Whole Body Vibration training for Multiple Sclerosis patients

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Rachael Ruth Mason

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Abstract

Introduction: The purpose of this study was firstly to investigate whether 8 weeks of whole body vibration (WBV) training was an acceptable form of exercise for patients with Multiple Sclerosis (MS) and secondly what effect it may have on measures of functional capacity.

Methods: Fifteen participants with MS volunteered for WBV training three times a week on a commercialised Galileo Sport™ vibration machine with an oscillating platform. Training consisted of two four week blocks based on an increasing stimulus training programme (overload principle). The first fours weeks involving five sets of 1-min WBV with 1-min rest in between with increasing vibration frequency (15-25Hz, 2.6mm-4.1mm amplitude); the second four weeks training increased to eight sets of 1-min WBV (15-20Hz, 6.1mm amplitude). Functional performance measures (Timed up and Go, Standing Balance, Functional Reach and Timed walk) and quality of life questionnaire (SF-36) were conducted prior to training, at 4 weeks, 8 weeks and 2 weeks (10wk) following the completion of the training.

Results: The 10m walk test showed significant improvements at the 2m, 8m and 10m measure between pre vs. 8wk ($P<0.05$) and pre vs.10wk ($P<0.05$). Timed up and Go demonstrated a significant time effect ($P<0.05$). Standing balance showed significant improvements at pre and 4 week ($p<0.05$) and pre and 10 week ($p<0.05$).

Conclusions: This is the first study to investigate WBV as an exercise training modality for MS patients. It was shown that not only is WBV training safe, well tolerated by MS patients but it also improved standing balance and walking speed in MS patients.

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Abbreviations

C	Celsius
cm	centimetres
CMAP	Compound muscle action potential
CNS	Central nervous system
CSA	Cross sectional area
EDSS	Expanded disability status scale
FP	Foot placement
Fri	Friday
FRT	Functional reach test
FS	Functional system
g	Gravity
HHV	Human herpes virus
HLA	Human leukocyte antigen
hrs	Hours
Hz	Hertz
Kg	Kilograms
Km	Kilometres
MHC	Major histocompatibility complex
m	metres
mm	millimetres
mmHg	millimetres of mercury
Mon	Monday
min	minutes

MS	Multiple Sclerosis
MU	Motor unit
mV	millivolt
MVC	Maximum voluntary contractile
PCr	Phosphocreatine
P_i	Inorganic phosphate
RPE	Rating of perceived exertion
RRMS	Relapsing remitting multiple sclerosis
SB	Standing balance
SD	Standard deviation
SF-36	Short form-36
TUG	Timed up and go
WBV	Whole Body Vibration
Wed	Wednesday
Wk	Week
y	Years

1 Introduction

Multiple sclerosis (MS) is the most commonly diagnosed neurological condition in young people. It affects 72 per 100,000 people in New Zealand with women affected at a rate three times that of men; most being diagnosed in their late 20's to early 30's (Taylor *et al.*, 2008).

The effect of the disease is highly variable in terms of both symptoms and progression. Muscle weakness and fatigue are the two symptoms most patients with MS report (White & Dressendorfer, 2004) and these can limit the ability to perform physical activity, which then impacts on their general health.

Recent studies have investigated Whole Body Vibration (WBV) as an exercise modality in participants who are either healthy (Delecluse *et al.*, 2003; Cochrane *et al.*, 2008) or have compromised health (Bautmans *et al.*, 2005; Ebersbach *et al.*, 2008). Observations from these studies have shown improvements in balance, mobility and strength. These improvements may benefit patients with MS, as impairments in these functions negatively affect the lives of patients with MS.

Longitudinal or training studies provide a way of evaluating the effect an intervention has on a population over time. Because the only study of the effect of WBV in MS patients used only a single bout of vibration (Schuhfried *et al.*, 2005) there is a need to perform a training study of WBV in MS patients. Therefore, this study examines how patients with MS are affected by 8 weeks of WBV training.

1.1 Hypotheses

The purpose of this study was to test two hypotheses. Firstly, it is hypothesised that 8 weeks of WBV will be an acceptable exercise modality for patients with MS. Secondly, it was hypothesised that WBV will improve functional performance in patients with MS.

2 Review of the Literature

2.1 What is Multiple Sclerosis

Multiple sclerosis (MS) is a chronic disease of the central nervous system characterised by demyelination and axonal loss that affects approximately 4,000 New Zealanders (Garner & Widrick, 2003; Drew *et al.*, 2008). The effect MS has on people's lives ranges from fatigue to severe disability of normal function. First described in the 1830s, the disease was depicted as causing multiple, irregular foci of discoloration and shrinkage throughout the neuroaxis (Hickey, 1999). Although the disease has been diagnosable for nearly 180 years the precise aetiology of MS remains unknown (Lutton *et al.*, 2004). Extensive investigations have studied the pathogenesis of infectious agents, autoimmune causes, the association with immune mimicry and environmental and familial associations. There has also been interest in the physiological changes that occur in the body, especially those at a skeletal level (Ng *et al.*, 1997).

2.2 Classification of MS

The clinical course of MS can present in different forms (Lublin & Reingold, 1996), the most common of which is that of relapsing remitting MS (RRMS) (Keegan & Noseworthy, 2002). It is characterized by discrete clinical "attacks" or "relapses" followed by a period of symptom stability (Figure 2-1) (Keegan & Noseworthy, 2002). Following diagnosis most RRMS patients will slowly deteriorate neurologically over many years, with or without additional clinical attacks. This is termed secondary progressive MS and is seen as the long term outcome for RRMS patients (Figure 2-1) (Lublin & Reingold, 1996). Some patients are diagnosed with primary progressive MS, characterised by disease progression from the onset

with no distinct relapse and only occasional plateaus (Lublin & Reingold, 1996). Progressive relapsing MS on the other hand shows progression from the onset with occasional relapses later in the disease (Lublin & Reingold, 1996).

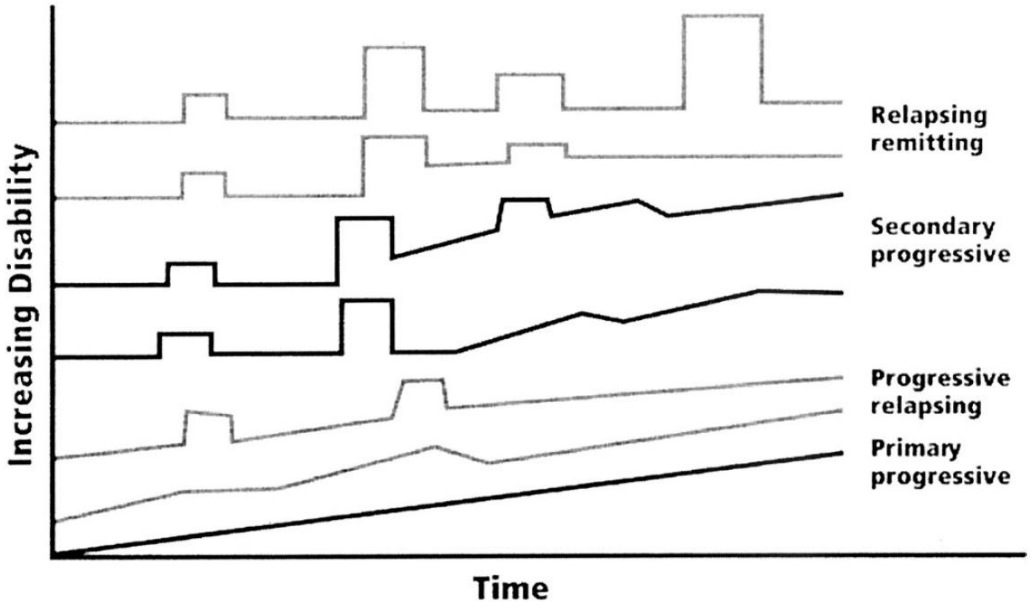

Figure 2-1. Clinical courses of Multiple Sclerosis (taken from (Rizvi & Agius, 2004))

2.3 Neurological classification of MS

MS is classified according to the degree of disability as defined by the expanded disability status scale or EDSS. The neurological symptoms reflect the location of the lesion within the central nervous system (CNS) (Keegan & Noseworthy, 2002). The scale used nowadays was redefined by Kurtzke in 1983, as the original scale was based only on neurological examination and did not take into account symptoms (Kurtzke, 1983). The EDSS is composed of nine functional system scores that are independent of the others but together they reflect all neurological impairment in MS (Kurtzke, 1983). The functional systems (FS) are divided into Corticospinal, Cerebellar, Brain Stem, Sensory, Bowel and Bladder, Visual, Cerebral or Mental and Other or Miscellaneous Functions (discussed below in more detail

from Kurtzke, 1983). Each FS with the exception of "Other" functions, are graded on a scale of 0-5 or 0-6, with 0 being normal to grade 5-6 being maximal impairment. The 'Other' functions are graded as being absent (0) or present (1). The EDSS score then uses the FS grades to classify the patient so that the disease process can be monitored over time, from normal neurological examination (0), to death due to MS (10) (Kurtzke, 1983).

Corticospinal functions

The corticospinal system is the centre specialised for making discrete movements and is one of the major motor tracts from the brain to the spinal cord. The score depends on the ability of the function of the limbs. This ranges from severe monoparesis or mild to moderate paraparesis or hemiparesis (grade 3) to quadriplegia (grade 6).

Cerebellar functions

The cerebellar system regulates balance and coordination of movements. In MS patients, mild ataxia or unsteadiness affects balance to the point where the patient is unable to perform coordinated movements (grade 5).

Brain Stem functions

The brain stem system consists of the midbrain, pons and medulla oblongata and controls involuntary functions of the body. Grade 2 on the EDSS scale is moderate nystagmus, characterised by rapid, rhythmic, repetitious involuntary eye movement. In addition to this disability there may be pathology of other cranial nerves that lead to dysarthia, marked by slurred, slow speech that may be difficult to produce and lack modulation. Severe disability is marked by the inability to swallow or speak.

Sensory functions

Sensory functions encompass the receptor mechanisms which monitor the external and internal environment such as pain, smell, taste, temperature, vision, hearing, touch and proprioception. In MS compromise can begin with decreased ability to write and move, to decrease in touch and pain, to a loss of sensation below the head.

Bowel and bladder functions

Bladder function can be disrupted by reduced neural control of the bladder muscles. Detrusor-sphincter-dyssynergia occurs when the muscle around the bladder neck fails to relax. The most severe rating (grade 6) is total loss of bowel and bladder function.

Visual or optic functions

Many patients experience visual disturbances that are caused by a scotoma or blind spot in the visual field or optic neuritis due to the presence of the lesion of the optic nerve. This is often associated with some level of decreased acuity (sharpness). These symptoms increase the patient's disability to the point where the worse eye is corrected to 20/200 and the better eye is 20/60 or worse.

Cerebral or Mental functions

This category applies to the mood state and level of mental activity in a patient. This can range from depression to dementia.

Other or miscellaneous functions

This is a dichotomous score either present or absent of any other neurological findings attributed to MS.

2.4 Aetiology

2.4.1 Infectious Agents

Infectious agents have been reported to be associated with MS although none of these associations are conclusive. There are infectious agents known to cause demyelinating diseases in animals, i.e. Theiler's murine encephalomyelitis virus. Infectious agents currently being investigated for a possible relationship to MS include Epstein-Barr virus, human herpes virus 6 and *Chlamydia pneumonia* (Keegan & Noseworthy, 2002).

Chlamydia pneumonia is a common respiratory pathogen and a major cause of pneumonia. Sriram *et al* (1999), with 37 MS patients (17 Remitting Relapsing MS, 20 Chronic Progressive MS) found that all Remitting Relapsing MS and 19 of 20 chronic progressive patients tested positive via polymerase chain reaction for a major outer membrane protein gene for *C. pneumonia*, although further studies by other laboratories have failed to repeat these data.

Human herpes virus 6 (HHV-6) is an ubiquitous organism that has a near 100% seroprevalance worldwide (Campadelli-Fiume *et al.*, 1999). The two variants of HHV-6, a and b, can remain latent in the CNS until reactivation by stress or co-infection with other microbes (Campadelli-Fiume *et al.*, 1999). This supports the theory of HHV-6 being a candidate for an infectious agent of MS as stress can trigger exacerbations of MS symptoms.

In a study of 83 Remitting Relapsing MS patients, Lucchinetti *et al* (2000), found that there were four distinct patterns of demyelination identified. Patterns I and II were consistent with demyelination via autoimmune-mediated mechanisms whereas types III and IV were more

consistent with demyelination via virus or toxin-mediated mechanisms. This was the first study to demonstrate differences in demyelination processes.

2.4.2 Autoimmunity

Autoimmune-mediated mechanisms can occur via cell-mediated autoimmunity or humoral and antibody-mediated contributions. Keegan and Noseworthy (2002) describe how autoreactive T lymphocytes apparently play a major role in demyelination. Activated T lymphocytes can cross the blood-brain barrier and bind with class II major histocompatibility complex (MHC). The secretions of cytokines by CD4 lymphocytes are thought to activate macrophage and microglial activity lead to damage myelin processes or the oligodendroglial cells. Conversely, cytotoxic T cells are thought to be able to directly damage the oligodendrocytes and myelin. Disruption of the blood-brain barrier in MS allows entry of B cells, antibodies and complement into the CNS. Myelin oligodendrocyte glycoprotein, found exclusively in CNS myelin, is thought to be the site of antibody attack via activation of B cells and the complement membrane attack complex.

2.4.3 Immune mimicry

There is a potential for pathogens to trigger disease by inducing an autoimmune disease. In a comprehensive review on the subject, Olson *et* al (2004) state that immune mimicry can be caused by a pathogen activating T cells in response to the foreign epitope but may also cross react with self-epitopes. It is postulated that infection of the target organ (the brain in the case of MS) is required for initiation of autoimmune disease via immune-mimicry. An infection may provide the inflammatory environment for local activation of cross-reactive T-cells. One hypothesis is that an early childhood infection may provide this situation, with a secondary

stimulation later in life required to restimulate autoreactive memory T-cells. This coincides with reports from patients that a stressful event, trauma or infection precedes onset of symptoms.

2.4.4 Environmental Factors

Extensive work studying the epidemiology of MS on the Faroe Islands created new ideas about the cause of MS. In extensive examination of the population medical records, MS was rare prior to the 1940s, so rare that not a single case was recorded (Kurtzke, 1993). In contrast, by 1986 there were 32 cases diagnosed in people living continuously on the island (9 other patients had lived off the island for a significant period of time). Further analysis revealed that the first clinically diagnosed onset of MS was in July 1943. From 1943 to 1949 there were 16 cases; from 1949 to 1973 another 16 cases and no cases seen from 1973 to 1986. In this time the population grew from approximately 25,000 to 45,000. From these data Kurtzke and colleagues suggest that there were three epidemics of MS in the Faroe Islands since 1941. The trigger of these epidemics occurred at the same time as British occupation of the Island during April 1940 to September 1945, with up to 7,000 soldiers stationed at any one time. It is thought that the army brought a transmittable infection to the Island; however no microbial agent has yet been identified.

2.4.5 Latitude

There has long been an awareness of differing prevalence of MS in relation to the distance from the equator. As reviewed by Ewing and Bernard (1998), this can be demonstrated in Australia and New Zealand, with the incidence of MS approximately 7 times more prevalent in Tasmania than in tropical Queensland; while the South Island of New Zealand has twice

the prevalence than the North Island. The origin of the initial settlers to New Zealand, mainly people of Scottish origin, is thought to be a likely reason for the differences in susceptibility, whereas in Australia this variation in ethnic origin cannot be attributed. Environmental factors are strongly linked to the susceptibility of the disease in Australia, as demonstrated by a reduction in risk when migration occurs before puberty from a high MS prevalence area to a low prevalence area (Hammond *et al.*, 2000).

2.4.6 HLA associations and gene susceptibility

Human leukocyte antigen (HLA) haplotypes have been linked with MS in various populations. Initial investigations discovered the MHC class I HLA alleles A3 and B7 to be linked with MS in European and North American populations (Chao *et al.*, 2007). Further work found that the class II allele, HLA-DR2 had an even stronger association (Haines *et al.*, 1998). This is consistent with large familial studies (Haines *et al.*, 1996; Sawcer *et al.*, 1996). In the Sardinian population, HLA-DRB1 region has been associated with MS (Marrosu *et al.*, 2001). The genes coding for the HLA-DR alleles are located on close together on chromosome 6 and show a strong linkage disequilibrium, possibly indicating a relationship between the two alleles (Ewing & Bernard, 1998).

2.5 Physiological effects

Two major symptoms that affect MS patient's day-to-day quality of life are fatigue and muscle weakness. Researchers have investigated how physiological systems contribute to these symptoms. Sheean *et al* (1997) investigated how MS patients respond to fatiguing activity. By performing a 45 second maximal contraction of the adductor pollicis of the hand, they found the MS group began with a similar force as the control group but the reduction in

force was greater (20% vs. 45%). This demonstration of exercise–induced reduction in force generating capacity is an illustration of the excessive fatigue seen in MS patients and is believed to be attributed to central fatigue origins.

To investigate if fatigue is caused by a reduction in muscle contraction, Garner and Widrick (2003) investigated the cross-bridge mechanisms of contraction in MS patients. By measuring neuromuscular strength with a dynamometer and taking a biopsy from the vastus lateralis, they showed MS patients had fewer fibres containing type IIa myosin heavy chain isoforms. This reduction in type IIa fibres goes against what normally happens with atrophy in humans except with aging. Normally with disuse, there is an increase in type II fibres and a reduction in type I fibres. This unique atrophy pattern seen in MS patients may be associated with a greater reduction in large motor unit function, due to the demyelination of neurons that control type IIa fibres and produces different degrees of atrophy. Edström (1970) was the first to demonstrate this pattern of change in patients with central paresis and Parkinsonism. The author suggested that the pattern of change seemed to be an effect of selective disuse of high-threshold phasic motor units due to the reduction in voluntary muscle use combined with the increased use of low threshold motor units caused by muscle spasticity (Edström, 1970).

Kent-Braun *et al* (1997) examined the strength, composition and enzyme activity in the skeletal muscle of MS patients. By biopsying the tibialis anterior muscle, they found there was a tendency toward greater atrophy in type II fibres and a lower cross sectional area compared to the control group. When comparing enzyme activity they found a reduction in succinate dehydrogenase activity although no difference in α-glycerol-phosphate dehydrogenase. This reduction in oxidative enzyme activity was comparable to that in spinal

cord injury patients rather than in short term disuse, indicating MS patients have decreased ability to use energy aerobically (Kent-Braun *et al.*, 1997).

Muscle strength and fatigue were investigated by Lambert *et al* (2001) by testing MS patients and a control group, with an isokinetic dynamometer. When body mass and age were accounted for, the MS group was weaker than the control group in non-dominant leg extension and flexion and dominant leg flexion. Muscle fatigue was induced in participants by performing three 30-contraction bouts. The degree of fatigue was measured with the Fatigue Index which is calculated by the ratio of the tension during the last 5 contractions to the tension during the first 5 contractions multiplied by 100. They found that MS patients had a 9.8% and 9.3% lower fatigue index for knee flexor and knee extensor muscle groups, respectively. The MS group did significantly less work (34%) with the knee flexion when compared to the controls. The authors suggest that the greater total work output for controls relative to MS patients reflects a combination of greater peak torque production and greater fatigue resistance in controls than in those with MS (Lambert *et al.*, 2001).

2.5.1 Neural Mechanisms

Central mechanisms for muscle weakness can occur due to a reduction in motor unit (MU) firing rate, changes in MU excitability, impaired recruitment or increased central motor conduction time (Garner & Widrick, 2003). Ng *et al* (2004) studied the functional relationship of central motor impairment and peripheral muscle functions. By using 16 patients with MS and 18 healthy controls, testing of central functions, showed the MS patients could perform only half the foot taps in a ten second period and had a slower maximal rate of force development compared to the controls. Muscle strength was significantly lower in the MS group despite having similar dorsiflexor muscle cross sectional area. Regarding

peripheral effects, the compound muscle action potential (CMAP) was used to indicate neuromuscular junction and muscle membrane activation and the muscle twitch and tetanic force indicated abnormal intramuscular calcium function or relative changes in muscle fibre type. The results showed no significant difference between CMAP amplitude or duration, twitch force and rate of force development between the two groups. Differences were seen in the force relaxation time, with the MS patients having slower half-relaxation time and maximal rate of tetanic force relaxation. The authors suggested that this evidence indicates the impairment of central motor drive as the primary role in the weakness of MS (Ng *et al.*, 2004). The impaired ability to perform successive voluntary contractions, such as the foot tap, is likely due to a slower rate of maximal voluntary force development which is dependent on both motor unit recruitment and rate coding (Ng *et al.*, 2004).

de Haan *et al* (2000) study of voluntary neural drive using electrical stimulation in patients with MS compared to healthy controls, to examine the contractile properties and fatigue of the quadriceps muscles. They found maximum voluntary contractile force (MVC) was 31% lower in the participants with MS when compared to controls. This lower contraction capability was also demonstrated in the lower percentage of the force production (11%) achieved when superimposed stimulation was used to determine whether participants were able to voluntarily activate their muscles maximally. The participants with MS were able to generate 75% of their maximum force-generating capacity compared to 94% for the controls. They also showed an increase in half-relaxation time in the MS group after 60 contractions at 30% of MVC. The authors suggest that most of the force loss was due to MS-related reduction in voluntary neural drive (de Haan *et al.*, 2000).

Ng *et al* (1997) looked at the central motor drive during maximal voluntary contractions in MS patients. By using surface electromyogram, which reflects both motor unit recruitment and motor unit firing rates, central motor drive can be determined. They showed that MS group could achieve the same relative force as a control group in dorsiflexor force but the MS group needed significantly greater central motor drive, *i.e. decreased efficiency in neural input*.

2.5.2 Metabolic alterations

Kent-Braun *et al* (1994) investigated the role of metabolism during voluntary exercise in MS. The exercise was performed on the ankle dorsiflexors while the leg was within a magnetic resonance spectroscopy machine. Changes in metabolism were seen with respect to phosphocreatine (PCr), inorganic phosphate (P_i) and pH. During the first 10 minutes of exercise all variables were similar between the MS patients and the control group. After 10 min, the controls showed significantly greater P_i/PCr increase and a greater pH decrease than the MS group. This finding suggested that at the same relative exercise intensity the magnitude of metabolic change was significantly smaller in the MS group. This, coupled with the earlier onset of fatigue also shown in the study, suggests the presence of activation failure in MS patients (Kent-Braun *et al.*, 1994).

2.6 Functional changes

The symptoms that lead a patient to the diagnosis of MS can vary widely. The functional changes that occur can be those that affect the ability to walk, balance and maintain physical activity.

2.6.1 Gait

Gait disturbances can be caused by plaques in the cerebral hemisphere, brain stem, spinal cord or corticospinal track or from proprioception involvement. Researchers have investigated the fluctuations in walking ability in MS patients. Martin *et al* (2006) found patients without corticospinal tract involvement showed reduced speed and stride length similar to those with corticospinal tract involvement. Patients in Morris *et al* (2002) performed a 10m walk test in the morning and afternoon and reported they felt physically worse in the afternoon, although their performance did not change. Albrecht *et al* (2001) showed that maximum walking distance measurements conducted on four consecutive days showed marked day-to-day variability in patients. Such a change could mislead clinicians into treating an exacerbation of symptoms with corticosteroids unnecessarily.

Various methods used to measure gait performance in MS patients include 25-foot walk (Yates *et al.*, 2002; Romberg *et al.*, 2004; Surakka *et al.*, 2004; Romberg *et al.*, 2005), 6min timed walk test (Freeman & Allison, 2004; Kileff & Ashburn, 2005), 2min walking test (Taylor *et al.*, 2006; van den Berg *et al.*, 2006), 7.62m walk test (Romberg *et al.*, 2004; Surakka *et al.*, 2004; Romberg *et al.*, 2005) and 10m walk test (van den Berg *et al.*, 2006).

2.6.2 Balance

The ability to perform functional activities such as walking and turning are impacted by balance disorders which affect many people with MS (Frzovic *et al.*, 2000). There are different ways in which balance can be measured: 1) standing balance (Lord *et al.*, 1998; Wiles *et al.*, 2001; Freeman & Allison, 2004; Cattaneo *et al.*, 2007) or 2) forward reach distance (Functional Reach Test, FRT; (Duncan *et al.*, 1990)).

The standing balance test or steady stance has been used to show differences between MS patients and controls (Frzovic *et al.*, 2000) but also differences between different forms of MS (Soyuer *et al.*, 2005). The FRT designed by Duncan *et al* (1990) measures the maximal distance a patient can reach forward without taking a step or losing balance. Martin *et al* (2006) found that two clinically distinct groups of MS patients, those with and without corticospinal tract involvement and minimal impairment, performed poorly with the FRT, with the authors suggesting anterior-posterior instability.

2.7 Treatment

Treatments for MS patients primarily aim to prevent further disability and to give relief of symptoms. There are two forms of disease modifying drugs that may be used: immunomodulators (interferon-ß and glatiramer acetate) or immunosuppressives (mitoxantrone). They have been found to delay the disability progression of the disease (Brown et al., 2007). Symptoms most commonly requiring treatment are pain, spasticity and mood disorders (Crayton & Rossman, 2006). More recently, there has been a change to the use of exercise prescription as a more widely accepted therapeutic option (Petajan & White, 1999).

2.8 Exercise and MS

The reduction in mobility, coordination and muscular strength greatly impact a patient's ability to maintain a regular exercise regime. With a decrease in physical activity comes the risk of developing co-morbidities such as obesity, cardiovascular disease and diabetes (Khurana *et al.*, 2009). Investigations into the effect exercise plays in reducing these conditions, as well as the symptoms associated with normal disease progression, are an important focus of research.

Disease management approaches have historically been conservative. Previously, exercise was deemed inappropriate for fear that excess activity might exacerbate the symptoms of the patient (Freal *et al.*, 1984). Prior to 1984, very little research had been conducted on the possible effects of an exercise program on MS patients. However, recent studies have investigated the effect of traditional exercise like walking/running and cycling but also aquatic exercise, resistance training, electrical stimulation and yoga. These studies have shown that various doses and modalities of exercise can induce a broad spectrum of physiological, functional and psychological adaptations in patients living with MS.

2.8.1 Exercise modalities prescribed

In a review of studies prescribing exercise for MS patients, 30 articles presenting the findings of 28 trials were found to focus on functional measures i.e. balance, gait, with an intervention period greater than 3 weeks. Fifteen trials prescribed some method of aerobic training (e.g. swimming, walking, cycling), while eight trials prescribed it as the sole exercise modality (Gehlsen *et al.*, 1984; Schapiro *et al.*, 1988; Ponichtera-Mulcare *et al.*, 1997; Rodgers *et al.*, 1999; Schulz *et al.*, 2004; Davis *et al.*, 2005; Kileff & Ashburn, 2005; van den Berg *et al.*,

2006) Resistance training was prescribed in nine trials and five of these prescribed it in isolation (DeBolt & McCubbin, 2004; White *et al.*, 2004; Gutierrez *et al.*, 2005; Taylor *et al.*, 2006; White *et al.*, 2006). Other modalities of exercise training included electrical stimulation (Kent-Braun *et al.*, 1996), yoga (Oken *et al.*, 2004) and physiotherapy based intervention (Lord *et al.*, 1998; Jones *et al.*, 1999; Wiles *et al.*, 2001; Yates *et al.*, 2002; Rasova *et al.*, 2006; Cattaneo *et al.*, 2007).

2.8.2 Adaptations to exercise training in MS patients

Physiological adaptations

Positive adaptations in MS patients were seen in response to a range of exercise interventions. Several trials have reported improved cardiorespiratory fitness in MS patients in response to aerobic training (Petajan *et al.*, 1996; Ponichtera-Mulcare *et al.*, 1997; Mostert & Kesselring, 2002; Davis *et al.*, 2005) and combined training (Rasova *et al.*, 2006; Bjarnadottir *et al.*, 2007). Improved lactate response was seen following aerobic training (Schulz *et al.*, 2004). Improvements in work rate during a graded exercise test were seen by Rampello *et al* (2007), which are indicative of improved cardiorespiratory fitness. Strength improvements were shown in response to cycle ergometer training (Petajan *et al.*, 1996; Rodgers *et al.*, 1999), aquatic training (Gehlsen *et al.*, 1984) and resistance training (DeBolt & McCubbin, 2004; White *et al.*, 2004; Gutierrez *et al.*, 2005; White *et al.*, 2006).

Functional performance

MS patients showed significant improvements in exercise capacity, through measures of walking ability (i.e. 6-min walk distance). This was shown in response to aerobic training (Kileff & Ashburn, 2005; van den Berg *et al.*, 2006), resistance training (White *et al.*, 2004; Taylor *et al.*, 2006), physiotherapy based training (Yates *et al.*, 2002) and combined training

(Freeman & Allison, 2004; Romberg *et al.*, 2004; Surakka *et al.*, 2004; Romberg *et al.*, 2005; Cattaneo *et al.*, 2007). The use of a physiotherapy based training programme showed significant improvements in transfer time (Jones *et al.*, 1999) and mobility (Wiles *et al.*, 2001).

Improvements in fatigue in MS patients studied were shown in response to aerobic training (Gehlsen *et al.*, 1984), resistance training (White *et al.*, 2004; Gutierrez *et al.*, 2005; White *et al.*, 2006), and combined training (Freeman & Allison, 2004; Oken *et al.*, 2004; Romberg *et al.*, 2004; Surakka *et al.*, 2004; Romberg *et al.*, 2005; Rasova *et al.*, 2006). Improvements in balance were demonstrated in patients in response to aerobic training (Schulz *et al.*, 2004), combined training (Freeman & Allison, 2004; Cattaneo *et al.*, 2007), and physiotherapy based training (Lord *et al.*, 1998; Wiles *et al.*, 2001).

The improvements in physiological and functional measures illustrate that exercise can be beneficial to MS patients. A new form of exercise, whole-body vibration (WBV), has shown improvements in compromised health populations (Cardinale & Wakeling, 2005). Currently, the only published study (Schuhfried *et al.*, 2005) studied acute (one bout) vibration using very low vibration frequency (2.0-4.4Hz, 3mm) on a Zeptor-Med system (Scisen GmbH, Germany) with some positive effects shown. Therefore, there is potential for focus on whole body vibration as a training intervention for MS patients.

2.9 Whole body vibration

Whole body vibration (WBV) exercise has been the focus of research over the past decade as a novel exercise form. The major focus of WBV has been the effect it has on physical performance of young, healthy athletes (Cochrane & Stannard, 2005; Delecluse *et al.*, 2005; Fagnani *et al.*, 2006). The effects WBV have on the body can be examined after a single bout (acute) or after multiple bouts (chronic). Multiple bouts of WBV can be prescribed in training programmes over a number of sessions, over a number of weeks.

2.9.1 Mode of action of WBV

The physiological mechanisms produced by WBV are thought to be neuromuscular in origin. The mechanical action of vibration causes fast and short changes in the length of the muscle-tendon complex (Cardinale & Bosco, 2003). These length changes are detected by sensory receptors that modulate muscle contraction through reflex muscular activity via the stretch-reflex loop and activation of the muscle spindles (Cardinale & Bosco, 2003). Activation of the muscles extrafusal fibres are initiated by α-motor neuron innervations. Interneurons may play a role in transferring signals to the higher centres in the cerebellum that in turn provide additional innervations to γ- and α-motor neurons. Additionally, the gamma motor neuron role ensures that the muscle spindle continues to fire action potentials during muscle contraction and to modulate muscle tone (Cardinale & Bosco, 2003).

The effect of the vibration is dependent upon the amplitude and frequency of the oscillations, and therefore the rate and length of muscular stretch. The amplitude is determined by peak to peak displacement of the platform, with the repetition rate of cycles of oscillation is denoted by the frequency of the vibration (measured in Hz) (Cardinale & Bosco, 2003). There are two

types of vibration platforms commonly used for clinical trials; an oscillating see-saw action like the action (Galileo) or an up and down-action (Power Plate™).

2.9.2 WBV acute studies

The research looking at acute WBV healthy participants has shown mixed results. Studies have found that WBV can: have a positive effect on cardiovascular measures (Rittweger, 2000; Cochrane *et al.*, 2008); enhance neuromuscular measures (Rittweger *et al.*, 2003); benefit (Torvinen *et al.*, 2002a; 2002b), reduce (Erskine *et al.*, 2007) or have no change (de Ruiter *et al.*, 2003a) on measures of strength; and enhance (Goto & Takamatsu, 2005) or have no change (Erskine *et al.*, 2007) on hormones.

Compromised Health Populations

Several studies have investigated acute WBV in participants who have compromised health. In an randomised controlled trial of 68 Parkinson's Disease patients, those who received 5x 1min WBV at 6Hz found that WBV improved tremor and rigidity, gait and posture and bradykinesia (Haas *et al.*, 2006). Stroke patients were shown to increase voluntary force and muscle activation of the quadriceps muscle (Tihanyi *et al.*, 2007).

2.9.3 WBV chronic studies

Chronic studies using WBV have used a wide range of durations. Roelants *et al* (2004a) 24 weeks of WBV 3 times a week found there was improvement in knee extensor strength following. These results were similar to those of Delecluse *et al* (2003) 12 weeks of WBV in young healthy non-athletes, which found isometric and dynamic knee strength increased. In a

shorter study, Paradisis and Zacharogiannis (2007) found WBV 3 times a week for 6 weeks participants improved step length, step rate and running velocity as well as jump height and number of jumps in 30sec.

de Ruiter *et al* (2003b), Cochrane *et al* (2004), Delecluse *et al* (2005) and Kvorning *et al* (2006) performed training studies ranging from 9 sessions over 9 consecutive days (Cochrane *et al.*, 2004) to 11 weeks of 3 sessions per week (de Ruiter *et al.*, 2003b). They found that WBV did not improve functional strength of the knee extensors (de Ruiter *et al.*, 2003b), jump height (Cochrane *et al.*, 2004), maximal leg muscle strength, knee-extension velocity, vertical jump height, sprint running velocity and force-time during sprint start (Delecluse *et al.*, 2005), nor was there any acute hormonal response (Kvorning *et al.*, 2006).

Elderly and Compromised Health

WBV training studies using older participants or those with compromised health have focused on maintaining or restoring function. By utilising tests that focus on functional measures i.e. balance and walking, the affect on quality of life can be assessed (discussed in detail below). Researchers have used a wide range of study duration; 3 weeks (Ebersbach *et al.*, 2008), 6 weeks (Bautmans *et al.*, 2005; Bruyere *et al.*, 2005), 8 weeks (Kawanabe *et al.*, 2007; Rees *et al.*, 2007), 12 weeks (Cheung *et al.*, 2007; Rietschel *et al.*, 2008) and 24 weeks (Roelants *et al.*, 2004b).

Effect on Balance

The effect WBV had on balancing ability was measured by Bautmans *et al* (2005), Bruyere *et al* (2005), van Nes *et al* (2006), Bogaerts *et al* (2007) Cheung *et al* (2007) and Ebersbach *et al*

(2008). Bruyere *et al* (2005), Bautmans *et al* (2005), van Nes *et al* (2006) and Bogaerts *et al* (2007) showed a significant improvement in body balance, whereas Ebersbach *et al* (2008) found no significant effect, perhaps due to the variation in dose effect in the two patient populations. Cheung *et al* (2007) found that the WBV group showed improvements in movement velocity and maximal sway but between group differences were not statistically significant. The fact that there was no standard test used to assess balance in all of the trails, identifies a need to validate and promote the use of a reliable test that can be used in all studies to assess the effect WBV has on balance.

Timed Up and Go test

Functional mobility can be measured by using the Timed Up and Go (TUG) test. The TUG uses the same parameters for all trials with the participants standing from a sitting position, walking 3m, turning then returning and sitting back down. This test has been used in WBV studies with compromised populations (Bautmans *et al.*, 2005; Bruyere *et al.*, 2005; Ahlborg *et al.*, 2006; Rees *et al.*, 2007). Bautmans *et al* (2005), Bruyere *et al* (2005) and Rees *et al* (2007) showed significant decrease in the time taken in the WBV group although Ahlborg *et al* (2006) found that times did not change significantly. An explanation for differences seen in the TUG may be associated with the use of a different population of participants for the studies; Rees *et al* (2007), Bautmans *et al* (2005) and Bruyere *et al* (2005) participants were elderly (>60 years) whereas Ahlborg *et al* (2006) Cerebral Palsy patients ranged from 21-41 years. Ahlborg *et al* (2006) suggest that these participants may require more vigorous training program to receive sufficient overload in order to get more marked effects on motor performance. There is also difference in that the Cerebral Palsy participants have a disability that affects them from birth, whereas the elderly participants generally have a progressive decline in function which could be restored.

Measures of walking ability

Measures of functional mobility include measuring walking over a set distance (Kawanabe *et al.*, 2007; Rees *et al.*, 2007; Ebersbach *et al.*, 2008) or over a set time (Ahlborg *et al.*, 2006). Rees *et al* (2007) group showed significant change in both the 5m and 10m fast walk tests and Kawanabe *et al* (2007) significantly improved over the 10m walking time, yet Ebersbach *et al* (2008) showed no change. Ahlborg *et al* (2006) used a 6 minute timed walk but showed no significant change. The reason for these differences may be due to the different study populations: elderly (Kawanabe *et al.*, 2007; Rees *et al.*, 2007), Parkinson's Disease (Ebersbach *et al.*, 2008) and Cerebral palsy (Ahlborg *et al.*, 2006).

The use of different WBV machines, Galileo (Bruyere *et al.*, 2005; van Nes *et al.*, 2006; Kawanabe *et al.*, 2007; Rees *et al.*, 2007; Ebersbach *et al.*, 2008; Rietschel *et al.*, 2008), PowerPlate (Bautmans *et al.*, 2005) and NEMES (Ahlborg *et al.*, 2006) makes it difficult to directly compare the outcomes to the studies. The different types of vibration stimulus coupled with the variation in additional exercises performed on the machines and varying study duration, complicate the validity of effectiveness of the WBV.

3 Methods

3.1 Participants

Eleven females with MS (mean age ± standard deviation [SD] 50.2 ± 6.9y; body mass 65.7 ± 19.2 kg; height 165.3 ± 6.1 cm; EDSS 3.5 ± 0.9) and four males with MS (mean age 50.5 ± 5.2y; body mass 85.3 ± 16.0 kg; height 175.3 ± 3.2 cm; EDSS 3.4 ± 0.5) volunteered to take part in the study. All participants had confirmed diagnosis of clinical MS (Poser *et al.*, 1983), with a mean disease duration of 10.9 ± 4.9y. Twelve participants had relapsing-remitting MS (RRMS), one primary progressive MS with secondary relapsing and two RRMS with secondary progressive. Seven participants were involved in organised physical activity ranging from stretching, yoga, Tai Chi, stationary cycling performed from 1x/week to 6x/week (Table 3.1). The other eight participants did not perform any type of organised activity.

The recruitment for MS volunteers involved placing an advertisement in the local MS society newsletter inviting potential volunteers to an information session. At this meeting the study was verbally outlined and an information sheet was provided (Appendix C), and an expression of interest was then called for. Participants approached the investigator in person or by phone to determine if they met the initial criteria (Appendix D). Those who meet the criteria underwent a full medical and neurological examination conducted by a Rehabilitation Consultant who was highly experienced in the clinical examination of MS patients. Participants were accepted for the study if they had a clinically definite MS, Kurtzke Expanded Disability Status Scale (EDSS) score between 2.0 and 5.5, had never undertaken WBV and were not suffering from uncontrolled hypertension or hypotension, bone tumours, herniated discs, recent fractures (<6 months), or had a recent acute relapse (<1 months).

Written informed consent was obtained from the participants and the study was approved by the Central Region Health and Disability Ethics Committee (CEN/08/07/038).

Table 3.1. Organised physical activity of participants

Participant	Exercise	Duration	Frequency
1	Stationary Cycle	4km	6 x per wk
2	No organised activity		
3	Stretching class	30-60min	1x per wk
4	No organised activity		
5	Gym programme	30min	3x per wk
	Yoga	60min	1 per wk
6	No organised activity		
7	Yoga and Tai Chi	60min each	2x per wk
8	Stretching class	30-60min	1x per wk
9	Stretching class	30-60min	1x per wk
10	No organised activity		
11	No organised activity		
12	No organised activity		
13	No organised activity		
14	No organised activity		
15	Yoga and stretching class	60min each	2x per wk
	Walking	30-60min	2-3 x per wk

3.2 Study Design

All WBV sessions and functional tests were conducted at the local MS Society rooms, which were carpeted and provided a constant environment [ambient temperature 18.9 ±0.7 °C; barometric pressure 760.1 mmHg ± 2.6]. All participants were familiarised with the WBV machine and the functional measures a week prior to the start of the WBV intervention. Participants were instructed to maintain their physical activity during the study and to not start any new activities. Activity levels were documented each week during the study.

The participants completed WBV three times per week (Mon, Wed, Fri) for a total of 24 WBV sessions with at least 24 hrs of rest separating each WBV session (Table 3.2). Health and functional measures were assessed prior to the start of the WBV intervention (pre), then at four (4wk), eight (8wk) and ten weeks (10wk) (Table 3.2). The ten week (10wk) assessment was a reassessment of the health and functional measures two weeks post-WBV training. To prevent variations in participant's symptoms affecting functional tests, participants underwent testing at a similar time day of time (±2hrs). In addition, subjective data covering participant's feelings of sleep quality, tiredness, fatigue, muscular pain and energy levels were also documented at the start of each WBV session.

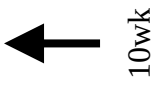

Table 3.2. Time line of training protocol. Arrows indicate when health & functional measures were

	WBV																								Post WBV	
Week	1			2			3			4			5			6			7			8			9	10
Session	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24		

3.3 WBV Machine

WBV was performed on a commercial machine (Galileo XS, Novotec, Pforzheim, Germany) which has a teetering board that produces side-to-side alternating vertical sinusoidal vibration to the body from 0 to 30 Hz. The WBV platform had marked foot placements that were numbered (Figure 3-1). A single axis ***i***MEMS® accelerometer (ADXL250, Analog Devices, Inc; Norwood, MA, United States) with a scaling factor of 76mV/*g* was fixed to the edge of the vibrating plate to measure the amplitude and magnitude of these foot placements; where foot position 2 (FP2) = 2.6mm (2.3-3.8*g*), FP2.5 = 4.1mm (6.4-10.9*g*) and FP3 = 6.1mm (5.4-9.7*g*).

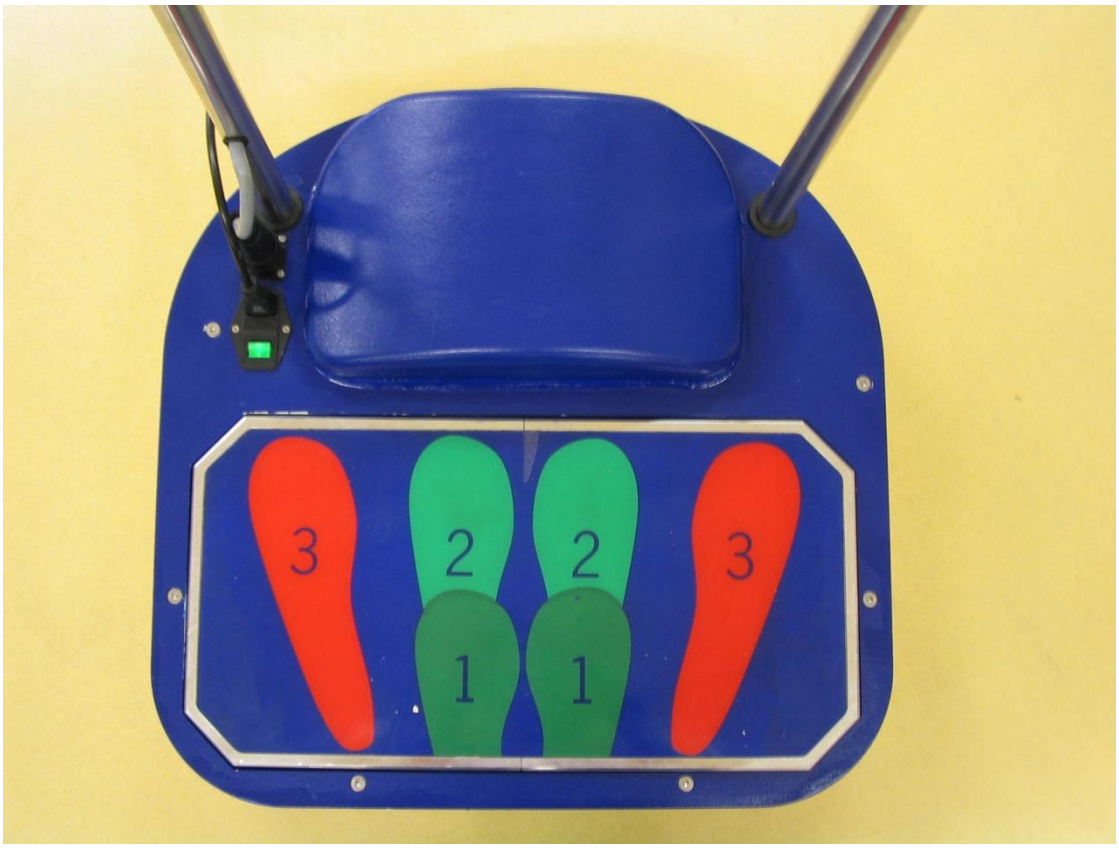

Figure 3-1. Photo of WBV machine platform illustrating foot positions

Figure 3-2. Photo of WBV machine with participant in position

Participants were asked to stand on the vibration platform in a static squat position where a manual goniometer was used to set the knee angle to approximately 110° of flexion (Figure 3-2). This knee angle was chosen based on previous vibration research using the *Galileo* vibration platform (de Ruiter *et al.*, 2003a; de Ruiter *et al.*, 2003b). Static rather than dynamic squatting was used as Abercromby *et al* (2007a) suggests the former maximises leg extensor activation, while the knee angle minimises the likelihood of negative side effects of vibration being transmitted through the spinal column to the head (Abercromby *et al.*, 2007b). If there was discomfort in the back or head, the participants increased flexion in their knees. The participants were instructed to place both feet over the central axis of the plate and to aid balance the participants were allowed to use the support bar when required. Participants had bare feet or wore socks to avoid footwear-dependent attenuation of vibrations. The ratings of

perceived exertion (RPE) using the modified 10-point Borg scale (Borg, 1998), which was recorded at the end of each minute of WBV.

3.4 WBV Training Programme

Currently, there are no scientifically based WBV training programmes available for people with MS. Therefore, we developed an eight week WBV programme in accordance to the overload principle (Kraemer & Ratamess, 2004) and from participant feedback. The training load increased systematically and progressively over the 8 weeks by increasing the vibration frequency, FP and/or session duration (Figure 3-3). Furthermore, in best practice it is recommended that exercise programmes are periodised to maximise adaptations to take place. Hence, a double periodised programme was implemented where the WBV training was separated into two 4 week blocks. The first 4 week block commenced with all participants starting at 15Hz (FP2; amp= 2.6mm) exposed for five x 1 minute bouts with 1 minute rest. The vibration frequency was then increased by 1 Hz increments in the proceeding sessions until 20Hz was reached, where the foot position increased to FP2.5 (amp= 4.1mm), thereafter the frequency increase continued until it reached 25Hz (Figure 3-3).

The second 4 week block of training commenced at 15Hz at FP3 (amp= 6.1mm) for 8 x 1 minute bouts with 1 min rest separating each repetition. The participants received 2 sessions at this frequency before it was increased by 1Hz over 12 sessions (Figure 3-3). If a new frequency was not tolerable, then the frequency was set to that of the previous frequency.

The selection of the vibration frequency was based on previous side-to-side vibrating platforms research where 18 Hz was used to treat lower back patients (Rittweger *et al.*, 2002) and 25-26 Hz has been used to enhance muscular performance (Bosco *et al.*, 1998; Bosco *et*

al., 1999; Torvinen *et al.*, 2002a; Cochrane & Stannard, 2005). The duration of the vibration was based on previous research with compromised health populations (Bruyere *et al.*, 2005; Kawanabe *et al.*, 2007; Rees *et al.*, 2007).

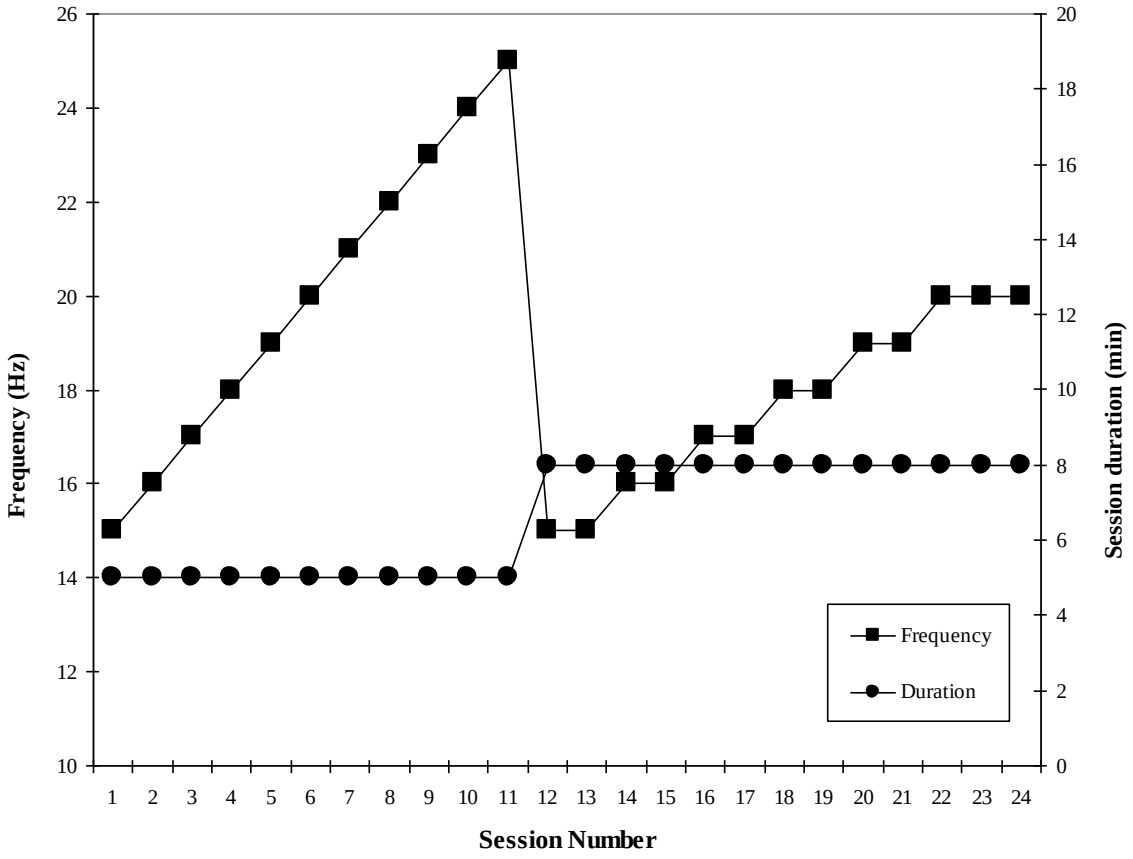

Figure 3-3 Vibration training protocol of frequency and session duration

3.5 General Health Scores and Functional Measures

3.5.1 Health-related quality of life

The Medical Outcomes Study Short Form-36 (SF-36) English version was used to assess quality of life (Appendix F). The SF-36 is a self-administered questionnaire that explores eight main health domains: physical functioning, role limitations due to physical health problems, bodily pain, general health, vitality, social functioning, role limitations due to emotional health problems and mental health (Pugliatti *et al.*, 2008). The SF-36 is based on eight multi-item Likert scales containing 2 to 10 items each. The results are reported on a scale of 0 to 100, with 100 indicating a high health status (Bjarnadottir *et al.*, 2007).

3.5.2 Functional Reach Test

In the Functional Reach test (FRT), participants were positioned next to the wall. A piece of paper was mounted on the wall in line with the acromion process. The participant held a marker in their hand and raised arm to 90° and marked the initial upright position. The participant was then instructed to lean as far forwards as possible keeping their arm in line (straight) with the line, without moving or lifting their feet. The maximal extension was marked on the paper by the participant. Every participant performed one practice and then three trials. The distances of the three trials were averaged as the FRT score, with a greater distance indicating better balance ability (Jonsson *et al.*, 2003; Lin *et al.*, 2004).

3.5.3 Timed Up and Go

In the Timed Up and Go (TUG) test, the participants were asked to stand up from a standardised chair (40-50cm, with arms), walk to a marker placed 3m in front of the chair,

turn and walk back to the chair and sit down. Timing was measured in seconds using a standard stopwatch. Timing started on the command 'go' and ended when the participants were seated in the chair. Every participant performed one practice and three trials with a maximum of 1 minute rest between trials if required. The distances of the three trials were averaged as the TUG score. A shorter time indicates better mobility (Podsiadlo & Richardson, 1991).

3.5.4 Standing Balance

The Standing Balance (SB) test requires participants to maintain steady stance positions as a measure of the ability to sustain an upright posture. Participants were asked to hold the following stance positions: (1) feet together (side-by-side position); (2) semi-tandem (heel of one foot along side the big toe of the other foot); and (3) tandem (heel of one foot directly in front of the other foot) for 10 seconds. The test was scored based on which position (1, 2, or 3) the participant was able to maintain (Ostir *et al.*, 2002). This test was performed only once through.

3.5.5 Timed Walk

In the measured walk test, participants were instructed to walk as fast as they could safely along a standardised 10m distance. The walk was measured to a hundredth of a second by dual beam timing gates (Swift Performance Equipment, Speedlight, Lismore, Australia). Each trial was started in a standing position behind the starting gate. Time-splits were measured at 2m, 8m and 10m. Each participant performed one practice trial and then three trials. Participants had a maximum rest of 2 minutes between the trials. The average time of these three trials was recorded.

3.6 Statistical Analysis

A repeated measures Analysis of Variance (ANOVA) was performed to determine a difference over time for the health and functional measures. Data was analysed using SPSS software (version 15.0 for windows; SPSS Inc, Chicago, IL, USA). SF-36 scores and substitutions for missing values were calculated according to standardised procedures (Ware *et al.*, 1993, 2000). An intention-to-treat analysis approach was used in all analyses for the participants whom at least baseline data were collected, with the last data carried forward for analysis (Wood *et al.*, 2005). The level of significance was set at $p < 0.05$. A Bonferroni correction post-hoc analysis was performed on any analysis that had a significant time effect. All values are expressed as means and standard deviations.

4 Results

4.1 Subject characteristics

Fourteen out of the fifteen participants completed all 24 WBV training sessions and all four health and functional measures tests. The protocol was occasionally adjusted if a subject missed a session due to personal reasons. One participant received WBV four times a week due to personal scheduling. There were no MS-related exacerbations reported from the WBV during the 8 weeks. One participant developed hip pain at the FP3 so they remained at FP2.5 for the remaining sessions. Two participants required treatment during the training period for symptoms unrelated to the WBV training. One participant requiring oral steroids to manage a potential flare of symptoms attended all the vibration sessions; another participant received intravenous corticosteroids, but did not attend sessions whilst receiving treatment and resumed training once treatment was completed. One participant completed Pre, 4wk and 23 WBV sessions before developing a back problem which prevented completion of the study. Their health and functional measures from 4wk were carried forward to the 8wk and 10wk as part of the intention to treat analysis.

4.2 Health-related quality of life (SF-36)

A significant time effect between Pre and 4wk measures was seen in the physical functioning measure (Table 4.1). No other significant interaction were seen with the other seven measures (Role-physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health).

Table 4.1. Change in SF-36 scores at Pre, 4 wk, 8 wk and 10wk (mean ±SD). # Significant difference between pre and 4 wk measure ($p<0.05$)

SF-36 Scores	Pre	4 wk	8 wk	10wk
Physical Functioning	49.3 ± 24.6	58.6 ± 26.3 # (p=0.013)	53.6 ± 27.1	56.8 ± 26.2
Role-physical	61.7 ± 37.6	53.3 ± 46.2	60.7 ± 44.6	69.6 ± 38.2
Bodily Pain	68.6 ± 24.4	64.7 ± 23.1	67.4 ± 14.4	70.1 ± 19.3
General Health	60.5 ± 20.3	66.1 ± 18.2	63.7 ± 18.6	70.1 ± 18.1
Vitality	41.3 ± 17.4	46.3 ± 14.4	42.3 ± 23.2	43.3 ± 21.1
Social Functioning	77.5 ± 22.8	78.3 ± 20.8	78.6 ± 18.0	78.6 ± 22.7
Role-emotional	82.2 ± 33.0	75.6 ± 40.8	74.4 ± 40.6	81.0 ± 31.2
Mental Health	73.4 ± 13.6	81.0 ± 11.0	80.0 ± 11.9	78.9 ± 13.0

4.3 Functional Reach Test

There was no significant effect of time on FRT (p=0.199) (Figure 4-1).

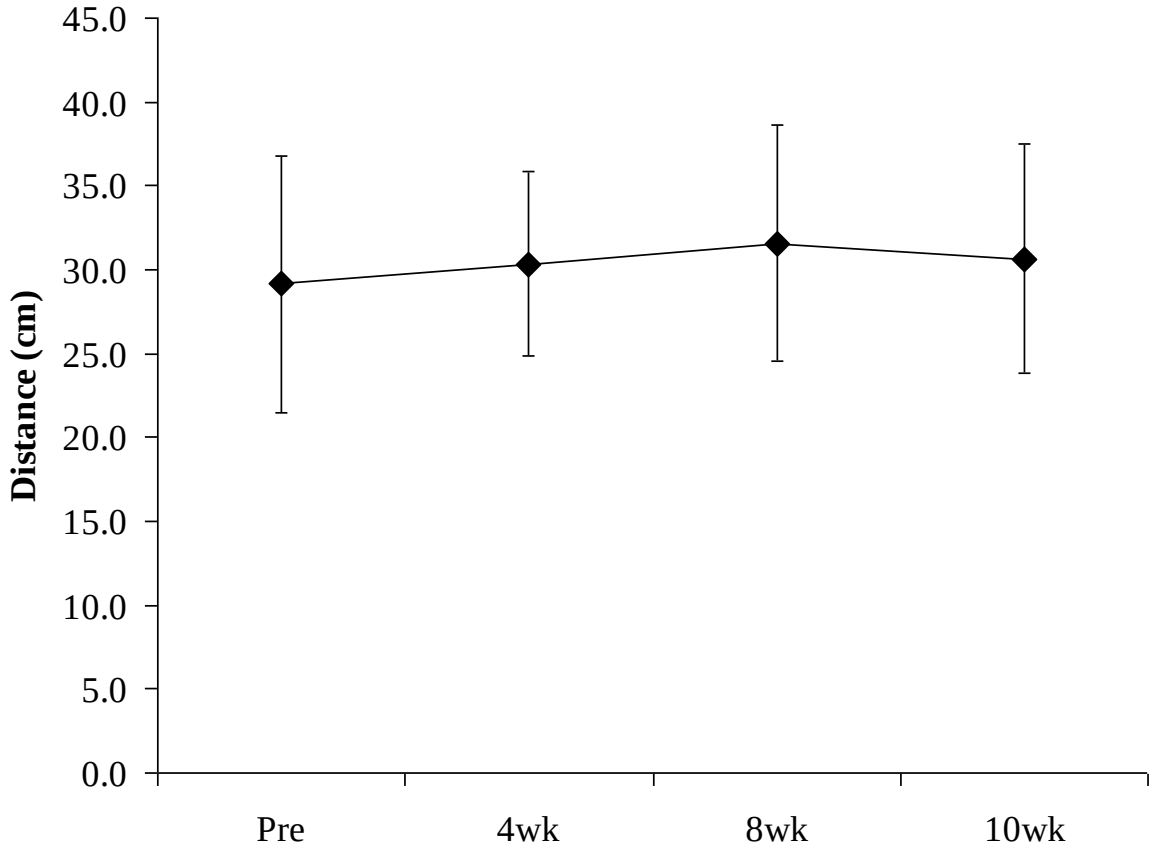

Figure 4-1. Mean (± SD) of Functional Reach Test distances pre-intervention, at four and eight weeks of WBV and two weeks after the WBV intervention (n = 15).

4.4 Timed Up and Go

There was a significant time effect on TUG (p=0.008). However, after Bonferroni correction post-hoc analysis could not identify where the interaction took place (Figure 4-2).

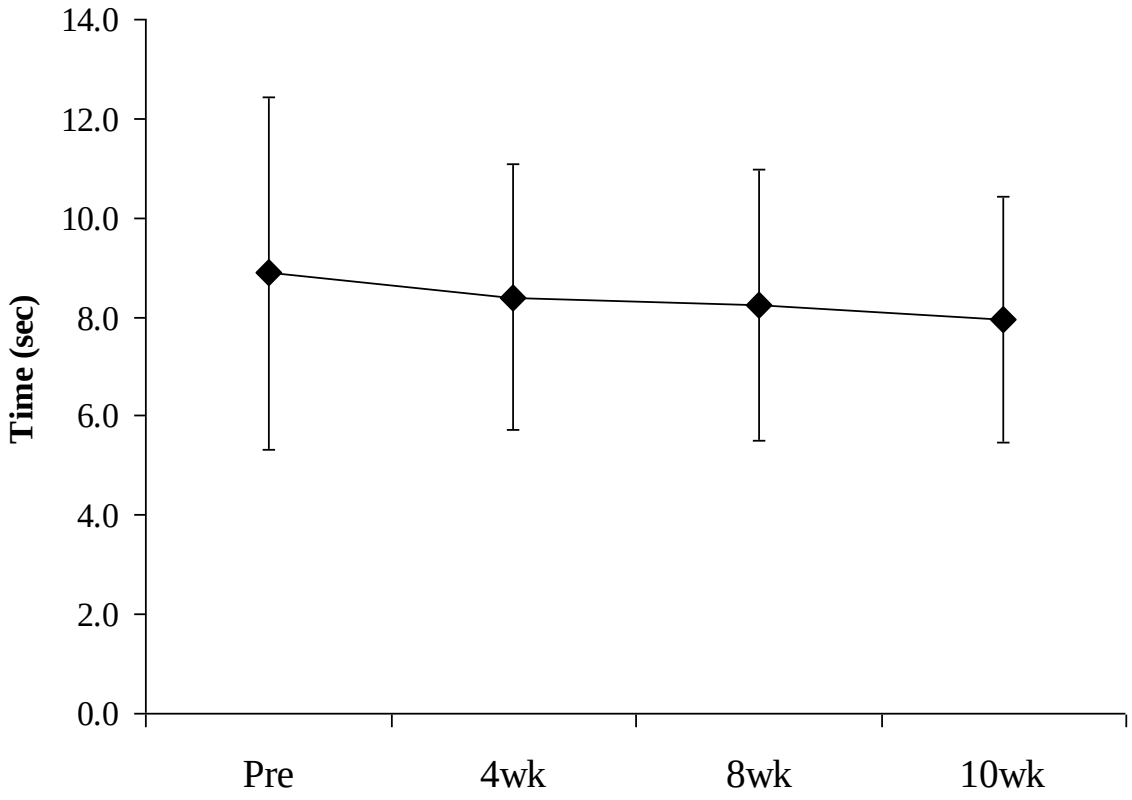

Figure 4-2. Mean (± SD) of Timed Up and Go for all participants at each of the functional tests (n=15).

4.5 Standing Balance test

There was a significant time effect in the standing balance test (p=0.004) displayed in Figure 4-3. After a Bonferroni correction, Post-Hoc analysis demonstrated a significant interaction such that the balance score at 4wk and 10wk were significantly higher (+12%) compared to Pre (p=0.03). However there were no other significant differences in balance scores between the different time points

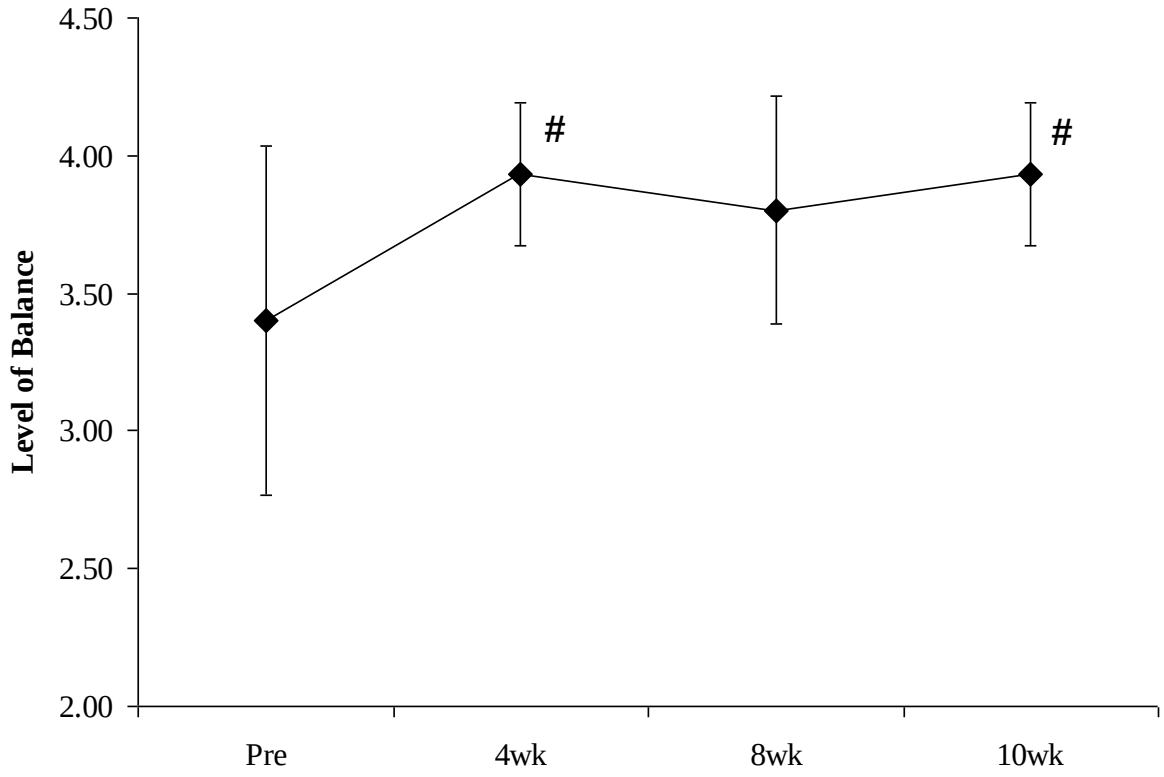

Figure 4-3. Mean (± SD) of Standing Balance distances pre-intervention, at four and eight weeks of WBV and two weeks after the WBV intervention. # Significantly higher measure compared to pre-intervention (p<0.05) (n=15).

4.6 Timed Walk

There was a significant time X distance interaction (Figure 4-4) between all three distance measures (2m, 8m and 10m). The time measures at 8wk and 10wk were significantly lower, compared to the Pre values ($p<0.05$). Thus, the timed walk was completed 10% and 13% faster at 8wk and 10wk respectively.

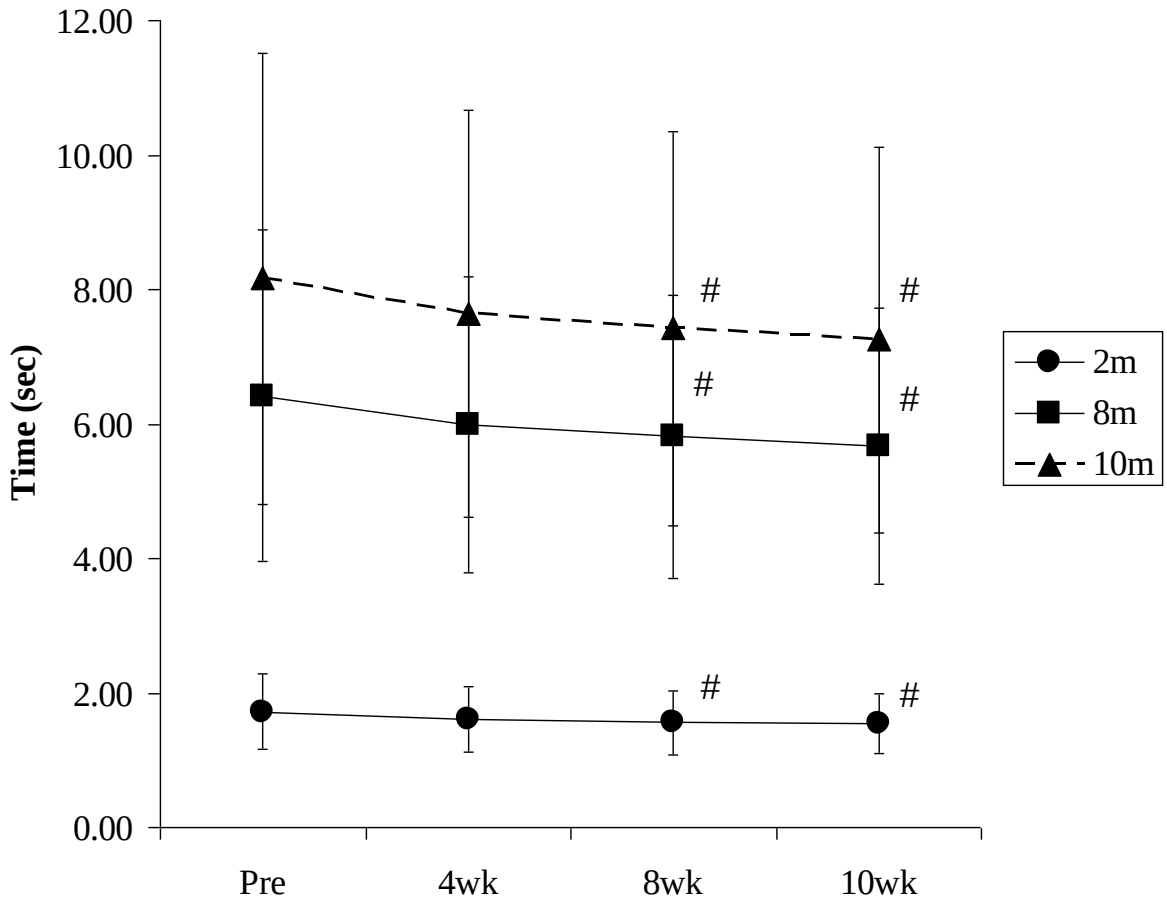

Figure 4-4. Timed walk measures for each of the distances (mean ± SD). # Significantly lower compared to pre-intervention ($p<0.05$) (n=15).

4.7 Rating of Perceived Exertion

There was a significant time effect on RPE (p=0.01). However, after Bonferroni correction post-hoc analysis could not identify where the interaction took place (**Figure 4-5**).

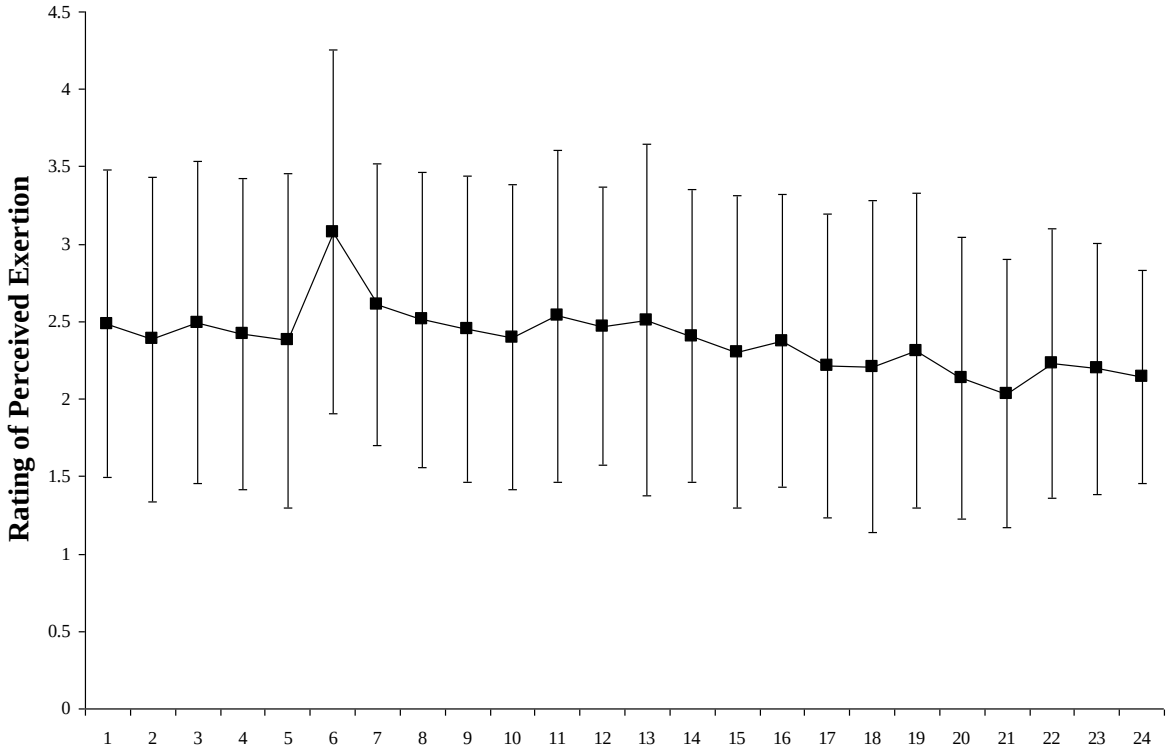

Figure 4-5. Mean (± SD) of Rating of Perceived Exertion for all participants at each of the WBV sessions (n=15).

5 Discussion

5.1 Timed walk

The most significant finding of this study was that WBV training significantly improved 10m walk time. These data thus show that MS patients may significantly improve their mobility within 8 weeks by exposure to WBV three times per week. Furthermore, the improvement was maintained following the completion of the WBV as shown by the results at the reassessment 2 weeks following. This suggests a residual effect of the intervention. These findings are consistent with previous exercise training studies with MS patients (Lord *et al.*, 1998; Wiles *et al.*, 2001; Freeman & Allison, 2004; Romberg *et al.*, 2004; Schulz *et al.*, 2004; White *et al.*, 2004; Kileff & Ashburn, 2005; Taylor *et al.*, 2006; van den Berg *et al.*, 2006; Cattaneo *et al.*, 2007) and WBV studies with compromised populations (Bautmans *et al.*, 2005; Bruyere *et al.*, 2005; Kawanabe *et al.*, 2007; Rees *et al.*, 2007).

Improvements shown by the 10m timed walk could be a reflection of improvement in lower limb strength in the participants. Improved lower limb strength coupled with improved walking ability has been associated with increased function and independence (Newman *et al.*, 2007). An eight week aerobic training programme has been shown to have positive effect on exercise tolerance, walking capacity, and improved health-related quality of life score in MS patients (Rampello *et al.*, 2007), whilst four weeks of treadmill training resulted in improved economy and increased voluntary walking speed (Newman *et al.*, 2007). The positive effect of WBV on gait seen in the present study could have the additional benefit of increasing the participation in physical activity which may then independently reduce their risk of disease associated with inactivity (Khurana *et al.*, 2009).

5.2 Standing Balance

A second important finding of this study is the significant improvement seen in the standing balance test. WBV training provided an early effect on standing balance (observable at the 4 week mark) and a residual effect 2 weeks after the completion of the intervention. The latter provides evidence of a residual effect, though familiarisation with testing procedures cannot be discounted.

The improvement in this functional measure parallels that seen in previous WBV training studies (Bautmans *et al.*, 2005; Bruyere *et al.*, 2005; van Nes *et al.*, 2006; Bogaerts *et al.*, 2007; Kawanabe *et al.*, 2007) as well as training studies with MS patients using other exercise modalities (Lord *et al.*, 1998; Frzovic *et al.*, 2000; Wiles *et al.*, 2001; Freeman & Allison, 2004; Schulz *et al.*, 2004; Cattaneo *et al.*, 2007).

Whilst our primary balance assessment was the tandem balance test, we also had an assessment for self-generated perturbations (FRT). Eleven out of the 15 participants showed improvement in the FRT at some point during the study although no significant training effect was seen. Differences in patients individual balance deficits need to be taken into account; a different type of assessment may be required for those patients that do not have an anterior-posterior balance problem.

Impaired balance not only limits mobility and participation in physical activity, but it is also associated with an increased the risk of falling. Repeated falls resulting in injury can further reduce functional capacity, especially if there is a loss of confidence in performing balance-requiring tasks. Any effect of simply standing on the platform without vibration needs to be taken into consideration; as previous studies focusing on balance exercises with MS patients

have shown to help balance and reduce risk of falls (Cattaneo *et al.*, 2007). Unfortunately, the present study was not designed with a control condition which would have been able to quantify the effect of passive standing on balance.

5.3 Timed Up and Go

A third finding of this study is the significant improvement seen in the timed up and go test. WBV training started to demonstrate improvements in TUG after 4 weeks of training with the results continuing at the 8 week assessment and after the completion of the WBV training at the reassessment 2 weeks following. The TUG improvement reiterates the positive effect on walking speed the MS participants demonstrated in the timed walk. Improvement in TUG not only illustrates the improvement in mobility but also has a balance component which mirrors the physical activities required during daily life. As MS patients have a high prevalence of gait and balance disorders, the TUG improvements illustrates the positive effect WBV training has on both of these aspects.

The time score of the TUG has been shown to be associated with risk of falls (Podsiadlo & Richardson, 1991). Five participants at pre-assessment were identified to have time above that which a healthy community-dwelling freely independent individual would be expected to have (≤10sec). Of these five, only the two participants that had the highest EDSS of this group failed to reduce their time to less than 10 seconds, though they did improve 12% (EDSS 4.0) and 32% (EDSS 5.5). This improvement shows that WBV training may improve MS patients' risk of falling in a high risk group.

5.4 Mechanisms

Overall, our results indicate that eight weeks of WBV training was able to improve mobility and balance in MS patients. WBV training is thought to initiate the stretch reflex which enhances central motor excitability, in particular large motor units (Rittweger *et al.*, 2003). It is thought that WBV recruits the under utilised large motor units and thus the type II fibres of MS patients and in doing so increases muscle strength. Consistent with these findings, are observations of improved strength and mobility following resistance training as an exercise intervention with MS patients (White *et al.*, 2004; Souza-Teixeira *et al.*, 2009).

It is generally agreed that improvements in strength initially stem from neural adaptations, which are then followed by hypertrophic changes in the muscle (Rutherford & Jones, 1986). Hypertrophy requires increased protein synthesis and satellite cell proliferation, and normally appears after 8-12 weeks of resistance training. However, Seynnes *et al* (2007) found that cross-sectional area (CSA) increased after only 20 days into a 35 day high-intensity resistance training program, which equated to 0.2% inc per day. Souza-Teixeira *et al* (2009) found that MS patients significantly improved their CSA by 3.6% following 8 weeks of resistance training contrasting White *et al* (2004) that showed no significant CSA increases after 8 weeks of resistance training. Souza-Teixeira *et al* (2009) suggest that the hypertrophic process in MS patients could be delayed and/or that the strength training stimulus needs to be improved. Unfortunately, the present study did not include measures of muscle cross-sectional area or specific motor unit training effects, so any effects of WBV on muscle size cannot be discounted, though the length of the intervention would possibly have been insufficient for this to occur. Further studies that include measures of strength i.e. isokinetic dynamometer or the use of MRI to directly assess muscle change and neural activation (EMG) would provide better understanding of the mechanisms WBV acts on the body.

5.5 Acceptability

This was the first study to assess the suitability of an 8 weeks WBV training programme in MS patients, and accordingly we showed WBV training to be an acceptable training modality for MS patients. Previous research had only exposed MS patients to an acute bout of WBV at 2.2-4Hz, with no ill effects (Schuhfried *et al.*, 2005). Similarly, we found our participants had no ill effects from incrementally increasing the vibration frequency to 25Hz.

Previous MS exercise training studies have found compliance to range from 65% (Mostert & Kesselring, 2002; Oken *et al.*, 2004) to 100% (White *et al.*, 2004; Gutierrez *et al.*, 2005; White *et al.*, 2006), while this study demonstrated high compliance of 99.2%. This high compliance may have been due to: flexibility in training time; short WBV sessions (20 minutes) or opportunity for social interaction. The participant/researcher interaction may have assisted participants achieving such high compliance. This interaction could be assessed in future studies with the use of a control group.

As the RPE in this study decreased as the WBV intensity increased, this suggests that the progressive increase in WBV training load required a lower physiologically demand (Noble & Robertson, 1996). Although MS patients report greater levels of baseline fatigue, Morrison *et al* (2008) showed that during sub-maximal and maximal exercise, MS patients had no significant difference in ratings of perceived exertion when compared to healthy controls, although Thickbroom *et al* (2006) demonstrated a greater perception of effort in order to obtain the required level of central motor drive. On the contrary, as WBV training gave similar functional changes to that of more physiological demanding exercise i.e. aerobic exercise or resistance training, MS patients may be more likely to be compliant with WBV training due to the less physiologically demand.

5.6 Limitations and Considerations

As this study was a pilot trial to assess the suitability of WBV for MS patients, there was no non-exercising control group employed in the study design. However, any control group in longitudinal studies with MS patients needs to match for not only age and sex but also for years of disease, type of MS, number of lesions, area of lesions, number of attacks/flares and current symptoms; all of these could effect the response to exercise. The use of a cross-over design would enable the patients to be their own control, as used by (Wiles *et al.*, 2001; van den Berg *et al.*, 2006; Rampello *et al.*, 2007), although the reconditioning the patient may experience in the first intervention may mask the outcomes of the second intervention. Ideally, a correctly powered randomised controlled trial, with a homogenous groups of patients based on the functional systems of the EDSS, would provide a way to determine how WBV can influence the different aspects of MS.

An increased intervention length would also provide a greater understanding of the long term effects of WBV on MS patients. As MS is a slow progressive disease the potential of WBV to maintain mobility and/or balance for an extended period of time could help patients to maintain their independence and therefore their quality of life. Additionally, there is a need for a longer follow-up period to assess how the long-term effects benefit the patients' well-being.

It must be acknowledged that the improvements seen in our results could potentially be due to familiarisation of (functional) testing procedures. However, to minimise any learning effect from these tests, a practice trial was preformed prior to each of the functional measures except the standing balance. As the tests were performed four times over a 10 week period, it could

be assumed that the learning effect would remain during this period as Wu *et al* (2003) found that the learning effect for a 6 minute walk test was maintained over a two month period.

5.7 Future Research

The majority of research investigating the effect of WBV training has been focused on healthy, young participants. It is often difficult to extrapolate the findings of these studies to different populations, especially populations with compromised health. In contrast, the present study relates to a condition that has a wide disease spectrum, the results of which can be applicable to a variety of MS patients.

As this was a pilot study, to be fully confident of the findings we would need to repeat the study with a group that mirrored the current study, but without vibration. Ideally, a concurrent study group that received a 'standard' exercise regime (resistance or aerobic training) would provide greater comparison. As stated previously, the difficultly with controlling for the different aspects of MS would be limiting.

6 Conclusion

Whole body vibration training was shown to improve functional measures of walking and balance in MS patients. The improvement in walking speed occurred after 8 weeks of WBV training with a residual effects maintained after 2 weeks of no training. The study showed that WBV was an acceptable form of exercise for MS patients. With the high completion rate and low attrition, this form of exercise was tolerated well by this group of participants. The findings from this study support the use of WBV as a training modality for MS patients. This supports the promotion of exercise to MS patients in order to maintain functional ability and quality of life.

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Appendix A

Massey University

Institute of Food, Nutrition and Human Health
Private Bag 11 222
Palmerston North
New Zealand
Telephone: 64 6 350 4336
Facsimile: 64 6 350 5657

PARTICIPANT CONSENT FORM

Effect of Whole Body Vibration on Multiple Sclerosis Patients

I have read the Participant Information Sheet for the above experiment and had the procedures and potential risks explained to me by the researchers. I am satisfied that my concerns and questions have been addressed fully.

I understand that I have the right to withdraw from the study at any time without giving reasons and this will not affect my current or future health care.

I understand that results from my physical examination may be passed on to my GP.

I have read the information sheet describing this project and I have no known medical or other condition which would exclude me from being a participant in this experiment.

I have been given one week to consider my involvement in the project.

1. **I agree to participate as an experimental subject.**
2. **I agree to my information being passed on to my GP.**
3. **I understand that I have the right to withdraw from the study at any time without reason and this will not affect my current or future health care.**

Signed: …….

Name: …….

Date: …….

Researcher Signature: .....

Appendix B

Massey University

Institute of Food, Nutrition and Human Health
Private Bag 11 222
Palmerston North
New Zealand
Telephone: 64 6 350 4336
Facsimile: 64 6 350 5657

Whole Body Vibration Training for Multiple Sclerosis Patients

Why?

Previous research with other patients with disabilities indicates whole body vibration (WBV) may enhance functional performance in Multiple Sclerosis (MS) patients. However, we need to investigate whether WBV is an appropriate form of exercise for the MS population.

Who?

We are looking for people with MS to volunteer for a medical screen to determine if you meet the inclusion criteria for the main study. If you are not pregnant, can walk 20m and have no recent bone fractures, bone tumors or herniated discs, we would like to hear from you.

How?

If you would like to participate, you will be assessed by a qualified medical practitioner to determine that you have no compromising conditions that could interfere with the study. If you meet all the inclusion criteria, you will be asked if you would like to volunteer for the main study. Once you volunteer for the study, you will be asked to attend vibration sessions 3 times a week for 8 weeks. You will also be asked to attend four sessions at the S.T.A.R. Centre at Palmerston North Hospital to assess your functional performance prior to the training, then at 4 weeks, 8 weeks and 10 weeks.

Contact

If you are interested please contact:

Rachael Mason 021 120 5254 or (06) 350 4336 EXT 4848 or R.R.Mason@massey.ac.nz or

Kristin Leslie 0276558573 or (06) 357 3188 or mmss@inspire.net.nz

WBV and MS Flyer 2008 v1

Rachael Mason 021 120 5254 R.R.Mason@massey.ac.nz	Rachael Mason 021 120 5254 R.R.Mason@massey.ac.nz	Rachael Mason 021 120 5254 R.R.Mason@massey.ac.nz	Rachael Mason 021 120 5254 R.R.Mason@massey.ac.nz	Rachael Mason 021 120 5254 R.R.Mason@massey.ac.nz	Rachael Mason 021 120 5254 R.R.Mason@massey.ac.nz	Rachael Mason 021 120 5254 R.R.Mason@massey.ac.nz	Rachael Mason 021 120 5254 R.R.Mason@massey.ac.nz

Appendix C

Massey University

Institute of Food, Nutrition and Human Health
Private Bag 11 222
Palmerston North
New Zealand
Telephone: 64 6 350 4336
Facsimile: 64 6 350 5657

Participant Information Sheet

Effects of Whole Body Vibration on Multiple Sclerosis Patients

Researchers:
Miss Rachael Mason
Ph: 0211205254
Email: R.R.Mason@massey.ac.nz

Dr. Steve Stannard
Ph: (06) 350 4336 ext 7465
Email: S.Stannard@massey.ac.nz

Mr Darryl Cochrane
Ph: (06) 350 4336 ext 2775
Email: D.Cochrane@massey.ac.nz

Dr. Greg Denny
Ph: (06) 350 8320
Email: Gregory.Denny@midcentraldhb.govt.nz

Dr. Elwyn Firth
Ph: (06) 350 5799 Ext 5061
Email: E.C.Firth@massey.ac.nz

You are invited to participate in a study on the effect Whole Body Vibrations on Multiple Sclerosis patients. Participation is entirely voluntary and you will have the right to withdraw without explanation at any time.

We are recruiting twelve participants with diagnosed Multiple Sclerosis with an EDSS between 2 and 5, who will participate in eight weeks of whole body vibration training. This will involve attending Carnation House (Manawatu MS Society Building) in Palmerston North for ten minutes of exercise, three times a week.

We hope to find that whole body vibration has a positive effect on MS patients. However, it is possible that your participation will reveal no beneficial effects from this type of training. Nevertheless, the knowledge we obtain from undertaking this study will be of benefit to patients undertaking exercise programs following diagnosis of MS.

Eligibility
If any of the following apply:

1. *You are currently experiencing a relapse of your condition.*
2. *You have a known heart or cardiovascular condition or if a member of your family died below the age of fifty (50) as a result of a heart condition.*
3. *You have any new bone fractures.*
4. *Diabetes with polyneuropathy.*
5. *You have any current or previous injury to your legs*
6. *You currently have a deep vein thrombosis.*
7. *In the last six months you have suffered from any painful injury or condition that lasted more than one week.*
8. *You have had an injury or medical condition that you think may affect your ability to sense pain or discomfort.*
9. *You have ever had persistent or regular lower back pain.*
10. *You have cultural or religious sensitivities about human body measurements.*
11. *If you currently have or have ever had renal and/or liver disease.*
12. *You are pregnant or breastfeeding.*
13. *You have any other reason to consider you will not be suitable for this investigation.*

…you should NOT participate in this project.

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Institute of Food, Nutrition and Human Health
Private Bag 11 222
Palmerston North
New Zealand
Telephone: 64 6 350 4336
Facsimile: 64 6 350 5657

Why Whole Body Vibration?

Whole Body Vibration is a novel exercise intervention performed on specialised vibration machines. It was originally developed in the former Eastern Block countries to improve power and strength development in athletes. Repeated exposure to WBV training improves measures of strength and power in the elderly, and significant benefits to balance and gait have been seen within as little six weeks in elderly physically inactive individuals. It has been shown to be an effective intervention for improving gait and coordination with patients suffering from Parkinson's disease. However, no studies have looked at vibration training on MS patients even though it is commercially available and in many gyms and leisure centre.

Test procedure

You will be asked to attend an appointment with Dr Greg Denny at the S.T.A.R Centre for a physical examination to assess that you have no compromising conditions that could interfere with participation in the study. If by chance any health condition of concern is identified in the examination your GP may be informed. If you meet the inclusion criteria, you will be asked to attend a session to assess your functional performance.

You will be asked to attend a familiarisation session at Carnation House a few days prior to beginning the training to become familiar with the whole body vibration machine.

You will then begin the vibration sessions. This consists of 5 minutes of vibration interspersed with 5 minutes of rest. You will need to attend these sessions three times a week for 8 weeks. At four weeks we will asked to repeat the functional performance tests that you did at the beginning. You will be asked to repeat these tests at the end of the eight weeks and ten weeks.

Compensation

Compensation will be given for travel costs to Carnation House of $15 per trip reimbursed at the end of each session.

Possible risks and discomforts

The procedures involved in this study are of low risk. Nevertheless, as with any physical activity, there are small risks and some discomfort may be experienced:

Whole Body Vibration

The vibration involves exercising on a specially designed machine that vibrates the whole body and causes muscle contractions. This is not harmful, however in some instances you may experience redness and muscle itchiness in your legs, up to 2-3 minutes after the vibration exercise, this is a normal side effect that is harmless and is due to the temporary changes in leg blood flow.

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Institute of Food, Nutrition and Human Health
Private Bag 11 222
Palmerston North
New Zealand
Telephone: 64 6 350 4336
Facsimile: 64 6 350 5657

Participants Rights

1. You can ask questions on any aspect of the project at any time, and we will do our best to answer them to your satisfaction.
2. As a participant in the study you will provide information on the understanding that your name will not be used unless you give permission to the researcher.
3. You have the right to view your own data at any stage and have it explained to you.
4. You will also be given access to a summary of the project findings when it is concluded.
5. You can withdraw from the project at any time, without giving any reason and this will not affect your current or future health care.

If you have any questions or concerns about your rights as a participant in this research study you can contact an independent health and disability advocate. This is a free service provided under the Health and Disability Commissioner Act. Telephone: (NZ wide) 0800 555 050; Free Fax (NZ wide): 0800 2787 7678 (0800 2 SUPPORT); Email (NZ wide): advocacy@hdc.org.nz. If there is a specific Māori issue/concern please contact Linda Grennell at 0800 37 77 66.

Compensation for injury

In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by ACC under the Injury Prevention, Rehabilitation and Compensation Act. ACC cover is not automatic and your case will need to be assessed by ACC according to the provisions of the 2002 Injury Prevention Rehabilitation and Compensation Act. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors such as whether you are an earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigators.

If you have any questions about ACC, contact your nearest ACC office or the investigator.

Ethical approval

This study has received ethical approval by the Central Ethics Committee. Study number CEN/08/07/038.

Appendix D

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Institute of Food, Nutrition and Human Health
Private Bag 11 222
Palmerston North
New Zealand
Telephone: 64 6 350 4336
Facsimile: 64 6 350 5657

Name:

Date:

Pre-Screening Checklist

Do you or have you ever had:			
	A heart condition?	Yes	No
	High blood pressure?	Yes	No
	A stroke?	Yes	No
	High cholesterol?	Yes	No
Has a member of your family died below the age of fifty (50) as a result of a heart condition?		Yes	No
If yes, who?			
Do you or have you previously had:			
	Deep vein thrombosis?	Yes	No
	Injury to your legs?	Yes	No
	Diabetes with polyneuropathy?	Yes	No
Have you currently or previously had:			
	A bone tumour?	Yes	No
	Herniated disc?	Yes	No
	Dizziness or vertigo?	Yes	No
Are you pregnant or breastfeeding?		Yes	No
How would you describe your mobility			
☐ Able to run	☐ Limited walking distance but **less than** 500m without rest		
☐ **Unlimited** walking distance without rest, but unable to run	☐ Unilateral supported, can walk **less than** 100m without resting		
☐ Limited walking distance but **greater than** or equal to 500m without rest	☐ Bilateral supported, can walk **less than** 100m without resting		
Do you currently take β-interferon?		Yes	No
Do you know your EDSS score?		Yes	No
If yes, what is it?			

Appendix E

Code:_____

Functional Test Form

Date		Temp (°C)		Test Number	
Time		BP (mmHg)			

Timed Up and Go	Test Number			
	1	2	3	Mean
Time (sec)				

Functional Reach Test	Test Number			
	1	2	3	Mean
Distance (cm)				

Tandem stance	Side by side	Semi-tandem	Tandem (3-9sec)	Tandem (10sec)
Score	1	2	3	4

10m walk	Test Number			
Distance	1	2	3	Mean
2m				
8m				
10m				
Comments				

Appendix F

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Institute of Food, Nutrition and Human Health
Private Bag 11 222
Palmerston North
New Zealand
Telephone: 64 6 350 4336
Facsimile: 64 6 350 5657

Effects of Whole Body Vibration on Multiple Sclerosis Patients

Your Health and Well Being

Instructions for completing the questionnaire: Please answer every question. Some questions may look like others, but each one is different. Please take the time to read and answer each question carefully by filling in the bubble that best represents your response.

Name:_____

Date: _____

1. In general, would you say your health is:
   - ❑ Excellent
   - ❑ Very good
   - ❑ Good
   - ❑ Fair
   - ❑ Poor

2. Compared to one year ago, how would you rate your health in general now?
   - ❑ Much better now than a year ago
   - ❑ Somewhat better now than a year ago
   - ❑ About the same as one year ago
   - ❑ Somewhat worse now than one year ago
   - ❑ Much worse now than one year ago

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3. The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports	☐	☐	☐
Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf?	☐	☐	☐
Lifting or carrying groceries	☐	☐	☐
Climbing several flights of stairs	☐	☐	☐
Climbing one flight of stairs	☐	☐	☐
Bending, kneeling or stooping	☐	☐	☐
Walking more than one kilometre	☐	☐	☐
Walking several hundred metres	☐	☐	☐
Walking one block	☐	☐	☐
Bathing or dressing yourself	☐	☐	☐

4. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

a. Cut down the amount of time you spent on work or other activities?
☐ Yes ☐ No

b. Accomplished less than you would like?
☐ Yes ☐ No

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- ❑ Not at all
- ❑ Slightly
- ❑ Moderately
- ❑ Quite a bit
- ❑ Extremely

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks.

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
Did you feel full of life?	☐	☐	☐	☐	☐
Have you been a very nervous person?	☐	☐	☐	☐	☐
Have you felt so down in the dumps nothing could cheer you up?	☐	☐	☐	☐	☐
Have you felt calm and peaceful?	☐	☐	☐	☐	☐
Did you have a lot of energy?	☐	☐	☐	☐	☐
Have you felt downhearted and depressed?	☐	☐	☐	☐	☐
Did you feel worn out?	☐	☐	☐	☐	☐
Have you been happy?	☐	☐	☐	☐	☐
Did you feel tired?	☐	☐	☐	☐	☐

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10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?

- ❑ All of the time
- ❑ Most of the time
- ❑ Some of the time
- ❑ A little of the time
- ❑ None of the time

11. How TRUE or FALSE is each of the following statements for you?

a. I seem to get sick a little easier than other people
- ❑ Definitely true
- ❑ Mostly true
- ❑ Don't know
- ❑ Mostly false
- ❑ Definitely false

b. I am as healthy as anybody I know
- ❑ Definitely true
- ❑ Mostly true
- ❑ Don't know
- ❑ Mostly false
- ❑ Definitely false

c. I expect my health to get worse
- ❑ Definitely true
- ❑ Mostly true
- ❑ Don't know
- ❑ Mostly false
- ❑ Definitely false

d. My health is excellent
- ❑ Definitely true
- ❑ Mostly true
- ❑ Don't know
- ❑ Mostly false
- ❑ Definitely false

Thank you for your time in completing these questions

Appendix G

Table 7.1. Clinical Data of Participants

ID	Age (y)	Gender	Height (cm)	Weight (kg)	Clinical course	EDSS Score	Disease duration since diagnosis (yrs)
1	59	F	173.9	66.4	RRMS	3.5	15
2	49	M	175.6	93.0	RRMS	3.5	17
3	47	F	161.3	50.0	RRMS/SPMS	3.5	9
4	51	F	164.0	113.0	RRMS	2.5	<1
5	60	F	166.0	59.0	RRMS/SPMS	4.5	18
6	50	F	166.8	54.0	RRMS	3.0	14
7	56	M	170.6	65.0	RRMS	4.0	9
8	53	M	177.2	102.0	RRMS	3.0	13
9	44	M	177.6	81.2	RRMS	3.0	14
10	55	F	162.0	70.2	PPMS/Secondary Relapsing	4.0	12
11	42	F	168.0	57.0	RRMS	5.5	12
12	50	F	176.6	88.8	RRMS	3.0	3
13	50	F	164.0	52.6	RRMS	3.0	8
14	52	F	155.0	56.4	RRMS	3.0	8
15	36	F	161.1	54.8	RRMS	3.0	1

Appendix H

Table 7.2. Raw data of Functional Reach Test

ID	Pre	4wk	8wk	10wk
1	44.7	38.6	49.4	37.6
2	27.6	34.7	31.8	39.4
3	29.6	28.9	30.7	29.8
4	37.3	36.1	36.5	41.3
5	29.2	31.0	32.7	28.9
6	15.6	26.2	30.0	23.3
7	23.0	27.0	23.5	20.4
8	28.3	30.3	32.1	31.5
9	27.2	25.8	30.8	33.1
10	26.5	30.6	27.4	26.5
11	19.7	19.8	19.8	19.8
12	42.7	41.3	41.0	39.6
13	28.9	29.1	26.6	28.4
14	28.2	26.5	28.2	33.6
15	28.8	29.6	33.3	26.9

Appendix I

Table 7.3. Raw data of Timed Up and Go

ID	Pre	4wk	8wk	10wk
1	6.7	5.4	5.6	6.0
2	10.0	10.4	9.6	9.5
3	7.0	6.7	7.4	6.8
4	6.0	6.2	5.8	5.9
5	10.0	9.7	8.7	8.7
6	6.0	6.9	7.0	6.7
7	8.7	7.8	8.2	8.1
8	8.0	7.8	6.8	6.0
9	7.3	7.6	7.0	7.1
10	12.2	12.3	12.5	10.9
11	19.7	14.9	14.9	14.9
12	5.7	5.3	5.0	5.4
13	11.1	10.8	11.1	9.3
14	8.0	7.2	7.0	7.0
15	7.1	7.2	7.0	7.0

Appendix J

Table 7.4. Raw data of Standing Balance

ID	Pre	4wk	8wk	10wk
1	4	4	4	4
2	3	4	4	4
3	3	4	4	3
4	4	4	3	4
5	3	3	4	4
6	4	4	3	4
7	2	4	4	4
8	3	4	4	4
9	3	4	4	4
10	3	4	3	4
11	3	4	4	4
12	4	4	4	4
13	4	4	4	4
14	4	4	4	4
15	4	4	4	4

Appendix K

of Timed Walk

	2m (sec)				8m (sec)				10m (sec)			
ID	Pre	4wk	8wk	10wk	Pre	4wk	8wk	10wk	Pre	4wk	8wk	10wk
1	1.44	1.12	1.08	1.17	4.90	3.75	3.75	3.90	6.09	4.68	4.69	4.80
2	2.17	1.85	1.71	1.81	7.95	7.08	6.54	6.65	10.04	8.96	8.42	8.46
3	1.51	1.39	1.53	1.40	5.36	4.84	5.31	4.78	6.65	6.14	6.59	5.98
4	1.24	1.19	1.17	1.20	4.65	4.26	4.20	4.24	5.83	5.41	5.33	5.31
5	2.12	1.94	1.95	1.93	7.49	7.18	6.87	6.85	9.29	8.99	8.60	8.59
6	1.36	1.24	1.23	1.23	4.86	4.64	4.68	4.51	6.07	5.87	5.91	5.68
7	1.57	1.53	1.51	1.51	5.82	5.58	5.42	5.31	7.37	7.03	6.91	6.78
8	1.45	1.42	1.30	1.35	5.53	5.20	4.68	4.78	7.11	6.61	5.91	6.01
9	1.46	1.54	1.45	1.35	5.43	5.69	5.32	5.29	6.79	7.10	6.63	6.73
10	2.10	2.37	2.25	1.99	8.12	8.92	8.26	7.26	10.31	11.40	10.41	9.22
11	3.29	2.79	2.79	2.79	13.92	11.96	11.96	11.96	18.58	16.28	16.28	16.28
12	1.13	1.11	0.99	1.08	4.10	3.61	3.56	3.47	5.18	4.58	4.48	4.35
13	2.22	1.92	1.77	1.71	7.98	7.00	6.59	6.28	10.21	8.87	8.38	8.03
14	1.36	1.33	1.30	1.32	5.10	4.88	4.96	5.02	6.41	6.12	6.25	6.27
15	1.39	1.38	1.36	1.37	5.10	5.22	5.09	4.95	6.45	6.58	6.49	6.26

Appendix L

Table 7.6. Raw data of Health Related Quality of Life SF-36

	Physical Functioning				Role-physical				Bodily Pain			
ID	Pre	4wk	8wk	10wk	Pre	4wk	8wk	10wk	Pre	4wk	8wk	10wk
1	85	95	95	95	100	100	100	100	82	72	100	100
2	50	40	35	40	25	25	75	75	62	41	72	62
3	20	20	15	20	0	0	25	50	82	72	72	100
4	65	65	65	65	75	0	100	100	82	51	62	62
5	40	50	40	45	100	0	0	25	100	62	62	72
6	75	89	75	80	100	100	100	100	100	72	72	62
7	60	65	65	60	50	0	100	100	82	51	72	51
8	30	40	45	45	0	25	0	75	62	100	72	72
9	40	70	40	55	75	100	100	100	40	52	72	72
10	10	15	10	10	25	25	25	0	22	22	41	32
11	40	50	50	50	75	100	100	100	72	100	100	100
12	75	95	85	90	100	100	100	100	61	72	72	72
13	35	45	45	50	25	25	25	50	41	41	41	62
14	90	95	95	95	100	100	100	100	100	100	72	100
15	25	45	40	45	75	100	0	0	41	62	62	62

	General Health				Vitality				Social Functioning			
ID	Pre	4wk	8wk	10wk	Pre	4wk	8wk	10wk	Pre	4wk	8wk	10wk
1	87	92	92	97	50	50	70	55	100	100	100	100
2	37	25	35	40	55	45	50	60	88	88	63	88
3	62	57	52	67	25	35	20	30	75	63	50	75
4	57	62	72	67	60	60	60	60	75	75	75	75
5	77	50	47	77	45	15	50	50	88	88	75	75
6	57	62	42	52	40	40	45	40	88	88	75	63
7	37	62	72	67	25	35	60	30	50	50	100	50
8	52	67	67	72	45	45	60	45	75	88	88	88
9	15	67	67	57	30	45	45	55	75	63	75	100
10	52	77	47	67	0	30	15	30	13	38	50	25
11	72	87	87	87	60	65	65	65	88	100	100	100
12	62	50	50	50	60	45	35	50	100	100	100	100
13	87	90	95	100	30	55	40	45	63	50	63	63
14	82	87	82	97	60	70	65	70	100	88	100	100
15	72	57	72	72	35	60	40	50	88	100	88	100

	Role-emotional				Mental Health			
ID	Pre	4wk	8wk	10wk	Pre	4wk	8wk	10wk
1	100	100	100	100	55	55	55	55
2	33	100	100	67	85	75	90	75
3	100	100	100	100	80	85	85	90
4	100	0	67	0	75	80	70	70
5	100	0	0	33	60	90	65	75
6	100	100	100	100	85	85	80	85
7	33	0	100	67	45	70	80	60
8	0	67	8	67	75	95	95	95
9	67	100	100	100	56	80	75	75
10	100	100	67	100	70	65	75	70
11	100	100	100	100	90	95	95	95
12	100	100	100	100	80	80	80	75
13	100	100	100	100	80	85	80	95
14	100	67	100	100	75	85	100	90
15	100	100	0	100	90	90	90	95