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Effects Of Controlled-Whole Body Vibration Training In Improving Disability Status And Functional Mobility Among People With Multiple Sclerosis

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EFFECTS OF CONTROLLED-WHOLE BODY VIBRATION TRAINING IN IMPROVING DISABILITY STATUS AND FUNCTIONAL MOBILITY AMONG PEOPLE WITH MULTIPLE SCLEROSIS

EDSON F. ESTRADA

Master’s Program in Kinesiology

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Edson F. Estrada

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Dedication

I dedicate this thesis to my students at the Universidad Autónoma de Ciudad Juárez.

Thank you for inspiring me to be a better professor and investigator.
EFFECTS OF CONTROLLED-WHOLE BODY VIBRATION TRAINING IN IMPROVING DISABILITY STATUS AND FUNCTIONAL MOBILITY AMONG PEOPLE WITH MULTIPLE SCLEROSIS

by

EDSON FRANCISCO ESTRADA, M.S., Ph.D.

THESIS

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MASTER OF SCIENCE

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Abstract

Multiple Sclerosis (MS) is a neurological disease that affects the central nervous system. The most common symptoms of MS are loss of mobility and thus restricted independence. The purpose of this study was to inspect the effects of an 8-week CWBV training course in modifying the disability status and functional mobility among people with MS (PwMS). Twenty-five participants diagnosed with MS (mean ± SD age: 50.3 ± 14.1 years; body height: 165.4 ± 9.2 cm; body mass: 73.9 ± 14.1 kg; disease duration: 15.3 ± 10.5 years; 18 females) participated in this study to experience an 8-week training intervention on a side-alternating vibration platform. Participants received the training three times weekly for eight weeks, totally 24 training sessions. Each training session consisted of five bouts of 1-min vibration exposure followed by a 1-min rest period. The vibration frequency and amplitude were respectively set at 20 Hz and 1.3 mm. The disability level quantified by the MS Functional Composite (MSFC) and Patient Determined Disability Steps (PDDS) and mobility characterized by gait spatiotemporal parameters. The results indicated that participants’ MSFC score was significantly increased at the post-training test in comparison with the pre-training test (0.00 ± 0.62 vs. 0.36 ± 0.68, p = 0.0001). The PDDS score reduced significantly from the pre-training to the post-training evaluation (3.66 ± 1.88 vs. 3.05 ± 1.99, p = 0.011). There were significant improvements in the gait speed (0.64 ± 0.32 vs. 0.71 ± 0.32 bh/s, p = 0.0002) and the double stance time (0.18 ± 0.12 vs. 0.15 ± 0.10 sec, p = 0.014). The step frequency (107.50 ± 29.35 vs. 112.33 ± 27.43 steps/min, p = 0.067) and the step length (0.37 ± 0.10 vs. 0.39 ± 0.11 bh, p = 0.053) displayed marginal improvements from pre- to post-training evaluations. Based on the results from this study, CWBV program could serve as an encouraging alternative exercise intervention among PwMS to reduce their disability level and improve functional mobility.
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1. Introduction

1.1. Basics of Multiple Sclerosis

1.1.1. Neuropathology.

Multiple sclerosis (MS) is a neurological disease presumably caused by an incorrect autoimmune response, which is characterized by a progressive demyelination of neuronal axons of the central nervous system (CNS). Despite considerable efforts, the precise MS pathology mechanisms remain unknown. It is believed that the inflammatory process is the key leading to the neurological lesions within the CNS, as evidenced by the fact that the inflammatory immune response produces demyelinated plaques in white and gray matter of the brain. Besides the brain, MS also affects other portions of the CNS that includes the brain stem, the optic nerves, the spinal cord and the periventricular areas (Cowan et al., 1984; van Waesberghe et al., 1998). Typically, MS is clinically diagnosed when formations of glial scars are identified through brain imaging techniques of the white matter (Lassmann, 2013). In the past decades, the understanding of the immunopathology of MS has been advanced by developing medical treatments that can control the activation of the involved leukocytes in order to delay the inflammation process and thus reduce the advancement of MS (Stadelmann, Wegner, & Bruck, 2011). However, there is no cure for MS as treatments are partially or selectively effective in halting or reversing the neurological effects of this disease.

1.1.2. Pathological progression of MS.

The pathology of MS is complex in nature. An accurate identification of the MS course, or type, is highly important for estimating the disease prevalence and the timely application of appropriate medical treatment, rehabilitation, and management. According to the classification criteria proposed by the National MS Society’s (NMSS) in 1996, the disease of MS may follow
different courses based on the neurological manifestations over time (Figure 1): a) the relapsing-remitting (RR) course is mainly characterized by intermittent relapses followed by a complete or partial recovery; b) the secondary progressive (SP) course, typically preceded by RR, is described by no well-defined relapse episodes but a continuous worsening of the person’s disability status; c) the primary progressive (PP) course is defined as a continuous worsening of symptoms after the onset of the disease; and d) the progressive-relapsing (PR) profile is similar to that depicted in PP stage with the occurrence of occasional relapses once the onset occurs (Lublin & Reingold, 1996).

Figure 1. Different courses of MS disability progression: a) relapsing remitting (RR), b) secondary progressive (SP), c) primary progressive (PP), and d) progressive remitting (PR) (Lublin & Reingold, 1996).

1.1.3. Prevalence.

According to Campbell, Dilokthornsakul, Nair, Corboy, and Valuck (2015), the estimated population of people with MS (PwMS) in the United States (US) was between 448,219 and 551,
770 persons in 2012. In 2013, the US prevalence of MS was estimated as 135 per 100,000 persons. Globally, this prevalence has increased steadily from 30 to 33 per 100,000 persons between 2008 and 2013. Although the average age of onset (i.e. MS diagnosis) is 30 years, MS has also been diagnosed at early stages of development such as childhood or adolescence (WHO, 2013). As a result, MS has been considered the leading cause of neurological deficits in young adults. By gender, the prevalence of MS in females triples that of males (the female-to-male ratio = 3.14:1) (Campbell et al., 2015).

1.1.4. MS in El Paso.

The city of El Paso, Texas is considered an MS cluster area by the NMSS because of the high regional prevalence of MS. During the past three decades, substantial efforts have been dedicated to estimating the number of PwMS at a regional scale by the epidemiologists in this area.

The first investigation of this kind reported that 14 former students of Mesita Elementary School and one student from E.B. Jones school were diagnosed with MS in 1994 (Henry, 2001). Findings of the retrospective study on the student cohorts in both schools suggest that the MS prevalence of Mesita School is about 360 per 100,000 persons. This estimated prevalence is higher than the national estimated prevalence of 87 per 100,000 at that period. The standardized morbidity ratio (SMR) of 1.93 (95% Confidence Interval (CI) = 1.06 – 3.24) depicted a doubled risk of MS for this cohort. However, it is likely that these results did not accurately reflect the actual prevalence and SMR of MS because values were extrapolated from the 1989-1994 National Institute of Health survey data.

In 2004, a follow-up study focused on providing better estimation of the manifestation of MS in Texas by reviewing medical records of neurological clinics located in 19 counties in northern Texas. With this new information available, the authors re-estimated MS prevalence of
the Mesita Elementary cohort and obtained a revised SMR estimate of 3.91 (95% CI = 2.24 - 6.35); a nearly four-fold greater risk compared with the national SMR level.

The cause of the higher prevalence of MS in El Paso is of significant interest to investigators. Although the exact reason is unknown, it is suspected to be related to the heavy metal exposure caused by some of the local industry. Such pollution may have triggered MS in this region, particularly on those genetically predisposed to the risk of MS (Neuberger et al., 2004).

1.2. Disability Status Evaluation Among MS

1.2.1. Disability status in MS.

The determination and the monitoring of the disability status through the course of the disease is a major component of any MS-related study. After the disease’s onset, an appropriate and timely evaluation of the disability status is critical for providing PwMS the necessary treatments based on the unique social, cognitive, psychological and physiological manifestations which each patient may encounter with this complex disease.

One challenge faced by many clinicians is the ability to differentiate the MS disease type among the RR, SP, PP, and PR courses. The continuous monitoring of the patient’s disability status is also of clinical significance when assessing the MS stage. Physiologically, there is a strong link between PwMS’s disability status and their neurophysiological condition. It has been established that the axonal damage found in the brain growths as the demyelination process occurs, results in a higher disability status experienced with little possibility of recovery (Ferguson, Matyszak, Esiri, & Perry, 1997). Another important purpose of assessing disability status is to provide clinicians tools to determine the effectiveness of different treatments when conducting experimental trials in order to reduce or delay the progression of the disease.
The damage to the CNS due to MS has an impact on the overall functional performance of PwMS. Consequently, the ability of PwMS to engage in activities of daily living is compromised, or in a worst case scenario, their participation in activities of daily living is halted. It was also reported that PwMS experience fatigue, pain, anxiety, and depression which can also affect their engagement in activities of daily living (Janardhan & Bakshi, 2002). Growing evidence indicates that the reduction of individuals’ participation in activities of daily living impacts their quality of life by being less independent and autonomous. The quality of life has served as an outcome measurement in MS, and it should be considered when selecting the appropriate medical treatment approach (Mitchell, Benito-Leon, Gonzalez, & Rivera-Navarro, 2005).

1.2.2. Instruments for evaluating disability status.

Since the discovery of MS, several approaches have been followed to diagnose and quantify the actual progression of the disease through different outcome variables. Medical biomarkers have been used to evaluate the damage to the CNS and to determine the effectiveness of medical treatments (Bielekova & Martin, 2004). However, biomarkers often do not correlate closely with the disability level. Similarly, magnetic resonance (MR) biomarkers were studied extensively in the past years to assess the damages to the CNS and to diagnose MS (van Waesberghe et al., 1998). The study conducted by Barkhof (1999) on magnetic resonance images (MRI) highlighted the importance of understanding the relationship between the lesion observed in the MRI scans and the disability status. However, the authors stated that this relationship is weak as the nature of lesions is dynamic rather than static because biological processes such as the remyelination of affected nerves often occurs in PwMS. Therefore, a straightforward relationship among MRI features and disability status may not be appropriate to estimate the latter.
Despite the high sensitivity and reliability of the MRI method, the availability of MRI machines and access to neurological third-level medical services are often factors limiting the use of MRI for the monitoring of the disability status on a large scale.

Due to the lack of reliable instruments to assess disability status in MS, physicians employed the available procedures designed for populations with other neurological diseases to assess different health-related outcome measurements of MS. However, this approach suffers from large methodological limitations. First, the generalization of those instruments may fail in detecting and assessing specific disease situations of PwMS that are not present in other populations. Second, the possible floor and ceiling effects with the existing instruments may not properly evaluate the full range of the health condition of PwMS. Third, those non-specific instruments may not be sensitive enough to accurately detect slight changes in the disability status among PwMS (Hobart, Lamping, Fitzpatrick, Riazi, & Thompson, 2001).

For all the aforementioned reasons, the clinical community has developed a series of instruments to assess the disability status of PwMS. The primary objective of an instrument of this nature is to assess the functional condition from different domains. Three evaluation schemes have been developed specifically for PwMS.

The first scale developed to estimate the disability level among PwMS was the Disability Status Scale (DSS) by Kurtzke (1955). This scale was based on the assessment of eight functional systems (FS): the pyramidal, cerebellar, brainstem, sensory, bowel & bladder, visual, cerebral, and miscellaneous functions. It allowed the definition of 10 possible stages of neurologic deficits, where 0 is considered normal status and 10 represents death due to MS. Later, this scale was revised and expanded by Kurstzke to enhance the sensitivity of the DSS scale, particularly in the middle part of the scale with the inclusion of 20 levels of disability status (0 =
normal and 10 = bed confined, with increments of 0.5 between each level) (Kurtzke, 1983). Since then, the Expanded Disability Status Scale (EDSS) has become the gold standard instrument to evaluate the impairment of PwMS based on the clinical evaluation of the mentioned functional systems. It has been used broadly to compare different sample populations of MS across various experimental trials. Nevertheless, the administration of the EDSS requires experienced physicians to score each functional system correctly. For instance, the cerebral functions require the assessment of different degrees of mental alterations, which needs specialty and may not be carried out by a general physician.

The second scale was a patient-centered outcome measurement tool to assess the disability status in a relatively rapid manner without the extensive involvement of very experienced physicians, and in which patients take a central role in describing their particular status (Hobart et al., 2001). New efficient and effective instruments are of vital importance for community-wide interventions where the medical resources and personnel may be limited. Recently, the Patient Determined Disease Steps (PDDS) scale has been presented as a valid alternative to the EDSS scale, where patients rate their own disability level based on the simple statements describing functional tasks such as being able to walk a 25-foot distance with or without a walking aid. A total of nine scenarios can be selected to describe the PDDS level (0 = normal, and 8 = confined to bed). Research has demonstrated that the PDDS outcome variable has a significant correlation with the EDSS outcome variable (correlation coefficient $\rho = 0.783, p = 0.0001$) (Learmonth, Motl, Sandroff, Pula, & Cadavid, 2013). The highest correlations among the FS and the PDDS score were found within the pyramidal and cerebellar domains ($\rho = 0.578, p = 0.01$; and $\rho = 0.501, p < 0.01$, respectively), whereas the mental FS depicted the weakest correlation with PDDS ($\rho = 0.169,$
In addition, studies have demonstrated that PDDS scores can be closely related to EDSS scores from the perspective of mobility (Learmonth et al., 2013).

The challenge of developing disability status measurement instruments is to consider the different dimensions that MS affects. For instance, the EDSS assesses vital mental capabilities. However, high-level functional dimensions such as leg-performance represented by the ability to walk are not accounted for in the EDSS instrument. Similarly, the PDDS does not consider some of the FS included in the EDSS, like cognitive function. Therefore, a new assessment system considering all domains possibly affected by MS was highly desired.

The third instrument, the MS Functional Composite (MSFC), was developed by an NMSS task force. The objective was to design an MS outcome measurement to quantitatively determine the disability level of PwMS by means of a more sensitive and inclusive assessment (Cutter et al., 1999). The new score was designed to include three dimensions: leg function, arm function, and cognitive status. Different clinical tests were evaluated for each dimension to determine which test would best represent each dimension. Among the different tests explored, the task force determined that the Timed 25-Foot Fast Walking Test (T25FWT), the 9-Hole Peg Test (9-HPT), and the Paced Auditory Serial Addition Test 3-second version (PASAT-3") were the most suitable clinical trials to evaluate the proposed dimensions (Fischer, Jak, Kniker, Rudick, & Cutter, 2001). Moreover, this approach uses the advantage of calculating a dimensionless index based on the calculated z-score for each dimension. The average of the three z-scores forms a solid composite score, called a MSFC score in which the arm and cognitive functions may provide more clinically relevant information that was not considered in the EDSS nor the PDDS (Kasser, Jacobs, Foley, Cardinal, & Maddalozzo, 2011). Since MSFC score is a continuous quantity, it is more sensitive
to changes in disability status than both EDSS and PDDS scales (Polman & Rudick, 2010; Rudick et al., 2009).

1.3. Effects of MS on Mobility Among PwMS

1.3.1. Quantification of mobility in MS.

Mobility is one of the functional dimensions debilitated in PwMS. Considerable efforts have been dedicated to examining the effects of MS on mobility (Benedetti et al., 1999; Givon, Zeilig, & Achiron, 2009; Holden, Gill, Magliozzi, Nathan, & Piehl-Baker, 1984; Martin et al., 2006). The demyelination process produces axonal damage in PwMS that affects the functional capacities in many aspects. Therefore, mobility of this population is compromised due to the presence of MS symptoms that include muscle weakness, central and peripheral fatigue, loss of balance, reduced flexibility, low muscle power capacity, compromised aerobic capacity and reduced vision (DeBolt & McCubbin, 2004; Rodgers et al., 1999). A study conducted by Heesen et al. (2008) suggested that among all bodily functions, walking was the most important domain reported by a group of 166 PwMS. This priority highlighted the importance of maintaining mobility among PwMS since independence and Quality of life are highly dependent upon mobility.

There are two main outcome variables that depict the configuration of the mobility test used in quantification: mobility restriction and walking speed. On the mobility restriction aspect, walking trials can be restricted either to space or time. Space-restricted clinical tests are often used to assess functional mobility and leg performance. It has been demonstrated that MS affects not only the mobility capacity but also the velocity at which PwMS navigate from one point to another (Sandroff, Sosnoff, & Motl, 2013). Time-restricted walking tests are more focused towards the resistance of walking, especially for those assessments lasting longer than one minute.
Using this approach, researchers can evaluate the distance covered over a restricted amount of time, while also being able to observe the covered distance profile during that given time.

Gait analysis is becoming a useful tool to assess ambulatory capability of PwMS. Gait analysis involves observing a person’s walking and analyzing their gait pattern in terms of kinetic and spatiotemporal parameters. This approach can provide insights into the mechanisms underlying the gait dysfunction. It can also be used to identify small gait impairments and abnormal postural control which cannot be captured by other methods. The commonly-used gait parameters include the gait speed, step length, step time, step width, step clearance, and step frequency.

1.3.2. Effects of MS on mobility.

Previous studies pertaining to disability status and mobility among PwMS found that individuals’ mobility capacity is closely related to their disability level. As MS progresses, the deteriorated disability level leads to the decline of Quality of life for PwMS (Benedetti et al., 1999). It has also been observed that PwMS change their walking profile as the disease progresses. For instance, Givon et al. (2009) found a reduction in the step length, an increase in the step width, and a prolonged double stance time in the early stages of MS. These adaptive changes in gait parameters have been described as a cautious gait pattern to avoid the possibility of balance losses or falls during walking (Martin et al., 2006).

The occurrence of falls among PwMS is a major concern as the present scientific evidence indicates that this population has an elevated risk of falling due to MS-related movement impairments. The risk of falling of PwMS is another detrimental factor affecting the quality of life. Since MS is not a terminal disease and it does not affect the life expectancy, it is important to reduce the risk of falling among PwMS (Koch-Henriksen, Bronnum-Hansen, & Stenager, 1998).
Given that the impaired mobility highly correlates with falls among PwMS, it is imperative to develop interventions to improve mobility. The improvement in mobility will, in turn, reduce the incidence of falls, further reducing or delaying the deterioration of the PwMS physical condition.

1.4. Interventions of Improving Disability Status and Mobility Among PwMS

1.4.1. Aerobic training.

Traditional aerobic training programs have been implemented as complementary resources to reduce the disability level and to improve the physiological capacity of PwMS. Most of the studies performed on this topic are related to the improvements of aerobic fitness and mobility rather than limb muscle performance. Ponichtera-Mulcare, Mathews, Barrett, and Gupta (1997) first explored the changes in the aerobic capacity of PwMS when being exposed to a six-month aerobic training program. Their findings, despite not achieving statistical significances, suggested an increase in the maximal oxygen uptake after the aerobic training program. Similar findings were presented by Mostert and Kesselring (2002) in which participants’ VO2max was significantly increased by 12% after a 4-week program. From the mobility perspective, aerobic training programs seem to improve the walking capacity of PwMS by increasing their gait velocity and distance covered within a given period of time (Kileff & Ashburn, 2005; Rampello et al., 2007; van den Berg et al., 2006). In spite of the positive effects detected in aerobic training programs of PwMS, this population may lack the physical capacity to undergo some aerobic training protocols which demand intensive physical activities (Mulligan, Hale, Whitehead, & Baxter, 2012; Romberg et al., 2004). Furthermore, muscular fatigue is a significant symptom of MS further limiting the ability of PwMS to participate in aerobic training programs (Romberg et al., 2004). Therefore, aerobic exercise is mainly suitable for PwMS with a mild level of disability.
1.4.2. Resistance training.

A study of the effects of anaerobic training programs for PwMS revealed that this type of exercise improves leg performance (DeBolt & McCubbin, 2004) quantified by the isometric strength capacity, muscular endurance, and muscular power (de Souza-Teixeira et al., 2009; Eftekhari, Mostahfæzian, Etemadifar, & Zafari, 2012). Also, gait spatiotemporal parameters have been improved after a 2-month resistance program (Gutierrez et al., 2005). Similarly, the enhancement of leg muscle performance has been reported with the reduction of muscular fatigue and improvement in functional capacity (White et al., 2004). However, resistance training is more suitable for individuals with mild to moderate levels of disability. Particularly in the resistance training activities, participants are required to perform high-level muscle contractions to overcome the external resistances. This may not be applicable to some PwMS. Therefore, alternative training paradigms to the traditional exercise training are pressingly needed to improve mobility and disability level of PwMS.

1.4.4. Other exercise-based therapies of PwMS.

Beyond the scope of conventional exercise-based interventions, some other types of exercise training, such as yoga, Pilates, Tai Chi, aquatic therapy, etc. have also been explored. Limited results showed that Yoga and Pilates exercise programs could be effective for improving body balance, walking endurance, and mobility among PwMS. These benefits probably can be attributed to the increase of thoracic muscular strength (Ahmadi, Nikbakh, Arastoo, & Habibi, 2010; Freeman, Fox, Gear, & Hough, 2012). On the other hand, Tai Chi, which is characterized by exercising at a slow motion, has been demonstrated to have a positive effect on lower limb performance and flexibility of individuals affected by MS. The peaceful nature of this unique exercise also showed influences on other elements closely linked to Quality of life, such as vitality,
mental health and cognition (Husted, Pham, Hekking, & Niederman, 1999). As for aquatic fitness programs, several studies showed its benefit to PwMS. For example, researchers have observed that chronic aquatic interventions improve the muscular performance and mobility of PwMS. Reduction in the fatigue level and improvement in Quality of life were also detected of some PwMS (Gehlsen, Grigsby, & Winant, 1984; Kargarfard, Etemadifar, Baker, Mehrabi, & Hayatbakhsh, 2012; Marandi, Nejad, Shanazari, & Zolaktaf, 2013).

1.5. Vibration Training

1.5.1. Controlled whole-body vibration.

Controlled whole-body vibration (CWBV) training has recently emerged as a promising alternative training modality within the physical therapy field. The vibration training principle relies on the delivery of a mechanical vibratory stimulation on the surface of the body limbs to induce involuntary muscle contractions (Bovenzi, 2005). Vibrations produce rapid changes of linear and angular limb position creating accelerations and decelerations of the stimulation zone. The acceleration of the segments’ mass develops inertial forces due to the movement; these forces are delivered over the area of application of the vibration stimuli. Thus, the conduction of these forces through the limb stimulates the activation of the involved muscles by developing constant cycles of muscles contractions (Abercromby et al., 2007). Parallel to this, the neuromuscular system is activated along with its proprioceptive and nociceptive components. Simultaneously, bones, tendons, and ligaments are stimulated by the exposure to the vibratory force.

Unlike occupational vibration, CWBV training has to be delivered in a well-controlled manner to ensure its effectiveness and reduce the risk of injury (Bovenzi, 2005). Four parameters can be adjusted to configure the vibratory stimulation. First, the amplitude (in mm) describes the displacement of the vibratory surface in the vertical direction. The vibration frequency (in Hz)
defines how rapidly the mechanical oscillation is produced. The duration of the stimulation determines the exposure time to the vibratory intervention within one bout. Finally, the vibratory stimulation can be conveyed under different body postures that are either static or dynamic. Different configurations of these parameters have been studied to determine how each individual training parameter affects the training effects.

During CWBV training, stimulation is delivered when one stands on a vibratory platform. This setup allows a direct stimulation to the contact area between the platform and human body which usually is the sole of the feet. Different types of vibration have been designed but the two most common are vertical-displacement and the side-alternating movement types. The side-alternating vibration machines are preferred to the vertical displacement platforms because the stimulation in the side-alternating platform is delivered in a safer way. The stimulation is alternatively delivered to the lower limbs, allowing the hips to pivot and to maintain the upper body almost isolated from the vibration stimulation. Thus, important regions which are sensitive to vibration, such as the spinal cord and the brain, are less exposed to the vibratory stimulation.

The use of CWBV has been studied in a variety of populations, and positive effects have been documented. In sport-related scenarios, the acute and chronic effects of CWBV have been explored as an alternative method to increase athletic performance. A recent review article by Wilcock, Whatman, Harris, and Keogh (2009) concluded that the observed chronic effects of CWBV might include modest improvements in maximal dynamic strength and lower-limb power development. However, the authors stated that CWBV may not induce a significant improvement in the speed or the neuromuscular activation of an athletic population. Few articles about the acute effects of CWBV indicated that joint mobility and flexibility are increased after a single bout of CWBV training among healthy participants and skilled gymnasts (Gerodimos et al.,
Nevertheless, it seems that the effects of CWBV among elite athletes are minimal possibly because the stimulation is not intense enough to produce muscular adaptations similar to those observed with traditional training programs (Delecluse, Roelants, Diels, Koninckx, & Verschueren, 2005). On the other hand, the CWBV stimulation appears to have large effects on populations with movement disorders (Pozo-Cruz et al., 2012) or frail older adults (Lam, Lau, Chung, & Pang, 2012). These findings align well with those reported by Rehn, Lidström, Skoglund, and Lindström (2007) in which a strong to a moderate effect size in the leg performance of untrained people or geriatric woman was illustrated.

The chronic effects of CWBV have also been examined in older adults to improve their overall functionality, their well-being, and Quality of life. A meta-analysis revealed that CWBV has positive effects on improving balance and mobility in community-dwelling older adults (Lam et al., 2012). The observed improvements in balance and mobility could be attributed to the CWBV-induced improvements in the muscular performance of lower limbs (Bogaerts, Verschueren, Delecluse, Claessens, & Boonen, 2007; Machado, García-López, González-Gallego, & Garatachea, 2010; Rehn et al., 2007; Yang, King, Dillon, & Su, 2015). Similarly, the bone density of older people exposed to CWBV training was improved significantly, particularly in those bones closer to the stimulation source (Merriman & Jackson, 2009; Totosy de Zepetnek, Giangregorio, & Craven, 2009; Verschueren et al., 2004; Yang et al., 2015). However, findings related to the effects of CWBV training on fall prevention are still inconclusive and require further investigation (Lam et al., 2012).

CWBV has also been employed among populations with neurological diseases (Pozo-Cruz et al., 2012) to determine its impact on various functional outcome variables such as muscle strength, leg performance, neuromuscular activation, mobility, and balance. Among people with

15
Parkinson’s disease, the chronic effects of CWBV include the improvement of body balance and mobility (Dibble, Addison, & Papa, 2009; Ebersbach, Edler, Kaufhold, & Wissel, 2008; Shariffifar, Coronado, Romero, Azari, & Thigpen, 2014). Researchers have also studied the benefits of using CWBV as a rehabilitation intervention for people who have suffered a cerebrovascular event. In this population, it seems that the acute effects of CWBV improved the flexibility of the affected lower-limb by reducing the muscle’s spasticity (Chan et al., 2012). With respect to mobility, some studies have determined that chronic exposure to a CWBV intervention may have improved the walking speed among people with stroke (Miyara et al., 2014). However, no study has reported a significant effect of CWBV training for improving lower-limb muscle strength or balance in stroke survivors (Brogardh, Flansbjer, & Lexell, 2012; Pang, Lau, & Yip, 2013; van Nes et al., 2006).

1.5.2. CWBV Among PwMS.

Seven studies have been published reporting the possible effects of CWBV training among PwMS. Table 1 below summarized these studies. Schuhfried, Mittermaier, Jovanovic, Pieber, and Paternostro-Sluga (2005) conducted a randomized, double-blind experiment for 12 PwMS assigned to either the training or control group. The training group received a multidimensional CWBV intervention while the control group received transcutaneous electrical stimulation while standing on a vibratory platform. The authors observed an improvement in mobility following acute exposure to CWBV training. The Timed-Up-and-Go test (TUG) values for the training group were lower when compared with baseline values immediately after the five minutes of CWBV training. In contrast, the placebo group did not demonstrate an improvement in the TUG score following the acute interventions. The experimental group showed significant differences in mobility one week and two weeks after the intervention, whereas the placebo group did not
show any significant changes. In the flexibility assessment, the Functional Reach Test did not display a significant change in participants’ flexibility immediately after or at the retention assessments. Similarly, the Sensory Organization Test (SOT) evaluating the body posture did not show any meaningful change. However, there was a marginal increment in SOT for the control group after the exposure. Thus, Schufi led et al. (2005) concluded that a 5-minute acute CWBV exposure had a positive effect on mobility, some on quality posture parameters, but may not induce any effect on functional flexibility of PwMS.

A similar experiment was conducted by Jackson, Merriman, Vanderburgh, and Brahler (2008) with outcome variables related to the muscle strength of the lower limbs. In this study, participants were included in a crossover experimental design to expose them to either a low or a high vibratory frequency of 2 or 26 Hz. Both treatments were delivered for 30 seconds with an amplitude of 6 mm but, regardless of the frequency used, no significant change in the lower-limb maximum torque was observed. However, there was a marginal increase in the isometric torque capacity produced by the hamstrings and quadriceps when participants were exposed to the 26 Hz vibratory frequency.

Schyns, Paul, Finlay, Ferguson, and Noble (2009) performed a pilot study to investigate the effects of a long-term CWBV intervention on modifying mobility, spasticity, muscle force, and sensation of PwMS. In this crossover study, sixteen participants were randomly assigned to one of two intervention groups. Group one underwent a 4-week exercise program that included a component of CWBV training. After a 2-week washout period, participants underwent a 4-week exercise program without the CWBV component. Group two performed the same two protocols in reverse order to achieve the crossover design. Results showed that the maximum isometric force production was greater after the exercise with CWBV exposure when compared to
the exercise exposure only. However, this improvement was not statistically significant. Similarly, the muscle force appeared depicted a marginal increment after training for the CWBV and exercise protocols with no statistical significance. Spasms in the group receiving the exercise with CWBV were reduced significantly compared to the exercise-only group. Significant improvements were observed in mobility as measured by the 10-m walk and TUG tests.

Broekmans et al. (2010) investigated the effects of CWBV on modifying leg performance and functional capacity of PwMS. Participants in the experimental group were exposed to a 20-week CWBV training program, whereas participants in the control group did not receive any intervention. Neither the main effect of group nor the time by group interaction effect was significant. The authors concluded that the CWBV training program did not have the capacity to improve leg performance or functional capacity.

Moreover, another study was conducted by Wunderer, Schabrun, and Chipchase (2010) to inspect the effects of a 6-week CWBV training course on modifying lower limb muscle strength and functional mobility. Results demonstrated that all three participants experienced a statistically significant increase in plantar flexion strength capacity. However, only two participants showed a significant increment in the knee flexion strength capacity. Two participants reflected a reduction in the time required to perform TUG. Nevertheless, the validity of the results was limited due to the relatively small sample size ($n = 3$) and the low statistical power.

Claerbout et al. (2012) investigated the effects of a 3-week CWBV program on lower extremity muscle performance and mobility among PwMS. Sixty-two participants were randomly assigned to the full-exposure CWBV group, the light-exposure CWBV group, or the control group. The authors reported a statistically significant time effect (pre vs. post) associated
with the strength capacity of the quadriceps and hamstrings muscles for the full-exposure CWBV group. Authors also observed a positive impact on mobility after the training program in both experimental groups.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Sample population</th>
<th>Study design</th>
<th>Training configuration</th>
<th>Summary of findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schuhfried et al., 2005</td>
<td>12 participants with MS Experimental group (n = 6, male = 1, age = 49.3 ± 13.3, EDSS = 3.9 ± 0.8) or the placebo group (n = 6, male = 2, age = 46 ± 12.7, EDSS = 3.7 ± 0.8).</td>
<td>Double-blind randomized experiment.</td>
<td>Training period: 1 session. Training parameters: 1 Hz up to the maximal frequency tolerated by each participant.</td>
<td>Improvement in functional mobility in the experimental group. Flexibility and posture were not improved.</td>
</tr>
<tr>
<td>Jackson et al. (2008).</td>
<td>15 participants (female = 12, age = 54.9 ± 9.6 years, EDSS = 4.2 ± 2.3).</td>
<td>Cross-over experimental design.</td>
<td>Training period: 1 session. Training parameters: 2 Hz and 26 Hz frequencies, duration = 30 sec, and amplitude = 6 mm.</td>
<td>Not a significant improvement in leg performance. However, a systematic increase was observed in lower limb peak torques.</td>
</tr>
<tr>
<td>Schyns et al. (2008).</td>
<td>16 participants. group 1, n = 8 (females = 3, disease duration 10 months to 23 years); group 2, n = 8 (female = 7, disease duration = 3.5 to 18 years).</td>
<td>Crossover pilot study.</td>
<td>Training period: 4 weeks. Training parameters: 40 Hz, duration = 40 seconds, and amplitude = 2 mm.</td>
<td>A systematic increase in isometric force, muscle tone, and mobility with no significant results. Improves mobility. Significant reduction of spasms.</td>
</tr>
<tr>
<td>Broekmans et al. (2010).</td>
<td>20 participants (age = 47 ± 1.9 years, EDSS = 4.3 ± 0.2).</td>
<td>Randomized experiment.</td>
<td>Training period: 20 weeks. Training parameters: Frequency was increased from 20 Hz to 35 Hz to 45 Hz (0, 10th, 20th week, respectively); duration 2.5 to 8.0 to 16.5 min; and amplitude = 2.5 mm.</td>
<td>No significant improvements in leg performance or functional capacity.</td>
</tr>
<tr>
<td>Wunderer et al. (2010).</td>
<td>3 participants (female = 2, age rage 43 -60 disease step scale range = 2-5).</td>
<td>Non experimental design.</td>
<td>Training period: 6 weeks. Training parameters: Frequency = 40 Hz, amplitude = 2 mm amplitude, duration from 30 to 45 min.</td>
<td>Some improvements in knee flexion strength and mobility.</td>
</tr>
<tr>
<td>Claerbout et al. (2012).</td>
<td>62 participants (age range from 20 to 65 years, EDSS from 1 to 7).</td>
<td>Randomized experimental design.</td>
<td>Training period: 3 weeks Training parameters: Frequency increased from 30 Hz to 35 Hz o 40 Hz, and duration from 7 to 13 min.</td>
<td>Significant improvement in maximal quadriceps and hamstring strength for the experimental group. Enhancement of functional mobility.</td>
</tr>
<tr>
<td>Manson et al. (2012).</td>
<td>15 participants (females = 11, age = 50.2 ± 6.9 years, EDSS = 3.5 ± 0.9).</td>
<td>Non experimental design.</td>
<td>Training period: 8 weeks. Training parameters: Frequency increased from 15 to 20 Hz, amplitude from 2.6 to 6.1 mm and duration from 5 to 8 min.</td>
<td>Significant impact on functional capacity, mobility and balance.</td>
</tr>
</tbody>
</table>

EDSS: Expanded Disability Status Scale.
Lastly, Mason, Cochrane, Denny, Firth, and Stannard (2012) explored the effectiveness of an 8-week CWBV program on the functional performance of PwMS. It was stated that this type of exercise was well tolerated by this population as no adverse effects, like anxiety or discomfort, were observed during the intervention. Their findings indeed suggested that an 8-week CWBV training program on a side-alternating platform significantly improved participants’ mobility immediately after the intervention. The body balance skill was also significantly improved in comparison with the baseline measurements.

Although various experimental protocols, training parameters, and measurement techniques were used across studies, the improvements in mobility were consistent between studies (Table 1). Therefore, CWBV training may be a valuable therapy primarily due to its attractive features, such as effectiveness, safeness, portability, and ease of operation. However, the studies examining the overall effects of CWBV training on improving disability status and mobility of MS are highly limited. In addition, despite the importance of reducing the disability level of PwMS, the effects of CWBV training for improving the disability status among PwMS has not been examined. Also, it is unclear to what extent PwMS could benefit from a CWBV program to improve their mobility due to the wide range of vibration parameters used in previous studies. The examination of these effects is critical to develop optimal vibration-based interventions to reduce the disability level and improve the mobility of PwMS. It would be of great interest to the MS community to delay their disease progression and to improve their Quality of life.

1.6. Purpose and Hypotheses

The primary purpose of this study was to investigate the effect of an 8-week CWBV training course upon the disability status and functional mobility among PwMS. Corresponding with our purpose and based on our pilot results, we hypothesized that an 8-week CWBV training
would improve the disability status of PwMS. We further hypothesized that the 8-week CWBV training program would improve the functional mobility of persons living with MS.
2. Methods

2.1. Participants

Participants were recruited from El Paso and its adjacent areas mainly via our connection with the Multiple Sclerosis Association of El Paso. Also, participants were invited to participate by using flyers, the university website, and advertising spots at local radio stations. Our target number of participants was 22 to achieve a statistical power of 90% (please see Appendix A for details). Participants were initially contacted to determine their eligibility for this study based on the following criteria:

To be eligible for this study:

- Participants must have been between 21 and 75 years old.
- Participants also must not have had a significant relapse within the past eight weeks.
- Participants were required to have a PDDS score less than 7.0, meaning they had the physical capacity to stand and walk independently with or without assistance.
- Participants must be free from other major general medical or surgical disorders or pregnancy.
- Participants must be medically stable.

Participants were excluded if:

- They had participated in whole-body exercise, balance training or resistance interventions in the past six months.
- They had undergone any vibration training.
- Participants had a concurrent severe medical illness.
- Participants were under 21 or over 75 years of age.
- Participants had experienced severe pain at shoulder, knee, cervical region, or back.
A total of 37 PwMS were initially identified as potential participants for the study. Thirty were screened to assess if they met the eligibility criteria. Five participants did not meet the inclusion criteria because of disability level, health condition, or not having a clinically confirmed MS diagnosis. Twenty-five participants were selected and enrolled into the study. Prior to participation, participants were required to sign an informed consent form approved by the Institutional Review Board at the University of Texas at El Paso. Table 2 lists the detailed demographic information of all participants for this study.

### 2.2. Study Design

This study adopted a one-group pretest-posttest longitudinal design. All participants went through an 8-week vibration training course. Before and after the training program, the disability status and mobility were evaluated for all participants (Figure 1a). The pre- and post-training evaluations were conducted immediately before first and last training session, respectively. The two evaluations were compared to examine the potential effects of CWBV training on disability status and mobility among PwMS.

Table 2. Demographic and medical description for study participants (N = 25, female = 18)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± SD</th>
<th>Range</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>50.3 ± 14.1</td>
<td>21.0 - 71.0</td>
<td>52.0</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>165.4 ± 9.2</td>
<td>152.3 - 186.0</td>
<td>162.3</td>
</tr>
<tr>
<td>Mass (kg)</td>
<td>73.9 ± 14.1</td>
<td>51.4 - 105.3</td>
<td>73.3</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>15.3 ± 10.5</td>
<td>2 - 43</td>
<td>13</td>
</tr>
<tr>
<td>Type of MS</td>
<td>RR = 16</td>
<td>PR = 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SP = 5</td>
<td>UN = 3</td>
<td></td>
</tr>
</tbody>
</table>

RR = Relapsing-Remitting, SP = Secondary Progressive, PR = Progressive Relapsing, and UN = Unknown. SD = Standard deviation.
Figure 2. a) Study design for an 8-week CWBV program to assess the effects of vibration therapy on the disability status and mobility among PwMS. Each training session consisted of five cycles of 1-min side-alternating CWBV training followed by a 1-min rest period. b) Participants stood on the vibratory platform with knees slightly flexed at 20° while the trunk was kept in an upright position.

2.3. Training Protocol

Participants underwent an 8-week CWBV training program consisting of 24 sessions in total (three sessions per week). Each training session consisted of five cycles of 1-minute vibratory stimulation followed by a 1-minute rest period (Figure 2a). A side-alternating vibration platform (Galileo Med-L, Germany) was used to deliver the stimulation at a frequency of 20 Hz and an amplitude of 1.3 mm (or the peak-to-peak displacement of 2.6 mm). Participants stood barefoot on the vibration platform over two marked positions that depicted the preferred stance width. Participants’ feet were closely monitored to correct displacements resulting from the vibratory stimulation. To keep balance, participants were told to hold the handlebar, to maintain a semi-squatted position at 20-degree knee flexion with respect to full knee extension while
maintaining the trunk upright, and to look forward to allow the correct propagation of the vibration to the lower limbs (Figure 2b). This position was preferred over a straight-legged stance position because the spinal cord and brain are more protected from receiving any unwanted vibratory stimulation. Finally, participants were instructed to distribute their body weight evenly on both feet to produce a symmetric stimulation of both legs. Participants were closely monitored to identify any adverse effects during the training course that may compromise their health status such as articular pain or muscle soreness.

2.4. Evaluations

2.4.1. Evaluation of disability level.

The disability status was evaluated via the PDDS and MSFC. During the evaluations, participants were allowed to pause or to stop the data collection procedure at any moment if they were not able to complete the tasks for any given reason. Observations were annotated in the records to identify side effect that could harm the health of participants.

2.4.1.1. Patient Determined Disability Steps.

The PDDS was used to determine the disability status of participants subjectively. The instruction and purpose of the PDDS test were explained to participants, and then they independently read each disability level statement. Each statement described a scenario in which participants assessed their current disability status base on their walking capacity. Then, participants rated themselves in a range between 0 (normal) and 8 (bedridden). Appendix B provides a full description of each disability level.

2.4.1.2. MS Functional Composite score.

The three dimensions of the MSFC score were collected following the guidelines and forms provided by the NMSS (Fischer et al., 2001). As discussed before, this composite score required
the assessment of three dimensions: leg function, arm function, and the cognitive component. The mean and standard deviation (SD) of baseline measurements were calculated for all three dimensions based on all participants’ values. The calculated mean and SD were then used as the reference values to convert each measurement of the three dimensions for each participant to corresponding z-scores (Kalkers, Polman, & Uitdehaag, 2002). The MSFC score for each participant was thus computed as the average value of the three z-scores as follow:

\[
MSFC \text{ score} = \frac{z_{\text{leg}} + z_{\text{arm}} + z_{\text{cognition}}}{3}
\]

where, \(z_{\text{leg}}\) represents the z-score for the leg function, \(z_{\text{arm}}\) stands for the z-score of the arm function, and \(z_{\text{cognition}}\) denotes the z-score for the cognitive dimension.

**Timed 25-Foot Fast Walking Test** For the Timed 25-foot Fast Walking Test (T25FWT), a distance of 25 feet was marked with two white lines in the middle of a 14-m linear walkway. The walking area was positioned in the center of the laboratory facilities in a well-illuminated and unobstructed space (Figure 3). Participants were instructed to walk as fast as possible but in a safe manner. The use of a walking assistive devices or lower-limb orthoses was annotated in the participants’ records to keep consistency through the pre- and post-training evaluations. The test was stopped if the participant was not able to complete a trial in less than 3-minute or after a 5-minute resting period. Each trial was timed by a stopwatch. The time (in sec) used in two successful trials was averaged to assess leg function in terms of speed mobility. A lower average time represented better mobility.
The 9-Hole Peg Test

The upper-limb function was assessed using the 9-Hole Peg Test (9-HPT). In this test, participants were asked to place a peg in each hole as fast as possible. Once this task was completed, participants were required to place back the pegs into the container one by one (Figure 4). Time was recorded to determine the level of the arm performance. Two trials each for the dominant (DH) and non-dominant (NDH) hands were conducted. The average time of the two trials for each hand was used as the score. In this test, a lower score indicated a better hand dexterity.

Figure 4. Schematic representation of the 9-Hole Peg Test (9HPT).

The Paced Auditory Serial Addition Test

The Paced Auditory Serial Addition Test 3-second version (PASAT-3") was adopted to determine the cognitive capacity for each participant. In this task, participants were instructed to listen to a sequence of 61 random numbers, and were asked to provide the sum total of the last two numbers heard (Figure 5). Participants were tested in their native language. The tester explained, aided with a piece of paper, the mechanism of the test verbally to demonstrate the task and the addition of the last two numbers. Then, the participants were allowed to practice three attempts with a total of 10 random numbers before the test. After this, the test was administrated, and the score for this component was computed based on the number of correct answers (0 = no correct answers and 60 = all answers correct). A higher score was indicative of better cognitive function.
Figure 5. Schematic representation of the Paced Auditory Serial Addition Test 3-second version (PASAT-3").

2.4.2. Evaluation of mobility.

The effects of CWBV training on functional mobility were determined by assessing spatiotemporal gait variables during the T25FWT. The parameters of interest included: gait speed, step length, step width, single-stance phase duration, double-stance phase duration, and step frequency (or cadence).

To collect these spatiotemporal parameters, an 8-camera motion capture system was used (Vicon, Oxford, UK) to gather each participant’s full-body kinematics at 120 Hz. A total of 26 reflective markers of 19 mm diameter were applied to bony landmarks on participant’s joints and limb segments to gather the full-body kinematics. Marker position data were bandpass filtered within a range from 4.5 to 9 Hz by means of a non-delaying fourth order Butterworth before calculating any kinematic parameter (Shiavi, Frigo, & Pedotti, 1998). The centroid of all major joints was calculated from marker positions based on anthropometric measurements, and the center of mass kinematics was determined using a sex-adjusted 13-segment body reductionist model (de Leva, 1996). Then, the positions of joint body centers were used to determine the following parameters:

*Touchdown and liftoff* Each foot’s touchdown was defined as the instant of heel strike, whereas the liftoff event was characterized by the instant when the foot takes off from the floor (Figure 6a). The computation of these two gait events was based on the markers’ vertical
velocity determined from the first-order discrete derivative of foot markers position (Ghoussayni, Stevens, Durham, & Ewins, 2004; O'Connor, Thorpe, O'Malley, & Vaughan, 2007).

Step length The step length was calculated as the anteroposterior distance between two heels at their touchdowns (Figure 6b) and was normalized to the body height ($bh$).

Step width The step width was calculated as the mediolateral distance between two heels at their touchdowns and was normalized to the $bh$ (Figure 6b).

Single-stance duration Single-stance phase is the portion of the gait cycle in which only one foot is in contact with the ground. Duration of the single-stance phase was determined as the time elapsed between the liftoff of one foot to the touchdown of the same foot.

Double-stance duration The double-stance duration is the period of the gait cycle when both feet are in contact with the ground. It was calculated as the duration from the instant of one foot’s touchdown to the following liftoff of the contralateral foot.

Gait speed This variable quantifies how quickly one progresses his/her body center of mass forward. It was calculated based on the T25FWT measurement. Specifically, the gait speed for each of the two walking trials was calculated as the distance (i.e., 25 feet = 7.62 m) divided by the time required to walk the distance. The average value of the two trials was used for analysis. Gait speed was also normalized to $bh$ to reduce the variability between participants.

Step frequency The step frequency represented the number of steps taken within one minute (i.e. steps/min). It was calculated by dividing the number of steps by the amount of time in minutes required to complete the T25FWT.
2.5. Statistical Analyses

The normality of all outcome variables was assessed using the Shapiro-Wilk test. To analyze the changes in disability status and functional mobility resulting from the training, the proposed outcome variables were assessed using either the paired $t$-tests or the Wilcoxon signed-rank tests for normally and non-normally distributed data, respectively. These outcome measurements included: the PDDS and MSFC scores, the scores of the T25FWT, the 9HPT, PASAT-3", step length, step width, double-stance duration, single-stance duration, gait speed, and step frequency. The Bonferroni step-down (Holm) correction was used to minimize the Type I error due to the multiple comparisons. Effect sizes were computed to evaluate the magnitude to indicate the difference between evaluations. The difference levels of effect size were defined as: large (> 0.8); medium (> 0.5), and small (> 0.2). For normally distributed measurements, the effects sizes were described using the Cohen’s effect size ($d_z$) (Lakens, 2013). For non-normally...
distributed measurements, the equation proposed by (Pallant, 2007) was used to compute the effect size.

\[
r = \frac{Z}{\sqrt{n_{pre} + n_{post}}}
\]

Where \( Z \) is the Wilcoxon signed-rank test statistic output and \( n_{pre} \) and \( n_{post} \) respectively represents the number of observations during the pre- and post-training evaluations.

All statistics were performed using GraphPad Prism 6.0, and a significance level of 0.05 was used throughout.
3. Results

Three participants did not complete the entire study, resulting in a completion rate of 88%. The remaining 22 participants finished all 24 sessions as described in section 2.3. No major adverse effects of discomfort were reported by participants. Participants expressed feeling an itchy sensation on the legs \((n = 4)\) or noses \((n = 3)\) after the first few training sessions. Nevertheless, this sensation quickly disappeared after 4-5 training sessions.

3.1. Normality Testing

Due to the paired nature of the analyses, the normality test was applied on the difference of each measurement between the pre- and post-evaluation results. The Shapiro-Wilk normality test determined for each outcome measurement the correct test: either the paired t-test for normally distributed variables (Shapiro-Wilk test \(p > 0.05\)) or the Wilcoxon test for the non-normally distributed parameters \(p < 0.05\). Table 3 showed the results of the Shapiro-Wilk test and the strategy selected to evaluate the changes in the outcome variables.

Table 3. Shapiro-Wilk normality test for outcome variables to define testing strategy

<table>
<thead>
<tr>
<th>Outcome Variable</th>
<th>(p) value</th>
<th>Normal distribution</th>
<th>Test strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDDS</td>
<td>0.010</td>
<td>No</td>
<td>Wilcoxon test</td>
</tr>
<tr>
<td>T25FWT</td>
<td>&lt;0.001</td>
<td>No</td>
<td>Wilcoxon test</td>
</tr>
<tr>
<td>9HPT DH</td>
<td>0.125</td>
<td>Yes</td>
<td>Paired t-test</td>
</tr>
<tr>
<td>9HPT NDH</td>
<td>0.901</td>
<td>Yes</td>
<td>Paired t-test</td>
</tr>
<tr>
<td>PASAT-3″</td>
<td>0.024</td>
<td>No</td>
<td>Wilcoxon test</td>
</tr>
<tr>
<td>MSFC</td>
<td>0.001</td>
<td>No</td>
<td>Wilcoxon test</td>
</tr>
<tr>
<td>Double stance time</td>
<td>0.007</td>
<td>No</td>
<td>Wilcoxon test</td>
</tr>
<tr>
<td>Single stance time</td>
<td>&lt;0.001</td>
<td>No</td>
<td>Wilcoxon test</td>
</tr>
<tr>
<td>Step length</td>
<td>0.881</td>
<td>Yes</td>
<td>Paired t-test</td>
</tr>
<tr>
<td>Step width</td>
<td>0.885</td>
<td>Yes</td>
<td>Paired t-test</td>
</tr>
<tr>
<td>Step frequency</td>
<td>0.686</td>
<td>Yes</td>
<td>Paired t-test</td>
</tr>
<tr>
<td>Gait Speed</td>
<td>0.004</td>
<td>No</td>
<td>Wilcoxon test</td>
</tr>
</tbody>
</table>
3.2. Disability Status

The reduction in the PDDS score reached a significant level from the pre-training to post-training evaluation (3.66 ± 1.88 vs. 3.05 ± 1.99, Wilcoxon signed-rank \( p = 0.0109 \), effect size \( r = 0.38 \), Figure 7a), indicating an improved subjective assessment of the disability status. The majority of participants (77%) exhibited a decrease in the PDDS value (Figure 7b).

The MSFC score was significantly greater during the post-training test in comparison with pre-training test (0.00 ± 0.62 vs. 0.36 ± 0.68, \( p = 0.0001 \), \( r = 0.61 \), Figure 8a). The improvement in the MSFC score was detected for 21 participants (96%, Figure 8b). Two of three MSFC components exhibited a significant change from pre-training test to post-training. Specifically, the time to complete the T25FWT significantly decreased (9.38 ± 4.92 vs. 8.14 ± 4.08 sec, \( p = 0.0009 \), \( r = 0.46 \), Figure 9a) and the score of the PASAT-3” significantly improved (30.55 ± 13.54 vs. 36.95 ± 15.07, \( p = 0.0016 \), \( r = 0.45 \), Figure 9b) from pre-training evaluation to post-training. The arm function displayed marginal changes between the two evaluations. In comparison to the pre-training test, the time of the 9-HPT for the dominant hand (DH) and the non-dominant hand (NDH) marginally improved during the post-training session (DH: 27.81 ± 5.96 vs. 26.19 ± 5.82 sec, \( p = 0.0527 \), \( d_z = 0.44 \), Figure 9c; NDH: 28.47 ± 7.40 vs. 27.43 ± 8.33 sec, \( p = 0.0586 \), \( d_z = 0.46 \), Figure 9d).

3.3. Functional Mobility

With respect to the spatiotemporal parameters (Table 4), there was a significant improvement in the gait speed (0.64 ± 0.32 vs. 0.71 ± 0.32 \( bh/s \), \( p = 0.0002 \), \( r = 0.52 \)) from the pre-training evaluation to post-training test. Also, a significant decrement in the double stance time (0.18 ± 0.12 vs. 0.15 ± 0.10 sec, Wilcoxon signed-rank \( p = 0.0142 \), \( r = 0.36 \)) was detected from the pre- to post-training test. The step frequency (107.50 ± 29.35 vs. 112.33 ± 27.43

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steps/min, \( p = 0.0666 \)) and the step length (0.37 ± 0.10 vs. 0.39 ± 0.11 \( bh, p = 0.0533 \)) displayed marginal improvements from pre- to post-training evaluations. No significant difference was observed in the step width (0.07 ± 0.03 vs. 0.06 ± 0.04 \( bh, p = 0.6745, d_z = 0.09 \)), or the single stance phase duration (0.45 ± 0.15 vs. 0.42 ± 0.08 sec, \( p = 0.2579, r = 0.17 \)) between pre- and post-training evaluations.

Figure 7. Comparisons of the Patient Determined Disease Steps (PDDS) between pre-training (Pre) and post-training (Post) evaluations in a) group mean and standard deviation and b) individual scores. A high score represents a poorer disability status. *Wilcoxon signed-rank test was used.*
Figure 8. Pre-training and post-training evaluations of Multiple Sclerosis Functional Composite (MSFC) score. a) Mean and standard deviations. b) Individual score. A low score represents a poorer disability status. #: Wilcoxon signed-rank test was used.
Figure 9 Pre-training and post-training evaluations of the MSFC components. a) The leg performance measured by the T25FWT, a smaller score represents a better mobility; b) the cognitive function evaluated by the PASAT-3”, a greater score represents better cognitive status; and the arm function assessed by the 9-HPT test on c) the dominant (DH) and non-dominant (NDH) hand, a lower score represents better arm function. 

+: Paired t-test and #: Wilcoxon signed-rank test.
Table 4. Comparisons of the spatiotemporal gait parameters in mean ± standard deviation between the pre-training (or Pre) and post-training (or Post) evaluations

<table>
<thead>
<tr>
<th>Outcome Variable</th>
<th>Pre</th>
<th>Post</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Double stance time (sec)</td>
<td>0.18 ± 0.12</td>
<td>0.15 ± 0.10</td>
<td>0.0142*</td>
</tr>
<tr>
<td>Single stance time (sec)</td>
<td>0.45 ± 0.15</td>
<td>0.42 ± 0.08</td>
<td>0.2579*</td>
</tr>
<tr>
<td>Step length (bh)</td>
<td>0.37 ± 0.10</td>
<td>0.39 ± 0.11</td>
<td>0.0533+</td>
</tr>
<tr>
<td>Step width (bh)</td>
<td>0.07 ± 0.03</td>
<td>0.06 ± 0.04</td>
<td>0.6745+</td>
</tr>
<tr>
<td>Step frequency (steps/min)</td>
<td>107.50 ± 29.35</td>
<td>112.33 ± 27.43</td>
<td>0.0666+</td>
</tr>
<tr>
<td>Gait Speed (bh/s)</td>
<td>0.64 ± 0.32</td>
<td>0.71 ± 0.32</td>
<td>0.0002*</td>
</tr>
</tbody>
</table>

*: Paired t-test.

#: Wilcoxon signed-rank test.
4. Discussion

This study sought to evaluate the effects of an 8-week CWBV intervention on the disability status and functional mobility of PwMS. To our best knowledge, this was the first study to explore whether the vibration-based intervention modifies the motor impairments caused by MS. This objective was approached not only by using a self-reported disability level score, but also by means of an objective measurement based on three functions that represent a comprehensive profile of participant’s functionality (i.e. leg, arm, and cognitive functions). After eight weeks of CWBV intervention, a significant improvement was observed in both the PDDS and MSFC disability status scores.

With respect to functional mobility, an 8-week CWBV training improved participants’ gait speed. Perhaps the most important contribution of this work, in terms of functional mobility, is to demonstrate which and how spatiotemporal gait parameters were modified after the intervention. In general, the findings from the present study further support the use of CWBV training as a safe and effective exercise method for PwMS despite the conservative configuration of the vibration parameters (i.e. frequency of 20 Hz and the amplitude of 1.6 mm) used in the intervention.

4.1. Disability Status

4.1.1. Patient Determined Disability Steps.

The finding of improved self-reported disability status following the training supported our hypothesis that an 8-week CWBV training would improve the disability status of PwMS. The PDDS score was significantly improved after the 8-week CVWB training program. Among the very limited studies which examined the effects of CWBV training of PwMS, the majority focused on variables such as mobility, balance, and muscle performance rather than disability status.
Because the PDDS score is based on items that rate the participant’s capability of walking a 25-foot distance with or without a walking aid, the significant improvement of the PDDS score could be attributed to the improved mobility performance of the gait speed due to the training. This notion supports previous findings about the relationship between disability status and mobility. Learmonth et al. (2013) conducted a study to explore the correlation among the PDDS score and outcome variables which have been traditionally used to assess different dimensions of disability status of PwMS. On the leg function, their findings depicted a strong correlation between PDDS value and clinical mobility tests such as the T25FWT (Spearman correlation coefficient $\rho = 0.627$, $p < 0.01$), the TUG test ($\rho = 0.717$, $p < 0.01$), and the 6-minute walk test ($\rho = -0.704$, $p < 0.01$).

The use of PDDS to gauge the self-reported changes of disability status after the 8-week CWBV training program in this study is in accordance with the finding reported by Liu et al. (2016). Previous studies that evaluated the correlation between PDDS and EDDS found a consistently strong correlation between these two instruments ($\rho = 0.783$, $p < 0.001$, (Hohol, Orav, & Weiner, 1995; Learmonth et al., 2013). The findings presented here reinforce the idea of using patient-rated outcomes as surrogates to the EDDS in order to determine the disability status with an easier and less cumbersome assessment (Gulick, Namey, & Halper, 2011; Riazi, Thompson, & Hobart, 2004). However, further studies are needed to corroborate the replacement of instrument of disability status determination as the EDDS was not measured in this study. With respect to unexpected decrement on PDDS score on some participants, it is recommended that future studies monitor minor and non-self-identified relapsing episodes that could affect the PDDS assessment.

4.1.2. MS Functional Composite.

Our results also supported the hypothesis that an 8-week CWBV training would significantly improve the disability status when measured objectively using the MSFC. Notably,
almost all participants (96%) showed an improvement of the MSFC score although not all the self-reported individual results demonstrated an improvement in the PDDS score. Prior studies have highlighted the better sensitivity of MSFC to determine the changes in disability status than the EDDS (Cohen, Reingold, Polman, & Wolinsky, 2012). The continuous nature of the MSFC measurement also represents a powerful approach to more precisely and sensitively evaluate the changes in the disability status of PwMS. Both, the EDSS or the PDDS are discrete variables, containing a finite number of levels. Therefore, the precision level of these two instruments would be much lower than the MSFC score. For example, PDDS would not be able to detect the difference in disability status if the two actual PDDS scores were just below and above 3. However, the MSFC is sensitive enough to detect the changes between these two PDDS values. This could be an explanation why few participants displayed the reverse changes from pre-training to the post-training sessions while 96% subjects showed positive changes in the MSFC score.

The improvements in the MSFC score were resulted from the changes in its three domains. Specifically, significant improvements on lower-limb and cognitive functions were observed (i.e. T25FWT and PASAT-3") whereas the upper limb function (i.e. 9-HPT) showed an encouraging improvement on both hands. In this study, the pre-training evaluation values were used to calculate the reference values for the MSFC calculation. In order to provide findings that could be compared to other studies findings, it is important to calculate the individual MSFC scores using a universal database.

With respect to the lower-limb function, these findings are similar to previous reports examining the acute and long-term effects of CWBV training (Santos-Filho, Cameron, & Bernando-Filho, 2012). For example, a double-blinded randomized controlled trial conducted by Schuhfried et al. (2005) investigated the acute effects of a single 5-minute session of CWBV on
the functional mobility among PwMS. The findings of Schuhfried et al. (2005) study suggested that the acute effects of the vibration therapy improved momentarily the leg muscle strength. Jackson et al. (2008) conducted a cross-over study to determine the acute effects of two vibration frequencies (2 vs. 26 Hz) on isometric torque capacity of the knee extensors and flexors among PwMS. Their findings suggested that the vibratory situation of higher frequency (i.e. 26 Hz) produced an increase in the lower-limb torques. This was in accordance with previous studies that demonstrated that CWBV-based interventions improved functional mobility among PwMS (Santos-Filho et al., 2012).

Most of the longitudinal studies concerning the long-term effect of CWBV on improving functions among PwMS are also consistent with the finding from the present study. Schyns et al. (2009) showed that a 4-week CWBV, combined with an exercise intervention, improved functional mobility when measured through the 10-min walking test and TUG. However, no statistical differences were found on the functional mobility tests when the same participants were exposed to a 4-week exercise-only intervention. Similarly, Wunderer et al. (2010) developed a single-group pretest-posttest study to examine a 6-week CWBV training program based on a 3-participant sample. Authors found some improvement in mobility; however, their findings could be affected by the lack of statistical power.

Recently, more robust experiments have provided a better understanding of the effects of CWBV on leg function and functional mobility. Claerbout et al. (2012) investigated the additional effects of a 3-week CWBV exercise with different exposure levels of vibration stimulation (CWBV-full vs. CWBV-light) to an only-exercise intervention. Authors were able to detect significant enhancement of functional mobility over time in the CWBV-full group and the CWBV-light group as well as in the exercise-only group. The author also reported a
significant improvement in the lower-limb strength for the CWBV-full group. A recent study which also adopted a single-group, 8-week, longitudinal design undertaken by Mason et al. (2012) reported similar findings that those in the present study. The intensity and volume of their 8-week CWBV training started with the frequency of 15 Hz, the amplitude of 2.6 mm, five minutes per session, and three sessions per week. The parameters were slightly increased up to 20 Hz, 6.1 mm and eight minutes respectively for the frequency, amplitude, and the duration of each session. Despite the discrepancy between the training parameters between studies, similar results were reported by both studies (Claerbout et al., 2012; Mason et al., 2012). This implies that a more conservative vibration training protocol could still be effective to improve the disability status among PwMS. This finding is particularly important for those with poorer disability status and highly limited physical capacity.

The findings about the significant enhancement in the cognitive function quantified by the PASAT-3" were somewhat surprising as the 8-week CWBV training did not include a specific cognitive training component. Nevertheless, the link between exercise, in the form of vibration training, and cognitive function can be inferred in different ways. One potential relationship was proposed by Sandroff, Pilutti, Benedict, and Motl (2015). In their study, 62 participants with MS were tested to determine the correlations between physical fitness and cognitive function. Sandroff et al. (2015) concluded that aerobic capacity and strength were related to cognitive processing speed. Furthermore, it is widely accepted that a strong correlation exists between the cognitive impairment and progress of disability status of PwMS (B. M. Sandroff, 2015). An improved disability status most likely indicates enhanced cognitive function.

We observed a marginal improvement in the upper-limb function. The 8-week CWBV program was focused on delivering a stimulus mainly to the lower limbs which possibly explain
the modest improvement in the upper-limb function. A novel theory explored by Anderson et al. (2011) studied the relationship between cerebral damage and upper-limb function. Anderson et al. (2011) described that a lower volume in white matter was associated to poor motor performance on the upper-limb function. Research conducted on MS disease progression has found that PwMS with higher aerobic fitness levels depicted larger volumes of gray and white matter. Similarly, PwMS, with a better preservation of gray and white matter integrity, showed a better cognitive capacity than those PwMS with lower levels of brain integrity (Prakash, Snook, Motl, & Kramer, 2010). It was suggested that the performance of the 9HPT is associated with the cognitive capacity among PwMS (Benedict et al., 2011). These results were further supported by a randomized-controlled study which investigated the effects of a 3-month aerobic exercised-based intervention in improving the gray matter volume. Results revealed that the experimental group, who receives the exercise training, displayed a 16.5% increase in the hippocampal gray matter volume. Also, participants exhibited a memory improvement by 53.7% after the exercise intervention (Leavitt et al., 2014). The vibration training, as one type of the exercise training, could have the effect to expand the gray matter volume and thus the cognitive function. Because previous research has linked the cognitive function with arm function of PwMS (Sbardella et al., 2013), it can be inferred that the CWBV training could have improved arm function by improving participants’ gray matter integrity. However, further studies are needed to explore these possible effects of CWBV.

4.2. Functional Mobility

The second hypothesis was also supported by these results where, the post-training mobility assessed via the T25FTW was improved after an 8-week CWBV training program. We observed a significant improvement of the double stance time, step frequency, and gait speed.
Additionally, a marginal increase in the step length was observed. This was in accordance with a previous systematic review that demonstrated that CWBV-based interventions improved functional mobility among PwMS (Santos-Filho et al., 2012). On the other hand, the single stance time and step width did not depict significant differences post training.

It was reported that the PwMS tend to walk more slowly with lower cadence, prolonged double stance phase, shorter step length, and greater step width in comparison with their healthy counterparts in order to maintain their stability during walking (Givon et al., 2009). These adaptive changes in the spatiotemporal parameters also become more and more significant with the progression of the disease (Martin et al., 2006). Hence, one of the goals of gait rehabilitation program designed for PwMS is to regain the capability of walking in a pattern similar to the healthy individuals (Benedetti et al., 1999; Crenshaw, Royer, Richards, & Hudson, 2006; Kaipust, Huisinga, Filipi, & Stergiou, 2012).

The observed changes in the gait pattern after the 8-week CWBV training program were in the desired direction regardless of whether or not these changes were significant. Specifically, the gait speed was significantly increased after the training among the participants included in this study. Such an increase in the gait speed could be attributed to the improved step frequency and marginal improvement of the step length (Yahia, Ghroubi, Mhiri, & Elleuch, 2011). The increased gait speed indicated an improved ambulatory ability. Gait speed is usually used as an index to gauge the progression of the disease (Crenshaw et al., 2006). An increased gait speed could mean an improved disability status or a delayed progression of the disease. The results also illustrated that the double stance time was significantly shortened after the training in comparison with pre training. The similar desired trend was also observed for the step length and step frequency from pre-training to post-training tests. Additionally, the step width after the
training showed a decrement within the participants in this study (Table 4). The changes in the spatiotemporal parameters demonstrated that an 8-week CWBV training program improves the gait performance among PwMS by adopting a more dynamic profile rather than a conservative or cautious gait pattern (i.e. wider base of support, longer time on double support, shorter steps, and slower gait speed).

Similar results have been found when using other types of exercise-based interventions among PwMS. For instance, Gutierrez et al. (2005) conducted an 8-week incremental resistance-training program to study the changes in gait parameters among PwMS. When comparing pre- and post-training evaluations, they reported a significant decrease in double support time (0.23 ± 0.07 vs. 0.21 ± 0.06 sec, \( p = 0.046 \)). Significant increments were also observed for stride length (1.06 ± 0.16 vs. 1.14 ± 0.12 m, \( p = 0.017 \)), and step length on the least-affected side (0.53 ± 0.07 vs. 0.56 ± 0.07 m, \( p = 0.025 \)). Physiotherapy treatment approaches have been found to improve gait parameters of PwMS. Lord, Wade, and Halligan (1998) investigated the effects of a 5- to 7-week intervention using a facilitation and a task-oriented approach. Both methods showed an improvement in gait parameters after training; stride length was increased from 0.75 ± 0.16 m to 0.93 ± 0.19 m for the facilitation group, whereas stride length significantly increased from 0.82 ± 0.10 to 0.98 ± 0.2 m for the task-oriented group. Therefore, a CWBV-based training program could achieve a similar training effect as other interventions. The improvement of functional mobility is crucial since gait is one of the most important body functions among PwMS (Heesen et al., 2008). Given the attractive features of CWBV training, such as portability, safety, ease-of-operation, and more acceptable intensity, vibration therapy has significant potential to improve mobility among the MS community.
4.3. Significance

Findings presented in this study have important implications that could impact the life and social functioning of PwMS. Despite this study only focus on the effects of an CWBV program on disability status and mobility, previous research has established a clear connection between these two outcome variables (Amato et al., 2001; Cohen et al., 2012; Hohol et al., 1995; Larocca, 2011; Mitchell et al., 2005).

First, the disability status is a constructed variable that can be measured in many different ways. In this study, the upper-limb, lower-limb, and cognitive functions were employed to estimate the disability status on participants. The lower limb function seemed to be the functional component that most benefits from the CWBV training program, whereas the improvement of upper-limb function was marginal probably due to the nature of the stimulation. Nevertheless, the improvement in cognitive functioning requires further investigation because of its relevant implications on quality of life and social functioning.

On the other hand, lower limb function is a determinant of mobility, and therefore there were observed improvements as those described by the spatiotemporal gait parameters. Notably, the increase in mobility reflected on the increment of gait speed and step frequency post training was significant in this population. According to Motl (2013), walking impairment is the primary consequence of the pathological changes of the CNS that limits PwMS from engaging in activities of daily life. In this study, the gait speed is the outcome variable demonstrating that the CWBV intervention improves mobility post training by allowing a more dynamic walking profile. Moreover, the increase in the gait speed could also be related to the improvement observed in step frequency. As the participants were able to step more rapidly, their gait speed would be increased. The improvements of lower-limb function and mobility were not only observed
objectively but also subjectively as reflected in the PDDS score. Even though the effects of the 8-week CWBV training program on the quality of life was not monitored in this study, previous studies suggested that disability status and mobility are two essential determinants of quality of life among PwMS (Amato et al., 2001). In this link, the improvements in the disability status and mobility could imply the promotion of the quality of life in this population.

4.4. Limitations

This study presented limitations that could influence our findings. First, the relatively small sample size did not allow us sufficient statistical power to implement a randomized-controlled design (Appendix A). Without an active control group or a placebo group, we cannot rule out the effects of other confounding variables on our findings. The confounders could include the gender, age, depression, disease course, fatigue effect, or other psychological factors. For example, the prevalence of depression is relatively high among PwMS. A descriptive study in a German sample of 1,675 participants showed a prevalence of depression of 60%. Half of this sample reported symptoms of fatigue via a Modified Fatigue Impact Scale Median-Split (Rupprecht et al., 2015). Fatigue and depression have been related to motor and human cognitive performance (Benito-León, Morales, & Rivera-Navarro, 2002; Schreurs, de Ridder, & Bensing, 2002). Second, the outcome variables were not evaluated in the middle of the intervention (i.e., at week 4). This limited our capability to track the changes in disability status of mobility performance across the training intervention. Third, it remains unknown the retention effects of the improvements in disability level or mobility resulting from vibration training or how much time the improvements are retained after the vibratory training intervention is ceased. Fourth, the clinical significance was not assessed in this study, and findings were based on the statistical significance. Future studies should include the calculation of clinical significance to determine
the practical effects of an 8-week CWBV on disability status and mobility among PwMS. Fifth, acute effects may have influenced the observed findings as the outcome variables were collected immediately after the post-training evaluation. Therefore, additional investigations are need to differentiate between the acute and chronical effects of CWBV. Each of these needs further investigation.

4.4. Future Research Directions

In order to further verify and strengthen the findings from this investigation, future studies adopting a more rigorous study design (like a randomized-controlled trial) with a large sample size is highly needed. Such a study would eliminate the possible effects of extraneous variables on the research findings.

Another possible direction would be to identify the optimal combination of the vibration training parameters including the frequency, amplitude, duration of each training bout, duration of the rest period, number of bouts within each session, and the volume of training. This would provide valuable guidance to develop effective vibration-based program to preserve or improve disability status and mobility among PwMS.

Lastly, with the advancement of technologies, the vibration platform could be designed for home use. Therefore, testing the effect of vibration training within a home environment could be of high interest to the rehabilitation community. If CWBV training at home is effective, it would largely increase the accessibility to the MS community. It may also provide evidence to the insurance industry to consider the coverage of vibration training. That could improve the MS management services and will have profound impact on the individuals, families, and the society.
5. Conclusions

In summary, the results from the present study demonstrated that an 8-week CWBV program is a promising exercise intervention for PwMS to reduce their disability level and improve functional mobility. Improvement of the disability level was reflected objectively and subjectively. Moreover, we observed improvements in the functional mobility and cognitive function. Given its practical and safe features, vibration training could become a well-accepted training modality, suitable for clinical settings, rehabilitation centers, or even home, to improve the disability level and mobility for PwMS.
6. References


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7. Appendix

7.1. Appendix A. Sample Size Estimation

A pilot study was performed to collect some preliminary data to test the feasibility of the training course briefly and to determine the required sample size. A group of four females (mean ± SD, age: 56.8±13.7 years, height: 162.7 ± 7.0 cm, body mass: 68.6 ± 13.2 kg, disease duration: 14.6 ± 8.9 years; and PDDS score: 4.25 ± 1.70) with physician-confirmed MS were enrolled into this pilot study. They all completed the 8-week vibration intervention. The 8-week CWBV training program consisted of 24 sessions. Each training session lasted 10 minutes consisting of five sets of 1-minute vibration training (frequency: 20 Hz, amplitude: 1.3 mm) followed by 1-minute rest.

Before and after the training course, their level of disability was assessed using the MSFC scores. The T25FWT, 9-HPT, and PASAT-3″ tests were used to assess the lower limb function, arm function, and cognitive function, respectively. Participants were also asked to rate themselves the perceived level of disability using the PDSS scale. An 8-camera motion capture system (Vicon, Oxford, UK) was used to collect the position of 26 markers in order to calculate the spatiotemporal gait parameters as proposed.

Because MSFC score is the most sensitive measurement to training, we deem the MSFC as the primary measure of disability status, whereas gait speed was selected as the primary outcome representing the mobility. Based on our preliminary results, the estimated effect sizes for these two measurements were 0.54 and 0.096, respectively. We computed the sample size for each of the two primary parameters based on a two-tailed paired t-test and the computed effect size at α level of 0.05 and a power of 90%. The sample size for these two outcome variables was calculated by means of an online sample size calculator (Biomath.info, US). The required sample
size was 8 and 18 respectively for the MSFC score and the gait speed. Taking the maximum, 18 participants would provide a statistical power of 0.90 for detecting a significant between-session difference at the level of 0.05 with respect to both primary outcome measurements. By applying a conservative attrition rate of 0.20, we plan to include 22 participants with MS in the study to ensure 18 participants would complete the 8-week training courses and two evaluations.

Table 5. Power analysis to determine the sample size of the study.

<table>
<thead>
<tr>
<th>Outcome variable</th>
<th>Effect size</th>
<th>Sample size (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSFC score</td>
<td>1.35</td>
<td>8</td>
</tr>
<tr>
<td>Gait speed</td>
<td>0.59</td>
<td>18</td>
</tr>
</tbody>
</table>
7.2. Appendix B. Patient Determined Disease Steps

The self-reported disability level was determined using the Patient Determined Disease Steps (Kister et al., 2013). Participants rated their current functional status based on the following eight-level scale.

- **0 Normal**: I may have some mild symptoms, mostly sensory due to MS but they do not limit my activity. If I do have an attack, I return to normal when the attack has passed.

- **1 Mild Disability**: I have some noticeable symptoms from my MS but they are minor and have only a small effect on my lifestyle.

- **2 Moderate Disability**: I don't have any limitations in my walking ability. However, I do have significant problems due to MS that limit daily activities in other ways.

- **3 Gait Disability**: MS does interfere with my activities, especially my walking. I can work a full day, but athletic or physically demanding activities are more difficult than they used to be. I usually don't need a cane or other assistance to walk, but I might need some assistance during an attack.

- **4 Early Cane**: I use a cane or a single crutch or some other form of support (such as touching a wall or leaning on someone's arm) for walking all the time or part of the time, especially when walking outside. I think I can walk 25 feet in 20 seconds without a cane or crutch. I always need some assistance (cane or crutch) if I want to walk as far as three blocks.

- **5 Late Cane**: To be able to walk 25 feet, I have to have a cane, crutch or someone to hold onto. I can get around the house or other buildings by holding onto furniture or touching the walls for support. I may use a scooter or wheelchair if I want to go greater distances.

- **6 Bilateral Support**: To be able to walk as far as 25 feet I must have two canes or crutches or a walker. I may use a scooter or wheelchair for longer distances.
☐ **7 Wheelchair / Scooter:** My main form of mobility is a wheelchair. I may be able to stand and/or take one or two steps, but I can't walk 25 feet, even with crutches or a walker.

☐ **8 Bedridden:** Unable to sit in a wheelchair for more than one hour.
8. Vita

Edson F. Estrada was born in Chihuahua, Chihuahua México on July 8, 1979. He is the fourth son of Mario Estrada and Maria Meneses. He moved to the border region of Juárez-El Paso in 2002. He graduated from the Centro de Bachillerato Tecnológico industrial y de servicios earning an associate degree in Electronics in 1994. Later in 2001, he received the degree of Bachelor of Science in Electronic Engineering by the Instituto Tecnológico de Chihuahua. In 2005 and 2010, he received the degrees of Master of Science and Doctor of Philosophy in Electrical and Computer Engineering, respectively, from the University of Texas at El Paso.

Currently, he is appointed as a full time professor with the Universidad Autónoma de Ciudad Juárez within the Health Sciences Department. To improve his knowledge in the field of Biomechanics, he enrolled in the Kinesiology graduate program at the University of Texas at El Paso to purse a second master in Kinesiology.

He has presented his research projects at various national and international conferences. Latest work was presented at the 2016 American College of Sports Medicine (ACSM) conference at Boston, MA. His poster was selected as one of the either finalists to compete for the Research Presentation Award in the 2016 Texas Chapter of the ACSM.

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