable the mediolateral movement. Although, the variability of mediolateral range was not significantly related to fatigue, the only significant relationships occurred during the fatigue sessions. As MS subjects were required to walk longer, there was an increase in the variability of mediolateral trunk movement. Trunk movement in the mediolateral direction alone was not significantly related to the severity of disease or fatigue level.

The change in anterior-posterior trunk movement between the afternoon sessions was significantly related to the severity of disease but not the change in fatigue. Therefore, the subjects that were more severely affected by MS had a greater increase in anterior posterior range. Recovery from trips from was dependent on trunk location in the anterior posterior direction (Pavol et al. 2001). Subjects who fell while trying to recover by stepping in the forward direction were more likely to fall if there was a more forward center of gravity of the head-arms-trunk (Pavol et al. 2001). Anterior-posterior theta movement during the individual sessions was not significantly related to the severity of the disease. Gehlsen et al. (1986) also did not find a significant relationship between anterior posterior theta range and disability level. The variability of anterior posterior movement was not related to fatigue. It was however related to the severity of disease during the morning trials. When comparing the control subjects and the MS subjects the variability of mediolateral range during the fatigue trials, the change in anterior posterior theta range between the afternoon fresh trials and the afternoon fatigue trials, and the variability of anterior posterior movement during the morning sessions were not significantly different between the two groups. When the effects of speed were removed only the changes in anterior-

posterior theta ranges between the afternoon trials remained significantly related to disability level. Therefore, the changes in speed were not solely responsible for the changes in anterior -posterior trunk movement. The changes may be due to the pathology of multiple sclerosis. While the variables were significantly related to the severity of disease in the MS patients, they were not different from the same measures than the control subjects.

Walking requires the ability to balance the upper body while controlling the center of gravity over a moving base of support (Winter et al. 1990a; Winter et al. 1993). Dynamic balance of the upper body and legs was guaranteed when the center of gravity movement stayed within the base of support in the frontal plane (MacKinnon and Winter 1993). If the center of gravity moved too far in one direction the action could cause a person to fall if he was unable to compensate fast enough (Chou et al. 2003). The more severe the disease or fatigue a person feels may contribute to that person's ability to control his center of gravity movement from stride to stride or while walking a straight line. In the present study, the more affected by MS the subject was the greater the center of gravity movement and the more variable the center of gravity movement was while walking in a straight line during the individual afternoon sessions. However, only the variability of center of gravity movement while walking in a straight line was related to the severity of disease when speed was used as a covariate during the afternoon fresh session. The change in the variability of the center of gravity movement over several strides was related to the change in fatigue level from the afternoon fresh trials to the afternoon fatigue trials, regardless of whether speed was used as a covariate. The change in center of gravity movement between morning sessions was significantly related to fatigue when speed

was used as a covariate. Only one of the variables was significantly different when comparing the MS group from the control group. The change in the variability of lateral COG displacement between afternoon sessions was significantly different between the MS group and the control group regardless of whether speed was used as a covariate. Therefore, the increase in variability seen in the MS group was not only associated with speed. The control group decreased in lateral COG displacement variability between afternoon sessions.

The change in the amount of center of gravity movement from the morning to afternoon sessions was also related to the change in fatigue when speed was used as a covariate. The variable was not significantly different when comparing the MS subjects and the control subjects. Chou et al. (2003) compared COG mediolateral displacement in healthy elderly subjects and elderly subjects that had balance impairments, the researchers also found no increases in COG displacement when walking over ground. The researchers did, however, find an increase in COG displacement when crossing obstacles as little as 5 cm. Therefore, just walking over ground might not be enough of a challenge to determine a significant increase in lateral COG displacement. The center of gravity movement variability between strides was significantly related to the severity of disease during the afternoon fatigued session. This variable was significantly different when comparing MS subjects and control subjects.

There were some limitations in the present study. The method of fatiguing the patients in this study was a limitation. Subjects had to walk until they increased their RPE level by three points or 15 minutes passed. After walking for a period of minutes, subjects might have become bored with walking and reported a

higher RPE level in order to stop walking sooner. Another concern with self-rated measures was that subjects might report their fatigue or RPE score based on what they feel was expected of them. The amount of subjects might have contributed to the lack of significant differences in the gait variables between the two groups. For example, the lateral COG displacement during the afternoon fatigue sessions, and the change standard deviation of lateral COG displacement between afternoon sessions showed a trend toward significance when comparing the MS2 group and the control group. With more subjects the variables might have been significantly different between groups.

Only two variables that were significantly related to EDSS or fatigue level were also different between the two groups: variability of center of gravity range between strides during the afternoon fatigue sessions and the change in the variability of center of gravity displacement between the afternoon sessions. Possible reasons for the lack of significant differences in the other variables could be the low level of disability in this MS sample. Since there were significant correlations between disability level and the different variables, having MS subjects that had a mean EDSS score of 4.5 might show more differences when compared to controls. An EDSS score of 4.5 represents a patient who can still work a full day but requires more rest when walking distances greater than 300 m (Kurtze, 1983). For future research it might be worthwhile to perform the study on a population that would be more affected by the disease and fatigue in order to determine if the variables studied would be appropriate when discussing dynamic balance in subjects with higher EDSS scores. Also, walking alone might not be sufficient enough to detect differences between MS patients and controls with respect to the selected measures. Since the variability of center of

gravity movement between strides and the variability of center of gravity movement while walking in a straight line were the only significantly different variables between groups it would be interesting to see what would happen if the Chou et al. (2003) study was repeated in the MS population. Most likely there would also be differences between the MS group and control group with respect to the mediolateral center of gravity displacement and center of gravity variability and when stepping over obstacles.

CONCLUSION

The temporal-spatial variables, trunk variables, and center of gravity variables were less related to the severity of disease than the standard deviations of the variables. The change in temporal-spatial variables and trunk movement variables were more related to the severity of disease than fatigue, in contrast the change in the center of gravity variables were more related to the change in fatigue than the severity of disease, specifically when speed was used as a covariate. The significant relationships of increased double support time and reduced step length when speed was used as a covariate with severity of disease or fatigue showed that MS subjects like elderly subjects had a more cautious gait. The increase variability of step rate, walking speed, mediolateral trunk movement, and center of gravity movement in relation to the severity of disease or fatigue showed an indication that MS subjects had impaired dynamic balance as the severity of disease or fatigue increased. However, with the exception of the variability of center of gravity motion the variables were not sensitive enough to detect differences between the two groups.

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