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Effects of Vibration on Spinal Circuitry Related to Spasticity and Walking

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Vibration is a form of afferent input known to influence the activity of spinal neural circuits. In individuals in whom neuropathology has disrupted the communication between the brain and spinal cord, vibration may mimic some functions formerly served by the lost or impaired supraspinal inputs. In individuals with SCI, vibration may influence spinal neural circuits in a manner that results in more normal reflex modulation and improved walking function. Three experiments were performed to assess the effects of vibration on spinal locomotor-generating circuitry, spinal reflex activity, and walking function.

In Experiment 1, localized leg vibration was used to elicit air-stepping responses in the lower extremities. We compared responses of individuals with SCI to those of non-disabled (ND) individuals, assessed the influence of severity of SCI, and assessed the influence of locomotor training on the air-stepping response in individuals with SCI. Our results indicate that vibration of the tensor fascia latae elicited more robust and consistent responses than did vibration of the quadriceps or hamstrings muscles. Individuals with SCI had less consistent and less robust responses than ND individuals. In those with SCI, neither severity of injury nor locomotor training influenced the robustness or consistency of the response.

In Experiment 2, we investigated the effect of whole-body vibration (WBV) on spasticity, as measured by spinal stretch reflex (SSR) excitability, in individuals with SCI. We also assessed differences in the influence of WBV among individuals who used antispastic medications and those who did not. Subjects were tested before and after participation in a 3 day/week, 12-session WBV intervention. There was a significant reduction in spasticity that persisted for several days following the WBV intervention. The amount by which spasticity was reduced was not different in those who used antispastic agents compared to those who did not use these agents.

In Experiment 3, we assessed the effects of the 12-session WBV intervention on walking function. WBV was associated with significant increases in walking speed, cadence, step length of the stronger leg, and consistency of hip-knee intralimb coordination. Increases in cadence and stronger-leg step length were correlated with improvements in walking speed.

These results suggest that WBV may represent an approach to decreasing spasticity, and may be useful for individuals in whom spasticity interferes with function. Furthermore, vibration appears to have a beneficial effect on walking function, perhaps by influencing spinal locomotor-generating circuitry.

This dissertation is dedicated to all the wonderful people who supported me throughout this process. Without the encouragement and support of those who believed in this research, this dissertation would not be possible.

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CHAPTER 1: INTRODUCTION: VIBRATION EFFECTS MAY IMPROVE FUNCTION IN INDIVIDUALS WITH SCI

Vibration is a form of afferent input that influences the activity of neural circuits in the spinal cord. The spinal circuits that are known to be influenced by vibration may be one of two types: those circuits that generate involuntary responses to sensory input (i.e., spinal segmental reflexes) and those innate circuits responsible for generation of cyclic, patterned motor output (i.e., central pattern generators; CPGs) underlying innate rhythmic behaviors such as walking, swimming, flying, and scratching.

In individuals with disorders of the central nervous system, there are multiple consequences of disrupted communication between the brain and spinal cord. One consequence is the disruption of descending modulation of spinal reflex circuitry. The disrupted modulation of spinal reflex activity manifests as reflex hyperexcitability. This hyperexcitability contributes to disordered motor output (i.e., spasticity, clonus, spastic gait patterns) and impaired motor function. Peripheral sensory input may activate modulatory systems with effects similar to those of the descending modulatory pathways. By this mechanism, sensory input may mimic the lost descending input, thereby decreasing motor dysfunction and improving functional movement.

In addition to loss of descending modulation of reflexes, the disruption of supraspinal influence also results in impaired activation of CPG circuits. The literature suggests that afferent input in the form of vibration[62] or electrical stimulation[36] may activate spinal circuits associated with the CPG for locomotion. In non-disabled (ND) individuals, vibration applied to the lower extremity has been used to elicit both unilateral air-stepping responses (while subjects are positioned in side-lying) and bilateral air-

stepping (when in an upright non-weight bearing position).[62] In individuals with motor complete SCI, invasive, epidural electrical stimulation has been used to stimulate the lumbrosacral region of the spinal cord to activate the locomotor CPG and elicit cyclic stepping patterns while the subject was in supine position.[36] Similar stimulation has been reported to decrease the effort of walking and increase walking speed in an individual with motor incomplete SCI.[64]

We were also interested in the influence of vibration on walking function. Evidence suggests WBV may be useful in modulating inappropriate muscle contractions after stroke.[107] The use of peripheral afferent stimulus (either in the form of electrical stimulus or vibration) has also been shown to alter the excitability of spinal circuits that are likely to be involved in walking.[28, 50, 88, 89] Periphery sensory stimuli may also be used in combination with motor training to induce spinal plasticity thereby improving motor function.[28] This evidence suggests WBV may be useful to augment improvements in walking function associated with a locomotor training intervention.

This project will focus on two groups of individuals with SCI differing degrees of injury severity: individuals with motor-complete SCI (MCSCI; having no voluntary, motor function remaining below the level of injury), and individuals with motor-incomplete SCI (MISCI; having some remaining voluntary, motor function below the level of injury). These injury severities are determined by the American Spinal Injury Association (ASIA) motor and sensory scores[2] comprise and ASIA Impairment Scale (AIS) classification.[79] According to this classification, in individuals with injuries classified as AIS A, sensorimotor function and anal sensation are absent below the neurological level. Whereas, the AIS B classification includes individuals who have no

motor function but have at least anal sensation below the neurological level. Individuals in the AIS A and AIS B categories are considered to have MCSCI. Individuals with injuries classified as AIS C have sensory and some motor function preserved below the neurological level with voluntary control of the anal sphincter muscle and less than half of the key muscles below the neurological level able to move the limb against gravity. Individuals with injuries classified as AIS D have sensory and motor function preserved, and at least half of the muscles are able to move the limb against gravity. Individuals in the AIS C and AIS D categories are clinically termed MISCI.[2]

Background and purpose

Individuals with SCI often experience a loss or impairment of both sensory and motor function below the level of injury. The impact the injury has on motor function is directly related to the level and severity of the injury. Regaining walking function is a high rehabilitation priority in individuals with SCI.[38] Some individuals with MISCI may be able to improve walking function given the appropriate rehabilitation interventions. To improve walking function after SCI, multiple obstacles must be overcome. As a result of the upper motor neuron injury, mechanisms of reflex regulation are disrupted and movement disorders such as spasms, extensor and flexor tone, spasticity, and clonus impede functional recovery.[102, 103] Innovative combinations of rehabilitation interventions have resulted in increased walking speed in individuals with motor incomplete SCI. Body weight support (BWS), electrical stimulation, and treadmill training are just a few examples of these interventions.[50] The exploration of innovative ways to use low-risk devices in combination therapies is a compelling goal in rehabilitation research related to individuals with motor incomplete SCI.

Spasticity

In non-disabled individuals, descending control modulates afferent input entering the spinal cord. The loss of the modulation results in hyperexcitability of reflex activity and the appearance of reflex-generated motor output most commonly referred to as spasticity. The exact cause of spasticity is currently unknown, but evidence from spinal reflexes provides the basis for these mechanistic theories. The Hoffman reflex (i.e., H-reflex), the electrical analog of the stretch reflex, is used to assess the excitability of the monosynaptic Ia reflex loop and measure changes in excitability of the spinal motoneuron pool that is excited by this reflex. Individuals with spasticity have a larger amplitude of resting H-reflex compared to those individuals without spasticity.[16, 80]

One theory for mechanism underlying the hyperexcitable of spinal reflexes is that decreased supraspinal modulation results in loss of presynaptic inhibition of the Ia inputs. Presynaptic inhibition controls synaptic efficacy by selectively gating sensory information before afferent information reaches the Ia-motoneuronal synapse. This loss of presynaptic inhibitory modulation is thought to result in increased Ia input to the motoneuron such that it responds to even small perturbations of muscle length.[91]

In individuals with SCI, spasticity may cause muscles to contract involuntarily, thereby impeding the ability for an individual to perform movement. Individuals with spasticity often take medications to deter the unwanted muscle contractions. If the anti-spasticity medication is taken orally, the influence of the medications is non-specific to spastic muscles and affects the whole body. The most commonly prescribed medication is baclofen which causes a variety of side effects including sedation, excessive weakness, vertigo, and psychological disturbances.[29] For some individuals with spasticity, side

effects may deter the use of some of medications and alternative non-medication options of reducing spasticity may be preferable.

Walking function and the role of the CPG

For humans with intact nervous systems, walking function requires input from supraspinal centers to initiate, guide, and adapt locomotion. In addition, spinal neural networks, the spinal locomotor CPG, produce rhythmic, patterned motor output subserving locomotion.[115] The CPG is a complex spinal network that produces the rhythm and timing of motor output during walking. In intact animals, the CPG is activated by tonic descending input from supraspinal centers, and uses proprioceptive feedback from sensory afferent input to refine motor performance.[34] This sensory input arises from cutaneous, joint, tendon, ligament and muscle receptors and is transmitted to the central nervous system by sensory nerve fibers.

While the locomotor output generated by spinal CPGs has been well characterized in animal models such as the lamprey,[113, 116] turtle,[49] and cat,[55, 56, 61, 113, 116] the evidence in humans is less direct. Some of the most persuasive evidence of the human CPG has been in experiments with individuals with SCI.[17, 36, 100] Studies of both incomplete[17] and complete SCI reported distinct patterns of involuntary stepping patterns in those with absent or impaired descending control.[36, 100]

Loss or impairment of walking function after SCI

Following a spinal cord injury, and depending on the severity of injury, individuals may experience loss or impairment of walking function. Maladaptive plasticity of the central nervous system and loss of descending control results in impairments such as muscle weakness, impaired balance, muscle stiffness, and impaired

sensation that contribute to walking deficits.[102, 103] Although in most cases, some sensation and motor function below the level of injury returns during the early stages of injury, most individuals with chronic SCI have difficulty with walking function.

Vibration as a possible rehabilitation intervention

Vibration is a non-invasive intervention that is increasingly being used in fitness and rehabilitation settings. With the low cost, ease of access, comfortable application, and FDA non-significant risk device classification, vibration is an attractive intervention that should be explored as an afferent input to modify the excitability of spinal circuitry to decrease spasticity and improve walking function in individuals with lower extremity impairment. Muscle vibration is used in human subjects research to produce reflex contractions[12, 30, 63] and to alter excitability of group Ia afferents.[16]

The vibration paradox

Localized vibration is usually applied to the body of the muscle or to the muscle tendon, imparting a series of rapid, repeated, low amplitude stretches. Because the muscle spindle (the receptor associated with the Ia afferent fiber) is the primary stretch receptor, vibration is a powerful stimulus to activate this receptor. Figure 1.1 illustrates how vibration input results in a paradoxical response[30, 33, 45] that may have implications for function. Vibration is known to elicit both excitatory and inhibitory influences on spinal reflex activity, resulting in a phenomenon called "the vibration paradox."[33] Excitatory influences are in the form of the tonic vibration reflex (TVR), a tonic muscle contraction arising from activation of muscle spindle afferents in the vibrated muscle. However, in individuals with SCI, the TVR may be absent or attenuated.[63] Vibration also activates inhibitory influences, thought to be due to presynaptic inhibition[42, 59, 96, 97] or

depletion of neurotransmitter,[3, 47, 67, 71, 74, 84] that result in a reduction of the excitatory Ia influences on the homonymous motoneuron.[33]

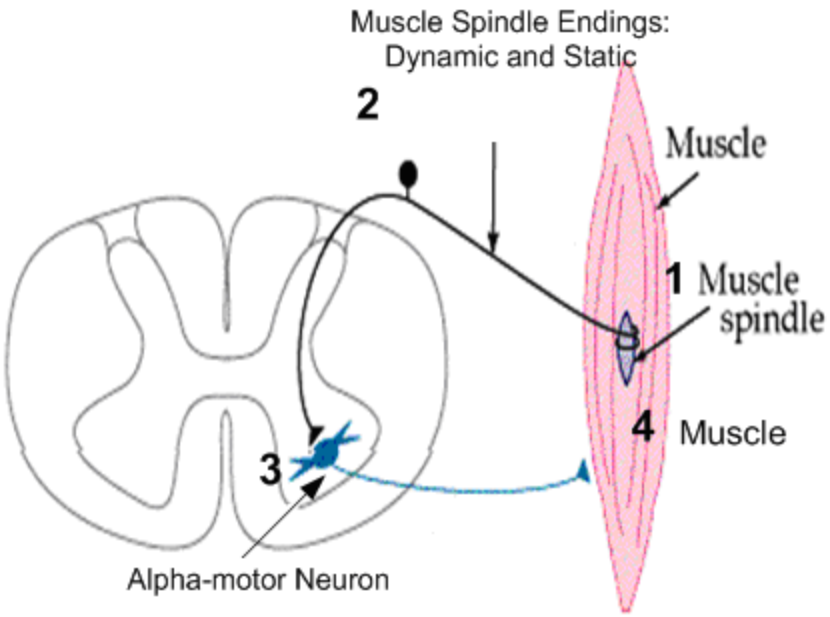

Figure 1.1: The Vibration Paradox. Vibration of a muscle or tendon results in a contraction of a homonymous muscle (TVR) and a depression of the Hoffman reflex.[33] Vibration can be used to increase muscle activity[32, 94] by exciting Ia reflex input. One result of this excitation is the TVR. The Hoffman reflex depression[11, 16] suggests that vibration modulates spinal stretch reflex excitability that may cause spasticity.

Functional implications of the influence of vibration on muscle activation

Vibration can be used to increase muscle activity[32, 94] by exciting Ia reflex input. This increase in muscle activity has been suggested to be the underlying mechanism for increased muscle strength.[32] In individuals who have loss of muscle strength as a result of SCI, vibration may be beneficial in improving muscle strength. However, this dissertation did not focus on the effects of WBV on muscle strength.

Functional implications of the influence of vibration on H-reflex

The mechanism for decreased amplitude of the H-reflex as a response to vibration is still under debate. The first mechanistic explanation is that vibration may result in an increase in presynaptic inhibition as previously described.[42, 59, 96, 97] Because vibration is a volley of afferent information, neurotransmitter depletion caused by the repetitive activation of the Ia motoneuron synapse is an alternative mechanism explanation.[3, 47, 67, 71, 74, 84] Vibration can depress the H-reflex[11, 16] suggesting that vibration modulates spinal stretch reflex excitability that may cause spasticity. Therefore, in individuals who have spasticity that interferes with walking function, vibration may decrease spasticity and thereby improve walking function.

Functional implications for the influence of vibration on the CPG

In addition to modulatory effects of spinal reflex activity, vibration is also known to elicit involuntary stepping responses when applied to the muscles of the leg. Gurfinkel et al.[62] demonstrated that air-stepping movements could be elicited by vibrating leg muscles in non-disabled individuals. Subjects were positioned in a gravity-minimized side-lying position with a single leg suspended by supports at the thigh and the shank to allow movement in the horizontal plane. Stepping-like movements were elicited when vibration was applied to various muscles of the leg. To rule out a series of TVRs as the mechanism underlying unilateral locomotor movements, vibration was applied to an immobilized, single leg and contralateral locomoto-like movements were found. These findings suggest that afferent input in the form of vibration activates bilateral mechanisms underlying cyclic behavior, and supports the hypotheses that vibration increased excitability of central neural structures and activates the locomotor CPG.[62]

Whole-body Vibration

The use of whole-body vibration (WBV) to increase muscle strength[9, 31, 46, 94] and improve specific task performance[9, 31] has been a recent trend in the fitness literature. In addition to indications that WBV has an effect on these movement-related variables, there is also evidence that WBV may have beneficial effects on some aspects of function in older individuals[4, 8, 72] as well as in some clinical populations of individuals with disability.[1, 58, 111, 112]

In adults with spastic diplegia due to cerebral palsy, an 8-week intervention of WBV has been associated with improvements in muscle strength.[1] Clinical results also suggested WBV reduces spasticity of the knee extensors as measured using the modified Ashworth scale, and improvements in tasks such as standing, walking, running, and jumping as assessed with the Gross Motor Function Measure.[1] In individuals with chronic, ischemic stroke, an improvement in functional balance was found immediately following a single session of WBV consisting of four 45-second bouts with one minute rest period between bouts. When the same balance tests were performed 45 minutes later, some of these improvements in balance persisted, although some of the influence of the WBV diminished when compared to the test results immediately following the bouts of WBV.[111] In individuals with acute stroke, a 6-week intervention of WBV improved clinical measures of balance, mobility, and sensation.[112] However, the improvements were not different compared to an alternative intervention. In individuals with acute stroke due to infarction and hemorrhage, a single session of WBV transiently increased maximum voluntary strength and EMG activity of the vastus lateralis muscle. In

addition, there was a significant decrease in co-activation of the vastus lateralis and biceps femoris muscles during isometric and eccentric contractions.[107]

The results from these studies suggest that WBV may be a useful intervention to reduce spasticity and improve walking performance in individuals with SCI. In individuals with SCI who were unable to stand without long-leg braces, a case series reported in a published abstract found that the use of WBV evoked reflex-induced standing, and subsequently some of the individuals were able to progress to walking.[58] More extensive evidence in the SCI population will provide valuable information about the influence of vibration on excitability of the spinal reflexes and spinal circuits underlying locomotor output.

The overall objective of this project was to investigate innovative ways of using vibration to reduce abnormal spinal reflex activity and to facilitate the recovery of walking function after spinal cord injury (SCI). This project focuses on two types of vibration interventions used for different purposes: localized vibration placed on the leg to activate spinal locomotor circuitry, and whole-body vibration (WBV) intended to modulate spinal reflex activity and thereby influence reflex excitability and walking function. The goal is to characterize how each of these forms of vibratory input influence spinal circuitry related to spasticity and walking function.

Experiment 1: Vibration Elicits Involuntary Air-stepping in Individuals with Spinal Cord Injury

The purpose of Experiment 1 was to determine if vibration can be used to elicit air-stepping responses in individuals with SCI, as has been observed in ND individuals, and to quantify differences in these responses. The hypothesis of this experiment is based on evidence that the spinal locomotor circuits remain active even after SCI.[13, 14, 17,

[36] We presumed that, like other neural circuits, these circuits would be strengthened and maintained through use,[122] and we predicted that the strength of the locomotor CPG outputs would there be dependent on the extent to which the spinal networks were used. Because of this use-dependent relationship, we predicted that individuals who made more frequent use of CPG spinal circuitry would have more consistent and more robust responses when compared to responses from a muscle that had a more postural function. We also predicted that vibration placed on extensor and flexor muscles that are critical to walking function would elicit the most consistent and robust responses when compared to muscles that are not involved in flexor or extensor activity. Kinematic data from 3D motion capture were used to measure hip and knee angles associated with the cyclic leg movements elicited by vibration of the quadriceps, hamstring, or tensor fascia latae (TFL) muscles. Consistency was defined as the agreement of the relative intralimb hip angle-to-knee angle position, which represents coordination over multiple vibration-elicited air-stepping cycles. Robustness was defined as the area of the space circumscribed by the air-step cycle, which represented the magnitude of the hip-knee movement during the vibration-elicited air-stepping cycles. The values of consistency and robustness were used to address the following aims:

Aim 1a: **Quantify the influence of severity of SCI on the consistency and robustness of the vibration-elicited air-stepping responses.** We hypothesized that individuals with remaining, voluntary motor function (MISCI group) would have a more consistent and more robust response when compared to those without remaining, voluntary motor function (MCSCI group).

Aim 1b: **Identify the placement of the vibration that elicits the most consistent and robust vibration-elicited air-stepping response.** We hypothesized that vibration placed on either the quadriceps or the hamstring muscles would elicit more consistent and more robust responses than would vibration of the TFL muscle.

Aim 1c: **Quantify the differences in the consistency and robustness of the vibration-elicited air-stepping responses between ND individuals and individuals with SCI.** We hypothesized that the responses of ND individuals would be more consistent and more robust when compared to responses of individuals with SCI.

Aim 1d: **Quantify the influence of locomotor training on the consistency and robustness of the vibration-elicited air-stepping response in individuals with SCI.** We hypothesized that individuals who participated in this training intervention would have a more consistent and more robust post-training response compared to those individuals who did not participate in the locomotor training intervention.

Aim 1e: **Quantify the influence of vibration history on the consistency and robustness of the vibration-elicited stepping-responses.** We hypothesized that with repeated test sessions those individuals who used their CPG spinal circuitry between test sessions would have similar consistency and robustness of the vibration-elicited stepping-response.

Experiment 2: Whole-body Vibration Reduces Quadriceps Spasticity in Individuals with Spinal Cord Injury

The purpose of Experiment 2 was to quantify the effect of WBV on quadriceps muscle spasticity in individuals with chronic, motor-incomplete SCI as measured by changes in spinal stretch reflex (SSR) excitability. Subjects were tested before and after participation in a 3 day/week, 12-session intervention of WBV. Weekly testing was also performed to assess differences between immediate and delayed within-session effects. Responsiveness of the quadriceps muscle to a gravity-provoked muscle stretch (i.e., the Pendulum Test) was used as a measure of SSR excitability. We operationally defined a decrease (or improvement) in spasticity as an increase in the first swing excursion (FSE) of the Pendulum Test. The following aims were addressed:

Aim 2a. **Quantify the change in SSR excitability before and after a 12-session intervention of WBV.** We hypothesized that there would be a reduction in quadriceps spasticity after a 12-session intervention of WBV.

Aim 2b. **Quantify the immediate and delayed change in SSR excitability following a WBV session.** We hypothesized that the within-session effects would be such that less spasticity would be observed in the immediate post-WBV test compared to the delayed post-WBV test.

Aim 2c. **Quantify the differences in response to the WBV intervention between individuals who used antispastic agents and those who did not.** We hypothesized that the individuals who reported daily use of antispastic agents would experience a smaller reduction in quadriceps spasticity associated with the WBV intervention when compared to those who reported no use of antispastic

agents. If antispastic agents are capable of reducing spasticity to the fullest extent possible, then there should be no further WBV-induced reduction in spasticity in those who used these agents.

Experiment 3: Whole-body Vibration Improves Walking Function in Individuals with Spinal Cord Injury

The purpose of Experiment 3 was to quantify the effect of WBV on walking function associated with a 12-session intervention of WBV. Analysis of 3D kinematic gait data captured as subjects performed a 10-meter walk was used to quantify walking function. The primary outcome measure was walking speed. Secondary gait characteristics of cadence, step length, and consistency of hip-knee intralimb coordination were also quantified. The outcome measures from the kinematic gait analysis were used to address the following aims:

Aim 3a. **Quantify the influence of a 12-session intervention of WBV on the walking function.** We hypothesized that walking function would improve after a 12-session intervention of WBV.

Aim 3b. **Quantify walking characteristics related to changes in walking speed associated with the 12-session intervention of WBV.** We hypothesized that gait characteristics would improve after a 12-session intervention of WBV.

CHAPTER 2: EXPERIMENT 1: VIBRATION ELICITS INVOLUNTARY, AIR-STEPPING IN INDIVIDUALS WITH SPINAL CORD INJURY

The pattern and timing of innate cyclic behaviors such as walking are generated by neuronal networks in the spinal cord. In non-human animals, these networks, or central pattern generators (CPGs), produce well-coordinated movements that are highly reproducible.[48, 49, 55, 55] Humans are thought to have similar organization of spinal circuitry [17, 35, 39, 40, 76] such that the locomotor output is largely produced by circuits in the lumbrosacral region of the spinal cord.[20, 36, 54] After a spinal cord injury (SCI), one consequence of disrupted communication between the brain and the spinal cord is impaired activation of the spinal locomotor CPG.

Proprioceptive input that has access to rhythm-producing CPGs has been demonstrated in a variety of animal models.[49, 60, 86] However, there is limited evidence of about the effects of afferent stimulation (i.e., vibration) on the locomotor pattern-generating circuitry in humans.[17, 62] In individuals with motor-complete SCI, invasive, epidural electrical stimulation to the lumbrosacral region of the spinal cord has been shown to elicit cyclic stepping patterns while the subject is in supine.[36] In individuals with motor-incomplete SCI, epidural stimulation to the lumbar enlargement has been suggested to improve walking function.[64]

When non-disabled (ND) individuals are positioned in side-lying and muscle vibration is applied at the quadriceps, hamstrings, or the tensor fascia latae (TFL) muscles, cyclic locomotor-like single-leg movements are elicited. Vibration to the contralateral limb muscles also elicits similar single-leg movements. Quadriceps muscle vibration applied to both legs elicits bilateral leg movements while subjects are in an upright, suspended position.[62]

This evidence suggests that continuous muscle vibration increases excitation from central structures that creates conditions that activate involuntary stepping.[62] Also in ND individuals, continuous vibration applied to either the quadriceps or hamstring muscles has been shown to increase walking speed depending on the combination of direction of progression and vibration placement.[68] Given evidence that continuous vibration to leg muscles in ND individuals elicits involuntary stepping responses that are thought to arise from activation of CPG circuitry, and that these spinal circuits are likely to remain intact following SCI, it is feasible that vibration may also elicit involuntary responses in individuals with SCI.

The primary objective of this study was to determine if vibration can elicit air-stepping responses in individuals with SCI (similar to that observed in ND individuals), to quantify these responses, and to assess the influence of the site of vibration in individuals with SCI that elicited the most robust and consistent response. We hypothesized that vibration to muscles that participated in the generation of stepping (either the quadriceps or the hamstring muscles) would elicit more robust and consistent responses than would vibration of a muscle that functioned primarily to stabilize the pelvis (the TFL).

Based on evidence that the spinal circuits are strengthened and maintained through use,[28, 43, 44, 119-121] we hypothesized that the strength of the locomotor CPG outputs would be dependent on the amount the spinal networks were used. Because of this use-dependent relationship, we expected that ND subjects (who routinely use their CPG spinal circuitry during walking) would have more consistent and more robust responses when compared to subjects with SCI who do not (as these subjects use a

wheelchair a their primary means of mobility). When considering the influence of severity of SCI on the response, we hypothesized that subjects with SCI who had remaining motor function (i.e., motor-incomplete SCI [MISCI]) in the lower extremities would have more consistent and more robust responses when compared to those without remaining motor function (i.e., motor-complete SCI [MCSCI]). We also hypothesized that those who participated in locomotor training (LT-MISCI) would have more robust and consistent responses as they would be using their CPG circuitry to a greater extent compared to those who did not participate in locomotor training (Control SCI). Finally, we quantified the influence of vibration history and hypothesized that in subjects who did not change their walking habits, the consistency and robustness of the vibration-elicited stepping-responses would be stable over time, such that there would be no change in these measures over two or more test sessions.

Methods

Subjects. Nineteen subjects with SCI and eight ND subjects (11 women, 16 men; ages 19-65) participated in this study. All subjects gave written and verbal informed consent to a protocol approved by the Human Subjects Research Office at the University of Miami, Miller School of Medicine. For the subjects with SCI, the subject inclusion criterion was chronic ($\geq$ 1 year duration) SCI at or above the level of T10. American Spinal Injury Association (ASIA) motor and sensory scores,[2] and ASIA Impairment Scale (AIS) classification[79] were evaluated by a physical therapist who was not otherwise involved in the study. The weaker leg was used as the test leg in subjects with asymmetrical lower extremity motor scores while the non-dominant leg was used as the test leg in both ND subjects and subjects with SCI who had symmetrical motor scores.

Information about the amount of walking that each subject performed per week was recorded prior to participation in the study.

All subjects were first grouped into one of three categories according to motor function status. The ND group (n=8) included subjects with no known neurological impairment. The motor-complete SCI group (*MCSCI*; AIS A or B; n=6) included subjects who had no voluntary motor function below the level of injury. The motor-incomplete SCI group (*MISCI*; AIS C or D; n=13) included subjects who had some preservation of sensory and voluntary motor function below the level of the lesion.

Of those subjects with MISCI, subjects were placed in one of two groups. The *LT-MISCI* (n=6) group included subjects who would concurrently be participating in body weight supported locomotor training five days per week for 10-12 weeks (for details related to training see Field-Fote et al., 2005).[52] The *Control MISCI* group (n=7) included subjects who did not participate in a locomotor training intervention. Demographic data for the subjects is given in Table 2.1.

Table 2.1: Subject Demographic Table. American Spinal Injury Association (ASIA) motor and sensory scores,[2] and ASIA Impairment Scale (AIS) classification[79] was used to classify subjects with spinal cord injury (SCI) into motor-incomplete SCI (MISCI) and motor-complete SCI (MCSCI) groups. The MISCI intervention group (LT-MISCI) included subjects participating in a locomotor training intervention and the Control MISCI group who did not participate in locomotor training.

Group/Subject Number	Gender	Age	Injury Level	AIS
ND 1	F	26	N/A	N/A
ND 2	F	24	N/A	N/A
ND 3	F	30	N/A	N/A
ND 4	F	25	N/A	N/A
ND 5	M	26	N/A	N/A
ND 6	M	23	N/A	N/A
ND 7	F	54	N/A	N/A
ND 8	M	35	N/A	N/A
Control MISCI 1	M	55	T7	D
Control MISCI 2	M	48	C5-C6	C
Control MISCI 3	M	62	C6	C
Control MISCI 4	M	41	C5-C6	C
Control MISCI 5	F	57	T6	C
Control MISCI 6	F	45	C4-C5	C
Control MISCI 7	M	53	C6	C

LT-MISCI 1	F	40	T10	C
LT-MISCI 2	M	30	C5-C6	C
LT-MISCI 3	M	33	T4-T5	C
LT-MISCI 4	M	50	T5-T8	C
LT-MISCI 5	M	47	C5-C6	C
LT-MISCI 6	M	20	C6	C
MCSCI 1	M	19	C7	B
MCSCI 2	F	46	T2-T3	B
MCSCI 3	F	49	C4-C7	B
MCSCI 4	M	33	C6	B
MCSCI 5	M	52	T5-T6	A
MCSCI 6	F	51	C7	B

Testing Procedure. For the purpose of collecting kinematic data, nine reflective markers were placed at the following points: C7, T10, sacrum, and on the test leg at the anterior superior iliac spine, trochanter, lateral knee joint line, lateral malleolus, lateral heel, and lateral 5th metatarsal head. Data was collected at 60 Hz using an 8-camera, 3D motion capture system (Peak Motus® Software, Peak Performance, Centennial, CO) in a calibrated test space.

Subjects were tested in a side-lying, gravity-minimized position on a padded table similar to previous studies.[62, 100] All subjects were secured to the table by a strap to ensure safety and to minimize the amount of trunk movement during leg movements. The test leg was suspended at a shoulder width distance apart by two straps, one placed at

the shank (above the ankle joint) and the other placed at the thigh (above the knee joint) so that the joints were not impeded. The height of the suspending straps was carefully adjusted to maintain the leg in neutral abduction/adduction. This positioning permits cyclic leg motion under conditions that reduce the influence of gravity. Subjects were blinded as to the purpose of the study being measurements of involuntary, air-stepping movements. An example subject with SCI in the testing position can be seen in Figure 2.1.

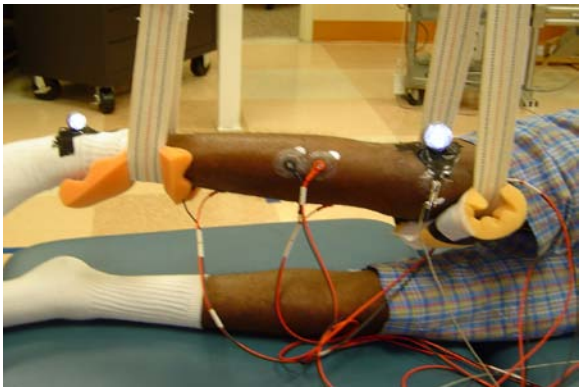

Figure 2.1: Individual with SCI in gravity-minimized side-lying position. This position permits cyclic movement under conditions that reduce the influence of gravity.

A 6.6 pound, hand-held vibrator (Pro-Massager USJ-301, U.S. Jaclean, Inc. Gardena, CA, USA; seen in Figure 2.2) was used to deliver vibration to target a specific leg muscle. The vibration was given at the frequency of 60 Hz with an unloaded amplitude of approximately 1 mm.

Figure 2.2: Hand-held vibrator. This device (Pro-Massager USJ-301, U.S. Jaclean, Inc. Gardena, CA, USA) was used to deliver vibration to target a specific leg muscle. The vibration was given at the frequency of 60 Hz with an unloaded amplitude of approximately 1 mm.

Each testing session consisted of five trials. In two trials subjects performed, or attempted to perform, voluntary air-stepping. The voluntary air-stepping trials were: forward air-stepping (to simulate forward walking; *volFW*) and backward air-stepping (to simulate backward walking; *volBW*). These voluntary air-stepping trials were used to ensure range of motion of the hip and knee joints was unrestricted in the test position. All subjects, including those with MCSCI, were asked to attempt voluntary air-stepping. Three trials consisted of involuntary, air-stepping elicited by vibration were recorded during vibration to each of three muscles: the quadriceps (*Qvib*), the hamstrings (*Hvib*), or the tensor fasciae latae (*TFLvib*). During involuntary, air-stepping trials, subjects were instructed to relax and, if they perceived movement, not to intervene. In all testing sessions, volFW and volBW were collected first, whereas, the sequence of the vibration trials was randomized for each test session to counter any possible effects of order of muscle vibration. During vibration-elicited air-stepping trials, vibration was applied to the belly of the target muscle for five minutes prior to the start of kinematic data collection and vibration to the muscle was maintained throughout the duration of the 30

second kinematic data capture period. This five minute time period was chosen to ensure that the response was in steady state during the data collection.

Six ND subjects and all 19 subjects with SCI participated in a minimum of two test sessions. For subjects in the LT-MISCI group, testing was performed prior to participation in the locomotor training program (*initial*) and after 10-12 weeks of locomotor training (*final*). For all other subjects, the initial and final test sessions were separated by the same 10-12 week duration to provide control comparisons. In some subjects, a follow-up test session was performed to assess the influence of vibration history on the stability of these measures. Subjects in the Control MISCI group and two subjects in the MCSCI group returned for the follow-up test 10-12 weeks following the second test session.

Data analysis. Air-stepping parameters were calculated from measures defined by the joint markers, with the hip angle defined by the trunk and thigh segments, and the knee angle defined by the thigh and shank segments. Kinematic joint angle data were filtered using a Butterworth filter with a 6 Hz cutoff. The relative motion plots of the hip and knee angles from each trial were used to quantify the consistency and the robustness of the responses. An example relative motion plot of the response during vibration to the TFL can be seen in Figure 2.3. These diagrams have been used to illustrate features that distinguish intralimb coordination between normal and pathological gait [21] and to assess cycle-to-cycle consistency of intralimb coupling relationships in cyclic behaviors such as locomotion.[53, 99, 106, 118] Analysis of the consistency over multiple cycles has been suggested to offer insights on the control mechanisms underlying coordination of cyclic behavior.[53, 106]

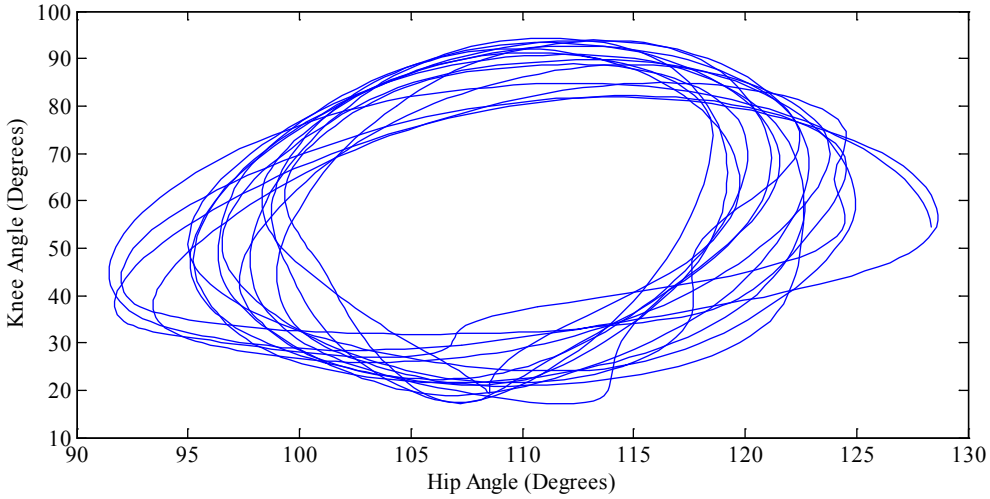

Figure 2.3. Relative motion plot of the hip and knee angles over multiple, involuntary air-step cycles. This example plot represents multiple, involuntary air-step cycles elicited by vibration to the tensor fascia latae. These plots were used to determine outcome measures of consistency (ACC) and robustness (AREA).

To quantify consistency and robustness of the vibration-elicited air-stepping responses, individual air-step cycles were identified; the onset of a cycle was defined as the frame of maximum hip flexion, with the end of the cycle defined by the frame preceding the subsequent maximum hip flexion frame. The total number of cycles was determined for each trial and used to calculate the mean number of kinematic frames per cycle within each trial. A spline interpolation was used to normalize all cycles to N number of frames per cycle. Figure 2.4 illustrates these calculations performed prior to quantifying consistency and robustness of the response.

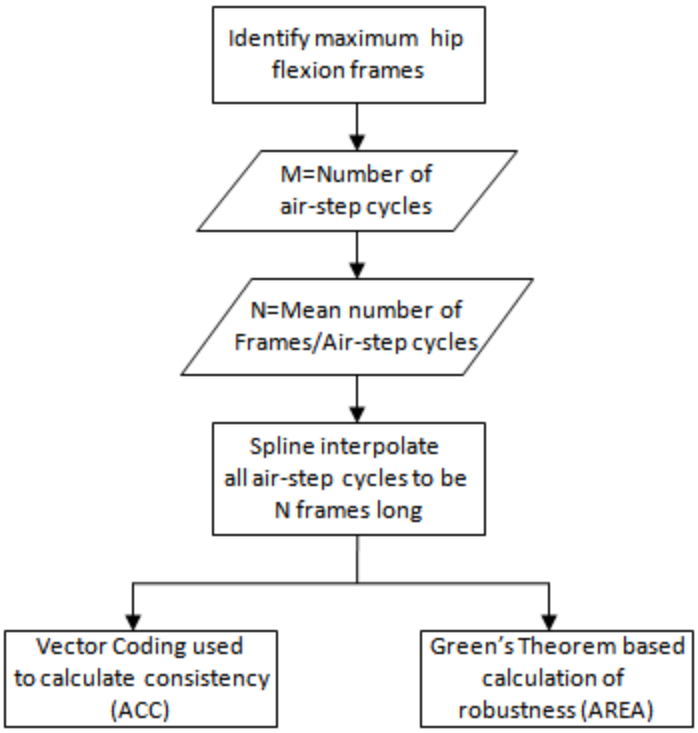

Figure 2.4: Calculations for each relative motion plot. This series of calculations were performed (example illustrated in Figure 2.3) prior to quantification of consistency (ACC) and robustness (AREA).

Consistency was defined as the repeatability of hip angle-to-knee angle coupling relationship over multiple cycles, which represents the strength of the interlimb coordination. Consistency was quantified using vector coding as seen in Figure 2.5, wherein the extent to which the hip angle-to-knee angle relationship is reproduced over multiple cycles is represented by the angular component of the coefficient of correspondence (ACC; 0= no consistency among cycles, 1= absolute consistency among cycles).[53, 106] In subjects with SCI, changes in the ACC value correlates well with improvements in walking function associated with locomotor training.[53] A larger value

of ACC was interpreted as a more consistent (less variable) intralimb hip-knee angle relationship in the vibration-elicited air-stepping response.

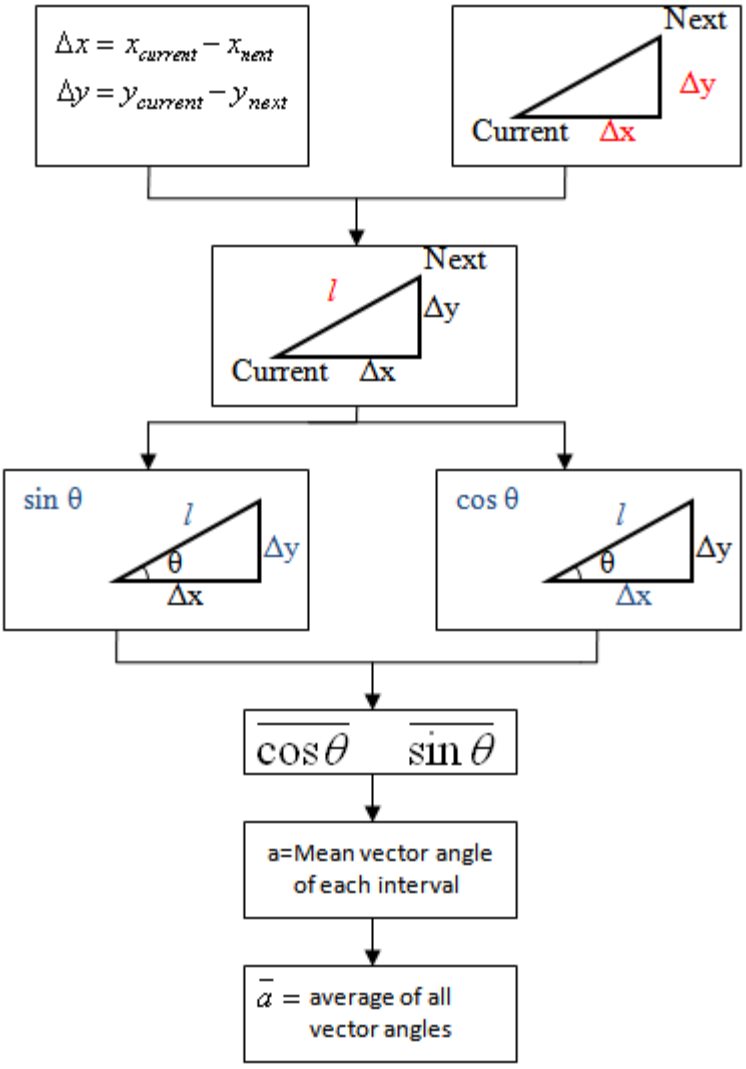

Figure 2.5. Vector Coding Flow Diagram. From relative motion plots (example illustrated in Figure 2.3), vector coding was used to defined the consistency (ACC) of intralimb coordination of the hip-knee coupling over mutliple air-step cycles.

For each interpolated air-step cycle, starting at the beginning of an air-step cycle, the difference was found between each current and subsequent frame (next) of the hip

(Δx) by Equation 2.1 and knee (Δy) found by Equation 2.2, and two orthogonal line segments (one for each hip and knee) were created from with lengths Δx and Δy .

$$\Delta x = x_{next} - x_{current} \qquad (2.1)$$

$$\Delta y = y_{next} - y_{current} \qquad (2.2)$$

The magnitude (*l*) between the two line orthogonal segments was calculated by Equation 2.3.

$$l_{next,current} = \sqrt{\Delta x^2 + \Delta y^2} \qquad (2.3)$$

The sine and cosine was then determined for the angle θ as found by Equations 2.4 and 2.5 and seen in Figure 2.5. These trigonometric functions were used to represent the frame-to-frame dispersion between the frame pairs of the relative motion plot. This process was repeated for N frame-to-frame intervals (until the end of the air-step cycle).

$$\cos\theta_{next,current} = \Delta x / l_{next,current} \qquad (2.4)$$

$$\sin\theta_{next,current} = \Delta y / l_{next,current} \qquad (2.5)$$

Over M air-step cycles, frame-to-frame intervals were averaged ($\overline{\cos\theta}, \overline{\sin\theta}$) by Equations 2.6 & 2.7.

$$\overline{\cos\theta}_{next,current} = \frac{1}{M}\sum_{i=1}^{M}\cos\theta_i \qquad (2.6)$$

$$\overline{\sin\theta}_{next,current} = \frac{1}{M}\sum_{i=1}^{M}\sin\theta_i \qquad (2.7)$$

Next, the length of the mean vector (a) denoted the dispersion of the knee and hip angle values over M air-steps for a single frame-to-frame interval was calculated by Equation 2.8.

$$a_{next,current} = \sqrt{(\overline{\cos\theta})^2 + (\overline{\sin\theta})^2} \qquad (2.8)$$

Finally, the arithmetic average of all the mean vector lengths ($\bar{a}$) was calculated by Equation 2.9. The value of $\bar{a}$ was the angular component of the coefficient of correspondence (ACC).

$$\bar{a} = \frac{1}{N}\sum_{i=1}^{N-1} a_{i,i+1} \qquad (2.9)$$

The mean hip angle and knee angle values of corresponding frames over all defined air-steps was calculated resulting in a single mean air-step cycle for each trial.

Equation 2.10 was used to determine the hip frames for a meaned air-step ($air\text{-}step_{avg,hip}$) and Equation 2.11 was used to determine the knee frames for a meaned air-step ($air\text{-}step_{avg,knee}$). By plotting the corresponding $air\text{-}step_{avg,hip}$ as the x coordinate $air\text{-}step_{avg,knee}$ as the y coordinate, a resulting average air-step ($air\text{-}step_{avg}$) was found. An example of $air\text{-}step_{avg}$ is illustrated in Figure 2.6.

$$air-step_{avg,hip} = \frac{1}{M}\sum_{i=1}^{N} x_i \qquad (2.10)$$

$$air-step_{avg,knee} = \frac{1}{M}\sum_{i=1}^{N} y_i \qquad (2.11)$$

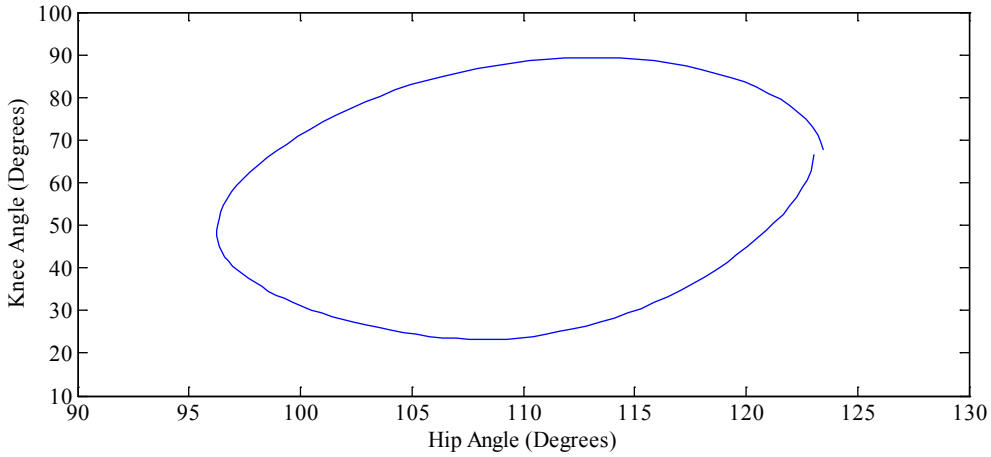

Figure 2.6. Average of multiple air-step cycles. This is an example of an average air-step cycle (air-step$_{avg}$) calculated from the example in Figure 2.3. Corresponding frames were averaged over all defined air-steps.

For each trial, air-step$_{avg}$ was used to quantify range of motion at the hip (hip_{ROM}) and knee ($knee_{ROM}$). Robustness was defined as the area of the space circumscribed by the step cycle, which represents the size of the hip-knee movement. To quantify the robustness of the air-stepping response, the net area (*AREA*; degrees squared) of the *air-step*$_{avg}$, was computed using Green's Theorem. Green's Theorem has two primary requirements: 1) a two-dimensional shape and 2) a closed loop (the beginning frame must equal the end frame). For cycles wherein the air-step$_{avg}$ did not meet the latter of the Green's Theorem requirements, the loop was closed by joining the first and last frame and the AREA was then computed. The resulting closed average air-step meets the Green's Theorem requirements and the net area was found by Equation 2.12. A larger value of AREA was interpreted as a more robust air-step.

$$NetArea = \sum_{i=1}^{M} (y_i \Delta x - x_i \Delta y) / 2 \qquad (2.12)$$

where, $\Delta x = x_{i+1} - x_i$ and $\Delta y = y_{i+1} - y_i$

Furthermore, in case of self crossing loops, Green's method is valid for determining net area as long as the criterion is met, but each intersection of must be considered as separate area regions.

From each *air-step*$_{avg}$, joint range of motion (ROM) of the hip and the knee were used to validate the AREA values. The hip joint range of motion ($hip_{\overline{ROM}}$) was defined as the difference from hip flexion (hip_{max}) to hip extension ($hip_{min)}$ by Equation 2.13.

$$hip_{\overline{ROM}} = hip_{\max} - hip_{\min} \qquad (2.13)$$

Similarly, ROM of the knee ($knee_{\overline{ROM}}$) was defined as the difference from hip flexion ($knee_{max}$) to hip extension ($knee_{min)}$ by Equation 2.14. An example of $hip_{\overline{ROM}}$ and $knee_{\overline{ROM}}$ can be seen in Figure 2.7.

$$knee_{\overline{ROM}} = knee_{\max} - knee_{\min} \qquad (2.14)$$

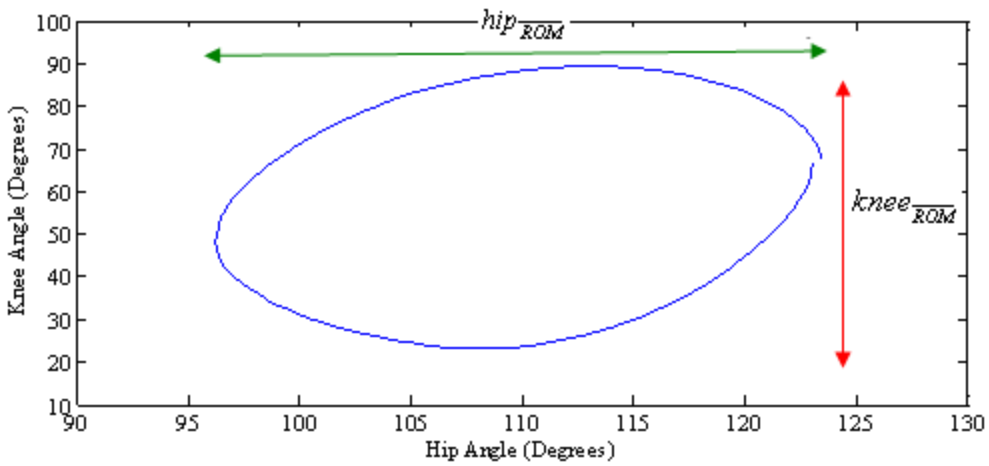

Figure 2.7. Range of motion for the hip and the knee. Example of range of motion for the hip (green arrow; $hip_{\overline{ROM}}$) and the knee (red arrow; $knee_{\overline{ROM}}$) for the example illustrated in Figure 2.6. The values of $hip_{\overline{ROM}}$ and $knee_{\overline{ROM}}$ were used to validate the methods for calculating of robustness (AREA).

Statistical Analysis. Statistical Package for the Social Sciences 15.0 (Chicago, IL) was used for all statistical analyses. Significance was set at α=0.05 except where adjustments were made for multiple comparisons.

We first established the validity of the AREA value as a measure of robustness of the air-stepping responses using a Pearson correlation to assess the strength of the relationship between AREA and hip_{ROM} and between AREA and $knee_{ROM}$. High correlation between these measures would indicate that the AREA value accurately represents, within a single value, the excursion of both the hip and the knee during the air-stepping cycles.

For analyses that had small and unequal sample sizes that did not meet the requirements of homogeneity of variance needed for use of parametric tests, comparisons were made using non-parametric statistical tests. To identify differences in the consistency of the vibration-elicited air-stepping responses due to degree of remaining

descending control in individuals with SCI, Mann-Whitney U Tests were used to compare initial ACC values for the three muscle vibration sites (Qvib, Hvib, or TFLvib) between the MISCI (n=13) and MCSCI (n=6) groups. Robustness was tested in the same manner, based on the initial AREA values. In both cases, a Bonferroni correction was performed to adjust the significance level for the 3 pair-wise comparisons, resulting in an adjusted significance level of α=0.017. This testing identified no between-groups differences (see Results), therefore, data from the MCSCI and the MISCI groups were pooled for all further comparisons.

To assess the influence of the site of vibration, the initial ACC and AREA values were compared for the three muscle vibration sites (Qvib, Hvib, or TFLvib) for subjects with SCI. This testing identified the TFL vibration to be the site of vibration (see Results). Therefore, all further comparisons were made based on the ACC and AREA values obtained from the TFLvib. To quantify differences between the responses of ND subjects and subjects with SCI, values of the initial ACC and AREA for all subjects with SCI (n=19) and ND subjects (n=8) were compared using Mann-Whitney U Tests.

To determine whether the consistency or robustness of the air-stepping responses were influenced by locomotor training, data obtained from subjects who participated (LT-MISCI; n=6) in locomotor training were compared to those who did (Control MISCI and MCSCI pooled; n=13). Mann-Whitney U Tests were used to compare the change in ACC values and to compare the change in AREA values from initial to final test sessions.

To determine the stability of these responses, the influence of vibration history on the consistency and robustness of the air-stepping responses was assessed. ACC and AREA values from the initial test were compared to those from final test for all subjects

with SCI (n=19) and ND subjects (n=6) using one-tailed, paired t-tests. Descriptive statistics were used to characterize the data obtained from subjects who participated in a follow-up test session (n=5) relative to data from the initial and final test sessions.

Results

All subjects with SCI demonstrated air-stepping responses to vibration, as did ND subjects. Relative motion plots of the hip and knee angle and air-step$_{avg}$ for a single subject from each of the ND, MISCI, and MCSCI groups are illustrated in Figures 2.8a, 2.8b, and 2.8c.

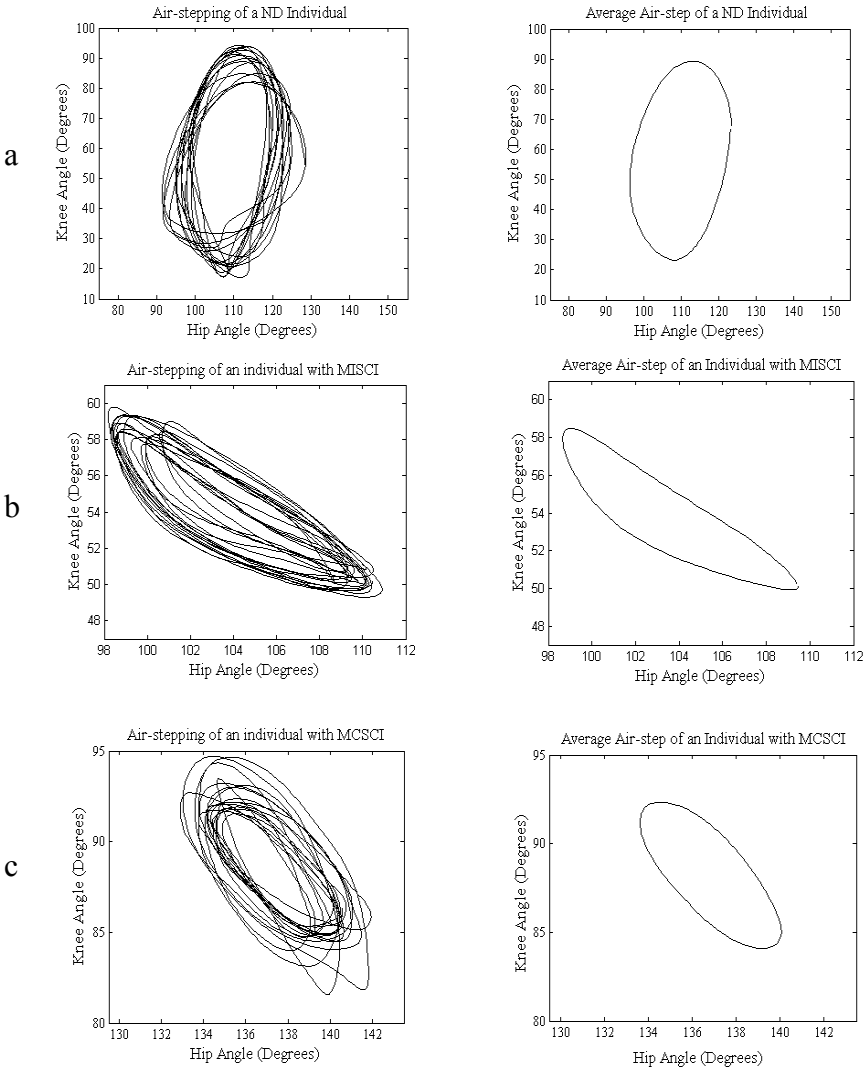

Figure 2.8: Examples of relative motion of hip-knee intralimb plots and average air-step cycles (air-step$_{avg}$). a) non-disabled (ND) individual b) Example relative motion of hip-knee intralimb plot and air-step$_{avg}$ of an individual with motor incomplete spinal cord injury (MISCI) c) Example relative motion of hip-knee intralimb plot and air-step$_{avg}$ of an individual with motor complete spinal cord injury (MCSCI)

There was an excellent [92] correlation between the AREA values and the respective measures of initial hip$_{ROM}$ and knee$_{ROM}$ with all correlations being r=0.865 or

greater, validating AREA is as measure of the combined excursion of both the hip and the knee during the air-stepping cycles. The Pearson correlation matrix for each muscle vibration site is given in Table 2.2.

Table 2.2: Pearson Correlation Values of robustness (AREA) with respective hip (hip_{ROM}) and knee ($knee_{ROM}$) range of motion measures for vibration to the quadriceps (QVib), hamstring (HVib), and tensor fascia latae (TFLVib) muscles.

	Qvib AREA	Hvib AREA	TFLvib AREA
hip_{ROM}	0.865	0.927	0.940
$knee_{ROM}$	0.948	0.902	0.943

There was no significant between-groups difference identified in the comparison of the vibration-elicited air-stepping responses between the MISCI and MCSCI groups for the initial ACC values at any of the vibration sites, including Qvib ($p=0.184$), Hvib ($p=0.208$), and TFLvib ($p=0.320$). There was also not a significant difference between groups for the initial AREA values at any of the vibration sites, including Qvib ($p=0.290$), Hvib ($p=0.162$), and TFLvib ($p=0.351$). ACC and AREA values for the vibration-elicited air-stepping responses of subjects with MISCI and MCSCI are illustrated in Figures 2.9a and 2.9b and Table 2.3. The finding of no between-group differences between MISCI and MCSCI permitted pooling of data across all subjects with SCI for all further comparisons.

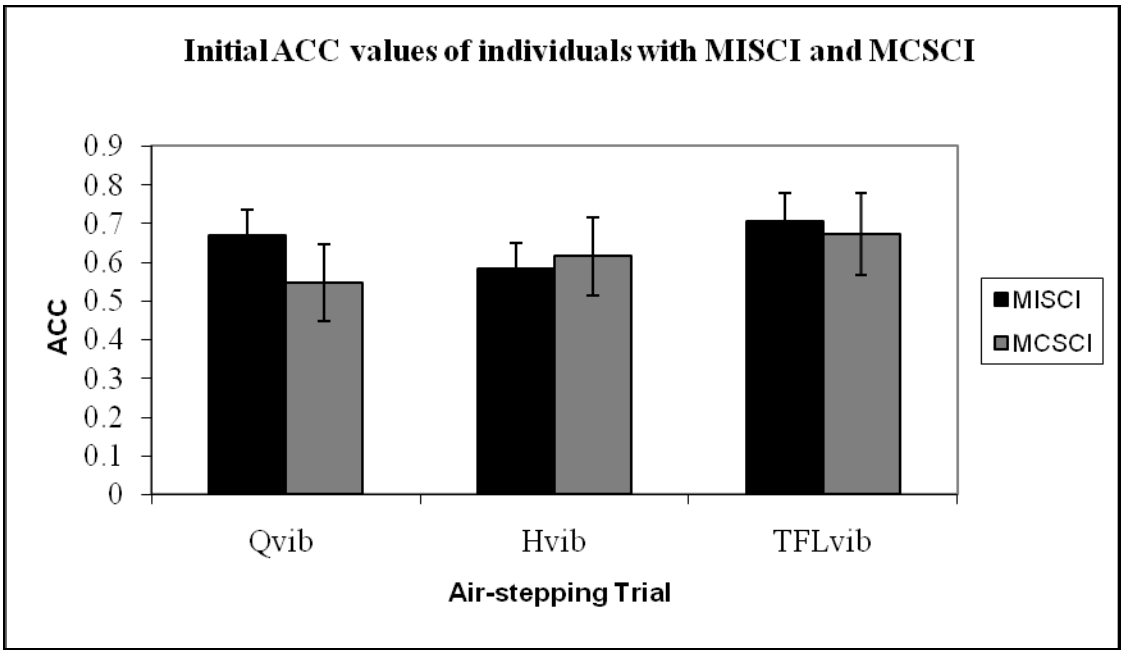

Figure 2.9a: Consistency (ACC) group mean values of vibration-elicited air-stepping responses of subjects with motor incomplete spinal cord injury (MISCI) and motor complete spinal cord injury (MCSCI). There was no significant difference in the consistency of the response between groups for Qvib (p=0.184), Hvib (p=0.208), and TFLvib (p=0.320).

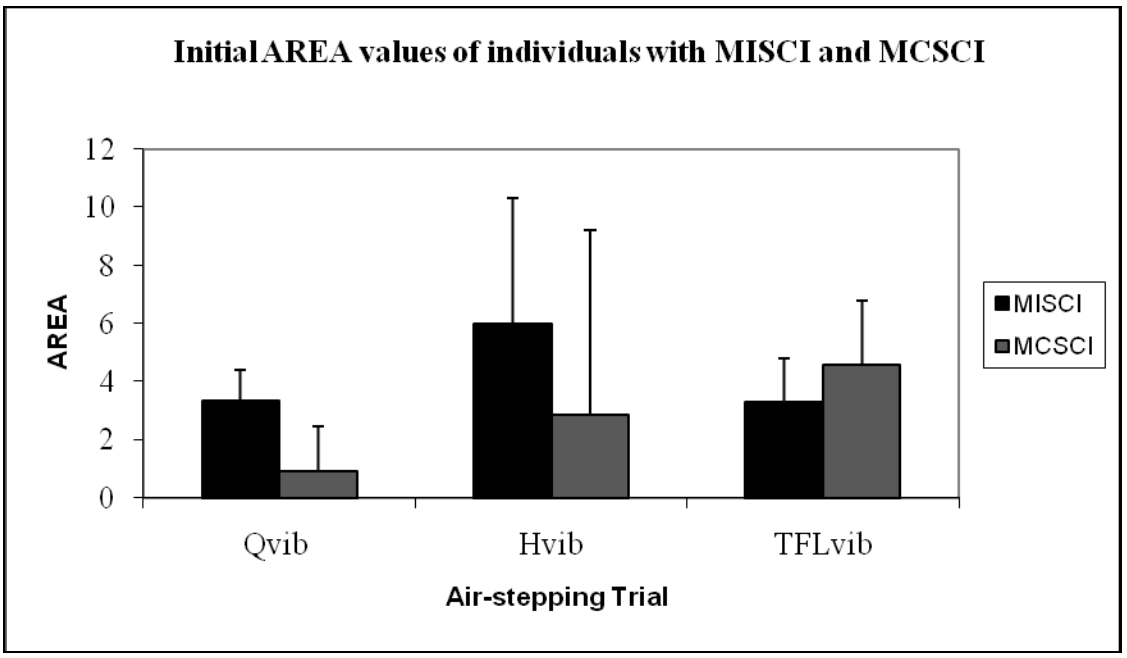

Figure 2.9b: Robustness (AREA) group mean values of vibration-elicited air-stepping responses in subjects with motor incomplete spinal cord injury (MISCI) and motor complete spinal cord injury (MCSCI). There was no significant difference in the robustness of the response between groups for Qvib (p=0.290), Hvib (p=0.163), and TFLvib (p=0.351).

Table 2.3: Comparison of the initial consistency (ACC) and robustness (AREA) of the vibration-elicited air-stepping responses. The ACC and AREA values for responses elicited from the three muscle vibration sites (Quadriceps (Qvib), Hamstrings (Hvib), and Tensor Fascia Latae (TFLvib)) for subjects with motor incomplete spinal cord injury (MISCI) and motor complete spinal cord injury (MCSCI) are shown. Mann-Whitney U and p-values are reported in the two right columns. There was no difference in consistency and robustness between subjects with MISCI and MCSCI.

Outcome	MISCI N=13		MCSCI N=6		Mann-Whitney U p-values	
Mean ± Standard Error (SE)	ACC	AREA	ACC	AREA	ACC	AREA
Qvib SE	0.669 ± 0.068	3.362 ± 1.056	0.547 ± 0.10	0.926 ± 1.554	U=28 p=0.184	U=32 p=0.290
Hvib SE	0.581 ± 0.069	5.989 ± 4.313	0.615 ± 0.101	2.863 ± 6.348	U=29 p=0.208	U=27 p=0.162
TFLvib SE	0.706 ± 0.072	3.32 ± 1.497	0.673 ± 0.106	4.586 ±2.204	U=33 p=0.320	U=34 p=0.351

There were differences in the consistency and robustness of the responses depending on the site of vibration. TFLvib produced the most consistent (ACC=0.836 ± 0.048) and most robust (AREA=26.6±11.04 degrees^2) response compared to Qvib

(ACC=0.763 ± 0.038; AREA=6.809±2.68 degrees^2) and Hvib (ACC=0.766 ± 0.061; AREA=13.45±5.305 degrees^2). The values from these three vibration placements are illustrated by the vibration-elicited air-stepping responses of subjects with SCI are illustrated in Figure 2.10a and 2.10b. With the finding that vibration of the TFL elicited the most consistent and robust responses, the TFLvib values were used for all further comparisons.

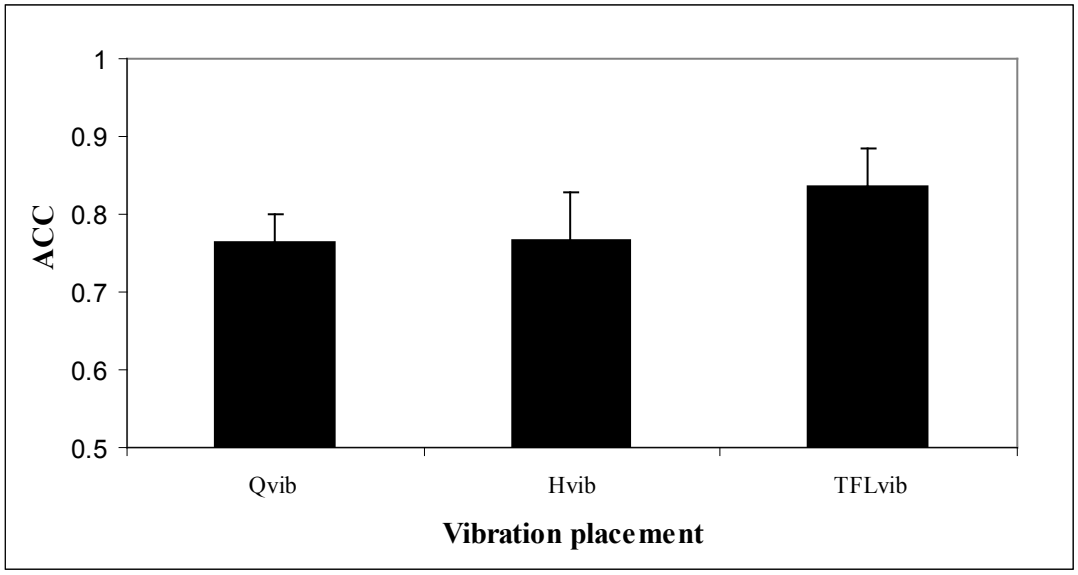

Figure 2.10a: Consistency (ACC) group mean values and standard error bars of the vibration-elicited air-stepping responses of subjects with SCI. The ACC values for the three muscle vibration site are illustrated (Qvib ACC=0.763 ± 0.038, Hvib ACC=0.766 ± 0.061, or TFLvib ACC=0.836 ± 0.048). TFLvib elicited the most consistent response in subjects with SCI.

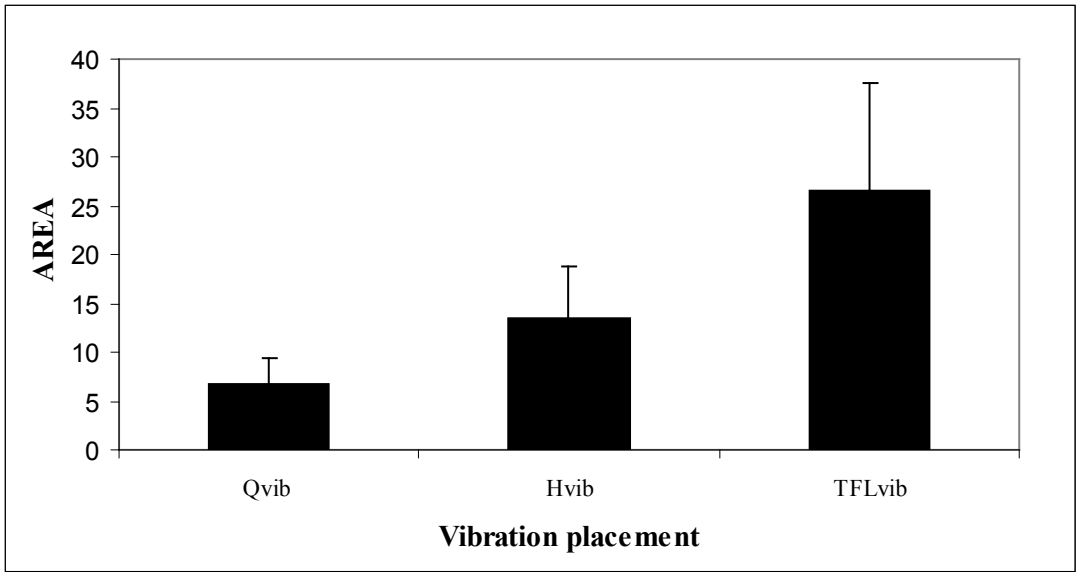

Figure 2.10b: Robustness (AREA) group mean values and standard error bars of the vibration-elicited air-stepping responses of subjects with SCI. The AREA values for the for the three muscle vibration site are illustrated (Qvib AREA=6.809±2.68 degrees^2, Hvib AREA=13.45±5.305 degrees^2, or TFLvib AREA=26.6±11.04 degrees^2). TFLvib elicited the most robust response in subjects with SCI.

There was a significant between-groups difference in the vibration-elicited air-stepping responses from the ND subjects compared to subjects with SCI. Differences were identified in both consistency (initial TFLvib ACC: p=0.026) and robustness (TFLvib AREA p=0.013) of the responses. Values for the vibration-elicited air-stepping responses of ND subjects and subjects with SCI are illustrated Figure 2.11.

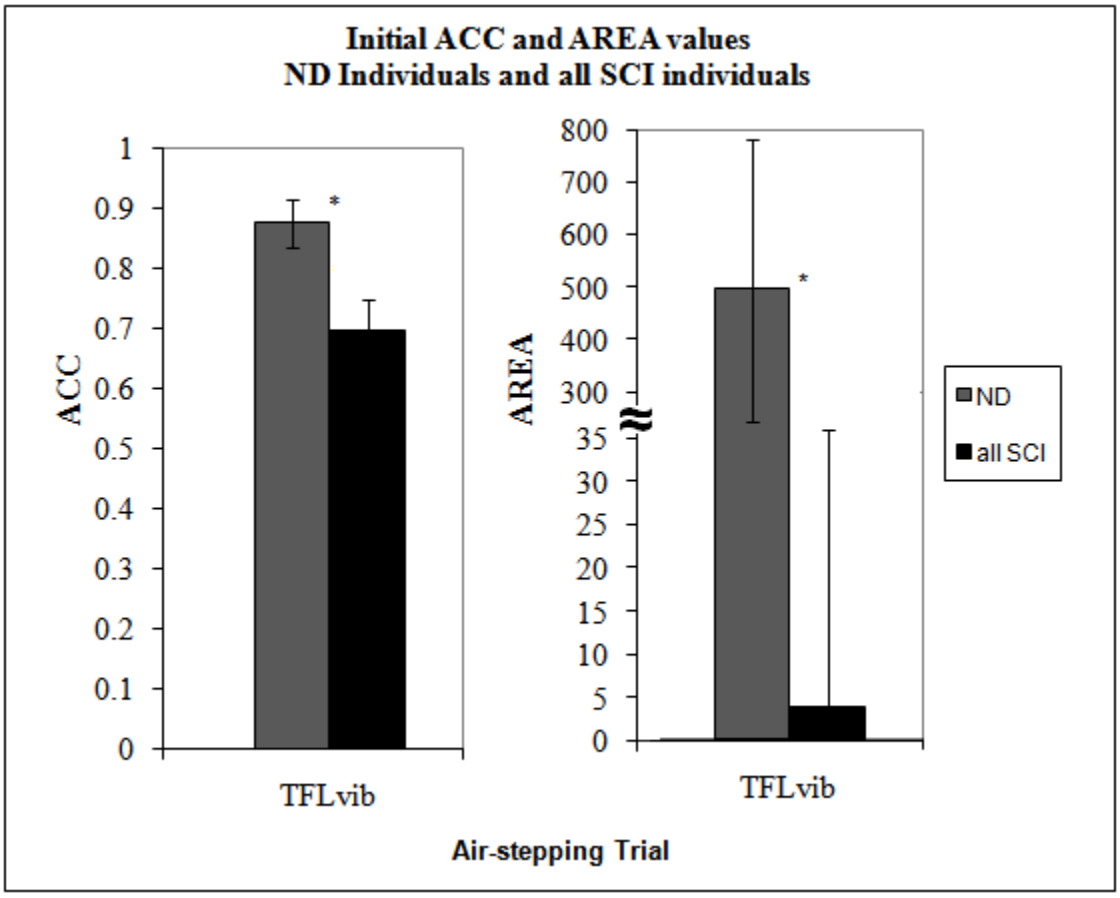

Figure 2.11: Consistency (ACC; left graph) and robustness (AREA; right graph) group mean values of vibration-elicited air-stepping responses of ND subjects and all subjects with spinal cord injury (SCI). There was a significant difference (denoted *) in the consistency ($p=0.026$) and robustness ($p=0.013$) of the response between groups for TFLvib. The y-axis of the right graph has been broken from 35 to 300 to accommodate the range of AREA values.

Locomotor training did not significantly influence either consistency or robustness of the vibration-elicited stepping responses. Comparison of the change in responses for those who did and those who did not participate in locomotor training identified no significant difference between-groups differences in consistency (TFLvib ACC: $p=0.105$) or robustness of the responses (TFLvib AREA: $p=0.351$). Change in these measures in the two groups is illustrated Figures 2.12a and 2.12b. Given the lack of

between-groups differences, data from the LT-MISCI and pooled Control MISCI and MCSCI groups were combined to assess the influence of vibration history.

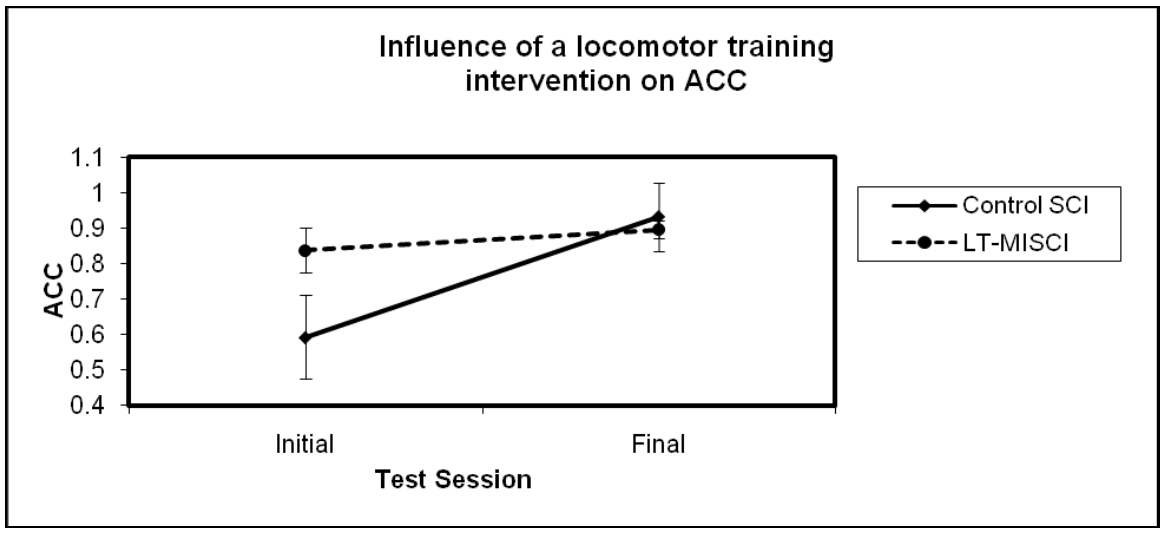

Figure 2.12a: Change in coordination (ACC) of vibration-elicited air-stepping responses in subjects who participated in a locomotor training intervention (LT-MISCI; n=6) and those who did not (Control SCI: Control MISCI and MCSCI pooled; n=13). There was no difference between groups for the change in coordination (TFLvib ACC: p=0.105).

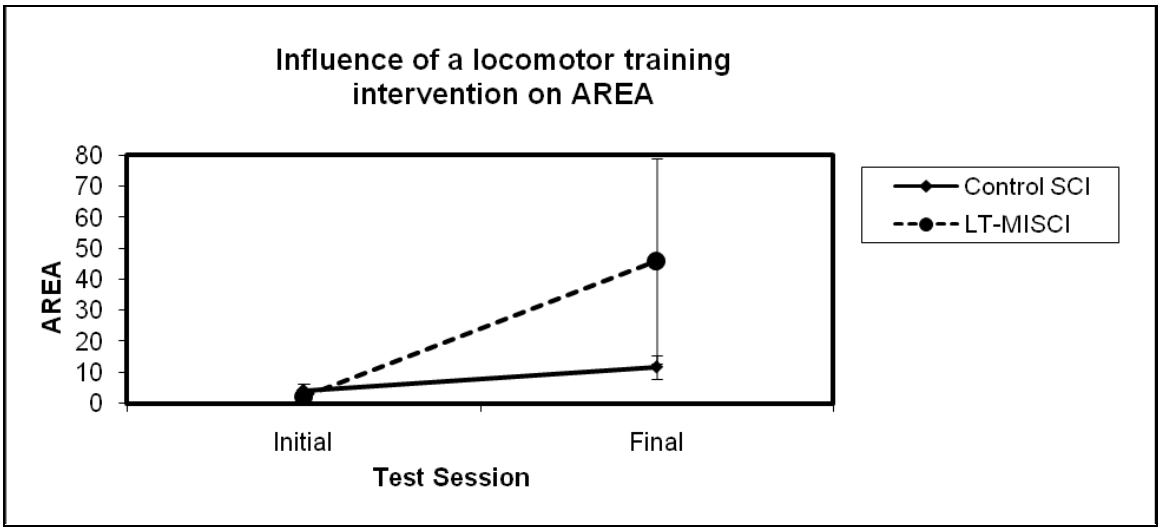

Figure 2.12b: Change in robustness (AREA) of vibration-elicited air-stepping responses in subjects who participated in a locomotor training intervention (LT-MISCI; n=6) and those who did not (Control SCI: Control MISCI and MCSCI pooled; n=13). There was no difference between groups for the change in robustness (TFLvib AREA: p=0.351).

Assessment of the influence of vibration history was measured by calculating differences between the responses generated in the initial test and those generated in the final test sessions. In ND subjects there was no change in the consistency (TFLvib ACC: p=0.216) or robustness (TFLvib AREA: p=0.059). For all subjects with SCI, there was a significant increase in the consistency (TFLvib ACC: p=0.046) and robustness (TFLvib AREA: p=0.035) of the response in the final test compared to the initial test session. The follow-up testing session responses were more consistent (TFLvib ACC: 0.863 ± 0.045) and more robust (TFLvib AREA: 17.295 ± 10.51 degrees^2) when compared to the initial testing session (TFLvib ACC: 0.561 ± 0.097; TFLvib AREA: 0.703 ± 0.097 degrees^2), however, the final testing session (TFLvib ACC: 0.92 ± 0.157; TFLvib AREA: 30.061 ± 13.638 degrees^2) was larger when compared to the follow-up testing session. The

influence of vibration history on the vibration-elicited air-stepping responses of all subjects are illustrated Figure 2.13a and 2.13b.

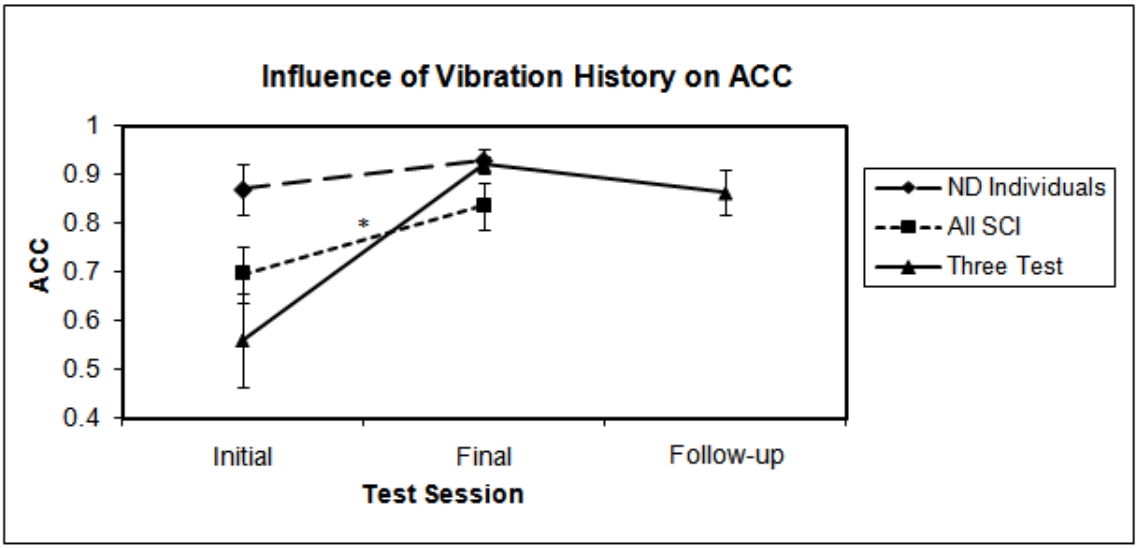

Figure 2.13a: Influence of vibration history on the consistency (ACC) of the vibration-elicited stepping-response. Consistency group mean values and standard error bars of the vibration-elicited air-stepping responses of ND subjects (n=6), subjects with SCI (All SCI: MISCI and MCSCI pooled; n=19), and subjects with SCI who returned for a follow-up testing session (Three Test; n=5). There was no significant change in consistency for ND subjects (p=0.216). There was a significant increase (denoted *) in the consistency between the initial and final testing session for subjects with SCI (p=0.046). For subjects with SCI who returned for a follow-up testing session, testing session responses were more consistent (0.863 ± 0.045) when compared to the initial testing session responses (0.561 ± 0.097). The final testing session responses (0.92 ± 0.157) were more consistent when compared to the follow-up testing session.

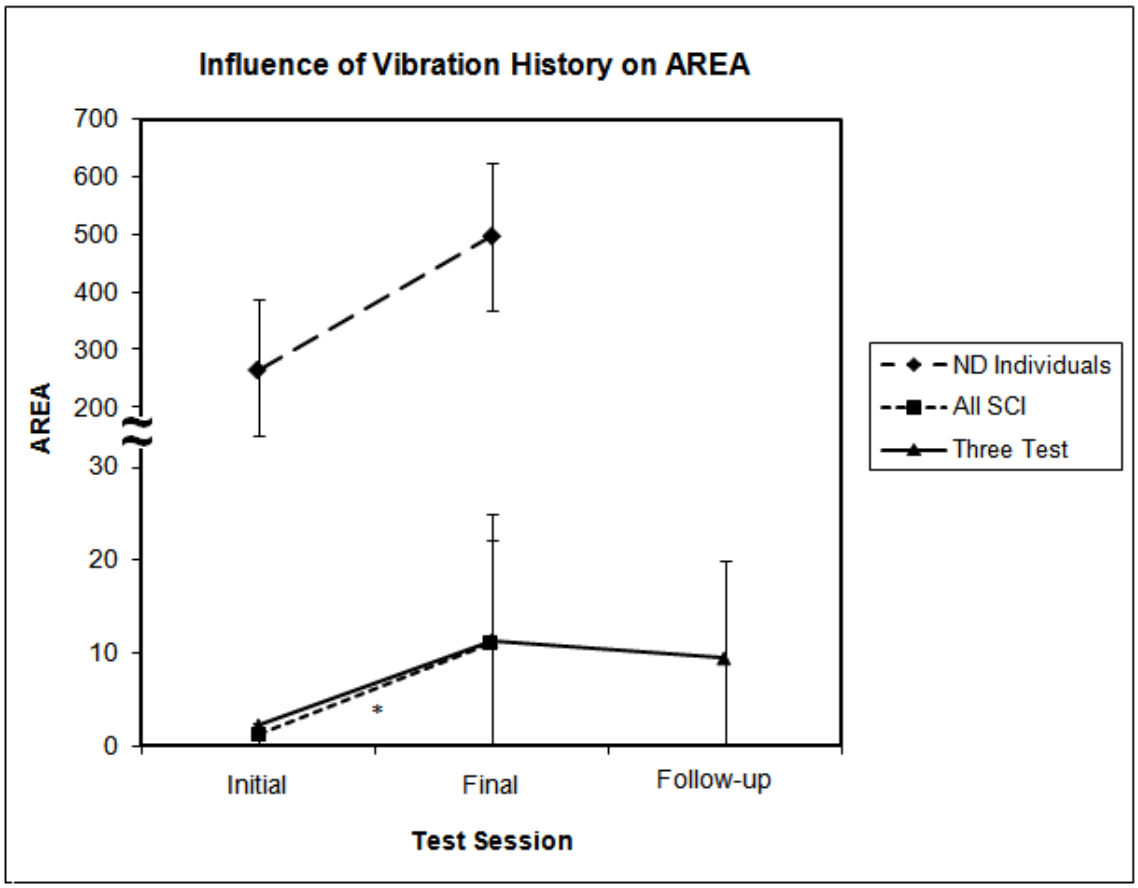

Figure 2.13b: Influence of vibration history on the robustness (AREA) of the vibration-elicited stepping-response. Robustness group mean values and standard error bars of the vibration-elicited air-stepping responses of ND subjects (n=6), subjects with SCI (All SCI: MISCI and MCSCI pooled; n=19), and subjects with SCI who returned for a follow-up testing session (Three Test; n=5). There was no significant change in robustness for ND subjects (n=6; p=0.059). There was a significant increase in the robustness (denoted *) between the initial and final testing session for all SCI (p=0.035). For subjects with SCI who returned for a follow-up testing session, the follow-up test session responses were more robust (17.295 ± 10.51 degrees^2) and when compared to the initial testing session (0.703 ± 0.097 degrees^2). The final testing session (30.061 ± 13.638 degrees^2) was more robust when compared to the follow-up testing session. The y-axis of the right graph has been broken from 30 to 200 to accommodate the range of AREA values.

Discussion

Our results indicate that vibration applied to the muscles of the thigh elicits involuntary air-stepping in subjects with chronic SCI. This is consistent with prior reports of involuntary stepping movements elicited with muscle vibration in ND subjects[62] and with epidural electrical stimulation in subjects with SCI.[36, 100] Interestingly, and contrary to our hypothesis, the site of vibration that elicited the most robust response was vibration of a pelvic stabilizer (i.e., the TFL) rather than a muscle involved in the generation of stepping (i.e., the quadriceps or hamstrings muscles). It is known that the effects of vibration can spread to muscles other than one being vibrated.[19] Because the TFL is situated midway between the hip flexor and extensor muscles, and all receive afferent innervation from the lumbosacral spinal cord, it is possible that vibration applied in this location produces widespread tonic, excitatory influences to the spinal circuitry innervating both the hip flexors and extensors. Hip muscle afferents are known to provide a powerful modulatory influence on the locomotor CPG,[17, 65, 73] therefore TFL vibration may create conditions of tonic excitation to the flexor and extensor half-centers of the locomotor CPG resulting in rhythmic oscillations as theorized by T.G. Brown[10] and others.[69, 77] Involuntary movements have also been elicited through electrical, epidural stimulation in subjects with MCSCI,[36, 100] and are reported to facilitate walking in subjects with subjects with MISCI.[64] Similar to the present study, the theoretical rational for the effect of epidural stimulation is that it provides non-specific excitation to the locomotor CPG, because responses elicited by vibration are non-focal in nature, it has been suggested that it may excite several segments of the spinal cord and trigger locomotor-like movements.[62]

Contrary to our hypothesis that responses would be more robust in those who habitually used their locomotor CPG in walking, there was no difference in the consistency and robustness of the vibration-elicited air-stepping patterns between subjects with MISCI and MCSCI. It could be argued that while the MISCI group included subjects who had the capability to perform walking, but who may actually have walked very little (or not at all) in daily practice there may have been no true difference between the MCSCI group and the MISCI group in terms of the extent of use of the locomotor-generating circuitry. This argument is supported by the fact that the consistency and robustness of the air-stepping responses was significantly greater in ND subjects compared to those with SCI. However, it is clear that there were differences between groups in terms of the extent of remaining voluntary drive to the lower extremities, as during each test session, both subjects with MCSCI and those with MISCI were asked to attempt the voluntary air-stepping trials. All six subjects in the MCSCI were unable to perform the voluntary movements, while all subjects in the MISCI group were able to perform at least minimal voluntary air-stepping. Further, the conclusion that it is not extent of use of the CPG that determines robustness of the vibration-elicited response is supported by the finding that the responses of subjects with SCI who participated in locomotor training were not significantly different from untrained subjects with SCI suggesting that locomotor training did not have an influence on the CPG. Based on this evidence, we must conclude that it is a factor(s) other than the extent to which the locomotor CPG is used or the amount of available descending supraspinal drive that accounts for differences in consistency and robustness of the vibration-elicited responses. Factors such as muscle stiffness (known to be greater in those with

spasticity[81]), which was not measured as part of this study, is one possible influence that should be considered.

Also unexpected, when we assessed stability of the responses by examining the effects of vibration history on the air-stepping response, we found that the responses increased in consistency and robustness in the 10-12 weeks between initial and final testing sessions in all subjects with SCI. In subjects who returned for a follow-up testing session, the consistency and robustness measured in the follow-up test session was similar to the measurements obtained during the final test session. Both of these tests were more consistent and robust compared to the initial test session suggesting that there is an influence of vibration that persists over time in subjects with SCI. This is consistent with evidence from prior studies that have shown that a single session of afferent stimulus may be sufficient to induce neuroplastic changes in the spinal cord[51] and cortex[25] and that these may persist following removal of the stimulus, for periods of as long as one month.[24]

Vibration may be a potent afferent stimulus in terms of its ability to influence neural excitability. In addition to it apparent effects on locomotor pattern-generating circuitry that are supported by this study and others,[62, 68] it also activates primary as well as secondary muscle spindle endings resulting in both phasic [101] and tonic reflex responses.[30, 45, 101] Vibration elicits a tonic vibratory reflex (TVR) that results in a muscle contraction, arising from activation of muscle spindle afferents in the vibrated muscle,[30, 45, 101] as well as antagonist vibratory reflexes,[18, 19] resulting in a contraction of the antagonist muscle, and activation of remote muscles.[19] Vibration reflex responses are found in subjects with SCI but are smaller and have higher activation thresholds

compared to ND subjects.[101] Although the circuitry related to the locomotor CPG is likely to be intact in all of our study participants, smaller vibration reflex responses found in subjects with SCI [37, 101] may indicate that the vibration-elicited air-stepping responses found in these subjects would also be smaller.

Implications for function

Vibration to the muscles of the thigh elicits air-stepping responses in subjects with SCI. While these responses are not as vigorous as those observed in ND subjects, the fact that these cyclic involuntary behaviors can be elicited indicates that the CPG-related circuitry is influenced by, and accessible through afferent input. These findings may have implications for the use of vibration in combination with locomotor training. Further investigation is warranted to assess the effect of vibration on walking function in subjects with SCI.

CHAPTER 3: EXPERIMENT 2: WHOLE-BODY VIBRATION REDUCES QUADRICEPS SPASTICITY IN INDIVIDUALS WITH SPINAL CORD INJURY

In individuals with disorders of the central nervous system, there are multiple consequences of disrupted communication between the brain and spinal cord. Among these is the loss of descending modulation of spinal reflex circuitry, which manifests as spastic hypertonia with increased reflex excitability and disordered motor output (i.e., spasticity, clonus, spastic gait patterns) that contribute to impaired motor function. The loss of presynaptic inhibition has been suggested by the increased amplitude of the Hoffman reflex (H-reflex; the electrical analogue of the stretch reflex) in individuals with spasticity.[11, 16] Peripheral sensory input in the form of localized vibration applied to specific muscle tendons may activate modulatory systems[15, 16, 89] that produce effects similar to those of the descending modulatory pathways. Localized vibration to the tendon or muscle belly suppresses the amplitude of the H-reflex in both non-disabled individuals and in individuals with spasticity.[16] While the depression is not as effective in those with spasticity as in non-disabled individuals, the depression of the H-reflex during vibration in individuals with spasticity suggests vibration may modulate the excitability of the underlying neural circuits.[11, 16] Further evidence for the modulatory influence of vibration in reflex activity in individuals with SCI, is offered by studies in our lab in which tendon vibration resulted in improved reciprocal inhibition, with effects of a single session persisting up to 15 minutes after vibration was removed.[89]

Whole-body vibration (WBV) has become popular in fitness centers with a myriad of benefits ascribed to its use. The research literature lends support to several of these claims

with findings that a program of WBV may be associated with increased muscle strength, [32, 46, 78, 93, 108, 110] flexibility, [23, 46, 110] and performance measures such as jump ability.[22, 26, 93, 108, 108, 109] In addition to indications that WBV has an effect on these movement-related variables, there are also reports that WBV may have beneficial effects on some aspects of function in older individuals,[7, 72, 93] as well as in some clinical populations.[1, 107, 111, 112]

In individuals with chronic stroke, a single session of WBV has been shown to be associated with improvements in balance function with effects persisting 45 minutes.[111] In individuals with acute stroke, improvements in balance and scores on tests of functional independence were found to be associated with a 6-week intervention of WBV. These improvements were observed both immediately after the 6-week intervention and at follow-up testing 6 weeks after the intervention, however, these changes were similar to those attained by subjects randomized to an alternate intervention group.[112] In another study designed to rule out the possible influence of simply standing in a squat position, individuals with subacute stroke were randomized into a group receiving a single session of WBV while performing a static squat or a group who only performed static squatting. The WBV group had an increase in maximal voluntary strength and reduction of the antagonistic hamstring muscle activity during eccentric contraction of the quadriceps muscle compared to no change in the squat-only group.[107] In adults with spastic diplegia due to cerebral palsy, WBV has been shown to be associated with improvements in muscle strength and reductions in spasticity of the knee extensor muscles.[1] In individuals with SCI who were unable to stand without long-leg braces, a case series reported in a published abstract found that the use of WBV evoked reflex-induced standing, and subsequently some of the individuals were able to progress to walking.[58]

The purpose of this study was to quantify the effect of WBV on quadriceps muscle spasticity in individuals with chronic, motor-incomplete SCI as measured by changes in spinal stretch reflex (SSR) excitability. Subjects were tested before and after participation in a 3 day/week, 12-session intervention of WBV. Weekly testing was also performed to assess differences between immediate and delayed within-session effects. Finally, we assessed differences in response to the WBV intervention between individuals who used antispastic agents and those who did not. If antispastic agents are capable of reducing spasticity to the fullest extent possible, then there should be no further WBV-induced reduction in spasticity in those who used these agents. We hypothesized that there would be a reduction in quadriceps spasticity after a 12-session intervention of WBV, that the within-session effects would be such that less spasticity would be observed in the immediate post-WBV test compared to the delayed post-WBV test, and that the individuals who reported daily use of antispastic agents would experience a smaller reduction in quadriceps spasticity associated with the WBV intervention compared to those who reported no use of antispastic agents.

Methods

Subjects. Seventeen subjects (3 women, 14 men; age 28-65) with SCI enrolled in the study. All subjects underwent clinical examination prior to testing. Subject inclusion criteria was motor incomplete, chronic ($\geq$ 1 year duration) SCI, and ability to stand with no more than moderate assistance. Exclusion criteria was a lack of quadriceps spasticity as defined by the Pendulum Test first swing excursion value (see Testing Procedures) equivalent to that of non-disabled individuals (96 degrees).[105] One subject who was screened was excluded, due to not demonstrating quadriceps spasticity as defined by the exclusion criteria. Therefore, sixteen subjects (2 women, 14 men; age 28-65) with spastic hypertonia due to SCI were

tested. American Spinal Injury Association (ASIA) motor and sensory scores,[2] and ASIA Impairment Scale (AIS) classification[79] were evaluated by a physical therapist who was not otherwise involved in the study. All subjects had injuries that were classified as either AIS C or AIS D. Individuals with injuries classified as AIS C have sensory and some motor function preserved below the neurological level, but more than half of the key muscles below the neurological level are unable to move the limb against gravity. Individuals with injuries classified in the AIS D have sensory and motor function preserved, but at least half of the muscles are able to move the limb against gravity.[2] All individuals had asymmetrical lower extremity motor scores, the weaker extremity was designated as the test leg. Information about daily use of medications and assistive devices for mobility was recorded. Seven individuals reported daily use of antispastic agents, while nine individuals reported no use of these medications.

Demographic data for the subjects is given in Table 1. All subjects gave written and verbal informed consent for participation in a protocol approved by the Human Subjects Research Office at the University of Miami, Miller School of Medicine and in accordance with the Declaration of Helsinki. All subjects were instructed to maintain their pre-enrollment exercise and medication habits until completion of the study.

Table 3.1: Demographics of participants; * Subject 6 was excluded from analysis due to initial first swing excursion (FSE) values > 96 degrees indicating no spasticity (i.e., equivalent FSE values are observed in non-disabled individuals).[105] LEMS = lower extremity motor scores represent the sum of the motor scores for the 5 key muscles of both legs graded according to ASIA guidelines[2] prior to the WBV intervention.

Subject	Gender	Age	Injury Level	LEMS Scores	Antispastic Agents	Primary Daily Assistive Device
1	M	41	C5	25	Zanaflex	Wheelchair
2	F	42	C4	23	Baclofen	Wheelchair
3	M	60	C6	17	Baclofen	Wheelchair
4	M	48	C5	33	None	Wheelchair
5	M	56	C5	38	Baclofen	Wheelchair
6*	F	60	T4	34	Baclofen	Wheelchair
7	M	43	T8	26	None	Personal Transporter
8	M	54	T4	36	None	Wheelchair
9	M	34	T4	29	None	Wheelchair
10	M	42	C4	24	Baclofen	Wheelchair
11	M	41	T6	23	None	Wheelchair
12	M	53	T7	34	None	Walker
13	M	42	C4	23	Baclofen	Wheelchair
14	M	43	T7	42	None	Wheelchair
15	M	58	C6	31	None	None
16	M	65	C3	36	None	Wheelchair
17	M	28	C4	39	Baclofen	Wheelchair

WBV Intervention. Subjects participated in an intervention consisting of WBV (Power Plate; Northbrook, IL) 3 days per week for 4 weeks. Each session included four, 45-second bouts with one minute of seated rest (without vibration) between bouts according to previously published protocols.[111, 112] The sequence of procedures for a single session of WBV is illustrated in Figure 3.1.

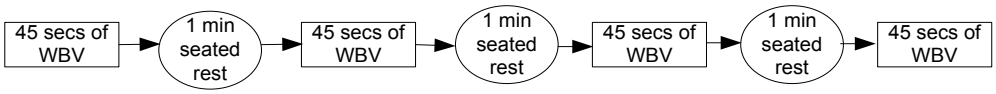

Figure 3.1: Procedure for a single session of whole-body vibration (WBV)

During each WBV bout, subjects stood on the vibration platform with knees slightly flexed (approximately 30 degrees from full extension) as seen in Figure 3.2. Vibration was delivered at 50 Hz with a vertical displacement of 2-4 mm (depending on subject weight).

Figure 3.2: Subject positioning during each whole-body vibration (WBV) bout. Subjects stood on the vibration platform (Power Plate; Northbrook, IL.) with knees slightly flexed (approximately 30 degrees from full extension)

Testing Procedure. Spinal reflex excitability (i.e., responsiveness to quadriceps muscle stretch) was assessed using the Pendulum Test. The Pendulum Test allows the application of a consistent, gravity-provoked stretch to assess responsiveness of the knee extensor muscles to rapid stretch. The test was performed according to previously published protocols, [57, 105] which have shown this test to be a reproducible,[105] valid, and sensitive measure for assessment of spasticity[57, 70, 82] that is well correlated with clinical measures of spasticity.[70, 82]

The Pendulum Test was performed with the subject in a semi-reclined position on a treatment table with the torso elevated (using a foam wedge) to approximately 40 degrees from horizontal. Both legs were positioned to hang freely over the end of the table with the knees flexed allowing a space of approximately two fingers width between the popliteal fossa and the edge of the table. The test was performed by an experimenter not otherwise involved in the data analysis.[57, 105] The examiner grasped the heel of the test leg to extend the knee, and the leg was dropped. Five tests, with at least 30 seconds of rest between, were performed in each test set. A test set was captured both prior to the start of the 12-session intervention (*initial test*) and following the 12-session intervention (*final test*). This arrangement allowed us to assess the overall influence of the 12-session WBV intervention. Once each week, following a session of WBV, two test sets were captured: the first test set was captured within five minutes following the vibration session (*immediate post-WBV test*), and the second test set was captured approximately fifteen minutes after the WBV session (*delayed post-WBV*). This test arrangement allowed us to assess the within-session timecourse of the effects of WBV on the SSR excitability. To avoid lower extremity use or weight bearing that might confound the influence of the WBV in the immediate post-session period, following

the last vibration bout for that session, the subject sat on a wheeled, padded table that was located next to the WBV platform, and was then wheeled into the 3D motion capture area for the immediate post-WBV test set. During the time between the immediate post-WBV test and the delayed post-WBV test, a support was placed under the subject's legs to maintain the knees in the extended position (limiting passive stretch of the knee extensors) and the subject rested quietly for 10 minutes. After 10 minutes, the testing procedure was repeated for the delayed post-WBV test set. The sequence of the weekly, within-session testing procedures is illustrated in Figure 3.3.

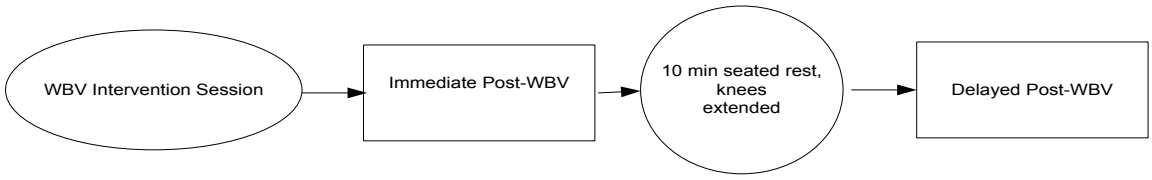

Figure 3.3: Weekly Pendulum Testing was performed immediately after a session of whole-body vibration (WBV) (Figure 3.1) during the 12-session WBV intervention.

Reflective markers were placed on the weaker lower extremity at the greater trochanter, the lateral knee joint line, and the lateral malleolus. Kinematic data associated with the Pendulum Test was collected at 60 Hz using an 8-camera, 3D motion capture system (Peak Motus® Software, Peak Performance, Centennial, CO) in a calibrated test space. For each Pendulum Test, we assessed change in the anatomical knee angle (i.e., 0 degrees = full knee extension). For each Pendulum Test, first swing excursion (FSE) was defined as the angle at which the swinging leg first reversed direction from flexion to extension indicating the point in the knee range of motion at which a reflex contraction of the quadriceps caused the knee to extend. The initial and final knee angles associated with the Pendulum Test in

one subject are illustrated in Figure 3.4 (arrows indicate initial and final FSE values). The number of oscillations (OSC) was determined by graphing the knee joint angle and summing the number of peaks before the leg returned to the resting knee angle. FSE has been shown to be the most sensitive measure to characterize severity of spasticity.[57] The number of oscillations completed prior to returning to the rest position has been shown to be a useful indicator of whether or not spasticity is present,[57] but is not sensitive to differences in amount of spasticity.[6, 117] Therefore, we considered FSE to be the primary outcome measure of interest. An increase in FSE suggests decreased excitability of the quadriceps SSR and therefore was interpreted as a decrease in spasticity. For each set of five tests, the mean of the five FSE and OSC was calculated and used for all statistical tests.

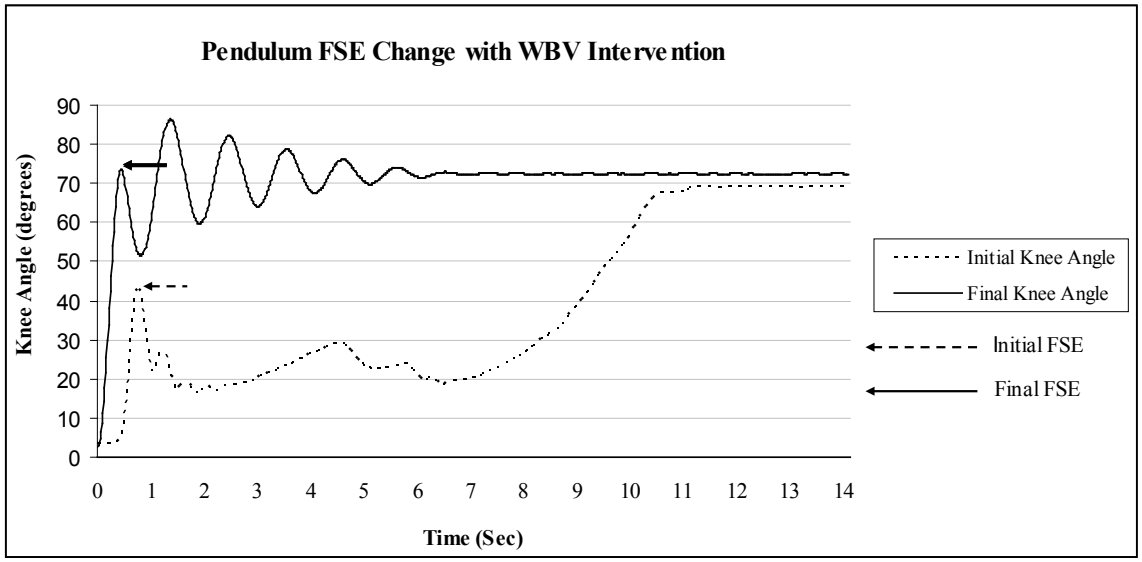

Figure 3.4: Changes in quadriceps spasticity in response to a 12-session whole-body vibration (WBV) intervention in an example subject. The first swing excursion (FSE) is marked for the initial (dashed trace) and final tests (solid trace), wherein an increase in FSE suggests a decreased responsiveness to quadriceps stretch.

Following the final WBV session, all subjects returned within 8 days for the final test session. Thirteen of the subjects returned for the final test session within 4 days of the final WBV session and three were tested 6-8 days after the WBV intervention. The data acquired for the subjects tested within 4 days was compared to that of that acquired from subjects tested 6-8 days after the WBV intervention to obtain a sense of the persistence of the effect of the WBV intervention.

To assess the possible impact of prolonged or repetitive squatting on the measures of interest, data from one subject (subject 7), who habitually used a Segway Personal Transporter (Bedford, NH) for daily mobility and stood in a slight squat for long periods, was considered separately.

Statistical Analysis. Statistical Analysis Software 9.1.3 (Cary, NC) was used for all statistical analyses. Significance was set at $\alpha=0.05$. One-tailed, paired t-tests were used to compare initial and final FSE values and to compare each of the four weekly immediate and delayed post-WBV FSE values. A Bonferroni correction was used to adjust the alpha level for these five pair-wise comparisons resulting in an adjusted value of $\alpha=0.01$. A separate one-tailed, paired t-test was used to compare initial and final OSC values.

To verify that there were no pre-intervention differences in spasticity in individuals who did and those who did not use antispastic agents, a one-tailed, independent sample t-test was used to compare the initial FSE values between the two groups. To determine whether there were differences in responsiveness to WBV between these two groups, a repeated-measures ANOVA was performed to identify any time x group interaction in the initial and final FSE values of those individuals who did and those who did not use antispastic agents.

Results

The 12-session intervention of WBV was found to be associated with a statistically significant increase in FSE from initial to final test (p=0.005), indicating that there was a reduction of quadriceps spasticity associated with the 12-session WBV intervention. The initial and final FSE values for each of the subjects is illustrated in Figure 3.5. There was not a statistically significant change in OSC (p= 0.195). Therefore, FSE was used for all further analyses.

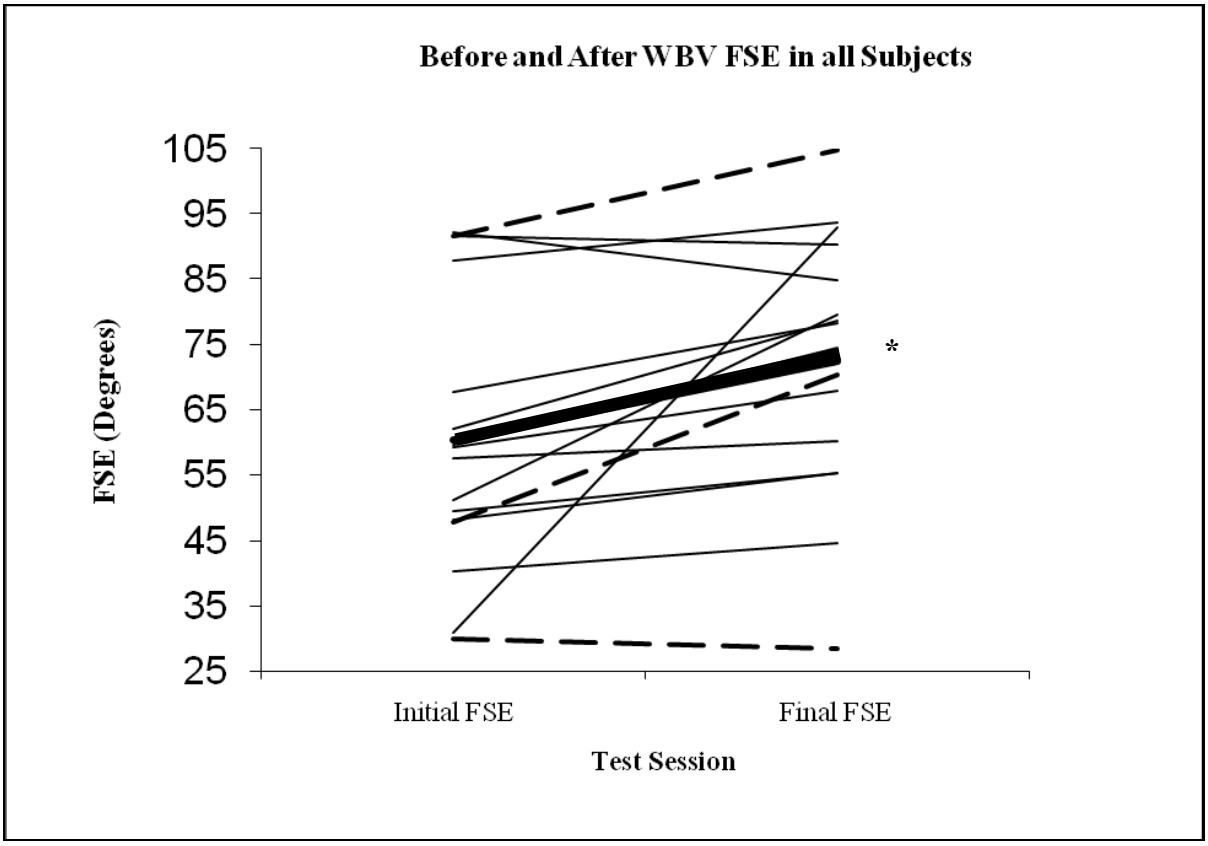

Figure 3.5: Change in first swing excursion (FSE) values associated with the 12-session whole-body vibration (WBV) intervention. Change in FSE values for all subjects (thin lines) and group mean change (thick line). Group mean initial (60.7 ± 2.7 degrees) and final FSE values (72.9 ± 3.3 degrees) were significantly different (denoted by *; p=0.005), indicating a decreased responsiveness to stretch associated with the intervention. Change in FSE values were similar for those individuals (n=3; dashed lines) for whom the final test as administered 6-8 days after the final WBV session.

Comparisons of the weekly immediate and delayed post-WBV FSE values identified a significant within-session difference for week 1 (p=0.005), week 2 (p=0.006), and week 4 (p=0.006). This indicates that in the post-vibration period quadriceps spasticity was lower after a delay of 15 minutes. The difference in the FSE for the within-session post-WBV tests for week 3 was not statistically significant (p=0.039). Values of the initial and final FSE, and weekly immediate and delayed post-WBV FSE values are illustrated in Figure 3.6.

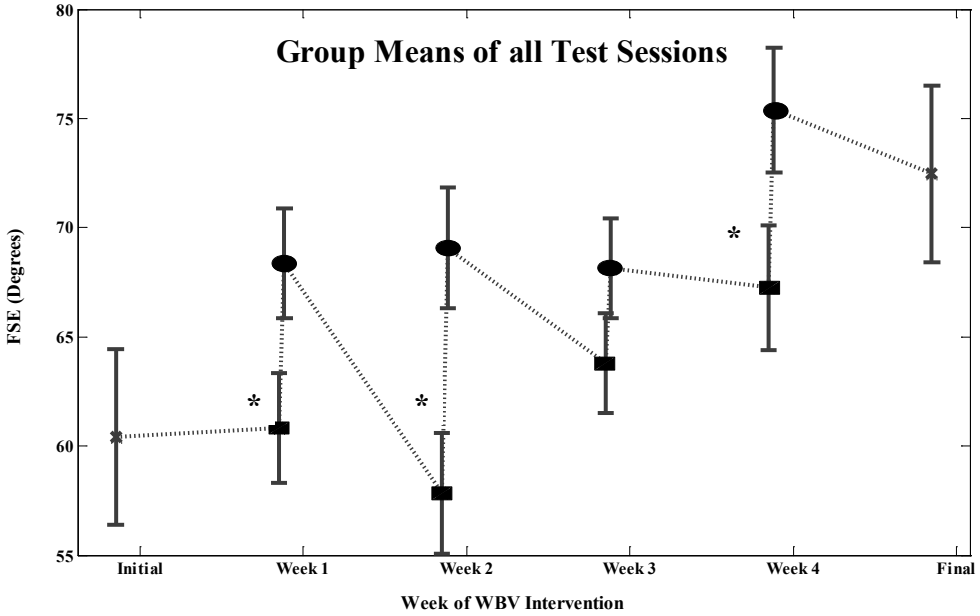

Figure 3.6: Within-session comparisons of weekly immediate and delayed post-WBV FSE values for the 12-session intervention. Delayed post-WBV FSE values (circles) were significantly different (as indicated by asterisk [*]) from immediate post-WBV values (squares) and for weeks 1 (7.07 ± 2.39 degrees), 2 (8.73 ± 3.02 degrees), and 4 (8.13 ± 2.87 degrees). The difference for week 3 (4.35 ± 2.29 degrees) was not statistically significant.

There was no significant difference between the initial FSE values of individuals who did and those who did not use antispastic agents (p=0.198). There was no significant time x group interaction between the initial and final FSE values of those individuals who reported daily use of antispastic agents and those who reported no use of antispastic agents (p=0.221),

indicating that the effects of WBV in individuals who use antispastic agents are similar to those who do not. The initial and final FSE values for the groups of subjects who did and did not use antispastic agents are illustrated in Figure 3.7.

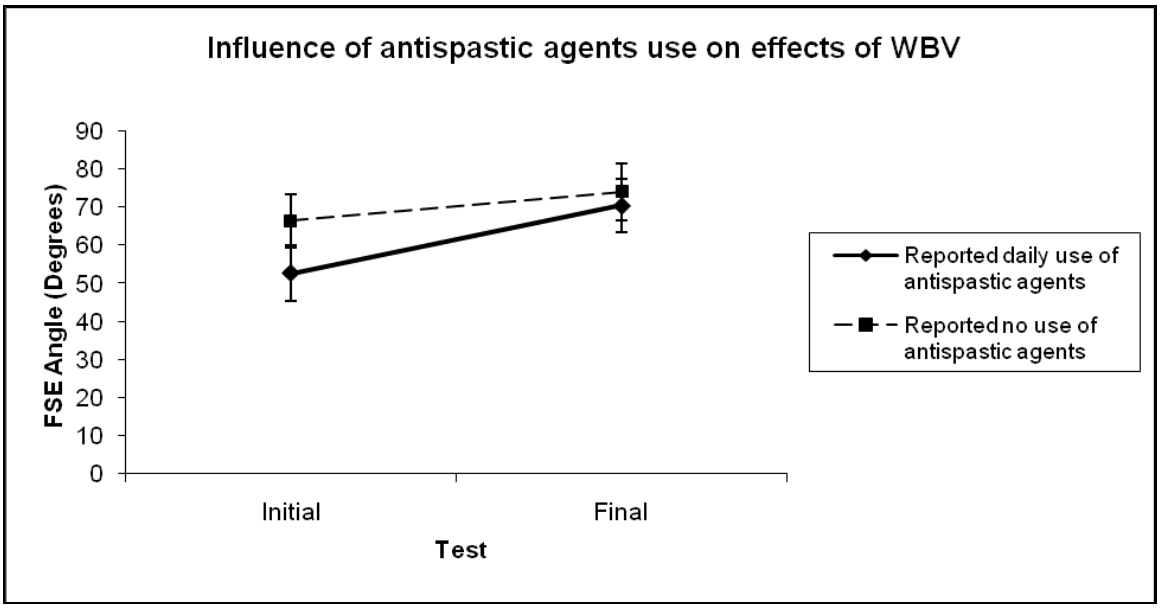

Figure 3.7: Influence of antispastic agent use on response to spasticity-reducing effects of whole-body vibration (WBV). There was no difference in the effect of a 12-session WBV intervention in individuals who used antispastic agents and those who did not.

The data from thirteen individuals who had their final test session within 1-4 days of the final intervention session were compared to that of the three individuals who had their final intervention session 6-8 days after the final intervention session. The mean change for each of these were 12.05 ± 4.04 degrees and 11.47 ± 18.31 degrees, respectively, for each of these (dashed lines in Figure 4 show FSE values for the latter subjects). The similarities between FSE values suggest that the effects of the WBV intervention persist for at least 6-8 days.

The data from one subject (subject 7), who used a personal transporter for daily mobility and always maintained a slight, standing squat while riding the device, was

examined individually. The change in FSE for this individual was 8.73 degrees. This was within the range of the mean change in FSE exhibited by the other subjects (12.05 ± 4.04 degrees).

Discussion

Our results indicate that use of WBV is associated with decreased excitability of the quadriceps SSR in individuals with spastic hypertonia due to SCI, as measured by an increase in the knee angle at which a stretch to the quadriceps first elicits a reflex muscle contraction (i.e., the FSE). This reduction in quadriceps spasticity is consistent with evidence of reduced knee extensor spasticity associated with WBV intervention in individuals with spastic diplegia due to celebral palsy.[1] In agreement with other studies that have quantified the severity of spasticity,[57] we did not find a significant difference in the number of oscillations of the swinging leg (i.e., the OSC) between the initial and final tests. The number of swing oscillations has been found to be useful only in distinguishing between non-disabled individuals and clinical populations with spasticity.[57] Therefore the OSC appears not to be sufficiently sensitive to detect changes within a sample of individuals with spasticity.

We hypothesized that WBV would be associated with a reduction in quadriceps spasticity immediately following a WBV session and this reduction would decay with time. However, data from weekly test sessions suggests that following a session of WBV the reduction in quadriceps spasticity is greater following a delay of 15 minutes than it is when tested within 5 minutes following a WBV session as seen in Figure 3.5. WBV has also been shown to be associated with improvements in balance and these effects have been reported to persist for up to 45 minutes after a session of WBV.[111] It is also possible that if we had

acquired post-WBV data at later time points, we may have identified the time at which the within-session effects associated with WBV reached a plateau.

Vibration is known to elicit both excitatory and inhibitory influences on spinal reflex activity, resulting in a phenomenon called "the vibration paradox." Excitatory influences are in the form of the tonic vibration reflex (TVR), a tonic muscle contraction arising from activation of muscle spindle afferents in the vibrated muscle. Vibration also activates inhibitory influences, thought to be due to presynaptic inhibition[42, 59, 96, 97] or depletion of neurotransmitter,[3, 47, 67, 71, 74, 84] that result in a reduction of the excitatory Ia influences on the homonymous motoneuron.[33] It is possible that effects of the TVR linger following WBV and are responsible for increasing the SSR excitability in the immediate post-WBV period, resulting in decreased FSE values (i.e., earlier onset of the reflex contraction). However, we are unable to verify this as we did not obtain pre-WBV FSE values on a weekly basis. The increase in the delayed post-WBV FSE values (i.e., later onset of reflex contraction) suggests activation of vibration-induced inhibitory influences and decreased SSR excitability.

Our data suggests that there was a progressive decrease in spasticity each week of the WBV intervention. Therefore, it is likely that the repetitive use of the afferent stimulus in the form of WBV induces persistent plastic changes in the neural circuits related to spinal reflex excitability.[51] This view is further supported by the decrease in quadriceps spasticity seen in the three individuals in whom the final test session was administered 6-8 days following the last WBV session. The reduction in spasticity was evident up to 6-8 days after the WBV intervention, as the final test values of these individuals was within the range of that obtained for subjects who were tested within four days.

This persistence of the reflex-modulating effects following a stimulus period has also been found in prior studies from our laboratory. In a preliminary study in non-disabled individuals, a single session of WBV resulted in a significant decrease in the Ia-mediated reflex circuit (as measured by the size of the normalized H-reflex amplitude; H/M ratio).[5] Our group has also shown short-term changes in reflex modulation following electrical stimulation in non-disabled individuals,[88] and following localized tendon vibration in individuals with SCI.[89] In individuals with chronic, motor-incomplete SCI, localized tendon vibration applied to the tibialis anterior tendon results in improved efficacy of reciprocal inhibition to the soleus muscles. Reflex modulation was greatest 5 minutes after the vibration was removed, and remained depressed relative to pre-vibration values for minutes thereafter.[89]

We hypothesized that individuals who used antispastic agents would have medication-induced depression of responsiveness to quadriceps stretch. We expected those who reported daily use of antispastic agents to have reached a plateau effect of spasticity reduction, and therefore, that these individuals would experience a smaller relative reduction in quadriceps spasticity associated with the WBV intervention compared to those who did not use antispastic agents. Contrary to our hypothesis, we found that individuals who used antispastic agents experienced similar reductions in quadriceps spasticity as those who did not use such medication. These results are consistent with a prior study demonstrating that localized tendon vibration causes a reduction of the excitatory Ia influences on the homonymous motoneuron even after use of antispastic agents. In a study of individuals with spastic hypertonia due to chronic SCI who were not previously using antispastic agents, administration of antispastic agents for 3 weeks resulted in an increase in the vibration-

induced inhibition of the H-reflex as measured by the vibration inhibition index (i.e., the H-reflex amplitude during vibration as a proportion of the H-reflex amplitude without vibration).[82]

Tension in the quadriceps muscle due to the slight squat that the subjects maintained during the WBV bouts may activate Ib fibers, which are classically thought to activate a homosynaptic inhibitory circuit. For this reason, we considered the possibility that the squat position, rather than the WBV, was responsible for the reduction in quadriceps spasticity. However, in a subject who habitually stood for hours each day in a semi-squat position while riding a personal transporter, the results of WBV were similar to those of subjects who habitually sat in a wheelchair for mobility. This suggests that the effects observed are not likely due to the influence of squatting alone (in the absence of WBV).

Our results are consistent with evidence in subjects with stroke in whom co-contraction of knee muscles decreased after WBV when compared to subjects who only performed a static squat.[107]

Implications for function

These results support the use of WBV as an intervention to decrease quadriceps spasticity in individuals with SCI. With a 12-session intervention of WBV, we found significant decreases in quadriceps spasticity. In individuals in whom spasticity interferes with function, WBV may represent an approach to decreasing spasticity. Furthermore, the effect of vibration on spasticity persists for several days, suggesting that WBV may be useful prior to motor rehabilitation interventions to enhance the goals of training. Future studies should investigate whether WBV could be an effective substitute for antispastic agents in some individuals.

CHAPTER 4: EXPERIMENT 3*:* WHOLE-BODY VIBRATION IMPROVES WALKING FUNCTION IN INDIVIDUALS WITH SPINAL CORD INJURY

Loss of walking function is often a result of spinal cord injury (SCI) and for individuals with SCI, regaining walking function is a high priority.[38] These individuals, and other populations with disorders of the central nervous system, often have various deficits that negatively impact walking function. For example, muscle weakness and sensory impairment result in reduced levels of muscle activation and decreased walking speed.[90] Spasticity may result in altered muscle timing and co-contraction associated with spastic gait patterns.[75, 90] Decreased walking function results from any one, or a combination, of these deficits.[90,104 ,23]

In non-disabled (ND) individuals, vibration to the muscle body or tendon increases walking speed depending on the combination of direction of progression and vibration placement.[68] In individuals with Parkinson's disease, vibration applied through the soles of the feet during walking increases walking distance, speed, stride length, and improves stride variability.[85] Electrical stimulation[36, 64] or vibration[62] may also excite spinal circuitry (i.e., locomotor pattern generators) involved in the production of locomotor output.

Whole-body vibration (WBV) is increasingly being used in elderly individuals[72, 93] and in clinical populations.[1, 41, 58, 111, 112] In individuals with SCI, our studies offer preliminary evidence that a 12-session intervention of WBV decreases spasticity of the quadriceps muscles.[83] The use of WBV has also been associated with changes in walking function.[1, 41, 58, 72] Elderly individuals who received a 2-month WBV intervention in

combination with balance, muscle strengthening, and walking exercises demonstrated increased walking speed and step length when compared to individuals who did the same exercise program without WBV.[72] In individuals with Parkinson's disease, a 3-week intervention of WBV is associated with improvements in walking speed.[41] In adults with spastic diplegia due to cerebral palsy, an 8-week intervention of WBV is associated with improvements in muscle strength and reductions in spasticity of the knee extensor muscles, but the distance walked in 6 minutes was unchanged.[1] In individuals with SCI who were unable to stand without long-leg braces, a case series attributed the use of WBV with the progression of function from standing to walking.[58]

The primary objective of this study was to quantify changes in walking speed associated with a 12-session intervention of WBV and hypothesized that this intervention would be associated with increased walking speed. In addition, we assessed changes in secondary gait parameters associated with the 12-session intervention of WBV. Gait parameters included step length, cadence, and consistency of hip-knee intralimb coordination. We hypothesized that the 12-session intervention of WBV would be associated with increased step length and cadence, and increased hip-knee intralimb coordination. We also assessed the relationship between the change in walking speed and the decrease in quadriceps spasticity found in Chapter 3 and hypothesized that the decrease in quadriceps spasticity would contribute to an increase in walking speed.

Methods

Subjects and WBV intervention. The 17 individuals who received the 12-session WBV intervention from Chapter 3 participated in this study. Subject height was recorded for the purpose of normalizing gait parameters.

Testing Procedure. The effects of the 12-session WBV intervention on walking function was quantified by comparing the kinematic data acquired prior to the intervention (initial test) to that collected within seven days of the last WBV session (final test), one subject returned an additional time at 5-weeks post WBV for a follow-up test session to allow assessment of persistence of intervention effects. An array of twenty-one reflective markers were placed bilaterally at the lateral malleoli, 5^{th} ray metatarsal-phalangeal joints, heels, lateral knee joints, greater trochanters, anterior superior iliac spines, shoulders, elbows, and wrists as well as at C7, T10, and the sacrum. Kinematic data was collected using an 8-camera 3D motion capture system (Peak Motus® Software, Peak Performance, Centennial, CO). Recording of kinematic data was performed in a calibrated space with data captured at 60 Hz.

For each walking test session, subjects walked 5 times across a 10-meter walkway at their preferred walking speed; subjects were allowed to rest between walking tests. During each walking test, subjects were given 30 seconds to complete the 10-meter walk, and all outcome measures were extracted from data captured within the central 6 meters of the walkway.

Subjects used assistive devices as required during testing. Fourteen subjects used a rolling walker, one subject did not have the necessary hand function to grip the handles of a standard rolling walker and performed the test using a rolling walker with bilateral forearm platform supports, and two subjects did not require assistive devices. If a subject required an assistive device, the same device was used both for the initial and final test sessions.

Data analysis and statistics. Statistical Analysis Software 9.1.3 (Cary, NC) was used for all statistical analyses. Significance was set at α=0.05.

Walking speed (SPEED; meters/second; m/s) was calculated from the distance traversed in the direction of forward progression as measured from the sacral marker. A one-tailed, paired t-test was used to compare the mean speed of the five walking trials from the initial and final test sessions. One individual returned for a follow-up walking test session 5-weeks after the last session of WBV. Walking speed for this subject was compared to both the initial and final tests to assess persistence of change in speed associated with the WBV intervention.

Gait parameters were calculated from the kinematic measures. Data were filtered using a Butterworth filter with a 6 Hz cutoff. Bilateral step lengths were extracted from the coordinates of the heel in the direction of progression. Step lengths (m) were determined by the distance between two consecutive contralateral heel strikes. Step length was normalized to subject height. A one-tailed, paired t-test was used to compare the mean initial and final test values of the strong leg step length (SSL) and weak leg step length (WSL). Gait cadence (CAD; steps/minute) was calculated by dividing the total number of steps by the time need to complete the steps. A one-tailed, paired t-test was used to compare the mean CAD of the initial and final tests.

Intralimb coordination was defined as the ability to produce a consistent relationship of hip-angle-to-knee-angle coupling over multiple step cycles.[53, 106] The hip angle was defined by the trunk and thigh segments. The knee angle was defined by the thigh and shank segments. Vector coding was used to quantify intralimb coordination wherein the angular component of the coefficient of correspondence (ACC) represents

the degree of consistency of the hip angle-to-knee angle relationship over multiple cycles.[53, 106] It has been suggested that ACC values offer insights into the organization of control mechanisms (i.e., locomotor central pattern generators) underlying coordination of innate, cyclic behaviors.[53, 106] In individuals with SCI, changes in the ACC value correlate well with changes in walking speed associated with locomotor training.[53] ACC was calculated for both the strong ACC (SACC) and weak ACC (WACC) legs. An increase in ACC value from initial to final was interpreted as increased consistency of intralimb coordination. A one-tailed, paired t-test was used to compare the average mean SACC and WACC from the initial and final tests.

A Bonferroni correction was used to adjust the alpha level for 4 pair-wise (SPEED, CAD, SLL, WSL) comparisons resulting in an α=0.0083. Because values of ACC are derived from joint angles of multiple reflective markers, whereas, SSL, WSL and CAD are directly derived from a single reflective marker, a Bonferroni correction was not performed for pair-wise comparisons of SACC and WACC.

To determine which gait parameters were most closely associated with changes in walking speed, Pearson correlations where used to identify the relationship between SPEED and the parameters of CAD, SSL, WSL, SACC, WACC, and the first swing excursion (FSE) as measured by the Pendulum Test in Chapter 3. Pearson r values were interpreted as follows: 0.00-0.25 was considered little or no relationship, 0.25-0.50 was considered a fair relationship, 0.50-0.75 was considered a moderate relationship, and 0.75-1.0 was considered to be a good to excellent relationship.[92]

Results

The 12-session intervention of WBV was associated with a statistically significant increase ($p<0.001$) in SPEED from 0.259 ± 0.248 m/s in the initial test to 0.321 ± 0.260 m/s in the final test .

The data from Subject 17, who returned for a follow-up test 5-weeks after the last WBV session, had an initial SPEED of 0.128 m/s, a final SPEED of 0.215 m/s and a 5-week follow-up SPEED of 0.241 m/s. SPEED values of all subjects, group mean, and Subject 17 are illustrated in Figure 4.1.

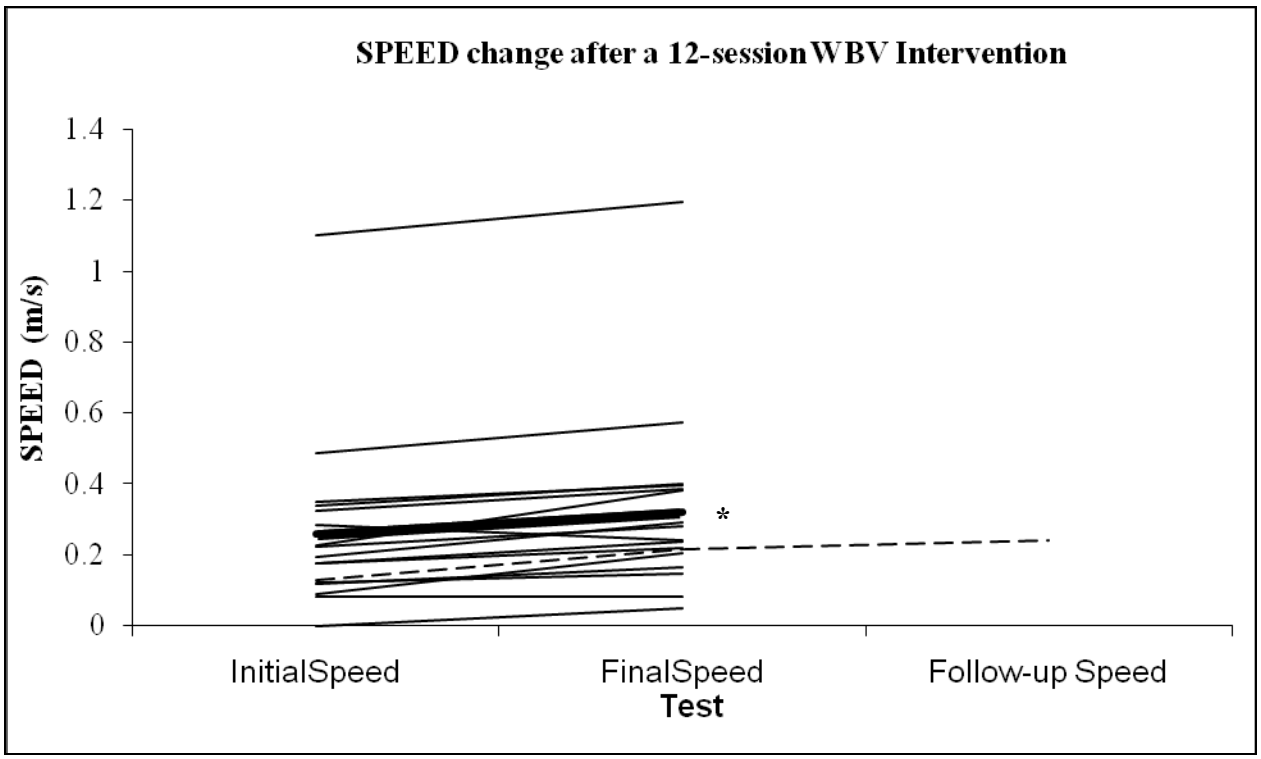

Figure 4.1: All subjects change in walking speed (SPEED) associated with 12-session whole-body vibration (WBV) intervention. Change in SPEED values for all subjects (thin lines) and group mean change (thick line). Group mean initial SPEED value (0.259 ± 0.248 m/s) and final SPEED value (0.321 ± 0.260 m/s) were significantly different (denoted by *; $p<0.001$). One subject returned for a follow-up test 5-weeks (dashed line) after the last WBV session, had an initial SPEED of 0.128 m/s, a final SPEED of 0.215 m/s and a 5-week follow-up SPEED of 0.241 m/s.

The 12-session intervention of WBV was also associated with a statistically significant increase ($p=0.002$) in CAD from 33 ± 5 steps/minute in the initial test to 36 ± 5 steps/minute in the final test. SSL significantly increased ($p=0.006$) from 0.194 ± 0.090 m in the initial test to 0.23 ± 0.063 m in the final test and WSL significantly increased ($p=0.003$) from 0.180 ± .082 m in the initial test to 0.212 ± 0.075 m in the final test. The relationship between change in SPEED to changes in, CAD, SSL, and WSL are illustrated in Figure 4.2.

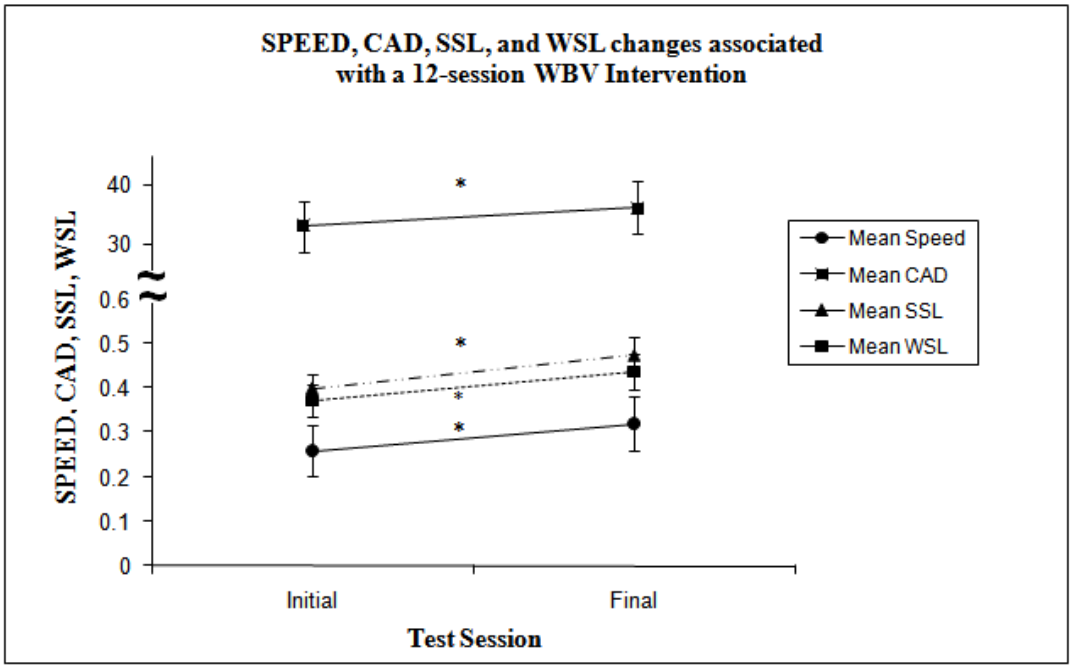

Figure 4.2: Group Mean Changes in walking speed (SPEED; m/s) and the relationship to change in walking cadence (CAD; steps/min) and change in weak (WSL) and strong (SSL) step lengths (m) after a 12-session whole-body vibration (WBV) intervention. CAD, WSL and SSL increased after the 12-session intervention of WBV. Theses gait parameters contributed to the increase in SPEED. The y-axis values are dependent on the reported measure. Note the break in the y-axis from 0.6 to 30 to accommodate for values of cadence. There was a significant increase in SPEED (denoted by *; $p<0.001$), CAD ($p=0.002$), SSL ($p=0.006$), and WSL ($p=0.003$).

There was a statistically significant change in SACC ($p=0.018$) from 0.68 ± 0.22 in the initial test to 0.77 ± 0.12 in the final test and in WACC ($p=0.026$) from 0.67 ± 0.22 in the initial test to 0.74 ± 0.14 in the final test. The relationship between change in SPEED to changes in SACC and WACC can be seen in Figure 4.3.

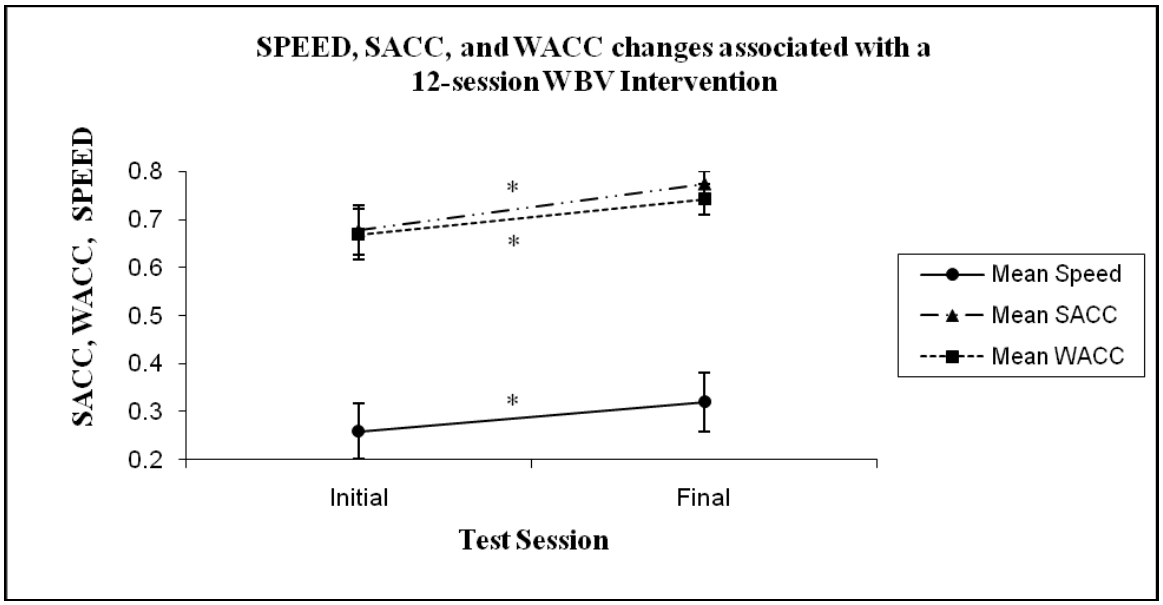

Figure 4:3: Group Mean Changes in walking speed (SPEED; m/s) and the relationship to change in strong (SACC) and weak (WACC) coefficients of correspondence (ACC) after a 12-session whole-body vibration (WBV) intervention. The y-axis values are dependent on the reported measure. There was a significant increase in SPEED (denoted by *; $p<0.001$), SACC ($p=0.018$), and WACC ($p=0.026$) associated with the 12-session intervention of WBV.

Changes in SPEED had a moderate, direct correlation with CAD ($r=0.528$), a fair, direct relationship with SSL ($r=0.344$) and a fair, inverse relationship with FSE ($r=-0.203$). Changes in SPEED had a weak, direct correlation with WSL ($r=0.154$), SACC ($r=0.018$), WACC ($r=0.204$).

Discussion

Our results indicate that consistent use of WBV is associated with an increase in walking function in individuals with SCI who have some ability to maintain voluntary standing. This is consistent with our hypothesis and with evidence in elderly individuals[72] and in individuals with Parkinson's disease who received a WBV

intervention.[17] In healthy, elderly individuals, a meaningful change in walking speed during a 10-meter walk test is 0.05 m/s.[87] However, this change in speed may be even more meaningful in individuals with SCI. As seen in Figure 4.1, 10 out of 17 of our subjects exceeded a change of 0.05 m/s after the 12-session intervention of WBV. Subject 13 was unable to take a single step in the initial test. After the 12-session intervention of WBV, the subject was able to take 4 steps. The increase in speed observed with the 12-session WBV intervention was equal to or greater than changes observed in our previously reported studies wherein individuals with SCI participated in a 3-month locomotor training intervention.[52] In that study, walking speed changes of 0.023 m/s, 0.05 m/s, 0.05 m/s, and -0.005 m/s were associated with manually assisted treadmill training, stimulation-assisted treadmill training, overground training, and robotic-assisted treadmill training, respectively. Our findings suggest that regular use of WBV intervention may be a potent intervention for improving walking function in individuals with SCI.

In the single subject who performed a follow-up test session 5 weeks after the WBV intervention, the effects on walking speed not only persisted, but increased 5 weeks after the WBV intervention. These are similar to findings in individuals with Parkinson's disease who had a persistent change in walking speed 4 weeks after receiving a 3-week WBV intervention .[41] The use of afferent input to induce positive plastic effects in the nervous system has received considerable attention in the recent research literature.[25, 66, 95] These plastic changes are most meaningful when they are associated with a lasting improvement in function.[25, 41]

We hypothesized that secondary outcome measures of cadence, step length, and consistency of hip-knee intralimb coordination would improve after a 12-session intervention of WBV. Consistent with our hypothesis, we found improvements in cadence, strong leg step length, weak leg step length, and strong leg and weak leg consistency of hip-knee intralimb coordination after a 12-session intervention of WBV. Furthermore, changes in walking speed and cadence were moderately correlated suggesting the increase in walking speed associated with the WBV intervention is related to an increase in the number of steps taken per minute. In addition to an increase in cadence, changes in walking speed also had a fair relationship with changes in the stronger step length, suggesting that increased stronger leg step lengths may also contributed to the improvements in walking speed. The improvements in walking speed and step length are consistent with increases in stride length reported in individuals with Parkinson's Disease during vibration.[85] However, this is contrary to evidence in ND individuals wherein no change in stride length during walking was observed with vibration applied to tibialis anterior, triceps surae, biceps femoris, rectus femoris, or quadriceps femoris.[114] Changes in stride length may not be evident in ND individuals because their strides are already longer when compared to individuals with a neuropathology. For this reason, individuals with neuropathology may have more aptitude for vibration induced improvement of spatial walking characteristics compared to ND individuals.

Consistent with our hypothesis, the degree of consistency of the hip-knee intralimb coordination of both legs improved but had only weak relationships with the change in walking speed. This is in agreement with evidence that a 3-month locomotor

training intervention improves hip-knee intralimb coordination from 0.56 before locomotor training to 0.65 after locomotor training.[53] However, contrary to our findings, in ND individuals, bilateral Achilles tendon vibration did not change walking speed or leg inter-segmental coordination.[27] Also in ND individuals, changes in intralimb ankle-knee coordination were not found with vibration applied to tibialis anterior, triceps surae, biceps femoris, rectus femoris, or quadriceps femoris.[114] Our findings and other evidence in individuals with SCI[53] suggest that the consistent use of afferent input improves the motor output of the control mechanisms that have been impaired after a SCI.

Spasticity negatively affects walking performance in individuals with SCI.[98] However, contrary to our hypothesis, although we found a significant decrease in quadriceps spasticity and an increase in walking speed as illustrated in Figure 4.4, the decrease in quadriceps spasticity was not related to the increase in walking speed. Our findings suggest that WBV modulates the quadriceps spinal stretch reflex, therefore, it is feasible to hypothesize that all hyperexcitable spinal stretch reflexes would also be modulated by an intervention of WBV. It is likely that quadriceps spasticity did not contribute to the impairment in walking function in these individuals prior to participation in the WBV intervention. However, if other hyperexcitable spinal stretch reflexes caused deficits in walking function, it is feasible to suggest that the WBV may have modulated these reflexes thereby improving walking function.

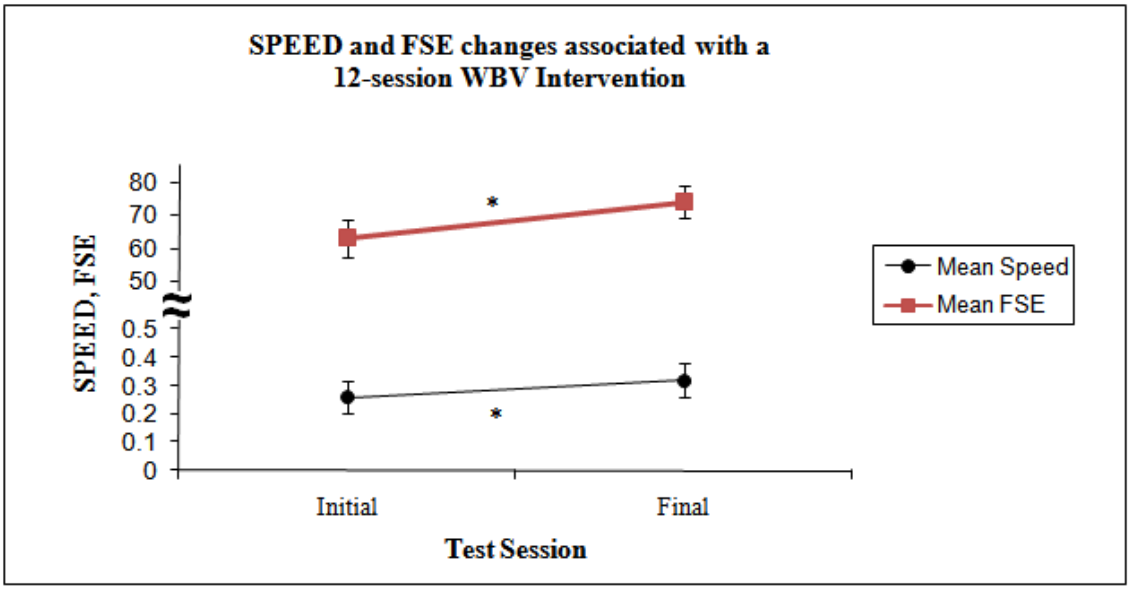

Figure 4:4: Group Mean Changes in walking speed (SPEED; m/s) and the relationship to change in first swing excursion (FSE; degrees; an increase in FSE was interpreted as a decrease in quadriceps spasticity), as measured by the Pendulum Test from Chapter 3 associated with a 12-session whole-body vibration (WBV) intervention. There was a significant increase in SPEED (denoted by *; $p<0.001$) and FSE ($p=0.005$). However, there was a fair, inverse relationship with FSE ($r=-0.203$) between the measures suggesting there was no relationship between the change in quadriceps spasticity and the improvement in walking function. The y-axis values are dependent on the reported measure. Note the break in the y-axis from 0.5 to 50 because no values were reported in this range.

Implications for function

Our findings and other evidence in individuals with SCI suggests that the consistent use of afferent input positively influences some aspects of the motor output that are been impaired by SCI. These results support the use of WBV as a possible intervention to improve walking function in individuals with SCI. With a 12-session intervention of WBV, we found significant improvements in walking speed, cadence,

step lengths, and intralimb coordination over multiple steps. Furthermore, the effect of WBV on walking function may continue to improve walking function even after the use of WBV has ended.

CHAPTER 5: *CONCLUSION:* IMPLICATIONS FOR THE USE OF VIBRATION AS A REHABILITATION INTERVENTION

Evidence from this dissertation suggests that vibration can be used to activate spinal circuits that provide similar effects as descending pathways. In individuals with spinal cord injury (SCI) have deficits in motor function because of the loss of descending pathways. Vibration influences spinal neural circuits, resulting in more normal reflex modulation and improved walking function. Localized muscle vibration mimics supraspinal input used to activate spinal circuits associated with the central pattern generator (CPG) for locomotion, thereby producing involuntary leg movements in individuals with SCI at or above T10. A 12-session intervention of whole-body vibration (WBV) provides modulatory effects on spinal reflexes that are hyperexcitable, resulting in decreased quadriceps spasticity. The WBV intervention was also associated with clinically meaningful changes in walking function. These results suggest that vibration is a powerful intervention for improving walking function in individuals with SCI.

In Chapter 2, we found that localized vibration to the quadriceps, hamstrings or tensor fascia latae (TFL) can be used to elicit involuntary air-stepping responses in individuals with SCI. TFL was identified as the vibration placement that elicited the most consistent and robust air-stepping responses in individuals with SCI. We concluded that these responses have implications for use in combination with locomotor training, but suggested that further investigation is warranted to assess the effectiveness of vibration during walking in individuals with SCI. Prior studies in our laboratory have

been used to compare changes in walking function associated with four different types of locomotor training interventions.[52] Two of these combination interventions used locomotor training with functional electrical stimulus (FES) and body weight support (BWS). Each step was facilitated by the FES, eliciting a robust flexion withdrawal response that caused simultaneous ankle dorsiflexion and hip and knee flexion.[52] Because FES and BWS combination interventions improve walking function in individuals with motor-incomplete SCI,[52] comparing changes in walking function associated with TFL vibration and FES would assess the effectiveness of vibration as a locomotor training intervention.

In Chapter 3, we found that a 12-session intervention of WBV decreased spinal stretch reflex (SSR) as measured by the Pendulum Test. However, it is unclear what mechanisms were responsible for the modulation of SSR found after the intervention. Elucidating the underlying neural circuits that are influenced after a 12-session WBV intervention will provide an essential understanding of the changes in spasticity. Specifically, electrophysiological tests could be used to quantify changes in the Hoffman reflex (i.e., H-reflex), presynaptic inhibition, and low-frequency depression. A decrease in the H-reflex amplitude after the intervention compared to before the intervention would further support our findings that the intervention modulated SSR excitability. An increase in presynaptic inhibition or low-frequency depression would help identify the mechanisms that caused the decrease in SSR excitability.

Within a session of WBV, electromyography (EMG) data and H-reflexes could also be collected before, during, and after a session of WBV to measure the vibration-elicited EMG activity and reflex responses. Data collected before the intervention would

provide a baseline measurement that could be used to compare with the measurements taken during and after the WBV session. In addition, this measurement would identify weekly changes in muscle activity and SSR excitability that would be useful in suggesting how many sessions of WBV can be used to cause plastic changes and dosage effects of WBV in individuals with SCI. After a session of WBV, data collected more than 15 minutes post-session could also be used to determine how long the decrease in spasticity persists. If this data was collected from the legs and the arms would also provide information about the multiple spinal segments that the WBV affects and may suggest use for decreasing spasticity in the upper limbs.

In Chapter 3, we concluded that our participants had more SSR excitability in the immediate post-WBV measurement compared to the delayed post-WBV measurement because of the vibration paradox. EMG data could be used to quantify the time-course of the vibratory reflex responses during and after a session of WBV. H-reflex data would quantify the time-course of SSR modulation. Comparisons of these two time-courses would identify the mechanisms responsible for the changes we found.

We also found that individuals who used antispasticity medication had similar changes in spasticity compared to those who did not use antispasticity medication. We concluded that further investigation was warranted to suggest that WBV may be used as a substitute for antispasticity medications. A randomized, controlled trial of individuals with spasticity assigned to either an intervention of an acute dosage of Baclofen (or any other antispastic agent) or WBV would provide a comparison of the effects of each intervention on spasticity. If the two interventions were equivalent, then WBV might be

considered as an alternative treatment of spasticity for those who do not use antispasticity agents because of the side-effects (as described in Chapter 1).

To suggest direct causality for changes in spasticity, certain variables should be controlled. For individuals who rely on a wheelchair for primary means of mobility, the slight squatting position during each WBV session may have confounded our results. Comparing individuals who receive sessions of squatting alone (in the absence of WBV) or a sham intervention (i.e., subsensory electrical or vibration in which the functional effects have been reported) to those who receive an equal intervention of WBV during the same squatting activity would provide evidence that WBV was the reason for the change in spasticity.

In Chapter 4, we found that walking function improved after participation in a 12-session intervention. In addition, the decrease we found in quadriceps spasticity did have a strong correlation with changes in walking speed. Perhaps if we had measured spasticity of other muscles (i.e., clonus) we would have found other relationships related to the change in walking speed. Electrophysiological tests of reciprocal inhibition may also identify changes in the underlying mechanisms related to walking function.

This dissertation did not focus on changes in specific muscle strength. However, in clinical populations, others have found improvements in muscle strength associated with WBV interventions.[7, 31, 32, 109] Therefore, it is feasible to suggest that increases in muscle strength may also be found in individuals with SCI. If an increase in strength is found in muscles critical for walking function, it may also contribute to changes in walking function.

These 17 individuals were given an intervention of WBV without walking training, and clinically meaningful improvements in walking function were found in the majority of individuals. These results suggest that use of WBV alone is effective in improving walking function. Our findings suggest that a combination intervention of WBV prior to locomotor training would be most effective in improving walking function.

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