Depression is A Predictor for Balance in People with Multiple Sclerosis

Alia A. Alghwiri PhD Associate Professor ,
Hanan Khalil PhD Associate Professor ,
Alham Al-Sharman PhD Assistant Professor ,
Khalid El-Salem MD, FAAN Professor of neurology

PII: S2211-0348(18)30173-1
DOI: 10.1016/j.msard.2018.05.013
Reference: MSARD 851

To appear in: *Multiple Sclerosis and Related Disorders*

Received date: 23 February 2018
Revised date: 16 April 2018
Accepted date: 16 May 2018

Please cite this article as: Alia A. Alghwiri PhD Associate Professor , Hanan Khalil PhD Associate Professor , Alham Al-Sharman PhD Assistant Professor , Khalid El-Salem MD, FAAN Professor of neurology , Depression is A Predictor for Balance in People with Multiple Sclerosis, *Multiple Sclerosis and Related Disorders* (2018), doi: 10.1016/j.msard.2018.05.013

Highlights

- Balance impairments are common in people with MS.
- Depression is a frequent disorder in individuals with MS.
- Depression is a predictor for balance deficits in people with MS.
- Management of persons with MS should cover both physical and psychological impairments.

Depression is A Predictor for Balance in People with Multiple Sclerosis

Alia A. Alghwiri[1]*; Hanan Khalil[2] ; Alham Al-sharman[2]; Khalid El-Salem[3]

Alia A. Alghwiri, PhD

Associate Professor

The University of Jordan

School of Rehabilitation Sciences, Department of Physical Therapy, Amman, Jordan

Hanan Khalil, PhD

Associate Professor

Jordan University of Science and Technology

Faculty of Applied Medical Sciences, Department of Rehabilitation Sciences, Irbid, Jordan

Alham Al-Sharman, PhD

Assistant Professor

Jordan University of Science and Technology

Faculty of Applied Medical Sciences, Department of Rehabilitation Sciences

Irbid, Jordan

Khalid El-Salem, MD, FAAN

Professor of neurology

Jordan University of Science and Technology

Faculty of Medicine, Department of Neurosciences, Irbid, Jordan

*Address all correspondence to Dr. Alia A. Alghwiri, Department of Physical Therapy, School of Rehabilitation Sciences, The University of Jordan, Amman 11942, Jordan. E-mail: alia.alghwiri@gmail.com. Phone number: 00962772155737.

Running title: Depression and Balance in People with MS.

Key words: Multiple sclerosis, Depression, Balance, Prediction.

Depression is A Predictor for Balance in People with Multiple Sclerosis

Abstract:

Background: Balance impairments are common and multifactorial among people with Multiple Sclerosis (MS). Depression is the most common psychological disorder in MS population and is strongly correlated with MS disease. Depression might be one of the factors that contribute to balance deficits in this population. However, the relationship between depression and balance impairments has not been explored in people with MS.

Objective: To investigate the association between depression and balance impairments in people with MS.

Methods: Cross sectional design was used in patients with MS. The Activities-specific Balance Confidence scale (ABC) and Berg Balance Scale (BBS) was used to assess balance. Beck Depression Inventory (BDI-II) was used to quantify depression and Kurtizki Expanded Disability Status Scale (EDSS) was utilized for the evaluation of MS disability severity. Pearson correlation coefficient was used to examine the association between depression and balance measurements. Multiple linear stepwise regressions were also conducted to find out if depression is a potential predictor for balance deficits.

Results: Seventy-five individuals with MS (Female=69%) with a mean age (SD) of 38.8 (10) and a mean (SD) EDSS score of 3.0 (1.4) were recruited in this study. Depression was present in 53% of the patients. Depression was significantly correlated with balance measurements and EDSS. However, multiple linear stepwise regressions found that only depression and age significantly predict balance.

Conclusion: Depression and balance were found frequent and associated in people with MS. Importantly depression was a significant predictor for balance impairments in individuals with MS. Balance rehabilitation may be hindered by depression. Therefore, depression should be evaluated and treated properly in individuals with MS.

Introduction

Multiple sclerosis (MS) is estimated to affect more than 2 million people worldwide, with an estimated prevalence of 30/100,000 (National Multiple Sclerosis Society, 2017; World Health Organization, 2008). Patients with MS suffer from a wide range of impairments and limitations. These impairments include physical, neuropsychiatric and psychosocial symptoms. Physical manifestations of MS may include spasticity, cerebellar, sensory, visual, and vestibular impairments that lead to balance and gait disorders.

Balance difficulties are important component for determining functional status in people with MS (Larocca, 2011). Deficits in balance usually occur early in the MS disease and typically worsen with the progression of the disease (Cavanaugh et al., 2011; Comber et al., 2017; Martin et al., 2006). Most of balance aspects were found impaired in people with MS including increased postural sway during standing (Huisinga et al., 2012; Spain et al., 2012), abnormal static and dynamic balance,(Fritz et al., 2015) and delayed postural reactions (Cameron & Lord, 2010). Several consequences were reported from poor balance in MS population including decreased physical activity, increased risk of falling and deterioration in quality of life (Klevan et al., 2014; Nilsagard, Denison, et al., 2009; Nilsagard, Lundholm, et al., 2009). Balance and walking abilities are closely related to each other (Cameron & Lord, 2010; Cattaneo et al., 2002). It is known that deficits in systems contributing to balance can impede dynamic stability during walking (Cattaneo et al., 2002; Fritz et al., 2015). It was reported that balance deficits are strong predictors of risk of falls in people with MS (Cattaneo et al., 2002; Kasser et al., 2011).

Recently, researchers have attempted to investigate factors that affect balance skills and may consequently contribute to the effectiveness of rehabilitation outcomes and reduction of risk of falling. However, balance is multifactorial and several interacting factors such as cognitive impairments (Sandroff, Hillman, et al., 2015; Sandroff, Pilutti, et al., 2015) and fatigue (Van Emmerik et al., 2010; Wolkorte et al., 2015) are found to be associated with impaired balance in people with MS. Despite the fact that depression is the most common psychological impairment in patients with MS (LaRocca et al., 1987) and found to present in 54% of this population

(Minden et al., 1987), research on the relationship between balance and depression specifically in patients with MS is deeply lacking.

In a study of geriatric population, authors found a significant correlation between depression (examined using the Geriatric Depression Scale) and balance skills utilizing the Berg Balance Scale and the Get Up and Go Test (Kose et al., 2005). Depression (examined by Beck Depression Inventory II) was also found correlated with balance and physical performance in patients post stroke (Alghwiri, 2016). Despite the possible explanations behind the relationship between depression and balance in geriatric and stroke populations, depression in people with MS has different characteristics.

Overall, an increase in investigating the relationship of MS and depression is driven by the introduction of MS drugs (such as steroids) that may aggravate or hasten depression in patients with MS. Additionally, depressive symptoms are experienced most often following initial diagnosis and during adjustment to having a chronic illness and then subsequently during an exacerbation (Siegert & Abernethy, 2005).

Depression, fatigue, and disability were found strongly correlated and represented strong predictors of quality of life in MS (Amato et al., 2001). Therefore, the existence of depression in MS population is attributed to multiple factors and may affect various body functions such as balance. This study aims to explore the relationship between depression and balance in people with MS, and whether depression can be used as a predictor to the balance status in this population. This is an important area as it would shed the light into important rehabilitative therapeutic options to comprehensively advise patients with MS.

Methods

Sample

A sequential sample of patients with MS participated in this observational study. Patients with MS were recruited from outpatient clinics from Amman and Irbid cities and through brochures about the study. The inclusion criteria were age of 18 years and older, a confirmed diagnosis of MS from a neurologist, ambulatory (able to walk independently with or without assistive devices), and the ability to follow commands. The exclusion criteria were patients using wheel chair for ambulation and pre-existing diagnosis of depression.

Procedures

Ethical approval was obtained from the ministry of health ethics committee. Interested patients were screened for eligibility by a neurology consultant. Research team explained the procedures of this study to eligible patients with MS who pass the inclusion criteria. Then patients signed informed consent. Demographic (Age, height, weight, gender) and health-related information (duration of the disease, type and location of MS) were collected from patients. Subsequently, a well-trained neurologist assessed the severity of the MS using the Kurtzke Expanded Disability Status Scale (EDSS). Finally, patients were asked to complete the Arabic versions of the Beck Depression Inventory (BDI-II) and Activities Specific Balance Confidence Scale (ABC). Balance was objectively assessed using Berg Balance Scale (BBS) by a physical therapist. It is well recognized that measuring balance using both subjective (ABC) and objective (BBS) measures is highly recommended to capture the full picture of patient's functional status. Physiotherapist who performed the assessment received training on conducting the assessments as per standard operating procedure. All tests were administered in a standardized manner and order of tests was kept the same for all individuals.

Outcome measures:

The Kurtzke Expanded Disability Status Scale (EDSS) is a widely used measure of disability in people with MS (Kurtzke, 1983). The EDSS scoring detects functioning and disability in a range of body functions such as pyramidal tract involvement and the total score of EDSS can range from 0 (indicates normal neurological functions) up to 10 (indicates death due to MS).

The Beck Depression Inventory (BDI-II) is a measure that quantifies the intensity of depression by asking about 21 behavioral characteristics of depression. Scoring of BDI-II is calculated by summing the items results that can range between 0-63 with higher score indicates more intense depression (Beck et al., 1961). The total score of BDI-II was categorized into 3 levels: 0-13 indicates no or minimal depression, 14-19 reflects mild depression, 20-28 indicates moderate depression, and 29-63 reflects severe level of depression (Huffman et al., 2010). The BDI-II has been translated and validated in Arabic language (Abdel-Khalek, 1998).

The Activities Specific Balance Confidence Scale (ABC) is a 16-item self-reported measure of balance confidence (Powell & Myers, 1995). The content of the ABC focuses on the activities and participation domain (87%) of the International Classification of Functioning, Disability and Health (ICF) (Alghwiri et al., 2011). The ABC was validated in several populations including people with MS (Nilsagard et al., 2012), and was translated to different languages including Arabic language (Alghwiri et al., 2016).

The Berg Balance Scale (BBS) is a performance-based measure of static and dynamic balance and risk of falling. The BBS has 14 items with a total score that a range from 0 up to 56 with higher score indicates better balance abilities. A cut-off score of 45 was reported as optimal for fall risk (Kornetti et al., 2004). BBS has been used with several populations and translated and validated in different languages including Arabic language (Alghwiri et al., 2016).

Data analysis

SPSS (version 20; Chicago, IL) was used for statistical analysis. Data were assessed for normality using histograms and Q-Q plots. Additionally, data were checked for the presence of skewness, kurtosis and outliers before proceeding into inferential analysis. The associations between BDI-II, ABC, BBS, EDSS, and age were calculated using Pearson correlation coefficient. Generally, r values <0.10 are considered to be a small effect, >0.10 to <0.50 a moderate effect, and >0.50 a large effect. Stepwise method of multiple linear regression was used to identify whether BDI-II significantly predicts ABC and BBS scores. Age, gender, body mass index (BMI) and duration of the disease were all entered to the regression analysis along with the BDI-II to examine their predictive role to balance (ABC and BBS). Index of goodness of fit of each estimated parameter was calculated after the construction of the regression model.

Results

Seventy-five patients with MS participated in this study. Demographic and health-related characteristics of participants are listed in Table 1. Fifty three percent of MS patients had mild to severe depression based on the BDI-II scores. Significant moderate correlations were found between BDI-II and balance (ABC and BBS) measurements and between BDI-II and EDSS as a measure of disability in people with MS (Table 2).

Simple linear regression revealed that BDI-II was a significant predictor for ABC and explained 17% of the variance. The BDI-II was also found as a significant predictor for BBS and explained 11% of the variance.

Multiple stepwise linear regression showed that BDI-II and age were found to significantly predict subjective balance using ABC (ABC=118.16 - 1.03 BDI - 0.94 Age; R^2= 0.24; P<0.001), accounting for 24% of the variance of the ABC total score of the sample after controlling for BMI, gender, and duration of the disease (Table 3).

Multiple stepwise linear regression also showed that BDI-II and age were found to significantly predict objective balance using BBS (BBS=62.58 - 0.43 BDI - 0.34 Age; R^2= 0.20; P=0.002), accounting for 20% of the variance of the BBS total score of the sample after controlling for BMI, gender, and duration of the disease (Table 4).

Discussion

The aim of this study was to explore the association between depression symptoms and balance impairments in people with MS. Our findings not only confirmed the increase in depression levels and deterioration in balance abilities but also established the association between depression symptoms and balance in people with MS.

Depression was present in 53% of patients with MS in this cohort. Investigating depression in people with MS started back to 1980 (Whitlock & Siskind, 1980), then numerous studies have been conducted and have shown the incidence of depression in people with MS (Millefiorini et al., 1992; Mohr et al., 1997; Sadovnick et al., 1996). In 2002, Chwastiak et al. reported that 41.8% of people with MS had clinically significant depression with 29.1% had moderate to severe depression (Chwastiak et al., 2002). Patten et al. in 2003 reported that 25.7% of people with MS had major depression (Patten et al., 2003).

Depression score was significantly correlated with the disability level (using the EDSS) in our sample which is consistent with Millefiorini et al. who found that depression in early stages of MS is correlated more to physical disability than to other factors (Millefiorini et al., 1992). The extent of neurological impairment has also been shown to have an effect on the severity of depression in people with MS (Chwastiak et al., 2002; Rabins et al., 1986). However, intervention studies reported that addressing depression in people with MS had a positive effect on improving patients to cope well with having the disease (Thomas et al., 2006).

Another important finding of this study is that depression was significantly correlated with balance impairments in people with MS. While the correlation between balance, motor ability and depression has been studied in the geriatric and stroke populations, this has not been studied in the MS population before. We used subjective (ABC) and objective (BBS) balance scales in the current study to capture the full picture of patient's functional status. Based on the mean score of the ABC (61.72±29.4), participants in this study had reduced balance ability and moderate level of functioning (Myers et al., 1998). Additionally, the average total score of BBS in our sample (42.15 ±12) is lower than the cut-off score; therefore, our sample was at high risk of falling (Shumway-Cook et al., 1997; Steffen & Seney, 2008). Balance impairments and risk of falls found in our sample are comparable to those found in other studies (Cattaneo et al., 2002; Frzovic et al., 2000).

Most importantly, depression was found to significantly predict the balance status even after accounting for confounding factors including BMI, gender, and duration of the disease. This provides the suggestion that as intensity of depression increased the participant's ability in performing functional balance tasks in their everyday life decreased. It can also be extrapolated that for participants in our study, as their depression increased, so did their risk for falls especially with the fact that ABC has been shown to reliably predict fall status (Frzovic et al., 2000).

In conclusion, findings from this study indicate that with appropriate treatment of depression and consultation, a resultant enhancement in a person's balance skills can be achieved. Depression and balance improved significantly after using Tai Chi posture treatment in a sample of MS (Mills et al., 2000). Similarly in a recent study, Tai Chi training significantly improved balance, coordination, and depression in mildly disabled individuals with MS (Burschka et al., 2014). The improvement of balance and depression together in MS population after certain interventions is an indirect evidence of their relationship.

Limitations:

The current study had several limitations. Patients were not screened by a neuropsychiatric for depression at the time of data collection. Moreover, we did not collect the data about participants’ medications that may contribute to depression. Additionally, other diseases that may affect balance should have been excluded such as peripheral poly neuropathy, vitamin B12 and vitamin E deficiency, cervical and lumbosacral spinal stenosis, visual and vestibular impairments.

Conclusion:

Balance impairments and depression symptoms were found to be frequent and associated in people with MS. It is essential to understand that balance rehabilitation may be hindered by depression. Therefore, regular assessment of depression by rehabilitation specialist is essential and addressing both balance impairments along with depression symptoms in intervention programs for people with MS may ensure better outcomes. Our study also confirms that the understanding of health-care professionals to a patient’s level of depression, they can predict the patient’s risk of falling, therefore, enabling them to create effective and tailored treatment plan.

Conflict of interest: all authors declare no conflict of interest.

Acknowledgement for funding is to the University of Jordan Deanship of Academic Research (Grant number 20/2012-2013 to AA) and Jordan University of Science and Technology (Grant number 0194/2014 to HK).

Table 1

Demographics and health-related information, (n=75).

	Mean	**SD**	**Range**	**N(%)**
Age (Years)	38.84	9.7	18-59	
BMI	24.9	4.3	16.8-35	
Gender (Female)				52 (69)
Onset	10	6.5	.13-28.39	
EDSS	3.0	1.4	1-7	
Type of MS:				
RR				48 (64)
SP				4 (5)
PP				2 (3)
Missing				21 (28)
Location of MS:				
Brain				29 (39)
Spinal cord				4 (5)
Both				21 (28)
Missing				21 (28)
BDI-II	17.28	10.3	0-41	
ABC	61.72	29.4	5.63-100	
BBS	42.15	12.0	10-56	
BDI levels of depression:				
No depression				35 (47)
Mild				12 (16)
Moderate				16 (21)
Severe				12(16)

BMI= Body mass index; EDSS= expanded disability status scale; RR= Relapsing Remitting; SP= Secondary Progressive; PP= Primary Progressive; BDI-II= Beck Depression Inventory; ABC= Activities Specific Balance Confidence Scale; BBS= Berg Balance Scale.

Table 2

Correlations between Beck Depression Inventory (BDI), Activities Specific Balance Confidence Scale (ABC), Berg Balance Scale (BBS), Kurtzki Expanded Disability Severity Scale (EDSS), and age, (n=75).

	ABC	BBS	EDSS	Age
BDI	-.41**	-.33**	.26*	-.01
ABC		.76**	-.33**	-.31**
BBS			-.33**	-.28*
EDSS				.28*

*P < .05. **P < .001.

Table 3

Regression analysis of explanatory variables of ABC, (n=75).

	Parameter Estimates	Standard Error	t value	P value
Constant	118.16	14.15	8.35	0.000
BDI-II	-1.03	0.33	-3.13	0.003
Age	-0.94	0.34	-2.75	0.008

Table 4

Regression analysis of explanatory variables of BBS, (n=75).

	Parameter Estimates	Standard Error	t value	P value
Constant	62.58	6.40	9.79	0.000
BDI-II	-0.43	0.15	-2.96	0.004
Age	-0.34	0.15	-2.24	0.029

References

Abdel-Khalek, A. M., 1998. Internal consistency of an Arabic Adaptation of the Beck Depression Inventory in four Arab countries. Psychological reports, 82(1), 264-266.

Alghwiri, A. A., 2016. The Correlation between Depression, Balance, and Physical Functioning Post Stroke. Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association, 25(2), 475-479.

Alghwiri, A. A., Alghadir, A. H., Al-Momani, M. O., & Whitney, S. L., 2016. The activities-specific balance confidence scale and berg balance scale: Reliability and validity in Arabic-speaking vestibular patients. J Vestib Res, 25(5-6), 253-259.

Alghwiri, A. A., Marchetti, G. F., & Whitney, S. L., 2011. Content Comparison of Self-Report Measures Used in Vestibular Rehabilitation Based on the International Classification of Functioning, Disability and Health. Phys Ther.

Amato, M. P., Ponziani, G., Rossi, F., Liedl, C. L., Stefanile, C., & Rossi, L., 2001. Quality of life in multiple sclerosis: the impact of depression, fatigue and disability. Multiple sclerosis, 7(5), 340-344.

Beck, A. T., Ward, C. H., Mendelson, M., Mock, J., & Erbaugh, J., 1961. An inventory for measuring depression. Archives of general psychiatry, 4, 561-571.

Burschka, J. M., Keune, P. M., Oy, U. H., Oschmann, P., & Kuhn, P., 2014. Mindfulness-based interventions in multiple sclerosis: beneficial effects of Tai Chi on balance, coordination, fatigue and depression. BMC neurology, 14, 165.

Cameron, M. H., & Lord, S., 2010. Postural control in multiple sclerosis: implications for fall prevention. Current neurology and neuroscience reports, 10(5), 407-412.

Cattaneo, D., De Nuzzo, C., Fascia, T., Macalli, M., Pisoni, I., & Cardini, R., 2002. Risks of falls in subjects with multiple sclerosis. Arch Phys Med Rehabil, 83(6), 864-867.

Cavanaugh, J. T., Gappmaier, V. O., Dibble, L. E., & Gappmaier, E., 2011. Ambulatory activity in individuals with multiple sclerosis. Journal of neurologic physical therapy : JNPT, 35(1), 26-33.

Chwastiak, Lydia, Ehde, Dawn M, Gibbons, Laura E, Sullivan, Mark, Bowen, James D, & Kraft, George H, 2002. Depressive symptoms and severity of illness in multiple sclerosis: epidemiologic study of a large community sample. American Journal of Psychiatry, 159(11), 1862-1868.

Comber, L., Galvin, R., & Coote, S., 2017. Gait deficits in people with multiple sclerosis: A systematic review and meta-analysis. Gait & posture, 51, 25-35.

Fritz, N. E., Marasigan, R. E., Calabresi, P. A., Newsome, S. D., & Zackowski, K. M., 2015. The impact of dynamic balance measures on walking performance in multiple sclerosis. Neurorehabilitation and neural repair, 29(1), 62-69.

Frzovic, D., Morris, M. E., & Vowels, L., 2000. Clinical tests of standing balance: performance of persons with multiple sclerosis. Arch Phys Med Rehabil, 81(2), 215-221.

Huffman, J. C., Doughty, C. T., Januzzi, J. L., Pirl, W. F., Smith, F. A., & Fricchione, G. L., 2010. Screening for major depression in post-myocardial infarction patients: operating characteristics of the Beck Depression Inventory-II. International journal of psychiatry in medicine, 40(2), 187-197.

Huisinga, J. M., Yentes, J. M., Filipi, M. L., & Stergiou, N., 2012. Postural control strategy during standing is altered in patients with multiple sclerosis. Neuroscience letters, 524(2), 124-128.

Kasser, S. L., Jacobs, J. V., Foley, J. T., Cardinal, B. J., & Maddalozzo, G. F., 2011. A prospective evaluation of balance, gait, and strength to predict falling in women with multiple sclerosis. Arch Phys Med Rehabil, 92(11), 1840-1846.

Klevan, G., Jacobsen, C. O., Aarseth, J. H., Myhr, K. M., Nyland, H., Glad, S., et al., 2014. Health related quality of life in patients recently diagnosed with multiple sclerosis. Acta neurologica Scandinavica, 129(1), 21-26.

Kornetti, D. L., Fritz, S. L., Chiu, Y. P., Light, K. E., & Velozo, C. A., 2004. Rating scale analysis of the Berg Balance Scale. Arch Phys Med Rehabil, 85(7), 1128-1135.

Kose, N., Cuvalci, S., Ekici, G., Otman, A. S., & Karakaya, M. G., 2005. The risk factors of fall and their correlation with balance, depression, cognitive impairment and mobility skills in elderly nursing home residents. Saudi medical journal, 26(6), 978-981.

Kurtzke, J. F., 1983. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). Neurology, 33(11), 1444-1452.

Larocca, N., 2011. Impact of walking impairment in multiple sclerosis: perspectives of patients and care partners. The patient, 4(3), 189-201.

LaRocca, N., Scheinberg, L., & Kaplan, S., 1987. Disease Characteristics and Psychological Status in Multiple Sclerosis. Journal of Neurologic Rehabilitation, 1(4), 171-178.

Martin, C. L., Phillips, B. A., Kilpatrick, T. J., Butzkueven, H., Tubridy, N., McDonald, E., et al., 2006. Gait and balance impairment in early multiple sclerosis in the absence of clinical disability. Multiple sclerosis, 12(5), 620-628.

Millefiorini, Enrico, Padovani, A, Pozzilli, C, Loriedo, C, Bastianello, S, Buttinelli, C, et al., 1992. Depression in the early phase of MS: influence of functional disability, cognitive impairment and brain abnormalities. Acta neurologica Scandinavica, 86(4), 354-358.

Mills, N., Allen, J., & Carey-Morgan, S., 2000. Does Tai Chi/Qi Gong help patients with Multiple Sclerosis? Journal of Bodywork and Movement Therapies, 4(1), 39-48.

Minden, S. L., Orav, J., & Reich, P., 1987. Depression in multiple sclerosis. General hospital psychiatry, 9(6), 426-434.

Mohr, David C, Goodkin, Donald E, Likosky, William, Beutler, Larry, Gatto, Nicole, & Langan, Michele K, 1997. Identification of Beck Depression Inventory items related to multiple sclerosis. Journal of behavioral medicine, 20(4), 407-414.

Myers, A. M., Fletcher, P. C., Myers, A. H., & Sherk, W., 1998. Discriminative and evaluative properties of the activities-specific balance confidence (ABC) scale. J Gerontol A Biol Sci Med Sci, 53(4), M287-294.

National Multiple Sclerosis Society. (2017). Who gets MS? (Epidemiology). Retrieved June 30, 2017, from http://www.nationalmssociety.org/What-is-MS/Who-Gets-MS

Nilsagard, Y., Carling, A., & Forsberg, A., 2012. Activities-specific balance confidence in people with multiple sclerosis. Multiple sclerosis international, 2012, 613925.

Nilsagard, Y., Denison, E., Gunnarsson, L. G., & Bostrom, K., 2009. Factors perceived as being related to accidental falls by persons with multiple sclerosis. Disabil Rehabil, 31(16), 1301-1310.

Nilsagard, Y., Lundholm, C., Denison, E., & Gunnarsson, L. G., 2009. Predicting accidental falls in people with multiple sclerosis -- a longitudinal study. Clin Rehabil, 23(3), 259-269.

Patten, SB, Beck, CA, Williams, JVA, Barbui, C, & Metz, LM, 2003. Major depression in multiple sclerosis A population-based perspective. Neurology, 61(11), 1524-1527.

Powell, L. E., & Myers, A. M., 1995. The Activities-specific Balance Confidence (ABC) Scale. J Gerontol A Biol Sci Med Sci, 50A(1), M28-34.

Rabins, P. V., Brooks, B. R., O'Donnell, P., Pearlson, G. D., Moberg, P., Jubelt, B., et al., 1986. Structural brain correlates of emotional disorder in multiple sclerosis. Brain : a journal of neurology, 109 (Pt 4), 585-597.

Sadovnick, AD, Remick, RA, Allen, J, Swartz, E, Yee, IML, Eisen, K, et al., 1996. Depression and multiple sclerosis. Neurology, 46(3), 628-632.

Sandroff, B. M., Hillman, C. H., Benedict, R. H., & Motl, R. W., 2015. Acute effects of walking, cycling, and yoga exercise on cognition in persons with relapsing-remitting multiple sclerosis without impaired cognitive processing speed. Journal of clinical and experimental neuropsychology, 37(2), 209-219.

Sandroff, B. M., Pilutti, L. A., Benedict, R. H., & Motl, R. W., 2015. Association between physical fitness and cognitive function in multiple sclerosis: does disability status matter? Neurorehabilitation and neural repair, 29(3), 214-223.

Shumway-Cook, A., Baldwin, M., Polissar, N. L., & Gruber, W., 1997. Predicting the probability for falls in community-dwelling older adults. Phys Ther, 77(8), 812-819.

Siegert, R. J., & Abernethy, D. A., 2005. Depression in multiple sclerosis: a review. J Neurol Neurosurg Psychiatry, 76(4), 469-475.

Spain, R. I., St George, R. J., Salarian, A., Mancini, M., Wagner, J. M., Horak, F. B., et al., 2012. Body-worn motion sensors detect balance and gait deficits in people with multiple sclerosis who have normal walking speed. Gait & posture, 35(4), 573-578.

Steffen, T., & Seney, M., 2008. Test-retest reliability and minimal detectable change on balance and ambulation tests, the 36-item short-form health survey, and the unified Parkinson disease rating scale in people with parkinsonism. Phys Ther, 88(6), 733-746.

Thomas, Peter W, Thomas, Sarah, Hillier, Charles, Galvin, Kate, & Baker, Roger, 2006. Psychological interventions for multiple sclerosis. The Cochrane Library.

Van Emmerik, R. E., Remelius, J. G., Johnson, M. B., Chung, L. H., & Kent-Braun, J. A., 2010. Postural control in women with multiple sclerosis: effects of task, vision and symptomatic fatigue. Gait & posture, 32(4), 608-614.

Whitlock, FA, & Siskind, MM, 1980. Depression as a major symptom of multiple sclerosis. Journal of Neurology, Neurosurgery & Psychiatry, 43(10), 861-865.

Wolkorte, R., Heersema, D. J., & Zijdewind, I., 2015. Reduced Dual-Task Performance in MS Patients Is Further Decreased by Muscle Fatigue. Neurorehabilitation and neural repair, 29(5), 424-435.

World Health Organization. (2008). *Atlas multiple sclerosis resources in the world*