AN ABSTRACT OF THE THESIS OF

Ruben J. Guzman for the degree of Master of Science in Movement Studies in Disability presented June 5, 2012.

Title: Effect of Whole-Body Vibration on Painful Diabetic Peripheral Neuropathy

Abstract approved:

________________________________________________________________________

Gianni F. Maddalozzo

Introduction. Painful diabetic peripheral neuropathy (DPN) is a common complication of diabetes that interferes with daily living and causes severe pain. Pharmacotherapy is the accepted treatment strategy, however, this strategy is associated with high cost, minimal reductions in pain, and adverse side effects. Thus, a critical need exists to develop alternative treatment strategies. Purpose. To determine if a 12-week whole-body vibration (WBV) intervention reduces pain in adults with DPN. Methods. Twenty-one adults with physician confirmed painful DPN volunteered to take part in a 26-week time series design study. Pain was assessed with the Brief Pain Inventory Short Form [BPI-sf] and a 0-10 numeric rating scale [NRS]. The BPI-sf contains two indices that respectively measure how pain interferes with daily living and severity. The intervention began after a 12-week control period. At week 13, participants were asked to stand on a WBV machine 3 d/week for 4, 3-min bouts at 30-50 Hz with 1-min rest intervals between bouts. Pain levels were reported using the NRS before and after each bout. Results. Comparing post- to pre-intervention, BPI-sf pain interference scores decreased from 5.61±1.40 to 2.39±1.82 (p≤0.001). BPI-sf pain severity scores decreased from 5.1±0.64 to 3.1±1.87 (p≤0.01). Analyses of the NRS scores indicate that pain decreased each week following WBV and that between weeks, pain continued to decrease. Conclusion. These findings demonstrate that whole-body vibration was effective at reducing pain in a sample of adults with painful DPN.
Effect of Whole-Body Vibration on Painful Diabetic Peripheral Neuropathy

by

Ruben J. Guzman

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Presented on June 5, 2012.

APPROVED:

________________________________________________________________________
Major Professor, representing Movement Studies in Disability

________________________________________________________________________
Co-Director of the School of Biological and Population Health Sciences

________________________________________________________________________
Dean of the Graduate School

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Ruben J. Guzman, Author
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Effect of Whole-Body Vibration on Painful Diabetic Peripheral Neuropathy

Chapter 1: Introduction

Diabetic peripheral neuropathy (DPN), characterized mainly by sensory nerve damage and dysfunction, is one of the most common long-term complications of diabetes, affecting 60-70% of all diabetics (National Institutes of Health [NIH] 2009). It is also the most common type of neuropathy in the Western world (Marchettini, Lacerenza, Mauri, & Marangoni, 2006) with the greatest prevalence among patients who are aged 65-74 years and have had diabetes for at least 25 years (Argoff et al., 2006). Despite the multiple pharmacological treatment methods available, efficacy, safety, and tolerability issues remain a major concern (Dworkin et al., 2003). Non-steroidal anti-inflammatory drugs (NSAID) are the most commonly prescribed class of analgesic, but have demonstrated limited efficacy for this population. To date, pharmacological agents have been accepted as the mainstay for the treatment of painful DPN. However, this approach includes high cost, minimal reductions in pain, side effects, and limited efficacy (Woolf & Mannion, 1999). There is, therefore, a critical need to develop safe and cost-effective treatment strategies that reduce pain.

Whole-body vibration involves the application of vibratory stimuli throughout the body by standing on a vibrating platform (Merriman & Jackson, 2009). The vibration is created by a mechanical, linear motion, which transfers energy upwardly through the body stimulating muscles to contract (Rittweger, 2010). Whole-body vibration has recently been used to reduce back pain and fibromyalgia pain in women (Alentorn-Geli, Padilla, Moras, Lazaro Haro, & Fernandez-Sola, 2008; Iwamoto, Takeda, Sato, & Uzawa, 2005). This training modality has also been identified for its potential clinical application for aging adults in improving physical function (Cardinale & Wakeling, 2005; Merriman & Jackson, 2009; Rittweger, 2010).

Our long-term research goal is to develop effective and innovative treatment strategies that improve quality of life and are cost effective. Moreover, we wish to improve overall population health by targeting the treatment strategy to the specific health needs of adults with painful DPN in
order to reduce many of the long-term neuropathy-related adverse outcomes associated with prescription medications. As part of our long-term goal, we have recently focused attention on whole-body vibration as an alternative, or adjuvant, strategy to reduce pain. This novel approach, with its demonstrated feasibility and safety, is a suitable alternative treatment strategy because it is simple, cost effective, easy to perform, and has few to no side effects. The objective was to evaluate the potential effects of whole-body vibration to reduce pain. The central hypothesis, was that exposure to whole-body vibration would result in reduced pain in individuals with DPN. The rationale was that by establishing the feasibility of whole-body vibration as a safe and well-accepted intervention for treating painful DPN, we would provide a cost-effective method of ameliorating the debilitating impact associated with this disease without the detrimental side effects of traditional pharmacological methods. We examined the following Specific Aims:

**Specific Aim #1:** To determine the effect of a 12-week whole-body vibration intervention on pain in a sample of adults with painful diabetic peripheral neuropathy. The working hypothesis was that pain would decrease.

**Specific Aim #2:** To determine the acute effect of a 12-week whole-body vibration intervention (i.e. during the intervention) on pain in a sample of adults with painful diabetic peripheral neuropathy. The second working hypothesis was that the acute pain would decrease following whole-body vibration exposure.

**Significance**

Recent estimates from the National Health and Nutrition Examination Survey (NHANES) indicate that approximately 23.6 million Americans currently have diabetes (NIH, 2009). Diabetic neuropathy, characterized mainly by nerve damage and dysfunction, is the most common long-term complication of diabetes, affecting 60-70% of all diabetics (NIH, 2009). Diabetic neuropathy is also the most common type of neuropathy in the Western world (Marchettini et al., 2006) with the greatest prevalence among patients who are aged 65-74 years and have had diabetes for at least 25 years (Argoff, Backonja, et al., 2006).
The yearly cost of pain medication per patient is over $1,000 and for those that take 2 or more medications, as most do, yearly costs can exceed $1600 (Able, 2005). Healthcare costs are more than triple for patients with painful DPN when compared to healthy, age-matched controls (Berger, Dukes, Oster 2004). Unfortunately, the specific mechanisms of neuropathic pain are still unclear making effective treatment strategies very difficult.

This project is significant because it serves as an important first step in developing innovative treatment strategies that improve quality of life, cost effectiveness and patient experience by safely reducing pain without the use of medication, which may also potentially mitigate disproportionate healthcare costs for patients, their families, and society. Reducing pain may also allow individuals with painful DPN to lead more physically active lifestyles, thereby conferring to them the potential health benefits of an active lifestyle.

Assumptions
• All participant responses on the pain surveys were truthful and not influenced by the researchers.
• All participants maintained their usual daily routines including medication schedules and daily activities.

Delimitations
• All participants were recruited from the surrounding community and were aged 45 – 75 years.
• Whole body vibration frequency was set at 30 – 50 Hz (2.3-2.8g) for 4, 3-minute bouts with 1-minute rest periods.

Limitations
• All participants were recruited from the surrounding community.
• The sample size is small size.
Definitions

• Pain is operationalized as two separate constructs for this study: 1) Pain Interference and 2) Pain Severity.

• Pain Interference: The degree to which pain interferes in: 1) general activity; 2) walking; 3) work; 4) mood; 5) enjoyment of life; 6) relations with others; and 7) sleep.

• Pain Severity: An average intensity in the sensory aspect of pain considering the normal fluctuation from least to worst that could be experienced.
Chapter 2: Manuscript

Effect of Whole-Body Vibration on Painful Diabetic Peripheral Neuropathy

Ruben J. Guzman
Abstract

Introduction. Painful diabetic peripheral neuropathy (DPN) is a common complication of diabetes that interferes with daily living and causes severe pain. Pharmacotherapy is the accepted treatment strategy, however, this strategy is associated with high cost, minimal reductions in pain, and adverse side effects. Thus, a critical need exists to develop alternative treatment strategies. Purpose. To determine if a 12-week whole-body vibration (WBV) intervention reduces pain in adults with DPN. Methods. Twenty-one adults with physician confirmed painful DPN volunteered to take part in a 26-week time series design study. Pain was assessed with the Brief Pain Inventory Short Form [BPI-sf] and a 0-10 numeric rating scale [NRS]. The BPI-sf contains two indices that respectively measure how pain interferes with daily living and severity. The intervention began after a 12-week control period. At week 13, participants were asked to stand on a WBV machine 3 d/week for 4, 3-min bouts at 30-50 Hz with 1-minute rest intervals between bouts of WBV. Pain levels were reported using the NRS before and after each bout. Results. Comparing post- to pre-intervention, BPI-sf pain interference scores decreased from 5.61±1.40 to 2.39±1.82 (p≤0.001). BPI-sf pain severity scores decreased from 5.1±0.64 to 3.1±1.87 (p≤0.01). Analyses of the NRS scores indicate that pain decreased each week following WBV and that between weeks, pain continued to decrease. Conclusion. These findings demonstrate that whole-body vibration was effective at reducing pain in a sample of adults with painful DPN.
Introduction

Painful diabetic peripheral neuropathy (DPN) is a common and debilitating complication of diabetes that has been consistently associated with impaired daily living and severe pain (Gore, 2005). According to the National Institutes of Health, it affects 60-70% of all individuals with diabetes (NIH, 2009). Pain is typically described as burning, lancinating, cramping, aching and vice-like. Impaired physical and mental functioning and greater rates of self-reported disability have also been consistently associated with painful neuropathies (Boulton, 1998).

To date, pharmacological agents have been accepted as the mainstay for treatment of DPN associated pain. However, recent research suggests that approximately 25% of all patients with painful DPN receive no treatment and that those that do may not be getting the most effective medication (Berger, Dukes & Oster 2004). Using pharmacological agents, most patients achieve no more than 30-50% reduction in pain and no medication completely relieves 100% of pain (Boulton, 1998).

Drug-related adverse effects are common due not only to the side effects of pain medications, but also due to interactions with other medications for diabetes and other co-morbidities (Dworkin et al., 2003). For instance, tricyclic antidepressants are associated with cardiac arrhythmias and blurred vision (Argoff, Backonja, Belgrade, Bennett, Clark, & Cole, 2006; Boulton, 2005); Gabapentin, a commonly used anti-convulsant, is associated with gait/balance problems, cognitive impairment, weight gain, and ataxia (Backonja, et al., 1998; Serpell, 2002); and opioids are associated with nausea, dizziness, seizures, and addiction (Gimbel, Richards, & Portenoy, 2003; Harati et al., 1998). The current pharmacological approach for the treatment of painful DPN warrants that other non-invasive approaches, without the known adverse pharmacological side effects be identified. One such potential method that has been shown to reduce pain, but not widely studied, is whole-body vibration.

Whole-body vibration involves the application of vibratory stimuli throughout the body by standing on a vibrating platform (Merriman & Jackson, 2009). The vibration is created by a mechanical, linear motion, which transfers energy upwardly through the body stimulating muscles to contract (Rittweger, 2010). Whole-body vibration has recently been used to reduce back pain and
fibromyalgia pain in women (Alentorn-Geli et al., 2008; Iwamoto et al., 2005). Since current theory suggests that pain operates through common mechanisms and that no pain mechanism is an inevitable consequence of a particular disease process (Woolf & Mannion, 1999), it extends to reason that whole-body vibration may be effective at reducing neuropathic pain in patients with diabetes. In a recent case study, the authors reported that whole-body vibration was effective at reducing painful symptoms associated with DPN (Hong, Barnes, & Kessler, 2011). The purpose of this study was to determine the effect of whole-body vibration on pain in a sample of adults with painful DPN. The first research question was to evaluate the effect of whole-body vibration on pain pre- and post-intervention. The second research question was to evaluate the acute effect of whole-body vibration on pain during the intervention, which also allowed for the evaluation of how pain changed from pre- to post-intervention.

**Methods**

**Participants**

A total of 21 participants (female=12 and male=9) diagnosed with painful diabetic neuropathy volunteered for this study. All participants met the following inclusion eligibility criteria: 1) aged 45-75 years; 2) physician confirmed diagnosis of painful DPN; 3) current pain level of ≥3 (0-10 scale); 4) ability to walk 50 feet without stopping; 5) ability to stand for at least 5 minutes; and 6) primary care physician’s clearance to participate. In addition, participants who met the eligibility criteria were excluded if they met the following criteria: 1) any foot wound (i.e. ulcer); 2) presence of any condition or injury that would preclude full participation; and 3) a score ≤23 on the Mini-mental State Examination indicating some degree of cognitive impairment (Folstein, Folstein, & McHugh, 1975). Table 1 summarizes the characteristics of the participants. The investigator’s Institutional Review Board approved all testing procedures and informed consent was obtained from all participants.
Table 1. Demographic Characteristics of Participants at Baseline

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<th>Characteristic</th>
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<tr>
<td>Age - yr</td>
<td>63.00</td>
<td>5.04</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>39.13</td>
<td>9.60</td>
</tr>
<tr>
<td>Duration of Diabetes - yr</td>
<td>11.82</td>
<td>8.17</td>
</tr>
<tr>
<td>Duration of Painful Neuropathy - yr</td>
<td>8.93</td>
<td>7.20</td>
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Measurement Instruments

Pain was measured using two pain measurement instruments: 1) the Brief Pain Inventory Short Form [BPI-sf] (Cleeland, 2009); and 2) a numeric rating scale [NRS] (Turk & Melzack, 2011; Williamson & Hoggart, 2005). The BPI-sf has been widely used for neuropathic pain assessment in both clinical and research settings (Cleeland, 2009). The BPI-sf contains 11 items designed to capture two dimensions of pain: interference (i.e. how pain interferes with daily living) and severity (i.e. sensory perception). The pain interference index contains seven items that are rated on an 11-point scale with a numeric range from 0 (does not interfere) to 10 (completely interferes). These items assess how pain interfered in the previous 24 hours with: 1) general activity; 2) walking; 3) work; 4) mood; 5) enjoyment of life; 6) relations with others; and 7) sleep. The average of these items are used to form a composite score that represents pain in this construct.

The pain severity index contains four items that are also rated on an 11-point scale with a numeric range from 0 (no pain) to 10 (pain as bad as imaginable). Since pain typically varies throughout any given day, this index asks participants to report their pain levels at their: 1) “worst”; 2) “least”; and 3) “average” during the previous 24 hours as well as pain levels 4) “now”. For example, the first pain severity item asks the participant to rate pain at its “worst” during the previous 24 hours. The average of these items are also used to form a composite score that represents pain in this construct.

The 2-factor structure of the BPI-sf has been well established in several large national studies (Cleeland et al., 1996; Cleeland & Ryan, 1994). Factor analysis yielded acceptable factor loadings (i.e. >0.3), which verifies the two separate factors. Internal consistency (Cronbach’s $\alpha$) ranged from 0.80 to 0.87 for the pain severity items and from 0.89 to 0.92 for the seven pain interference items. Test-retest reliability values have ranged from 0.83 to 0.98.
for the pain severity items and from 0.83 to 0.97 for the pain interference items. Pain cut-points for the BPI have been established at 0-3 for mild, 4-6 for moderate, and 7+ for severe (Zelman, Dukes, Brandenburg, Bostrom, & Gore, 2005).

The acute effect of whole-body vibration was measured using the NRS, which has a numerical range of 0 (no pain) to 10 (worst pain possible) (Turk & Melzack, 2011). This scale is widely used in clinical settings to assess a patient’s subjective rating of pain. Adequate validity of the NRS has been established with correlation coefficients ≥0.80 between the NRS and visual analog and verbal rating scales (Bijur, Silver, & Gallagher, 2001; Lara-Munoz, De Leon, Feinstein, Puente, & Wells, 2004; Ponce de Leon, Lara-Munoz, Feinstein, & Wells, 2004). The NRS has also demonstrated moderate reliability with a reported kappa coefficients of 0.59 (Lara-Munoz et al., 2004; Ponce de Leon et al., 2004). Additionally, the NRS has greater sensitivity to changes in acute pain when compared to a visual analogue scale or a verbal rating scale and has been identified as being more useful in pain assessment and research than both the visual analog and verbal rating scales (Williamson & Hoggart, 2005).

Testing Procedures

Participants were recruited from the state of Oregon (Linn, Benton, and Polk counties) through physician referrals and local advertisements to take part in a 26-week time series design study. From April to August of 2011, a total of 50 respondents were screened for eligibility and of these, only 30 met all of the inclusion criteria and were consented (Figure 1). After obtaining informed consent, nine participants withdrew for various reasons (Figure 1) and 21 participants returned for baseline testing. After baseline testing, all participants entered a 12-week control period during which participants were asked to continue with their usual daily routines including medication schedule. During this period, one participant withdrew for travel/time concerns. At the completion of the 12-week control period (week 13), 20 participants began the 12-week whole-body vibration intervention. Participants were again asked to maintain their regular medication schedules. During the intervention, three participants withdrew citing unrelated health reasons and one withdrew citing time commitment concerns. Additionally, two participants that developed
unrelated ulcers (self-inflicted) completed the study, but were removed from the analysis. A total of 14 participants (female \( n=8 \)) remained for the purposes of analysis. The BPI-sf was employed at baseline, pre-intervention, and post-intervention to assess pain. The NRS was used during the intervention immediately following each bout of whole-body vibration exposure to evaluate the acute effect of whole-body vibration on pain.

Figure 1. Participant Recruitment and Retention Flowchart
Whole Body Vibration

During the intervention, participants were instructed to stand on a vibration platform three days per week, without shoes, with knees slightly bent and while holding onto a railing. Participants were provided with non-skid slipper socks to wear so that shoe sole thickness would not create discrepancies between participants in the amount of vibration transmitted through the lower extremities. Before the initial whole-body vibration exposure and after each subsequent exposure, participants were asked to report their pain levels using the NRS. This scale was used during the intervention to evaluate the acute effect of whole-body vibration on pain levels (i.e. immediately following each exposure to whole-body vibration) and also to evaluate how pain changed from pre- to post-intervention.

At the start of the intervention, participants were initially instructed to stand on the vibration platform for four, 1-minute bouts of whole-body vibration at 30 Hz (2.8g) with 1-min rest intervals between bouts of whole-body vibration. The intensity of the vibration was set at a range of 30-50 Hz (2.3-2.8g) because of its demonstrated efficacy to improve skin blood flow (Lohman, Petrofsky, Maloney-Hinds, Betts-Schwab, & Thorpe, 2007; Maloney-Hinds, Petrofsky, & Zimmerman, 2008). The intensity and duration was then adjusted weekly according to each participant’s response of tolerability. The change in intensity and frequency was as follows: Week 1) four 1-minute exposures at 30 Hz with 1-minute rest periods between vibration bouts; Week 2) four 2-minute exposures at 40 Hz with 1-minute rest periods between vibration bouts; Week 3) four 3-minute exposures with 1-minute rest periods between vibration bouts. By the sixth week of the intervention, all participants received four, 3-minute bouts at 50 Hz with 1-minute rest periods between bouts per week or 36 total weekly minutes of whole-body vibration.

Statistical Analysis

A one-way repeated-measure MANOVA was performed to examine overall levels of pain. The dependent variables were pain interference and pain severity. The independent variable was time at three levels: baseline, pre-intervention, and post-intervention. Follow-up univariate tests (ANOVA)
were performed for each dependent variable. As post-hoc analysis, polynomial contrasts and pairwise comparisons between time points (with Bonferroni correction) were performed. A visual analysis of the data collected using the NRS was performed by averaging the change in weekly pain scores for all participants during the intervention. This was performed in order to evaluate the acute effect of whole-body vibration on pain during the intervention. For all outcome variables, an alpha level of 0.05 was considered statistical significance. Statistical analyses were performed with the Statistical Package for Social Sciences software version 18 (IBM SPSS).

Results

The means and standard deviations for the BPI-sf scores are presented in Table 2. At the conclusion on the intervention, mean pain interference scores decreased from 5.61±1.40 to 2.39±1.82. Mean pain severity scores decreased from 5.1±0.64 to 3.1±1.87. Pain index scores did not change from baseline to pre-intervention.

| Table 2. Brief Pain Inventory-Short Form (BPI-sf) Mean Pain Scores By Index at Baseline, Pre-Intervention and Post-Intervention |
|-------------------------------------------------|----------|----------|----------------|----------------|----------|----------|
|                                                 | Baseline | Pre-Intervention | Post-Intervention |
|                                                 | M        | SD        | M        | SD        | M        | SD        |
| BPI-sf Interference Index                       | 5.76     | 1.58      | 5.61     | 1.40      | 2.39     | 1.82††    |
| BPI-sf Severity Index                           | 4.78     | 1.71      | 5.10     | 0.64      | 3.1      | 1.87†     |

††Indicates a statistically significant difference from pre-intervention and baseline (p<0.001).
†Indicates a statistically significant difference from pre-intervention but not baseline (p<0.01).

The results for the MANOVA indicate a significant time effect (Wilks’ \( \lambda=0.21, F(4,10)=9.23, p\leq0.01, \eta^2=0.79 \)). Follow-up univariate tests indicated that there was a significant main effect for pain interference (\( F(2,12)=20.99, p\leq0.001, \eta^2=0.62 \)). Post-hoc analysis indicated a statistically significant effect for pain interference (\( p\leq0.05, \eta^2=0.75 \)) with scores decreasing over time. A statistically significant decrease was observed between pre- and post-intervention (Figure 1). The mean difference between these time points was 3.22 with a standard error of 0.68 (\( p\leq0.01 \)) and with upper and lower bounds of -5.09 and -1.34. Baseline was also observed to have a statistically significant difference from post-intervention. The mean difference between these points was 3.37 with a standard error of 0.54 (\( p\leq0.001 \)) and with upper
and lower bounds of -4.85 and -1.89. There was no significant difference between baseline and pre-intervention.

For pain severity, the follow up univariate tests indicated that there was significant main effect \( F(2,12)=8.11, p\leq0.01, \eta^2=0.38 \). Post-hoc analyses also indicated a statistically significant effect for pain severity \( (p\leq0.05, \eta^2=0.35) \) with scores decreasing over time. For pain severity a statistically significant decrease was observed between pre- and post-intervention. The mean difference between these time points was 2.11 with a standard error of 0.57 \( (p\leq0.001) \) and with upper and lower bounds of 0.54 and 3.68. Comparisons between post-intervention and baseline and between pre-intervention and baseline were not significant.

Analyses of the NRS scores indicate that there was a weekly trend in decreasing pain levels (Figure 2). Each singular, descending line represents the average weekly change in pain levels immediately following whole-body vibration. The polynomial trend line indicates that pain levels across the 12-week intervention continued to decrease.
The purpose of this study was to evaluate a new method of treating or managing pain symptoms in adults with painful DPN. It is important to note that although pain is a subjective interpretation of an unpleasant sensory experience, it is also a multidimensional construct that has a large effect on nonphysical aspects of one’s life ("Classification of chronic pain", 1986; Shulamith, Beltrutti, Lamberto, & Niv, 2007). The results of this study indicate that pain interference (i.e. how pain interferes with daily living) may be managed and its effects on daily living ameliorated with the use of whole-body vibration.

A significant change in pain interference was observed at the conclusion of the intervention. The change in the physical sensation of pain observed throughout the intervention would suggest that pain interference would decrease because of this change. However, a change in only this physical component would not explain the extent of change in pain interference. A more plausible explanation is that there was some change in actual physical functioning (i.e. improvements in walking, sit-to-stand, climbing stairs, etc), which would be consistent with findings in the literature (Rehn, Lidstrom,
Whole-body vibration has consistently been observed to increase lower extremity strength and improve physical functioning (Rehn, et al., 2007). A systematic review of whole-body vibration studies involving leg muscular performance concluded that, “there is strong to moderate evidence that long-term whole-body vibration exercise can have positive effects on the leg muscular performance of untrained people and elderly women” (Rehn, et al., 2007). In a randomized trial by van Nes and colleagues (2006), statistically significant improvements in functional ambulation, mobility, and trunk control were observed in a group of post-stroke patients. In other clinical trials, improvements in walking function, including gait speed, have been observed in adults with spinal cord injury, adults with Parkinson’s disease, and adults with spastic diplegia due to cerebral palsy (Ahlborg, Andersson, & Julin, 2006; Ebersbach, Edler, Kaufhold, & Wissel, 2008; Ness & Field-Fote, 2009). These studies indicate that whole-body vibration seems to have similar benefits to lower extremity strength training in both clinical and older populations with significantly less training time (Bogaerts et al., 2007; Roelants, et al., 2004; Verschueren et al., 2004).

There is also anecdotal evidence reported by our participants regarding improvements in lower extremity functioning and strength. Several participants reported being able to walk for longer distances and at faster speeds than before beginning the whole-body vibration intervention. One participant reported that she was able to walk the length of her driveway while pulling two garbage cans behind her. A task she had been unable to do for over a decade. Several participants also reported improvements in their sleeping patterns, that is, they were able to sleep throughout the night without awaking. It is unknown as to whether this observation is attributable to a reduction in pain or some other phenomena. However, the anecdotal evidence in addition to the statistical evidence, strongly suggests that whole-body vibration may be a suitable method of ameliorating the effect of pain on daily living in this population. Moreover, given that the BPI-sf evaluates the effect of pain on sleeping, walking, mood, and other constructs, we can reasonably attribute the change of 3.22 points ($p \leq 0.01$) from pre-intervention to post-intervention to
changes in these items. Interestingly, in a study by Alentorn-Geli et al. (2008) that evaluated the use of whole-body vibration to reduce pain in women with fibromyalgia, significant changes in pain and Fibromyalgia Impact Questionnaire (FIQ) scores were observed in the whole-body vibration group. The FIQ is a common measure of fibromyalgia that assesses the degree to which Fibromyalgia interferes with daily living including work, walking, mood, and several other components similar to the BPI-sf pain interference index. It appears that the use of whole-body vibration to reduce pain may be largely attributable to positive benefits of mitigating the effect of pain on daily living through an enhancement of lower extremity functioning.

At the conclusion of the intervention, pain severity index scores decreased by approximately 2.11 points ($p \leq 0.001$) from pre-intervention. This is considered clinically significant given the change of pain severity classification from moderate to mild (Hoffman et al., 2010, Zelman et al., 2010). Pain classifications have been consistently associated with patient outcomes and medical utilization (NIH, 2009) and in the United States pain is the leading cause of physician consultation (Turk & Dworkin, 2004). In a cross-sectional study of 602 patients with neuropathic pain, 20% of those with moderate pain severity reported reductions in scheduled work time compared to only 12% of those with mild pain (Marchettini et al., 2006). Nearly half of all patients with moderate pain severity in this sample reported visiting their physician at least twice for pain-related issues in the previous week compared to only 27% of patients with mild pain. Although no differences in pain severity were found in our sample between baseline and post-intervention, this is likely attributable to a lack of sufficient statistical power.

Using the NRS to evaluate the acute effect of whole-body vibration on pain, NRS scores were observed to decrease every week and continued to decrease throughout the intervention. By the 12th week, pain levels were approximately two points lower when compared to the values reported during the first week of the intervention. This decrease in pain is also clinically significant (Farrar, 2000). A change of two points on a 0-10 numeric rating scale has been noted as being clinically meaningful in particular if the change results in a score on the lower end of the scale (Farrar, 2000). Hoffman, Sadosky, Dukes, & Alvir (2010) also note that although a $\geq 50\%$ reduction has
been used to classify treatment response in painful DPN trials, a reduction of two points should also be considered clinically meaningful. The NRS data also shows how the sensory aspect of pain changed during the intervention, that is, the BPI-sf pain severity index scores are similar at pre- and post-intervention with the NRS scores at weeks 1 and 12 of the intervention, respectively. The changes observed in the sensory aspect of pain are in-line with other studies.

Iwamoto et al. (2005) evaluated whether whole-body vibration would enhance the effect of alendronate (a commonly prescribed medication for osteoporosis) on lumbar bone mineral density and chronic back pain in women with osteoporosis. Post-intervention pain scores indicated a significant decrease in pain for the alendronate and whole-body vibration groups and the change in pain reached the level of clinical significance (i.e. ≥2 points).

Although no specific mechanism for the change in the sensory aspect of pain was identified, painful symptoms have been most strongly associated with erratic blood glucose control (Thacker, Clark, Marchand, & McMahon, 2007). Several participants noted improvements in HbA1c levels throughout the intervention. HbA1c or glycated hemoglobin is a common test of average plasma glucose concentration and in diabetes mellitus it is used as an indicator of blood glucose control. A recent study that evaluated the effect of whole-body vibration on blood glucose control in patients with diabetes would support our participants’ observations (Baum, Votteler, & Schiab, 2007). Baum et al. (2007) evaluated the effect of whole-body vibration and strength training on fasting glucose concentration, maximal glucose concentration measured by an oral glucose tolerance test (OGGT), and HbA1c in a sample of 40 adults with non-insulin dependent diabetes. After 12 weeks of training, there was no change in fasting glucose; however, maximal glucose concentration for OGGT had decreased significantly in both the strength training and whole-body vibration groups. There was no difference between groups in the magnitude of change. More interesting is the change in HbA1c levels between groups. There was an increase in HbA1c in the strength training and control groups, but a significant decrease in the whole-body vibration group.

Although this study may face the limitation of a relatively small sample sizes, these findings should be explored further. Moreover, we cannot claim that our anecdotal evidence in any way attributed to the changes in the
sensory aspect of pain, however, future studies involving whole-body vibration and painful DPN should certainly evaluate measures of blood glucose control in tandem with other primary outcomes. Future studies should also entail better control conditions such as randomization and blinding, which may preclude any potential Hawthorne effects. Nevertheless, the change in the sensory aspect of pain observed in this study should be considered promising given that a change in classification could reduce medical costs, improve one’s ability to work, and improve quality of life.

**Conclusion**

The results of this study indicate that whole-body vibration may be effective at managing pain in adults with painful DPN. Rather than eliminating medications entirely, patients may be able to use whole-body vibration as part of an integrative treatment plan that encompasses educational and dietary interventions, along with pharmacological and alternative treatment methods to reduce pain and improve quality of life. Moreover, such methods may be cost effective given the potential to reduce medication use and improve one’s ability to work. Although the changes in pain cannot be explained given the design of the current study, future research should evaluate potential mechanisms such as improvements in lower extremity functioning and blood sugar levels. This may provide insight into the changes observed and may also provide a means of improving current treatment strategies.
References


Chapter 3: Conclusion

The following summary will provide a discussion for each of the research questions that were presented in the introduction, as well as provide suggested future research directions. The primary purpose was to evaluate the use of whole-body vibration to reduce pain in patients with painful DPN. From this, two specific questions were asked. The first question was to determine the effect of a 12-week whole-body vibration intervention on pain in a sample of adults with painful diabetic neuropathy. Our working hypothesis was that pain would decrease.

The results of this study indicated that a significant decrease in pain was observed after the 12-week intervention ($p \leq 0.05$). Overall, pain levels dropped by approximately three points for each index of pain, resulting in a change of pain classification from moderate to mild. This is clinically significant.

The second research question was to determine the acute effect of a 12-week whole-body vibration intervention (i.e. during the intervention) on pain in a sample of adults with painful diabetic neuropathy. Our working hypothesis was that pain would decrease.

The results reveal that the whole-body vibration intervention reduced pain. This conclusion is based on the visual analysis of the 12-week trend graphic. A decreasing trend was observed during the 12-week intervention for pain. On average, pain levels dropped after every weekly exposure to whole-body vibration. Initially there was a drop in reported pain levels during the first two weeks, which subsequently plateaued until the sixth week. After this point in the intervention, reported pain levels continued to decline every week until the conclusion of the intervention.

Future Directions

Future research should entail designs of greater methodological rigor. For example, randomization and blinding may eliminate any potential Hawthorne effects. Additionally, potential mechanisms of pain reduction should be evaluated such as improvement in lower extremity function and strength as well as markers of blood sugar control. These potential mechanisms could elucidate the process by which pain was reduced in this study.
Bibliography


Appendices

Attachment A: Literature Review

Diabetic Neuropathy

Recent estimates from the National Health and Nutrition Examination Survey (NHANES) indicate that approximately 23.6 million Americans currently have diabetes (National Institutes of Health, 2009). Diabetic neuropathy, characterized mainly by nerve damage and dysfunction, is the most common long-term complication of diabetes, affecting 60-70% of all diabetics (NIH, 2009). Diabetic neuropathy is also the most common type of neuropathy in the Western world (Marchettini et al., 2006) with the greatest prevalence among patients who are aged 65-74 years and have had diabetes for at least 25 years (Argoff, Backonja, et al., 2006).

Diabetic neuropathy is classified into 4 subtypes: peripheral, autonomic, proximal, and focal, with each subtype affecting different areas of the body differently (NIH, 2009). Of these subtypes, peripheral neuropathy is the most prevalent and can be one of the most debilitating complications of diabetes (Boulton, 1998). Symptoms of diabetic peripheral neuropathy include numbness/insensitivity, extreme sensitivity, sharp pains, cramps, loss of balance and coordination (reduced proprioception), muscle weakness, loss of reflexes, and foot deformities (NIH, 2009). Also a common outcome of neuropathy is ulceration, the leading cause of amputation in the United States (Argoff et al., 2006).

Pain is one of the most distressing symptoms of diabetic neuropathy and has been consistently been associated with reduced quality of life, disrupted sleep, reduced physical activity, depression and anxiety (Argoff, et al., 2006). Impaired physical and mental functioning and greater rates of self-reported disability have also been associated with painful neuropathies (Gore, 2005). The yearly cost of pain medication per patient is over $1600 per patient (Able, 2005). On average, healthcare costs are more than triple for these patients than for healthy, age-matched controls (Woolf, 2004). The potential financial consequences caused by disproportionate healthcare costs and lost productivity, warrants that innovative and cost-effective treatment methods that reduce pain be identified.
Causes and Mechanisms of Painful Neuropathy

Neuropathic pain is not unique to diabetes and is typically caused by mechanical trauma, metabolic diseases (diabetes), cancer chemotherapeutic agents, viral infection, surgery, radiation, nerve compression, tumor infiltration and idiopathic (Dworkin, 2002). These damaged nerves undergo functional changes which cause persistent hyper-excitability and can last for periods well after the original nerve trauma has been resolved (Dworkin et al., 2003; Woolf & Mannion, 1999). Many of the changes that occur in response to neural damage are potentially adaptive, however many of the maladaptive responses suggest that genetic determinants may also potentially predispose or protect a person from the onset of neuropathic pain (Costigan, Scholz, & Woolf, 2009).

Neuropathic pain is distinguished from other types of pain in that the spectrum of symptoms are caused by unique changes in the function, chemistry, and structure of the peripheral nervous system (Campbell & Meyer, 2006). That is to say, the variability of symptoms a person experiences, depends upon the nature of those changes. This also suggests that similar neuropathic pain symptoms, despite the etiology of the pain, may operate through common mechanisms (Woolf & Mannion, 1999). Thus, it seems that no pain mechanism is an evitable consequence of a particular disease and that different diseases may be more similar to each other with respect to their pain mechanisms (Costigan et al., 2009; Dworkin et al., 2003). Yet, no specific mechanisms for neuropathic pain have been identified partly because of the heterogeneity of symptoms and partly because such research is labor intensive and impractical for routine clinical use (Dworkin et al., 2003).

Another important distinction of neuropathic pain is that it may be stimulus-dependent or stimulus-independent (spontaneous pain), both of which have different mechanisms (Argoff, et al., 2006; Dworkin, 2002). The different types of stimulus-dependent pain include allodynia (painful response to normally non-painful stimulus) and hyperalgesia (increased pain to normally painful stimulus) and are a consequence of increased neuronal excitability (Woolf & Mannion, 1999). Stimulus-independent pain is present in the absence of any stimulus and patients often report having continuous and intermittent pain of different qualities (Dworkin et al., 2003). This type of pain, described as
burning, shooting or shock-like, is likely caused by functional changes in sodium ion channels found in peripheral nerves, which alter the excitability of the nerve (Woolf & Mannion, 1999). In addition to stimulus-dependent and stimulus-independent pain, patients with neuropathy also report having abnormal unpleasant sensations (dysesthesia) and abnormal sensations that are not unpleasant (paresthesia) (Dworkin, 2002). Symptoms of dysesthesia and paresthesia include itching, numbness, tingling, and crawling.

Among patients with diabetic neuropathy, painful symptoms have been most strongly associated with erratic blood glucose control (Argoff, et al., 2006; Boulton, 2005). However, the specific risk factors for neuropathic pain are less clear and despite the association between diabetic peripheral neuropathy and hyperglycemia being well established, it is still uncertain if glycemic control is a risk factor (Argoff, et al., 2006). Nevertheless, nerve damage is most likely due to a combination of factors such as abnormal levels of blood lipids and insulin, decreased oxygenation to tissues and lifestyle factors like smoking and inactivity (NIH, 2009). These factors vary greatly among patients with painful neuropathies and it’s this combination of factors that may explain different symptoms of pain.

Of increasing interest to researchers investigating the mechanisms of neuropathic pain is the role of inflammation (Thacker, Clark, Marchand, & McMahon, 2007). Inflammation is characterized by a cascading immune cell response to damaged tissue and although inflammatory pain is thought to be distinct in terms of etiology, it may share common mechanisms with neuropathic pain (Costigan et al., 2009). For example, multiple immune cells and other inflammation markers have been shown to create neuropathic pain symptoms in animal models and small-scale human studies (Thacker et al., 2007). Pain receptors (nociceptors) respond directly to these immune cells and elicit action potential discharges in the nerves, which contribute to inflammatory pain and potentially to neuropathic pain (Costigan et al., 2009).

Nerve growth factor (NGF) is one such signaling molecule that has been associated with inflammation and diabetic neuropathy (Thacker et al., 2007). Its larger function is in the growth, maintenance, and survival of nerves however, after a nerve injury has occurred, NGF production is increased,
which causes sensitization (increased sensitivity) and pain (Thacker, et al., 2007). It is believed that as nerve damage progresses in diabetic neuropathy, there is more available NGF, which subsequently leads to pain-signaling maladaptations (Apfel, 2002). However, anti-NGF treatments have not been successful and other pharmacotherapy methods addressed at the immune response for the treatment of neuropathic pain have shown mixed results (Apfel, 2002). Overall, pharmacotherapy has been disappointing due to the frequency and severity of side effects (Woolf & Mannion, 1999). Thus, identifying alternative treatment methods of neuropathic pain and establishing their efficacy is of great concern.

**Current Treatment**

Recent data suggests that approximately 25% of all patients with diabetic neuropathic pain receive no treatment and that those that do may not be getting the most effective medication (Berger et al., 2004). Despite numerous pharmacological therapies in current use, including anti-depressants, anti-convulsants, opioids, and topical agents, many patients achieve no more than 30-50% reduction in pain and none relieve 100% of pain for 100% of patients (Boulton, 1998). Moreover, tolerability issues are of major concern. Drug-related adverse effects are common in this population due not only to the side effects of pain medications, but also due to interactions with other medications, age, and other co-morbidities (Dworkin et al., 2003).

The first class of drugs that are most often used to treat painful diabetic neuropathy and other chronic pain conditions are tricyclic antidepressants (TCAs) despite never having been approved by the FDA for the treatment of any type of pain (Boulton, 2005). Nevertheless, research has shown that the neuro-circuitry involved in pain modulation has common mechanisms with responses to mood (Blackburn-Munro & Blackburn-Munro, 2001; Schweinhardt et al., 2008). This suggests that emotional pain (i.e. depression) and physical pain share the same central nervous system pathways (Eisenberger, Lieberman, & Williams, 2003; Maletic & Raison, 2009). Yet, the specific mechanism of action is still unclear and because of side effects, despite the low cost and shown efficacy, up to one third of all patients cannot tolerate TCAs (Argoff, et al., 2006; Boulton, 2005).
Of the many anti-convulsants used over the years to treat painful neuropathies, Gabapentin is now widely used though the FDA has not approved it specifically for painful diabetic neuropathies (Argoff et al., 2006). Nevertheless, multiple studies have demonstrated its efficacy but tolerability remains problematic (Backonja et al., 1998; Gorson, Schott, Herman, Ropper, & Rand, 1999; Serpell, 2002). Common side effects include somnolence, dizziness, dry mouth, postural hypotension, weight gain, and ataxia. Even more problematic is that for elderly patients, Gabapentin may cause or exacerbate gait and balance problems and worsen cognitive impairment (Dworkin et al., 2003). For those who are already at risk of falling and/or cognitive impairment, Gabapentin may not be a viable treatment method.

Two opioids that have not traditionally been used, but are now commonly prescribed are Oxycodone and Tramadol (Argoff, et al., 2006; Boulton, 2005). Studies have shown the efficacy of both drugs, however the side effects remain a concern (Gimbel et al., 2003; Harati et al., 1998). Side effects include nausea, sedation, dizziness, seizures, pruritus (unpleasant itching sensation), and most problematic is the potential for addiction. Due to these side effects, opioids are considered as adjunctive therapies only when patients fail to respond to non-opioid medications (Argoff, et al., 2006).

Topically applied agents (capsaicin cream, nitrate spray and 5% lidocain patch) are not as commonly used to treat neuropathic pain, but are generally well tolerated and have demonstrated efficacy in several small, randomized trials (NIH, 2009). However, there are some concerns with the administration of these agents. For example, capsaicin use (active ingredient in chili peppers) requires that the patient endure several weeks of stinging and burning sensations, particularly during the first week, which may discourage patients (Argoff, et al., 2006). Additionally, the evidence supporting the efficacy of these treatment methods has been limited to small studies, which may restrict their use until larger randomized studies can be completed.

Other treatment methods with limited efficacy include selective serotonin reuptake inhibitors, acupuncture, yoga, vitamin therapy, magnetic field therapy, nerve stimulation, and laser light therapy (Head, 2006). Though there is evidence to support the efficacy of these methods, none have been
confirmed with large, randomized controlled trials and thus none are commonly used. Over-the-counter pain medications such as ibuprofen and acetaminophen are not recommended for neuropathic pain due to the severity of side effects (NIH, 2009).

The potential side effects of the pharmacological therapies currently in use warrant that other non-invasive and non-pharmacological approaches be identified. Furthermore, the financial burden and quality-of-life issues related to the treatment of neuropathic pain warrants the investigation of alternative treatment methods. One such potential method that has been shown to reduce pain is whole-body vibration.

**Whole-body Vibration**

The application of whole-body vibration involves standing or performing exercises on a vibrating platform, which transmits vibratory stimuli throughout the body (Merriman & Jackson, 2009). The oscillatory motion of the platform transfers energy upwardly through the human body and stimulates muscle contractions (Rittweger, 2010). These contractions occur during the upstroke of the vibration platform. Similarly, during the down-stroke the muscles relax. This continuous oscillating input of force causes the soft tissues to vibrate at the same frequency, which dampens the externally applied vibration (Cardinale & Wakeling, 2005). This process occurs naturally during any sporting activity in which there are impact forces (e.g. heel strike in running, hitting with a racket). Although whole-body vibration training is a relatively new method of exercise training, the muscle dampening that occurs during any sporting activity is similar in nature.

An important aspect of whole-body vibration training is intensity. The intensity of vibration is determined by the frequency (rate of oscillation measured in Hz), amplitude (peak to peak displacement measured in mm), and magnitude (gravitational acceleration imposed on the body measured in g). Though there is no clear consensus regarding optimal training parameters to induce physiological responses, these three parameters must be considered when designing any research protocol (Merriman & Jackson, 2009). In fact, the interaction of these parameters (i.e. training intensity) is related linearly to the rate of oxygen uptake during whole-body vibration,
which may explain why studies with greater training intensities tend to show better results in various outcomes (Cardinale & Wakeling, 2005).

Intensity levels ranging from 30-100 Hz have been shown to decrease pain (Guieu, Tardy-Gervet, Blin, & Pouget, 1990; Kakigi & Shibasaki, 1992; Lundeberg, 1984) and to improve skin blood flow (Lohman et al., 2007). As a therapeutic modality, whole-body vibration has recently been reported to reduce pain associated with fibromyalgia in women (Alentorn-Geli et al., 2008) and low back pain in women with vertebral osteoporosis (Iwamoto et al., 2005). In a randomized trial (n=36, mean age=56), Alentorn-Geli et al. (2008) observed that participants in the experimental group experienced statistically significant pain reductions from baseline while no differences were observed in the control groups. In a cohort study (n=50, mean age=72±8) Iwamoto et al. (2005) also observed reductions in pain that were statistically significant even though the experimental group only received whole-body vibration once per week for 4 minutes. Since current theory suggests that pain operates through common mechanisms and that no pain mechanism is an inevitable consequence of a particular disease process, it extends to reason that whole-body vibration may also be effective at reducing neuropathic pain in adults with diabetes (Woolf & Mannion, 1999). Some researchers have also argued that neuropathic pain and fibromyalgia may be variations of the same condition (Martinez-Lavin, 2007; Martinez-Lavin, Lopez, Medina, & Nava, 2003).

Several studies have also reported that whole-body vibration improves skin and muscle perfusion (Lohman et al., 2007; Maloney-Hinds et al., 2008). It is hypothesized that increases in perfusion are a result of vasodilation and though the specific mechanism is still unclear, populations with poor blood circulation, such as those with diabetes, may benefit greatly through improved circulation and healing (Maloney-Hinds et al., 2008).

Further evidence of the efficacy of whole-body vibration to reduce neuropathic pain comes from published case study of a 70 year-old male with severe peripheral neuropathy (Hong, Barnes, & Kessler, 2011). This individual had numbness, tingling, heaviness, and occasional burning in both feet as well as decreased sensation from the mid-foot distally on both feet. Traditional
pharmacotherapy for his pain was unsuccessful and in 2009 he began receiving whole-body vibration 4-5 times per week. He soon began to report improvements in foot pain and after several weeks, he discontinued use of all pain medications. This evidence further suggests that whole-body vibration may alleviate pain in adults with painful diabetic peripheral neuropathy.

Concerns over the safety of whole-body vibration training have been expressed because of the known hazards associated with occupational vibration exposure (Astrom et al., 2006). However, the dose of vibration used in therapeutic trials is orders of magnitude less than that associated with occupational vibration. Very few adverse events have been reported in interventions conducted in frail elderly and chronically ill populations (Arias, Chouza, Vivas, & Cudeiro, 2009; Brooke-Wavell & Mansfield, 2009; Bruyere et al., 2005; van Nes et al., 2006). Examples include isolated cases of head discomfort (when knees are locked out) and increased fatigue (Roth et al., 2008). However these diminish with increased exposure and by flexing the knees to absorb the vibration stimulus. More importantly, the potential benefits of this therapy for individuals with chronic disease, pain, impaired muscle function, and physical de-conditioning far outweigh the minimal risk associated with vibration since the majority of these individuals can not participate in traditional therapeutic exercise programs. Whole-body vibration may prove to be a safe and cost-effective approach as an exercise intervention for those who may not tolerate traditional exercise modalities (Brooke-Wavell & Mansfield, 2009).

Adherence and compliance may also influence the responsiveness of the musculoskeletal system to whole-body vibration (Rubin et al., 2004). Data from published studies are encouraging and suggest that compliance is near to or exceeds that of traditional exercise modalities even among older adults (Totosy de Zepetnek, Giangregorio, & Craven, 2009). The adherence and compliance to whole-body vibration protocols should be similarly established in trials that explore the feasibility in clinical populations that have not been previously studied. It is uncertain whether the benefits of whole-body vibration extend to adults with painful diabetic neuropathy, but its potential to reduce pain and improve the quality of life for these individuals needs to be explored.
Attachment B:

**Background Survey**

1. **Gender:**  
   - Male  
   - Female

2. **Date of birth (dd/mm/yyyy):** _______________________

3. **Marital status (check only one):**  
   a) Married/living with a partner  
   b) Single/divorced/separated/living alone

4. **Education (please choose the highest level of education completed):**  
   a) Elementary school  
   b) Middle school  
   c) High school  
   d) Community college  
   e) University (BA, BS, etc)  
   f) Graduate school (MA, MS, etc)  
   g) Post graduate (PhD, etc)

5. **Total household income (check one):**  
   a) Under $4,999  
   b) $5,000 - $9,999  
   c) $10,000 – 14,999  
   d) $15,000 - $19,999  
   e) $20,000 - $24,000  
   f) $25,000 - $29,999  
   g) $30,000 - $39,999  
   h) $40,000 - $49,999  
   i) $50,000 - $59,999  
   j) $60,000 or more

6. **Do you consider yourself Hispanic or Latino?**  
   Y  
   N

7. **Which race do you consider yourself to be?**  
   a) Native American  
   b) Asian  
   c) African American or black  
   d) Pacific islander  
   e) Caucasian or white  
   f) Other: __________________
8) How many years have you had type diabetes? ____________
9) How many years have you had painful peripheral neuropathy? _________
10) Have you fallen in the past 6 months?  Y    N
11) Please indicate the degree to which you are afraid of falling:
   Not at all afraid 1  2  3  4  5 Very afraid
12. Do you drink alcoholic beverages?  Y    N
13. If yes, how often?
   Less than once/week  1-2 times per week  3-4 times per week  5-6 times per week  Every day
14. Tobacco use?  Never  Ex-smoker/chewer  Current smoker/chewer
15. Please indicate if you have had any of the following conditions:
   a) Arthritis
   b) Heart disease
   c) High blood pressure
   d) Chronic lung disease
   e) Osteoporosis
   f) Depression
   g) Chronic back pain
   h) Cancer
   i) Stroke
   j) Thyroid disorder
   k) High cholesterol
Attachment C: Brief Pain Inventory - Short Form

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Please rate your pain by circling the one number that tells how much pain you have right now.

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Attachment D: Numeric Pain Rating Scale
Attachment E: Physician’s Medical Clearance

Bone Research Laboratory
Department of Nutrition and Exercise Sciences

**Project Title:** Can whole-body vibration reduce peripheral neuropathic foot pain in adults with diabetes?

**Principal Investigator:** Gianni F. Maddalozzo, Ph.D., FACSM
Oregon State University
Department of Nutrition and Exercise Sciences

**Personal Physician Clearance**

My patient __________________________________________ has notified me about his/her interest in participating in the aforementioned project. I have read the consent form that outlines the walking test, nerve conduction test, questionnaires and the whole body vibration training intervention. I understand that participants will consist of women and men who have been diagnosed with diabetic peripheral neuropathy of the feet and meet the following criteria:

- a) Aged 45-75 years
- b) Diagnosis of type I or type II diabetes
- c) Diagnosis of neuropathic pain of the feet
- d) Current pain level of 3 or greater in at least one foot measured by the Universal Pain Scale

To the best of my knowledge, this patient satisfies all of the criteria outlined above and does not have any additional conditions or symptoms that would preclude this individual from participating in a 12-week whole body vibration training intervention.

I understand that if I have any questions about the testing or training procedures, I may contact Dr. Gianni Maddalozzo at 541-737-6802 or by email at gianni.maddalozzo@oregonstate.edu

__________________________ __________________________
Physician printed name Date

__________________________ __________________________
Physician signature Date

__________________________
Address Phone
Attachment F: Informed Consent

APPENDIX E-4761
INFORMED CONSENT

Title: Can whole-body vibration reduce diabetic peripheral neuropathic foot pain in adults with diabetes?

Principal Investigator: Gianni Maddalozzo, Ph.D., FACSM,
Department of Nutrition & Exercise Sciences

Student Researcher: Ruben Guzman, B.S.

Co-Investigator(s): Mark Hoffman, Ph.D., FACSM; and Bradley J. Cardinal, Ph.D., FACSM, Kerri Winters-Stone, Ph.D., FACSM

Study Staff: Ryan Haran, Ben Jelinek, Kathryn Collins, and Walker Maddalozzo, Jakson Clark

Version Date: 12/20/2010

1. WHAT IS THE PURPOSE OF THIS FORM?
This form provides you the information you will need to help you decide whether to take part in our study. You may ask any questions about the study, the possible risks and benefits, your rights as a volunteer, and anything else about the study or your participation. When all of your questions have been answered, you can decide if you want to be in this study.

2. WHY IS THIS STUDY BEING DONE?
The purpose of this study is to see if whole-body vibration (WBV) training can be used to reduce foot pain caused by diabetic neuropathy. We also want to see if your walking improves as a result of the vibration training. Up to 30 people will be invited to take part in this study. This study will also be used for a student thesis. If you agree to take part, you will be given a copy of this form for your records.

3. WHY AM I BEING INVITED TO TAKE PART IN THIS STUDY?
You are being invited to take part in this study because you have been diagnosed with neuropathic pain of the feet related to diabetes.

4. WHAT WILL HAPPEN IF I TAKE PART IN THIS RESEARCH STUDY?
If you decide to take part in this research study, we will ask you to complete a series of questionnaires regarding your pain and several tests to measure your foot nerve damage. We will also measure your overall walking ability and ask you to participate in the WBV training.

Study Duration: This study will take about 26 weeks. Visits will last between 40 and 90 minutes.

Study Activities: You will be asked to complete the following questionnaires and physical tests:

- Questionnaires: There are two questionnaires that will ask you to report your current pain level, the quality of your pain (shooting, burning, etc) and how pain interferes with your daily life. Pain questionnaires will also be used to monitor changes in your perceived pain levels throughout the study. We will also ask you to complete a background information questionnaire (completed only once) and a list of medications (weeks 1, 13 and 26) you are currently taking
for your pain. A research assistant will review these questionnaires with you in a private setting. Time commitment 25 minutes

- Nerve conduction test: This test measures the effects of neuropathy on nerve conduction in your feet. If necessary, hair on the feet and ankles where the electrodes will be placed will be shaved and the skin will be cleaned with alcohol pads. For this test you will lay face down on a padded table while electrodes are placed on the calf and ankle. If your feet are cold, we may warm them with a warm blanket before starting the test. During this test you may feel several (10-15) slight shocking sensation (every 3-5 seconds), which will feel similar to a static electricity shock (carpet shock). We will ask you to avoid caffeine and smoking for 2 to 3 hours prior to the test and to avoid aspirin and non-steroidal anti-inflammatory drugs (Advil, Motrin, and Aleve, etc) for 24 hours prior to testing. Time commitment 30 minutes.

- Foot sensitivity test: A Semmes-Weinstein thin filament will be used to measure the loss of sensation in your feet. This test involves the application of a nylon thread to the soles of your feet. Time commitment 10 minutes.

- Walking ability test: You will be asked to walk without shoes at your normal walking speed and as quickly as possible under control on a carpeted walkway 20 feet in length. You will be asked to perform two trials for each condition. Time commitment 5 minutes.

- Visual foot inspection: We will visually inspect your feet for redness, swelling, ulcers, and foot deformities during week 13 and before and after each vibration training session. This foot inspection is similar to the inspections you may have received in the past or are receiving currently. We will provide you with diabetes foot care guidelines if necessary. Time commitment 5 minutes.

WBV training: You will be asked to stand on a vibrating platform without shoes during the training. When standing on the WBV platform you will feel a slight buzzing and/or vibrating sensation throughout your entire body. Your body will adjust to the vibrations naturally by contracting and relaxing your leg muscles. We will gradually increase the amount of vibration and the amount of time you will stand on the platform over the 1st three weeks. Initially, we will ask you to stand on the platform for four 1-minute periods vibrating at a low frequency. These periods will be separated by 1-minute breaks. By the 3rd week we will ask you to stand on the platform for four 3-minute periods vibrating at a high frequency. We will measure and record your blood pressure, heart rate, perceived effort, and pain level before and after each vibration training session. Time commitment 40-90 minutes.
• Pictures/video may be taken during your participation in the WBV intervention and testing sessions. These photographs and/or videos will only be used for class presentations, seminars, thesis defense, and presentations at conferences. If your pictures are used for these purposes, your face will be obscured so that it cannot be identified. Please initial one of the options below.

You may use my images for presentations. Initials: ______

You may NOT use my images for presentations. Initials: ______

Study Visits: You will receive a written schedule showing the activities that will take place at each visit. All visits will take place in the OSU Bone Research or Sports Medicine Labs in the Women’s Building (rooms 8 & 13).

Week 1 Visit 1
After signing this consent form, we will ask you to perform several tests to determine your eligibility to participate. These tests are: walking for 50 feet without stopping and without assistance; standing for 5 minutes without assistance; and your cognitive ability. If you are unable to successfully complete these tests, you will not be able to participate. If you are able to successfully perform these tests, we will provide you with the following documents: 1) a physician’s release form for you to take to your primary care doctor (we need your doctor to sign this form indicating that it is okay for you to participate in this study); 2) a copy of the study consent form; and, 3) a health history information questionnaire. Once we receive your doctor’s signed release form you will be enrolled in the study. If you are unable to obtain your doctor’s release you will not be able to participate in the study.

Week 1 Visit 2
During this visit you will complete the pain questionnaires and the following physical tests.
  1. Nerve conduction
  2. Foot sensitivity (thin filament)
  3. Walking test

Week 13 Visit 3
During this visit you will complete the pain questionnaires and the following physical tests.
  1. Nerve conduction
  2. Foot sensitivity (thin filament)
  3. Walking test
  4. Foot inspection

Weeks 14-25 WBV training sessions
We will schedule you for three visits per week for these 12 weeks. Each visit will last between 40 and 90 minutes. We will monitor and record your heart rate, blood pressure, assessment of your feet, and perceived rate of exertion. We will also ask you about your pain level in each foot before and after every time you train on the vibration platform. We will also ask you to complete the pain questionnaires every 4 weeks during this period.
Week 26
This will be your final visit to the OSU campus for testing. During this visit you will complete the pain questionnaires and the following physical tests.
   1. Nerve conduction
   2. Foot sensitivity (thin filament)
   3. Walking test

**Significant new findings:** Your participation may help to establish the use of whole-body vibration to reduce foot pain associated with diabetes.

**Termination of Participation**
Your safety is our main concern. If you begin to experience an increase in pain (greater than 2 points from pre-session WBV training), redness, swelling, excessive heat or you develop a new ulcer as a result of the vibration training, we will immediately stop the vibration and refer you back to your doctor. Your participation in the vibration training will resume once your doctor clears you to do so. If you are unable to obtain clearance from your doctor to resume vibration training, we will notify you by telephone that your participation in the study has been terminated.

**5. Future Use of Data**
We may store all of the information we collect about you indefinitely. Because it is not possible for us to know what studies may be a part of our future work, we ask that you give permission now for us to use your information without being contacted about each future study. Future use of your information will be limited to studies about diabetes and whole-body vibration. If you agree now to future use of your personal information, but decide in the future that you would like to have your personal information removed from our research database, please contact Dr. Gianni Maddalozzo at 541-737-6802 or gianni.maddalozzo@oregonstate.edu.

You may store my information for use in future studies. Initials: _____

You may NOT store my information for use in future studies. Initials: _____

Future Contact: We may contact you in the future for another similar study. You may ask us to stop contacting you at any time.

Study Results: We will send you report of your walking tests when the study is over.

**6. WHAT ARE THE POTENTIAL RISKS OF THIS STUDY?**
During your participation in this study it is unknown if your neuropathy will improve, worsen or stay the same. You may experience side effects from the study procedures that are not yet known to the researchers. There is a chance that you might feel uncomfortable answering some questions on our surveys. You may skip any questions that you do not want to answer. You may also be provided with study material via email. The security and confidentiality of information sent by email cannot be guaranteed. Information sent by email can be intercepted, corrupted, lost, destroyed, arrive late or incomplete, or contain viruses.
There are potential risks associated with the following testing procedures.

Nerve conduction: Due to the use of electrical stimulation, there may be a slight level of discomfort associated with this test. If at any time you are uncomfortable continuing with this test you can ask a member of the study team to stop the test. Although the possibility of a harmful stimulation is possible anytime electrical stimulation is being used, we are unaware of any injuries that have occurred due to this type of testing. For safety, the equipment for these tests has internal controls against excess stimulation. In the unlikely event that you receive a harmful shock, immediate steps will be taken to assist you. The testing will be discontinued immediately and your vital signs will be evaluated.

Whole-body vibration: The possible risks and/or discomforts associated with the vibration training include itching, muscle soreness, headaches, and lower body pain.

Walking test: There is a small chance of tripping or falling during this test. One of the research assistants will walk alongside you at all times.

Foot sensitivity (thin filament test): You may feel some pressure when the thin filament is applied to the bottom of your foot.

7. WHAT HAPPENS IF I AM INJURED?
Oregon State University has no program to pay for research-related injuries. If you think that you have been injured as a result of being in this study you should immediately contact Dr. Gianni Maddalozzo at 541.737.6802 or gianni.maddalozzo@oregonstate.edu. You should also contact your doctor if you believe you have been injured. If an injury occurs that prevents you from participating, we will inform you by telephone that you will no longer be able to participate.

8. WHAT ARE THE BENEFITS OF THIS STUDY?
This study is not designed to benefit you directly. However, others may benefit from the results of this study if we are able to determine that whole-body vibration is an effective alternative or supplement to current treatments for neuropathic pain relief.

9. WILL I BE PAID FOR BEING IN THIS STUDY?
You will not be paid for being in this research study.

10. WILL IT COST ME ANYTHING TO BE IN THIS STUDY?
You are responsible for the cost of all physician visits associated with this research study. You will also responsible for your transportation costs. We will pay for parking costs when you visit the OSU campus.

11. WHO IS PAYING FOR THIS STUDY?
The John C. Erkkila M.D. Endowment for Health & Human Performance.
12. WHO WILL SEE THE INFORMATION I GIVE?
The information you provide will be kept confidential. To protect your confidentiality, the researchers will not use your name on the questionnaires and data forms. All of your information will be kept in a locked filing cabinet and on password protected computers. If the results of this project are published, your identity or any information that could identify you will not be published. Federal agencies and the Oregon State University Institutional Review Board (a committee that reviews and approves research studies) may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

13. WHAT HAPPENS IF I CHOOSE NOT PARTICIPATE?
It is your decision if you want to be in this study. You will not lose any benefits or rights you would normally have if you choose not to participate. You can stop at any time. You will not be treated differently if you decide to stop being in the study. You may also skip any questions that you don’t want answer or decline any tests you do not wish to participate in. If you choose to withdraw before the study ends, the researcher may keep information collected about you to use in study reports.

14. WHAT IF I HAVE QUESTIONS?
If you have any questions about this research project, please contact: Dr. Gianni Maddalozzo at 541.737.6802 or gianni.maddalozzo@oregonstate.edu. If you have questions about your rights or welfare as a participant, please contact the Oregon State University Institutional Review Board (IRB) Office, at (541) 737-8008 or by email at IRB@oregonstate.edu

15. WHAT DOES MY SIGNATURE ON THIS CONSENT FORM MEAN?
Your signature indicates that this study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a copy of this form.

Participant’s Name (printed): ________________________________

Signature of Participant __________________ Date ____________

Signature of Person Obtaining Consent __________________ Date ____________