Acute Effects of Whole Body Vibration on Central and Peripheral Hemodynamics and Oxygen Consumption in Individuals with Spinal Cord Injury

by

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A dissertation submitted to the Graduate Faculty of
Auburn University
in partial fulfillment of the
requirements for the Degree of
Doctor of Philosophy

Auburn, Alabama
August 6, 2011

Keywords: Whole Body Vibration, Spinal Cord Injury, Cardiovascular Fitness, Oxygen Consumption, Blood Flow

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Abstract

A substantial body of evidence suggests spinal cord injury (SCI) increases cardiovascular disease and mortality risk in aging individuals with SCI. Based on retrospective assessments, excess mortality after SCI has been related to neurological level and completeness of injury. Performing routine arm exercise moderately stimulates the cardiovascular system; whereas functional electrical stimulation (FES) has been shown to elicit greater venous return and myocardial performance. FES is potentially painful and can induce adverse responses such as autonomic dysreflexia especially in quadriplegics and high paraplegics. Therefore, developing a safe and effective exercise intervention to improve cardiovascular health must be a priority for this population. Whole-body vibration (WBV) exercise is emerging as a potential treatment to improve locomotor capabilities in individuals with SCI. The use of WBV exercise to improve on cardiovascular response in the SCI population has yet to be investigated. Thus, the purposes of this study were: 1) to determine the acute effects of whole body vibration (WBV) exercise on central and peripheral hemodynamics and oxygen consumption, and 2) to compare the physiological responses to WBV between three different frequencies (30, 40, and 50 Hz) in individuals with SCI compared to age and activity matched able-bodied individuals. Eleven males with SCI (injury levels: C5-T6; ages: 50.39 ± 8.16) and ten age and gender matched able-bodied controls (ages: 48.17±6.78) completed three WBV exercise protocols at 30, 40 and 50 Hz. Heart rate, systolic blood pressure, diastolic blood pressure, stroke volume, cardiac output, oxygen consumption, and relative changes in oxyhemolobin, de-oxyhemoglobin and total

hemoglobin values were obtained during pre-WBV seated steady-state, pre-WBV standing steady-state, WBV first minute, WBV steady-state, post-WBV standing steady-state, and post-WBV seated steady state. Moreover, leg skin temperatures were obtained pre-WBV, immediately post-WBV, 10 minute post, and 15 minute post-WBV. Multi-analysis of Covariance with random subject-effect was used to analyze the effect of the treatments on the dependant variables. Follow up univariate ANCOVAs and t-tests were utilized to compare the treatment and con¬trol groups on the outcome measures. 30, 40, and 50 Hz of WBV elicited slight increases in heart rate, stroke volume and cardiac output both in the SCI and able-bodied group. Systolic blood pressure was significantly increased following WBV at 30 and 40 Hz in the SCI group. Both groups demonstrated significant increases in oxygen consumption during and following WBV; yet the increase in oxygen consumption was more pronounced in the SCI group. Muscle oxygenation and lower leg skin temperature was significantly increased following WBV only in the SCI group. Moreover no specific frequency effect was revealed within or between groups. The WBV parameters used in the present study do not appear to induce significant cardiovascular benefits for the individuals with SCI as well as for able-bodied individuals. Physiological responses to 30, 40, and 50 Hz were similar.

Acknowledgments

This dissertation is dedicated to my parents Mustafa and Hulya Yarar who have given me the opportunity of an education from the best institutions and support throughout my life. I would also like to thank my extended family Rahmiye, Turgay, Deniz, Ediz Akyalcin, Filiz Karaduman, and Zeynep Gunal for encouraging me throughout this endeavor. I would like to thank Dr. JoEllen Sefton for her mentorship, friendship and patience throughout my doctoral work. I greatly appreciate her belief in me. I would also like to thank our undergraduate researchers Andrea Hartis, Matt Homan, Sara Sellers and my good friend Franklin Butts for their great assistance with this project. Their support and care helped me to overcome setbacks. I greatly value their friendship and support. I would like to thank each member of my committee, Dr. David Pascoe, Dr. John Quindry, and Dr Eleanor M. Josephson, Dr Bruce Gladden for providing insight and support as both teachers and committee members. I also would like to thank Dr Pascoe for his amazing effort and patience on making our research laboratory's restrooms accessible to our paralyzed participants. Without this addition to our lab, this project would have been impossible. I would like to thank Dr. Judith Hudson for teaching me lab skills to perform echocardiography measurements for this project. I would particularly like to thank Dr Gladden and Jim McDonald for their time, insight, encouragement, and untiring help during my difficult moments. I would like to thank the participants for volunteering for this study. Without their time and effort it would have been impossible for me to finish this work. I would like to thanks Dr. Craig Darch for serving as my outside reader. Finally, in addition to everyone else

who assisted with this project, I would like to thank my husband Gordon Fisher for his support and patience with me throughout this project. None of this would have been possible without his love and patience.

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CHAPTER I

INTRODUCTION

It is estimated that approximately 12,000 new cases of spinal cord injury (SCI) occur each year. There are currently 255,700 individuals living with SCI in the United States.[1] To date, no treatments exist that are capable of reversing the neurological impairment resulting from SCI. Improved care has increased the average life span for those with SCI; however, due to medical issues associated with the injury cardiovascular disease has become highly prevalent in this population.[2] One third of SCI patients older than 65 years and nearly half of the patients who live with SCI for more than 30 years die of cardiovascular disease (CVD).[3] Moreover, CVD accounts for a major portion of post-injury treatment costs.[4-6]

Higher neurological level (C4-T6) and greater completeness of injury are associated with lower levels of heart function.[2,7] Rather than experiencing pathological increases in cardiac mass that occur with aging, aging SCI individuals with high level injuries lose nearly a quarter of total cardiac and left ventricular mass.[8] The myocardial atrophy observed in SCI individuals may be related to physical inactivity and/or abnormal autonomic circulatory regulation.[9] Previous studies of SCI patients[9] have shown that the application of functional electrical stimulation (FES) on the paralyzed muscles can reverse the cardiac atrophy and mediate the detrimental effects of SCI on cardiovascular health. However, FES is potentially painful and can induce adverse responses such as autonomic dysreflexia, which is characterized by a substantial sympathetic response to a painful stimulus or activation of non-nociceptive afferents from viscera and skin. This is

particularly prevalent in quadriplegic and high paraplegic patients. Hypertension resulting from autonomic dysreflexia can be life threatening. To date, a novel and safe exercise intervention that can reverse paralysis related loss of cardiac mass and can induce muscle contractions in paralyzed skeletal muscles is not available.

The first application of whole-body vibration (WBV) as an exercise intervention was conducted by Russian scientists who found that vibration was effective in enhancing strength in well-trained able-bodied individuals.[10] Subsequently, the effects of acute and chronic vibration exercise on the body's neuromuscular system have been examined using different treatment protocols.[11-13] Skeletal muscle can be forced into a tonic contraction by prolonged percutaneous mechanical vibration of the muscle belly via discharge from both primary and secondary endings.[14-17] Several studies have investigated the effect of WBV on energy metabolism and hemodynamic responses in able-bodied indivuduals.[12,14,18-19] A specific energy demand arising from exposure to vibration[20] and an increase in energy turnover[21] have been demonstrated. Furthermore, the mechanical forces produced by muscle contraction and relaxation acting on the muscle vasculature are thought to produce a significant increase in muscle blood flow.[22] An optimal response to varying frequencies of vibration has been demonstrated in able-bodied individuals,[23] with increased improvements in heart rate, blood pressure and oxygen consumption found with increasing frequencies.[20]

WBV has emerged as a potential intervention to improve locomotor capabilities in people with SCI.[24-25] However, the effects of WBV on the hemodynamic responses and energy metabolism, and effective vibration frequencies to improve these physiological responses have not been studied in the SCI population. If WBV exercise can be shown to improve energy metabolism and hemodynamic responses, WBV could become an important therapeutic modality

in the prevention of cardiovascular complications that affect individuals with SCI. Thus the purposes of this study were twofold: 1) to investigate the acute effects of WBV on central and peripheral hemodynamic responses and oxygen consumption; 2) to compare the physiological responses to WBV between three different frequencies (30, 40, and 50 Hz).

CHAPTER II

REVIEW OF LITERATURE

Epidemiology of Spinal Cord Injury

Injury to the spinal cord disrupts its structural and functional integrity resulting in partial or complete motor paralysis, sensory loss, and autonomic dysfunction below the level of the injury. A spinal cord lesion causes quadriplegia or paraplegia depending on the neurologic level of the injury.[26] Individuals with quadriplegia have sustained injuries to one of the eight cervical segments of the spinal cord; whereas those with paraplegia have lesions in the thoracic, lumbar, or sacral regions of the spinal cord. The annual incidence of spinal cord injury is approximately 12,000 new cases each year in the U.S. [27] The most common cause of SCI is motor vehicle accidents which account for 41.3%, followed by falls (27.3%), acts of violence (15%), and recreational sports activities (7.9%).[27] Approximately 81% of the SCI population is male [1] , 66.2% are Caucasian, 27.0% are African American, 2.0% are Asian, and 7.9% are Hispanic.[28-29] The average age at which SCI occurs has increased over time. For example, from 1973 to 1979 the average age at SCI was 28.7 years; however the current average age at SCI has shifted to 40.2 years of age.[27]

Life expectancies for individuals with SCI continue to increase; however mortality rates are still significantly higher during the first year after injury in severely injured persons (Table 1). The leading cause of death among persons with SCI has been renal failure; however significant advances in urologic management have decreased the mortality from renal

complications among SCI individuals. More recently mortality among SCI individuals has resulted from pulmonary complications during the first year after injury.[1]

Table 1. Life expectancy is the average remaining years of life for an individual with SCI.[1]

Life expectancy for post SCI injury by severity of injury and age at injury

	For persons who survive the first 24 hours						For persons surviving at least 1-year post-injury				
Age at Injury	No SCI	Motor Function at Any Level	Para	Low-Tetra (C5-C8)	High-Tetra (C1-C4)	Ventilator Dep.	Motor Function at Any Level	Para	Low-Tetra (C5-C8)	High-Tetra (C1-C4)	Ventilator Dep.
20	58.4	52.6	45.2	40.0	35.7	17.1	53.0	45.8	41.0	37.4	23.8
40	39.5	34.1	27.6	23.3	19.9	7.3	34.5	28.2	24.2	21.2	11.4
60	22.2	17.7	12.8	9.9	7.7	1.5	18.0	13.2	10.4	8.6	3.2

Note: SCI: Spinal cord injury; Tetra: tetraplegia; Ventilator Dep: Ventilator dependent; Para: paraplegia

SCI individuals continue to be at an increased risk for secondary medical complications such as deep venous thrombosis, autonomic dysreflexia, pressure ulcers, urinary tract infections, and bone loss.[2,4] Additionally, common risk factors for cardiovascular disease (both ischemic and non-ischemic) such as orthostatic hypotension, impaired cardiovascular reflexes, , quadriplegic cardiac atrophy (loss of left ventricular mass), glucose intolerance, type-2 diabetes, dyslipidemia, and alteration in body composition (increase in fat mass and decrease in lean mass) are frequently observed in aging individuals with SCI.[2] These secondary complications have increased the average annual health and living expenses in this population. The average

yearly expenses for medical care are estimated to be $826,843 during the first year and $148,625 for each subsequent year for high quadriplegia (C1-C4), $535,877 during the first year and $60,887 for each subsequent year for low quadriplegia (C4-C8) , and $303,220 during the first year and $30,855 for each subsequent year for paraplegia.[6] This increase in medical expenses along with the secondary complications that accompany SCI highlights the need for improved therapeutic interventions to prevent adverse cardiovascular and metabolic complications and to reduce the annual health care costs in aging individuals with SCI.[29]

Clinical Manifestations in the Chronic Stage of SCI

After surviving the acute stage of injury, patients with SCI are able to maintain stable cardiac function. However, they continue to have impaired cardiovascular reflexes and are prone to other complications such as conduction disorders, orthostatic hypotension, and autonomic dysreflexia due to interruption of the sympathetic outflow to the effector organs such as the myocardium, adrenal medulla and smooth muscle of the arteries and veins.[30]

The autonomic nervous system plays a significant role in the modulation of electrical properties of the heart. Complete or incomplete injury to the cervical spinal cord results in disruption of central sympathetic system outflow while peripheral sympathetic nerves may remain intact.[2] Sympathetic innervation to the heart occurs from T3-T6, thus individuals with quadriplegia (C4-C8) and high-level paraplegia injuries (between T1-T6) present significant cardiac complications related to vagal hyperactivity making them prone to persistent symptomatic bradycardia.[31]

Individuals with quadriplegia are prone to orthostatic hypotension commonly because of their inability to regulate and maintain blood pressure through neurogenic pathways. The

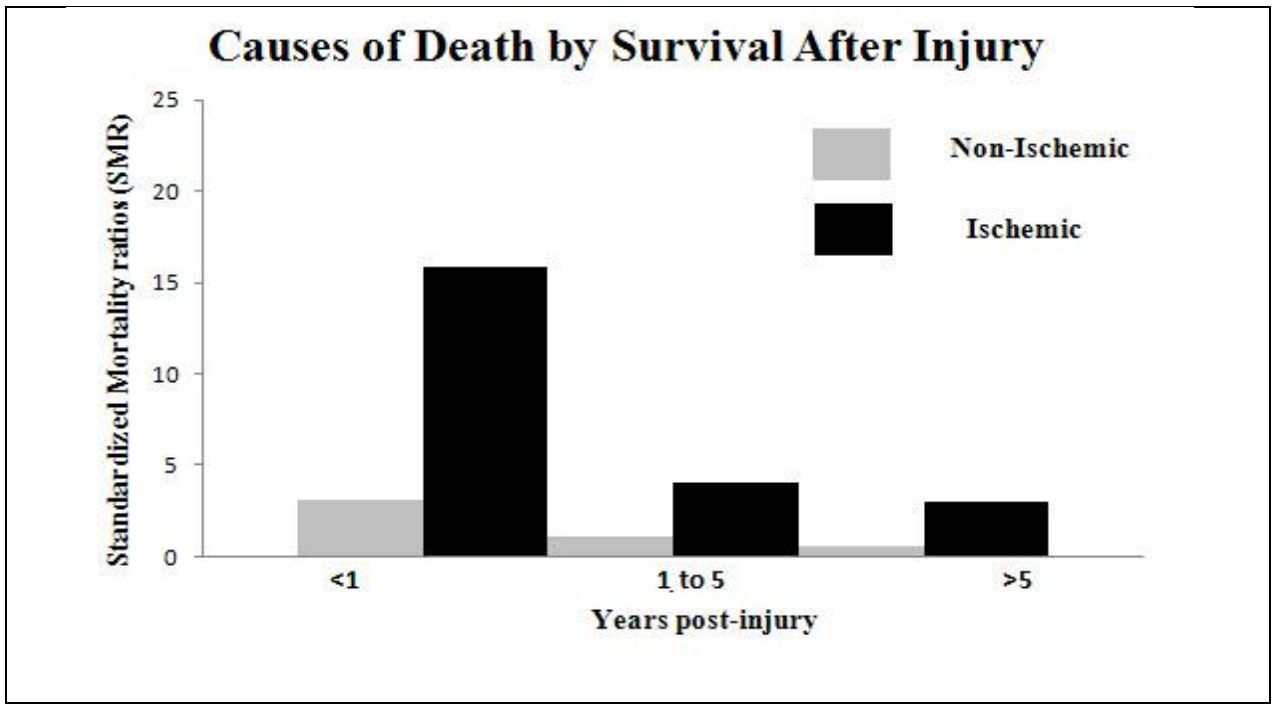
neurogenic pathways are accountable for short-term regulation of blood pressure through the baroreceptor reflexes, including the afferent nerves, vasomotor system, intraspinal sympathetic system, and postganglionic outflow..[31] The central disruption of the descending intraspinal pathways interferes with short-term regulatory mechanisms. Renin-angiotensin-vasopressin system is utilized for long term blood pressure control to prevent critically low blood pressures. In the absence of sympathetic vasoconstrictor tone, mean resting arterial blood pressure is approximately 70mmHg in individuals with high SCI as compared to 70 to 110 mmHg in able-bodied individuals.[2]

Autonomic dysreflexia in individuals with high level SCI (above T6) results from noxious stimuli below the level of injury that cause sympathetic hyperactivity.[32-33] Individuals experience a sudden and significant increase (20-40mmHg) in both the systolic and diastolic blood pressure. An increased number of spinal and peripheral adrenoreceptors, accumulation of other neurotransmitters, hormones and neuropeptides have been suggested to play a role in this massive sympathetic response to peripheral perturbations.[2,32] Intact sensory nerves below the level of the injury transmit impulses to the spinal cord and stimulate sympathetic neurons in the inter-medio-lateral gray matter; yet sympathetic inhibitory impulses that originate above T6 are blocked as a result of the injury.[34] The result is severe vasoconstriction in the arterial vasculature from the release of neurotransmitters (norepinephrine, dopamine-[3-hydroxylase, and dopamine)[2,30,35] resulting in significant elevations in blood pressure. Hypertension resulting from autonomic dysreflexia can be life threatening and typically persists until the noxious stimulus below the level of injury is removed.[35]

Cardiovascular Mortality in the Chronic Stage of SCI

The earlier in life SCI occurs the more likely it is that cardiovascular diseases will develop. [2] Individuals with quadriplegia and high paraplegia are more prone to cardiovascular problems later in life as higher neurological level and greater completeness of injury are associated with lower levels of heart function.[2,7] One third of SCI individuals older than 65 years and nearly half of the individuals living with SCI's for 30 years or more experience death from comorbidities associated with cardiovascular diseases.[8] Individuals with SCI often have multiple cardiac risk factors due to a sedentary lifestyle and limited physical activity, which contribute significantly to higher cardiovascular mortality rates.[36] In comparison with the general population, individuals with SCI have a 2-fold increase in rate of mortality from non-ischemic heart disease, and a 1.4-fold increase for ischemic heart disease (Figure 1)[37] Heart failure has been commonly found in these individuals, particularly in association with autonomic dysreflexia. SCI has also been shown to be associated with risk factors for ischemic heart disease.[2]

Figure 1. Causes of death by survival after injury in individuals with SCI[28]



Note: Reproduced from DeVivo M J, Black K J, and Stover SL: Causes of death during the first 12 years after spinal cord injury. Arch Phys Med Rehabil*:* 1993; 74:248.

Metabolic disorders and cardiovascular disease risk

Metabolic disorders that predispose SCI individuals to ischemic heart disease include hypertension, lipid abnormalities, glucose intolerance, diabetes mellitus, adiposity, and smoking. Poor peripheral utilization of insulin results in an increased intolerance to glucose and a tendency toward diabetes mellitus.[36] There is also a tendency for abnormal lipid patterns even though total cholesterol and triglyceride levels are similar to those of the general population.[38-39] Several reports[39-41] have described depressed levels of high density lipoprotein cholesterol in this population, possibly due to the lack of physical activity and the extreme sedentary lifestyles

imposed by paralysis. Moreover the level and completeness of the lesion has been shown to affect serum high density lipoprotein cholesterol values. (Table 2)[38,42]

Table 2. Lipid profile by group and subgroup in individuals with SCI

	Tetra (n=247) mean +SEM		Para (n=294) mean +SEM		Com Tetra (n=156) mean +SEM		Incom Tetra (n=94) mean +SEM		Com Para (n=206) mean +SEM		Incom Para (n= 88) mean +SEM	
TC (mg/dL)	184	2.6	198	2.6*	181	3.1	190	4.5	116	2.4	205	5.3
TG (mg/dL)	122	5.5	122	5.5	122	7.3	121	8.2	199	6.2	128	11.6
HDL (mg/dL)	39	0.7	45	0.8*	38	0.9	40	1.1	44	0.9	47	1.4
LDL (mg/dL)	121	2.4	129	2.3*	118	2.8	125	4.4	128	2.6	138	4.6

Note: TC= total cholesterol; HDL= high density lipoprotein cholesterol; LDL= low density lipoprotein cholesterol; *$p \leq 0.01$ for tetra (tetraplegic) vs. para (paraplegic)

Obesity is also a prevalent issue in this population. The changes in body composition that follow SCI (reduction in muscle and bone mass), resultant changes in metabolic rate, and mobility limitation may contribute to the development of weight gain.[43] Studies exploring differences due to injury type concluded that BMI is higher in the paraplegia group compared to quadriplegia.[44] One potential explanation for this is that BMI measures total body weight (which includes lean mass and fat mass) adjusted for height. Lean body tissues (muscle and bone) have higher density (greater weight per volume) than fat tissue. It is possible that individuals with paraplegia may have a higher percent lean mass than individuals with tetraplegia possess. Thus, BMI may underestimate obesity when it is defined as percent body fat to a greater extent in individuals with tetraplegia than in paraplegia.[45]

De-conditioned heart and cardiovascular disease risk

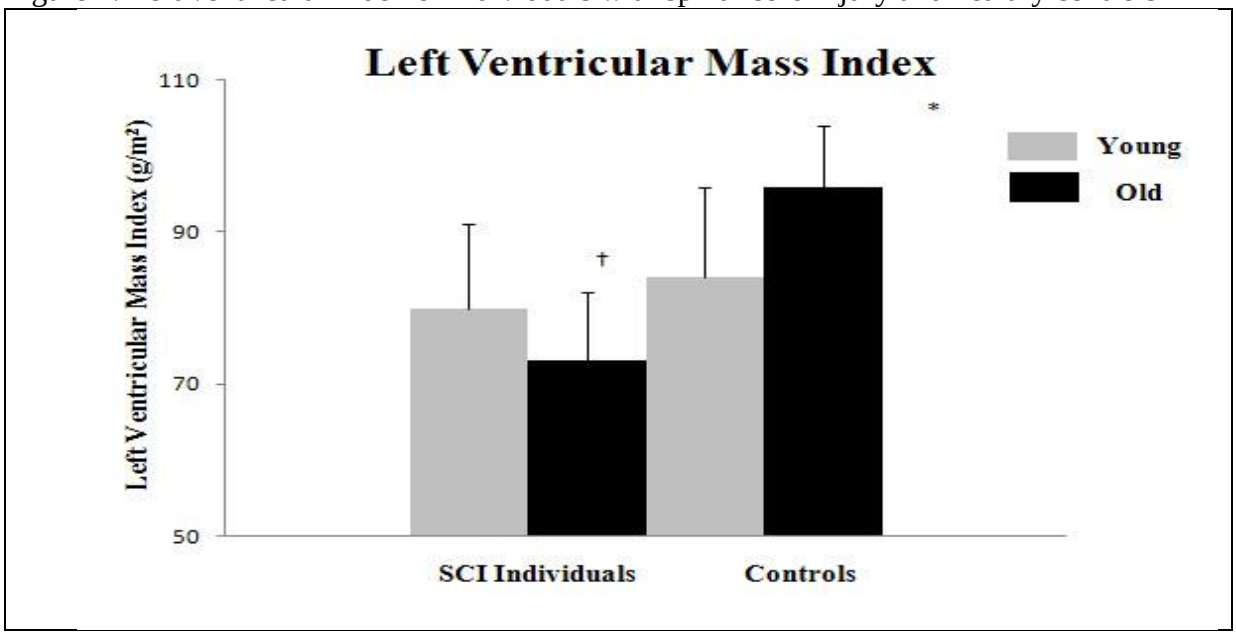
Physical activity can lead to significant modification of cardiac structure, from myocardial hypertrophy for endurance trained athletes[46] to myocardial atrophy for chronically de-conditioned individuals.[47] Quadriplegic and high paraplegic individuals typically develop an inactive life-style, as shown by maximal oxygen uptake values of approximately 0.7 L/min or 12 ml/kg/min.[26] representing the most extreme degree of inactivity possible in otherwise able-bodied individuals. (Average maximal oxygen uptake value in able-bodied individuals who are between 35- 65 is 30-35kg/ml/min).

The most obvious physiological and functional problem associated with this significantly lower aerobic fitness in individuals with quadriplegia and high paraplegia is skeletal muscle paralysis. Voluntary arm and leg muscle activity is limited due to partial innervation of the arm and leg muscles. The inability to perform voluntary large muscle group (leg muscles) activity limits the ability to acutely stress the otherwise healthy cardiovascular system. Absence of the venous muscle pump in the legs leads to venous pooling in the lower body. The accumulation of blood in the veins of the legs, with the subsequent decrease in circulating blood volume, significantly reduces cardiac volume [2,9,31] and left ventricular mass.[9,48] Therefore, rather than experiencing the pathological increases in cardiac mass that occur with aging, individuals with quadriplegia lose nearly a quarter of total cardiac and left ventricular mass.[49] Cardiac atrophy of this nature has been shown to increase with aging and is independent of body surface, or other underlying diseases that normally lead to cardiac atrophy (Figure 2).[50] Moreover the development of left ventricular diastolic dysfunction has been reported in individuals subjected to prolonged physical inactivity,[47,51] suggesting that individuals with SCI might also be at a

higher risk of developing abnormalities in left ventricular function which has been shown to be associated with exacerbated cardiovascular outcomes[52] such as increased incidence of heart failure.[4]

These complications associated with paralyzed-induced de-conditioning of heart are a frequent cause of morbidity and mortality and result in decrease in quality of life in individuals with SCI.[53] In the general population, physical activity has several beneficial effects with respect to cardiovascular disease risk; including improved lipid profiles, increased insulin sensitivity, and increased cardiovascular fitness;[54] yet everyday mobility and activities of daily living are inadequate to meet the requirements for cardiovascular fitness in individuals with SCI.[55-57] Additionally this population faces major exercise related challenges stemming from skeletal muscle paralysis, limited muscle mass, and autonomic dysfunction.[31]

Figure 2. Left ventricular index of individuals with spinal cord injury and healthy controls[35]



Note: Reproduced from Eysmann et al., Left ventricular mass and diastolic filling patterns in quadriplegia and implications for effects of normal aging on the heart

Exercise and SCI

Skeletal Muscle Paralysis

Voluntary arm exercise capacity is often limited in individuals with quadriplegia due to the smaller muscle mass and partial innervation to upper extremities. Limited venous return resulting in venous pooling in the lower extremities is due to the absence of a functional skeletal muscle pump. During arm exercises this may contribute to peripheral fatigue before the cardiovascular system reaches the limits of its pumping capacity.[31] The accumulation of blood in the lower extremities causes a decrease in circulating blood volume that may result in ischemia in the active muscles of the upper extremities. Therefore, in the absence of any cardiovascular disease the peak oxygen consumption and upper body aerobic exercise capacity will be limited by peripheral factors such as small muscle mass and decreased venous return rather than central cardiac factors such as limited stroke volume and cardiac output. [31,58]

Sympathetic Nervous System Impairment

Normal blood redistribution during upright exercise is impaired due to vasomotor paralysis in individuals with high (C4-T6) SCIs. Voluntary arm exercise cannot activate the sympathetic nervous activity due to an interruption of the efferent sympathetic innervation to the myocardium, smooth muscle of arteries and veins, and the adrenal medulla.[59] This impairs positive cardiac chronotropy, inotropy, adrenal medulla catecholamine production, and thermoregulation during aerobic exercise.[31] When arteries and veins of active muscles vasodilate without compensatory vasoconstriction, the exercise capacity and tolerance may be limited by orthostatic hypotension.[31] In addition to limited venous return due to reduced activity of the

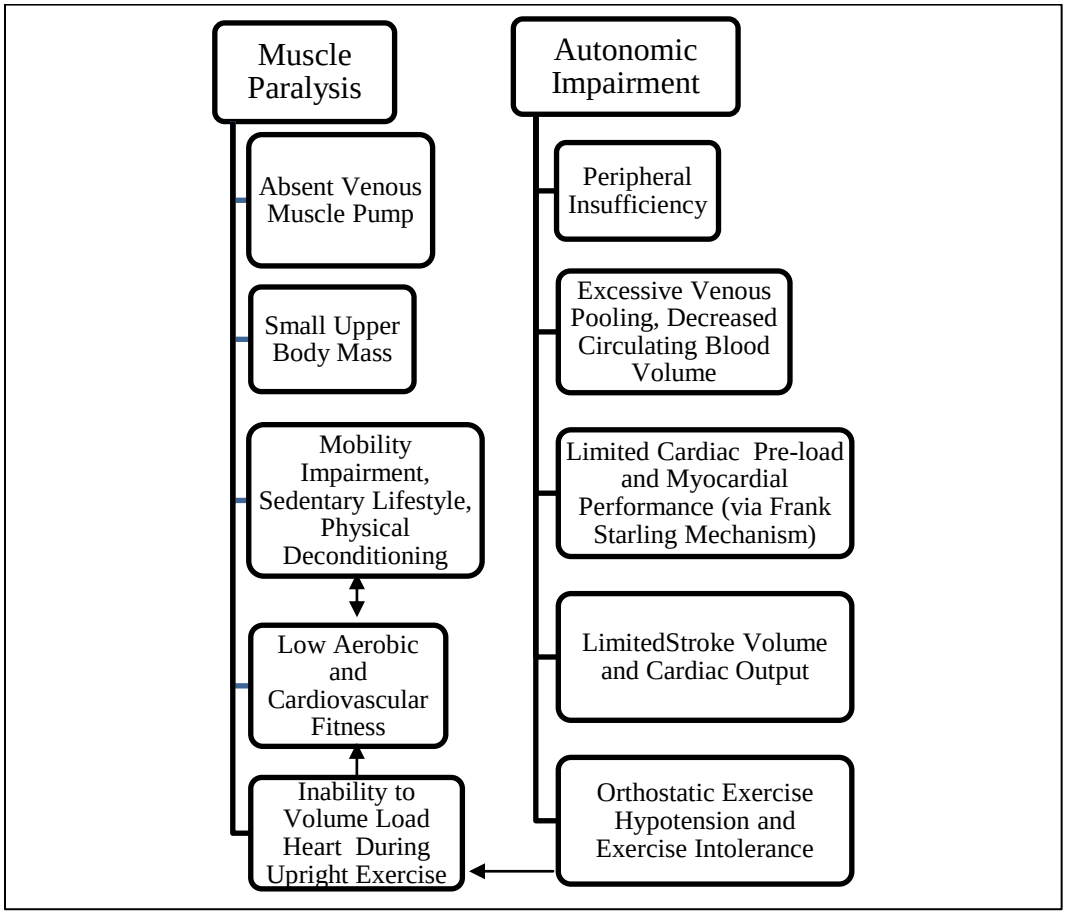
skeletal muscle pump, the vasomotor paralysis may also result in venous pooling in the lower extremities and decreased venous return. Normally, the increased volume of blood stretches the ventricular wall, causing cardiac muscle to contract more forcefully (Frank Starling mechanism); however the decrease in venous return in SCI individuals results in limited cardiac pre-load and decreased myocardial performance.[9,31] This may further compromise cardiovascular fitness and health in the chronic stages of SCI.[9,49] Potential factors that may negatively affect the cardiovascular fitness and health in quadriplegic and high paraplegic individuals are presented in Figure 3.[31]

Upper Body Exercise

Voluntary use of upper extremities has been commonly used to facilitate independence in daily activities (wheel-chair mobility, transfers, and soft tissue ulcer relief) both at home and in the society .[2,31,60-61] In quadriplegic and high paraplegic individuals who are confined to arm exercises, the ability to generate higher levels of oxygen consumption is reduced due to a number of separate but related metabolic, hormonal, and hemodynamic disturbances related to their injury. In able-bodied individuals, blood is directed to active muscles from inactive tissues to supply the working muscles during arm exercise. Cardiac output is also increased due to an increase in stroke volume and heart rate. This vasoregulation could be attributed to the increased activity of the sympathetic nervous system in able-bodied individuals; however individuals with high (C4-T6) SCIs the sympathetic nervous system is either completely or partially absent in direct relation to the level of the spinal cord lesion.[2,31] As a result of limited sympathetic nervous system function, the myocardial contractility is reduced. This may limit maximal cardiac output

and stroke volume and thus significantly limit the potential to improve cardiovascular fitness/health in this population.[62]

Figure 3. Flowchart of factors that influence cardiovascular fitness in individuals with SCI



Arm cranking exercise: It is important to consider potential limitations in improving cardiovascular fitness with arm cranking exercise in this population. The amount of muscle mass available is inadequate to elicit "volume loading" of the heart to maximally stress central hemodynamic mechanisms. Problems in eliciting volume loading are related in large part to the hemodynamic obstacles that SCI individuals must overcome during exercise as a result of impaired sympathetic outflow, a reduced or impaired ability for peripheral vasoconstriction of

non-exercising tissue, and an increased potential for blood pooling. Accordingly, their ability to stress central hemodynamic mechanisms is further compromised when exercising in the conventional upright seated position.[63-64]

Despite the fact that this type of exercise cannot stress the heart adequately, arm cranking exercise training has been shown to improve exercise performance capacity as reflected by significant increases in peak oxygen consumption values.[61] Previous studies have shown that an arm cranking program could lead to a significant increase in power output parallel with a significant increase in aerobic power and physical capability;[65-67] however the majority of the physiological benefits take place in peripheral muscles.[68] Peripheral training effects include an increased number and size of mitochondria, myoglobin, oxidative enzyme concentration and activity, muscle fiber size and capillary density.[58,69] Evidence supporting peripheral improvements in SCI from arm crank exercise include an unchanged heart rate response or mild bradycardia during exercise involving non-trained muscles,[60,70] and increases in aerobic (55%) and physical work capacity (37%) after 8 weeks of arm cranking training.[71] These studies suggest that individuals with SCI can improve their work capacity and power by participating in arm cranking exercise programs; however greater muscle mass involvement resulting in greater volume load in the heart is required for central cardiac adaptations in this population.

Disruption of spinal cord function leads to interruption of the sympatho-adrenal system, resulting in alterations in circulating catecholamines and lipid metabolism. Hyperlipidemia, due to accumulation of triglycerides and cholesterol, has been well documented in this population.[38-39,72] Cross sectional studies in sedentary wheelchair users and physically active wheel chair users have shown that the more active individuals have better blood lipid profiles as indicated by a lower total cholesterol, lower low-density lipoprotein-cholesterol and greater high-density

lipoprotein cholesterol level.[40,73] A possible explanation of this increase is an increase in the activity of cholesterol transport enzymes, lipoprotein lipase, and acyltransferase.[74] The most recent evidence indicates that lower concentration of high-density lipoprotein is associated with higher coronary heart disease risk for sedentary individuals with SCI. If high-density lipoprotein cholesterol does possess a protective effect against coronary heart disease, the increase in high density lipoprotein cholesterol that appears with arm exercise suggests that the risk of coronary heart disease in individuals with SCI may be decreased with arm exercise intervention.

Patients with SCI usually apply an excessive overload on the upper limbs, particularly the shoulders, using them more frequently and in a greater range of activities when compared to able-bodied participants. The shoulder joint has smaller muscles and tendons and a shallower joint capsule which makes shoulder joint weaker and less stable structure relative to hip joint. Able-bodied individuals use their hip and lower extremities for locomotion ; whereas many SCI individuals use wheelchairs for locomotion, aerobic exercise, soft tissue pressure relief, and sports practice.[75] Yet, this functional demand on shoulder joints may lead to shoulder pain, interfering with these patient's daily activities. The shoulder joint is subjected to a heavy load during wheelchair propulsion. Researchers have shown that wheelchair propulsion even at a low intensity placed stress on the rotator cuff muscles which may lead to subsequent development of rotator cuff ruptures.[76] Chronic pain incidence was investigated in 384 adults with pediatric-onset SCI in a previous study; 75.6% of the cohort reported pain in the upper limbs which limited their function and independence.[77] Additionally, shoulder pain was shown as the most relevant musculoskeletal complaint, present in 8% of 216 studied patients.[78] One long-term study with 64 SCI individuals using a wheelchair showed a high incidence of shoulder pain during functional activities requiring an extreme range of motion on the shoulder. The most

painful activities included; climbing slopes, reaching for something above the head, sleeping, moving to unequal surfaces, and washing their backs.[79] Furthermore, the influence of the SCI level on shoulder muscle activation during the push up maneuver (elbow extension) was studied in 57 SCI individuals. The push-up maneuver is commonly performed by this population for avoiding soft tissues' ulcers caused by an unrelieved pressure and by friction forces. Intramuscular electrodes recorded EMG activity on 12 shoulder muscles, including pectoralis major and triceps muscles among tetraplegic and paraplegic individuals. The results indicated tetraplegic patients had significantly stronger activity on anterior deltoid and infraspinatus muscles when compared to paraplegic patients. The authors concluded that a stronger activation of the anterior deltoid aided by elbow extension may be a potential contributor to glenohumeral joint pinch.[80]

Considering that arm cranking exercise has been often utilized to improve the health status of individuals with SCI, alternative methods should be studied as a replacement for arm exercise in individuals with SCI due to the musculoskeletal problems potentiated by arm cranking. Furthermore, clinical instructions must be provided to patients regarding the technique to insure safe wheelchair propulsion and arm exercise. Improving arm muscle strength, together with efforts to utilize more lower extremity exercise should be considered for preventing the development of shoulder pain. Hence, the combination of various types of physical activities that safely increase independence and improve cardiovascular health is important for individuals living with SCI.

Lower Body Exercise

In the search for more effective techniques for improving cardiovascular fitness in this population, electrical stimulation of paralyzed skeletal muscle has been introduced as a better alternative compared to arm exercises. This type of exercise has been suggested as having great physiological appeal due to the ability to recruit large lower extremity muscles mass.

Functional Electrical Stimulation: Recruitment of large lower extremity muscles and activation of the skeletal muscle pump through functional electrical stimulation (FES) is thought to increase venous return, providing an aerobic exercise mode[59,81-82] similar to able bodied cycling or jogging.[31] This type of exercise has a potential to increase the blood circulation by activating the skeletal muscle pump and reverse left ventricular atrophy,[9] which is likely to be the result of both pressure and volume changes to the heart imposed by FES exercise. FES involves the external application of electrical impulses, applied by skin-surface electrodes, to the motor points of paralyzed muscles to directly induce tetanic contractions.[83-84] Most electrical stimulation devices that are approved by the FDA apply surface (not implanted) electrical stimulation.[85] Most forms of FES require that the lower motoneuron system remain intact; so the direct activation of peripheral nerve induces muscle contractions. [86]

Static FES: Initial studies of FES were conducted in non-exercising patients to initiate contraction in the target muscles with no motion in the involved limb (called static FES). Following studies with able-bodied individuals , researchers utilized static FES on the calf muscles as an exercise modality for individuals with SCI. Results revealed significant increases

in systolic and diastolic blood pressures, heart rates, orthostatic tolerance,[87] and decrease in venous statis. [81] Moreover several investigators have demonstrated a central hemodynamic response to FES when utilized on larger lower extremity muscles.[2] According to their results stroke volume increased by 19% and cardiac output increased by 30%; however no significant change in oxygen consumption over resting condition has been reported. Additionally, significant increases in stroke volume (20%) and cardiac output (%16) were shown in response to FES combined with application of negative lower body pressure.[88] Negative lower body pressure was utilized to create a hypotensive state for this population and induced by a lower body negative pressure chamber. Study results demonstrated that FES applied to calf and thigh muscles can improve the orthostatic hypotension tolerance in individuals with SCI.

Dynamic FES: Dynamic FES involves movement of the stimulated limb as a consequence of electrical stimulation of target muscles. Dynamic FES has been used to improve health and fitness,[89-91] perform skilled activities, standing [92-93] and locomotion.[94-96] The ability to meet functional demands of FES depends on the paralyzed muscle becoming more fatigue resistant; [97] therefore a preparatory strengthening protocol may be needed for making FES effective and safe to utilize it in this population.

i. *FES-Induced Resistance Exercise***:** Typical FES resistance protocols involve dynamic contractions through a specific range of motion,[98] with stimulation intensities up to 150mA. Progressive overload and multiple sets of exercise consisting of a low number of repetitions at relatively high loads are highly recommended for FES-resistance exercise protocols.[89] Studies that have utilized FES-resistance protocols

reported significant increases in strength and endurance,[99] skeletal muscle cross sectional area and muscle mass,[100] and significant reductions in plasma glucose levels and muscle fatigue.[101]

ii. *FES-induced leg cycling exercise*: The disuse atrophy found in paralyzed muscles makes utilization of FES problematic in this population; hence a strength preparation protocol for cycling FES must be employed prior to cycling exercise. A typical preparation protocol involves stimulation intensity up to 150 mA, a pulse frequency of 35 Hz, and a pulse width of 0.3 ms. Knee joint range of motion is normally kept at 60 degrees. Increases in the training load can be made when 15 minutes at a given resistance can be completed at 5 knee/extension cycles per minute.[2] The training duration may vary from 1 to 12 weeks (depending on the participant's condition). The individual can start the cycling FES protocol as soon as she/he completes 35-45 maximal repetitions in the resistance program.[90,102-103] A leg cycle ergometer is operated via FES-induced movement of the paralyzed lower leg muscles. Computer controlled FES is utilized to induce contractions of the bilateral quadriceps, hamstrings, and gluteal muscle groups at specific position of the pedals.[104] A microprocessor that receives pedal position and velocity feedback information from the sensors, controls the cycling pattern and stimulation intensity.[105] The FES current increases automatically up to 140 mA to recruit extra muscle fibers to maintain revolutions per minute. When the pedal rate falls below 35 revolutions per minute, FES cycling exercise is automatically ceased.[104] Poor muscle strength and endurance could be a limitation for FES cycling exercise for the SCI population; however , individuals who were involved in the preparation phase with resistance training have demonstrated enhanced levels of fitness,[90,106]

improved gas exchange kinetics,[107-108] and increased muscle mass[109] with FES cycling training. Moreover reversal of left ventricular atrophy was reported in individuals with quadriplegia. This change may be associated with pressure and volume change to the heart induced by the exercise,[9] and greater lower body blood circulation following training.[110-111] Changes in skeletal muscle fiber distribution following 1-year (3 times per week) as well as a shift towards more fatigue resistant contractile proteins were also reported (61% increase in myosin heavy chain isoform IIA) with FES cycling exercise. This shift was accompanied by doubling of the oxidative enzymatic activity.[112] Furthermore, FES-induced cycling exercise of paralyzed muscles has been shown to elicit increases in lean mass, decreases in fat mass,[113] enhancement in whole body insulin uptake, and increase expression of GLUT-4 transport protein in the related muscles.[114-115] These skeletal muscle adaptations to FES are very important as skeletal muscle plays a vital role in the regulation of energy homeostasis.[116] Moreover, maintenance of energy balance is critical for metabolic disease prevention in this population.[42]

iii. *Hybrid exercise protocols with FES*: Recent efforts to increase the amount of muscle mass involved in exercise for individuals with SCI have focused on combining conventional upper body exercise with FES. Hybrid exercise protocols utilize both static and dynamic muscular contractions combined with different forms of upper body exercise such as; wheelchair ergometry/propulsion,[2] arm ergometry,[106] and rowing.[117] Hybrid exercise has been shown to have potential advantages over arm exercise or FES cycling alone. The potential advantages are: (1) maximum exercise capacity may increase as a result of an increase in active muscle recruitment, (2) FES may increase upper body blood flow, improving exercise performance

and tolerance by making more blood available to upper extremities; (3) upper body exercise may elicit a greater sympathetic nervous system response and improved leg exercise performance. Studies utilizing FES with arm cranking exercise reported greater cardio-respiratory stress as indicated by greater peak oxygen consumption, immediate post-exercise blood lactate levels,[118] steady state ventilation,[60] stroke volume, cardiac output, and mean arterial pressure.[119] Furthermore, studies utilizing rowing with FES have shown significant increases in oxygen consumption, minute ventilation and respiratory exchange ratio compared to rowing only.[117]

Ambulatory FES: Ambulatory FES has been used to achieve bipedal ambulation in individuals with both motor complete and incomplete SCI.[120-121] Surface neuroprostheses have been developed to employ electrical stimulation of the quadriceps and gluteal muscles during ambulation. They apply FES to the motor branches of the peripheral nerve in which paralyzed muscles are electrically stimulated to produce muscle contraction.[122] Muscle activation is controlled by a microprocessor worn on a belt, with activation of step initiated by a finger sensitive switch. When activated the electrical stimulator sends electrical current to the stance limb, which initiates quadriceps and gluteal muscle contraction. Contralateral hip flexion is produced by inducing an ipsilateral flexor withdrawal reflex via an electrical current over the common peroneal nerve. This process allows the contralateral hip, knee and ankle to start with flexion, followed by extension of the knee joint.[104,123] As in the leg cycling exercise, the stimulation intensity can be increased in order to continue to exercise if fatigue occurs. Electrically induced strength training programs may be required to increase the fatigue threshold prior to ambulation with FES. Ambulation distances up to 1 mile, despite the limitations in

ambulation velocity have been reported after training with ambulatory FES in individuals with SCI.[124] Additional training adaptations with ambulatory FES involve improved resting blood flow,[125] increases in lower extremity muscle mass,[126] upper extremity strength (determined with a dynamometer),[127] and hyperemic response to experimentally induced ischemic stimulus.[125] Clearly, FES only or hybrid FES exercises can potentially elicit improved physiological responses compared to arm exercise alone; however ambulatory FES can only be used in individuals with lower level injuries who possess some lower extremity motor function. Additionally, it is recommended that before participating in any FES exercise program, the individual with SCI should receive a medical examination that includes a neurological examination, EKG testing, radiographs of the lower extremities, and range of motion tests because FES may induce some adverse effects in individuals with high (C4-T6) SCIs.

Precautions for FES Exercise: High intensity level of stimulation is required to induce powerful contractions; thus FES may cause pain or discomfort at this intensity level in individuals who preserve some degree of sensation on the skin. Autonomic Dysreflexia can result from the painful stimuli that cause sympathetic hyperactivity.[84,128] Individuals with SCI at level T6 or above are at risk of autonomic dysreflexia[2]. Blood pressure should be monitored periodically during FES and FES exercise must be ceased immediately if any response is observed that can place the individual at risk. In addition to the risk of experiencing autonomic dysreflexia, musculoskeletal injury is very likely to result from FES. Musculoskeletal system tends to deteriorate following SCI; hence contraction forces generated by the electrical stimulation must be kept at a safe level to prevent musculoskeletal injury. Therefore, FES

exercise must be performed cautiously given that training the muscles may produce more force than the bones can bear.[129]

In summary, arm exercises utilized for this population are not well-suited to elicit "volume loading" of the heart to maximally stress central hemodynamic mechanisms due to small muscle mass involvement. FES has been suggested as a better way to improve cardiovascular fitness because greater lower extremity muscle mass can be activated; however FES may induce adverse effects such as autonomic dysreflexia and musculoskeletal injury in this population. Moreover, FES exercises, particularly ambulatory FES, are therapist and time-intensive and expensive interventions. Hence safe; time and therapist-efficient novel exercise protocols are needed to reverse myocardial regression by promoting central and peripheral cardiac adaptations. During the past decade there has been increasing interest in the use of whole-body vibration (WBV) as a therapeutic modality in able-bodied individuals as well as individuals with SCI. One area of potential benefit that has not been investigated is the effect of WBV exercise on cardiovascular response in the SCI population.

Whole Body Vibration Exercise

Vibration is a mechanical oscillation characterized by a periodic alteration of force, acceleration, and displacement over time. Energy generated by these oscillations is transferred from an actuator (the vibration device) to a resonator (the human body). Most vibration devices produce sinusoidal oscillations that are described by amplitude (*A*), frequency (*f*) and phase angle. There are six types of waveforms of oscillatory motion (sinusoidal, multi-sinusoidal, transient, shock, stationary random, non-stationary random; Figure 4).[130] Vibration exercise is mostly practiced as whole body vibration (WBV), while standing on a sinusoidal oscillating

platform. There are two broad categories of therapeutic WBV: synchronous and side-alternating. Synchronous vibration transfers vibrations to both feet synchronously whereas side-alternating operates in a side alternating way, with the right foot lowest when the left foot is highest and vice versa (Figure 5).[20] When a body with a mass *m* is attached to the vibration device, it will follow the sinusoidal trajectory elicited by the platform. However, the human body is not a rigid structure. Muscles have damping properties,[131] which influence the way that vibrations are transmitted from one segment to another (from foot to lower leg and from lower leg to upper leg, and on up the kinetic chain, Figure 6). Musculoskeletal stiffness and the damping effect of the muscles will influence how much vibration energy will be transmitted from the platform to human body.[132-133] Four variables can be manipulated by the operator during WBV exercise training: frequency, duration, amplitude, and mass. Frequency, measured in Hertz (Hz), is the number of oscillations per second produced by the WBV platform. Duration is the total amount of time spent on WBV platform,[13] and amplitude is the displacement between positive and negative peaks.[130]

Figure 4. The six common forms of oscillatory vibrations[130]

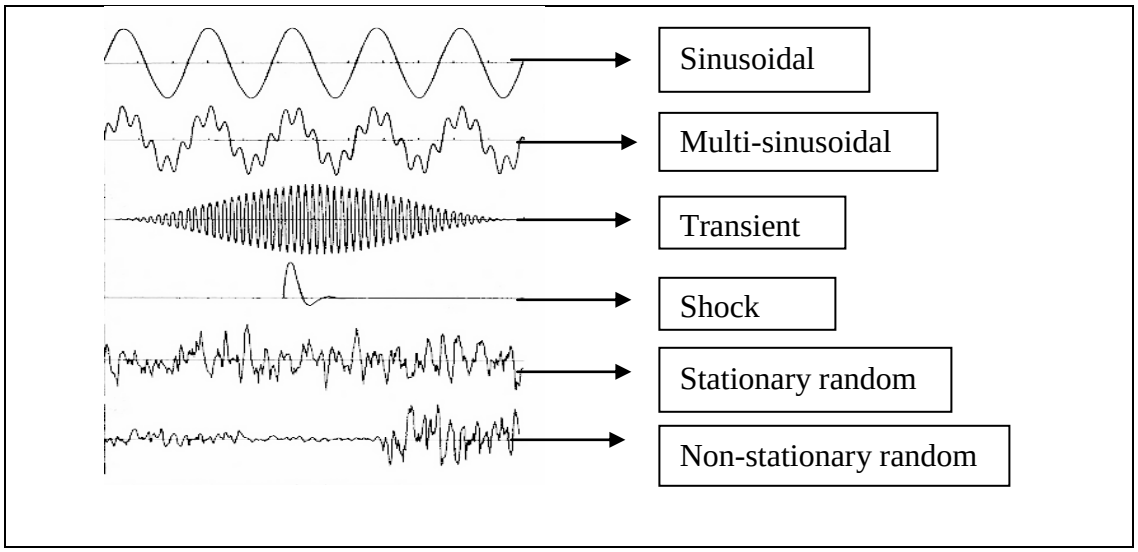


Figure 5. Illustration of the two principle modes of vibration transmission[134]

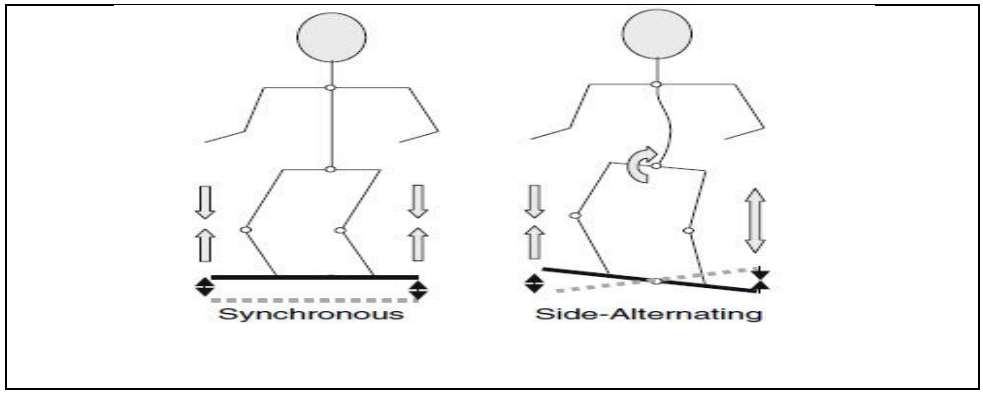
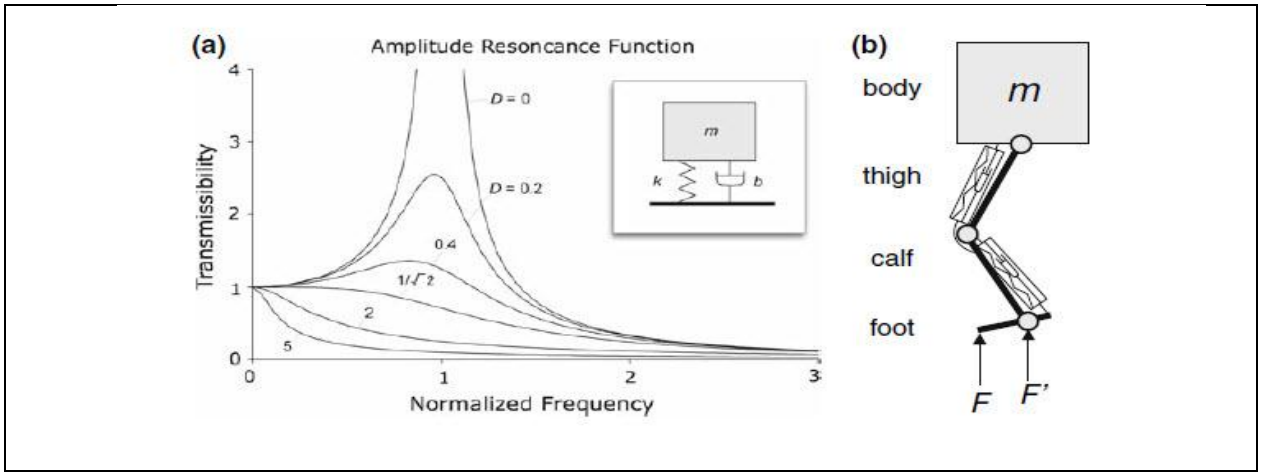


Figure 6. Model of the human body as a resonator, composed of a single (a) or multiple (b) segments with spring-like and damping behavior[134]



Physiological Responses to WBV Exercise

Neuromuscular Responses to WBV Exercise: A commonly observed motor effect of vibration is a phenomenon called the tonic vibration reflex.[16] The vibration applied to a muscle or its tendon elicits a tonic reflex contraction in that muscle or its antagonist.[135] This motor response is a result of the vibration-induced activity of the primary afferent endings (Ia) in the muscle spindles which are highly dependent on central influences.[136] The tonic contraction increases progressively with exposure time and can persist a few seconds after vibration ends. In addition to the spindle afferents, Ib-afferents from Golgi tendon organs are similarly responsive to muscle vibration.[137] Like the spindle endings, afferents from Golgi tendon organs become more responsive to vibration when the muscle is contracting.[138] Contrary to the reflex contraction initiated by the Ia-loop, the stretch reflex and the H-reflex are suppressed during vibrations.[139] GABAergic interneurons,[140] a reduction in the sensitivity of primary spindle endings,[141] and transmitter depletion[142] have been suggested as mechanisms for inducing H-reflex inhibition.

Electromyography (EMG) Studies: Several studies have demonstrated immediate effects of vibration on EMG activity.[13-14,143] Seated vibration with frequencies between 0.3 and 5 Hz (amplitude levels between 1.2 and 2.0g) has been shown to elicit vibration-synchronous EMG activity in the erector spinae muscles.[144] This modification of EMG activity has been suggested to be due to tonic vibration reflex response. Evidence also suggests that WBV increases the EMG activity by 9.4% in the triceps surae,[145] and 10%-103% in the muscles of the upper leg.[14] The vibration effects on upper leg muscles have been demonstrated to vary with different frequencies of vibration. For example, EMG amplitude has been shown to be larger at 30 Hz than at 40 or 50 Hz in vastus lateralis.[146] EMG activity has also been found to be more pronounced in side-alternating vibration as compared to synchronous vibration.[14] In contrast to these studies, there are studies showing no significant change in EMG activity of tested muscles after an acute bout of vibration. A study that applied vibration (65Hz) to the biceps tendon during biceps curls at 70% of the one-repetition maximum did not demonstrate any effect of vibration on the EMG. One possible explanation is that vibration usually increases motor activity during sub-maximal, but not during maximal contractions. Golgi tendon organ afferent inhibition elicited by large contraction forces was thought to account for the absence of EMG activity during WBV exercise.

Examining EMG during and following WBV exercise is difficult due to the number of artifacts in the data. The potential artifacts include electric induction in vibrating cables and piezoelectric or bi-layer currents. A stop-band filter (a filter that passes most frequencies unaltered, but attenuates those in a specific range to very low levels) has been suggested for eliminating potential artifacts from the EMG data.[134] Moreover, comparisons of the WBV EMG

activity among different studies have been difficult due to the different data processing parameters.[14] Future studies should focus on minimizing the noise associated with WBV EMG recording.

Energy Metabolism Responses to WBV Exercise: In addition to significant evidence for the involvement of muscular contractions during vibration exercise, applying vibration to intact or single fiber preparations has been shown to lead to specific increases in ATP turnover,[147] suggesting a potential specific energy demand from the exposure to vibration. Under various conditions, such as standing, and squatting with or without an additional load, this specific energy demand is 4.5 ml/kg/min (f = 26 Hz, A = 3 mm).[20] This specific response can be further enhanced by increasing frequency and amplitude of vibration as well as by adding additional loads.[148] Based on the linear relationship between vibration frequency and oxygen uptake, a specific oxygen demand (2.5 ml/kg per vibration cycle for an amplitude of 5 mm) to WBV has been demonstrated; however a non-linear relationship has been demonstrated between oxygen uptake and vibration amplitude.[134]

It is important to consider that WBV by itself may not significantly improve aerobic fitness due to the moderate energy turnover and cardio-respiratory responses that were shown in previous work; however the physiological effects of this type of exercise on energy metabolism in compromised physiological systems may be considerable. Hence, future studies are needed to explore the effects of WBV exercise on energy metabolism in individuals with SCI.

Intramuscular Temperature and Perfusion responses to WBV Exercise: Elevations in intramuscular temperatures with WBV exercise have been reported.[149] The production of additional heat within muscle during vibration has been related to the vibration-related increase in energy metabolism.[134] The effects of conventional warm-up techniques (warm bath and stationary cycling) were compared with the effect of WBV on muscle temperature. Temperature elevations in both modalities have been reported; yet the temperature elevations were faster in WBV than in stationary bicycling, even though both modalities were matched for oxygen uptake. This vibration related warm-up effect in the muscle was explained partly by shock-absorbing mechanisms within the muscle that transform mechanical energy into heat.[131] Because vibration exercise increases muscular energy turnover and heat production, there is a clear requirement for increased blood flow to the exercising tissue to comply with increased energy demands.

Acute hand-transmitted vibration (40-200 Hz) from hand held industrial tools has been shown to reduce digital blood flow at 120 Hz. Increased sympathetic tone in heart and extremities were suggested as a potential mechanism for decreased blood flow.[150] Consequently, vibration was thought to decrease perfusion to the treated sites. This belief was challenged later when the same kind of hand-transmitted vibration (f = 120 Hz) was shown to increase digital blood flow rather than to decrease blood flow. This increase in skin blood flow was explained by reduced secretion of endothelin-1 from vascular smooth muscle cells.[151] Subsequent to hand-transmitted vibration studies, alterations in skin blood flow were assessed during WBV. An enhancement in skin blood flow as measured by Laser Doppler Flowmetry has been shown during WBV.[23,152] One study has also demonstrated an optimal response to WBV. Significant increases in skin blood flow with both 30 Hz and 50 Hz vibration were reported, with the greater

increase in skin blood flow found at 50 Hz.[23] The effect of WBV exercise in skin blood flow was partly explained by the vasodilation brought by vibration-induced shear forces in the skin. Future studies should be completed to determine if these increases on skin blood flow could be beneficial to populations with compromised peripheral circulation such as those with individuals with SCI.

Significant increases in gastrocnemius and vastus lateralis oxygenation and blood flow have been reported after termination of WBV (f= 26 Hz, a= 3mm, side alternating).[153]. One could also expect that increase in oxygenation and flow could be a result of a reactive hyperemia that takes place after WBV exercise;[134] thus hypoxia may be elicited during WBV exercise. This idea has been supported by studies that measured tissue oxygenation by Near Infrared Spectroscopy. WBV combined with squatting exercise has been shown to reduced vastus lateralis oxygenation more than squatting alone (muscle oxygenation was measured by Near Infrared Spectroscopy).[154] It was concluded that vibration exercise induces muscle de-oxygenation and may induce an effective training stimulus for the skeletal muscle. Other studies have challenged this view and suggest that vibration affects muscle oxygenation only at certain frequencies.[155-156] These results have shown that WBV exercise with frequencies 30, 40, and 50 Hz and small amplitudes (1-2mm) did not affect oxygenation in vastus lateralis and gastrocnemius muscles to a higher degree than a non-vibration condition. Taken together it is suggested that muscle blood flow attempts to match the metabolic demands of the contracting musculature during vibration exercise.[157] Moreover, decrease in muscle oxygenation during WBV may be an indicator of increased metabolic activity imposed by muscle contractions. At the moment it is not clear whether WBV represents a training stimulus strong enough to influence muscle metabolism and/or blood flow. Further studies are needed to elucidate the

blood flow and oxygenation to WBV exercise, with particular reference to the interactions between neuromuscular and metabolic demands of this novel and promising exercise intervention in special populations.

Considering the potential of WBV for activating paralyzed muscles via the reflex loop and increasing the skeletal muscle metabolism, WBV exercise may provide a sufficient training stimulus for the cardiovascular system in individuals with SCI. Furthermore, if compromised cardiovascular systems can be shown to benefit from WBV exercise, FES of the lower extremities may be replaced with WBV exercise since FES may induce adverse effects among individuals with residual sensory function and is time and labor intensive. Frequencies of 30-50 Hz of WBV exercise have been shown to increase oxygen consumption and muscle blood flow in able-bodied people, however, it is not clear if there is a frequency that can elicit an optimal physiological response to vibration in both able-bodied or in individuals with SCI. The observation that participants receiving higher WBV exercise frequencies present augmented hemodynamic responses compared to lower frequencies would indicate a potential optimal response existing with WBV exercise. This optimal response would aid a clinician in choosing a vibration frequency that can most effectively optimize central and hemodynamic responses to WBV exercise.

Therefore, the purposes of this study are twofold:

1) To investigate the acute effects of WBV on central and peripheral hemodynamic responses and oxygen consumption
2) To compare the physiological responses to WBV between three different frequencies (30, 40, and 50 Hz) in individuals with SCI compared to age and activity matched able-bodies individuals.

The first purpose will be accomplished by measuring stroke volume and cardiac output by echo and Doppler cardiography; heart rate and blood pressure by an automated blood pressure cuff; oxygen consumption by a metabolic cart; muscle oxygenation and blood flow by Near Infrared Spectroscopy (NIRS), and skin temperatures by Dynamic Infrared Thermography (DIRT) before, during and after WBV exercise in health and SCI participants. The second purpose will be accomplished by comparing the central and hemodynamic responses to WBV exercise applied with 30, 40, and 50 Hz.

CHAPTER III.

JOURNAL MANUSCRIPT

Acute Effects of Whole Body Vibration Exercise on Central and Peripheral Hemodynamics and Oxygen Consumption in Individuals with Spinal Cord Injury

Abstract

A substantial body of evidence suggests spinal cord injury (SCI) increases cardiovascular disease and mortality risk in aging individuals with SCI. Based on retrospective assessments, excess mortality after SCI has been related to neurological level and completeness of injury. Performing routine arm exercise moderately stimulates the cardiovascular system; whereas functional electrical stimulation (FES) has been shown to elicit greater venous return and myocardial performance. FES is potentially painful and can induce adverse responses such as autonomic dysreflexia especially in quadriplegics and high paraplegics. Therefore, developing a safe and effective exercise intervention to improve cardiovascular health must be a priority for this population. Whole-body vibration (WBV) exercise is emerging as a potential treatment to improve locomotor capabilities in individuals with SCI. The use of WBV exercise to improve on cardiovascular response in the SCI population has yet to be investigated. Thus, the purposes of this study were: 1) to determine the acute effects of whole body vibration (WBV) exercise on central and peripheral hemodynamics and oxygen consumption, and 2) to compare physiological responses to WBV between three different frequencies (30, 40, and 50 Hz) in individuals with SCI compared to age and activity matched able-bodied individuals. Eleven males with SCI (injury levels: C5-T6; ages: 50.39 ± 8.16) and ten age and gender matched able-bodied controls

(ages: 48.17±6.78) completed three WBV exercise protocols at 30, 40 and 50 Hz. Heart rate, systolic blood pressure, diastolic blood pressure, stroke volume, cardiac output, oxygen consumption, and relative changes in oxyhemolobin, de-oxyhemoglobin and total hemoglobin values were obtained during pre-WBV seated steady-state, pre-WBV standing steady-state, WBV first minute, WBV steady-state, post-WBV standing steady-state, and post-WBV seated steady state. Moreover, leg skin temperatures were obtained pre-WBV, immediately post-WBV, 10 minute post, and 15 minute post-WBV (A schematic representation of an experimental session can be found in Figure 7). Multi-analysis of Covariance with random subject-effect was used to analyze the effect of the treatments on the dependant variables. Follow up univariate ANCOVAs and *t*-tests were utilized to compare the treatment and control groups on the outcome measures. 30, 40, and 50 Hz of WBV elicited slight increases in heart rate, stroke volume and cardiac output both in the SCI and able-bodied group. Systolic blood pressure was significantly increased following WBV at 30 and 40 Hz in the SCI group. Both groups demonstrated significant increases in oxygen consumption during and following WBV; yet the increase in oxygen consumption was more pronounced in the SCI group. Muscle oxygenation and skin temperature was significantly increased following WBV only in the SCI group. Moreover no specific frequency effect was revealed within or between groups. The WBV parameters used in the present study do not appear to induce significant cardiovascular benefits for the individuals with SCI as well as for able-bodied individuals. Physiological responses to 30, 40, and 50 Hz were similar.

Introduction

Individuals with spinal cord injuries (SCI) are living much longer than in the past, surviving to an age at which secondary complications become very common.[2] One third of SCI patients older than 65 years and nearly half of the patients living with SCIs for longer than 30 years die of cardiovascular disease (CVD).[3] Higher neurological level and greater completeness of injury are associated with lower levels of heart function.[2,7] Rather than experiencing pathologic increases in cardiac mass that occur with aging, quadriplegic patients lose approximately 26% of total cardiac and left ventricular mass.[49] The myocardial atrophy is possibly related to inactivity[31] that could potentially be lessened by promoting venous return via mechanical or electrical stimulation of lower extremity muscles.[9]

Voluntary arm exercises have been utilized to improve cardiovascular fitness in this population; however these exercises only involve a small muscle mass that is not well suited to stress an otherwise healthy cardiovascular system.[158] Another physiological limitation of arm exercises is that the skeletal muscle pump in the lower extremities cannot be activated which may result in excessive venous pooling in the lower extremities. The sequestration of blood in the lower extremities may decrease circulating blood volume which may promote ischemia in the active muscles. This ischemia may induce early fatigue during voluntary arm exercises before cardiovascular system reaches its limits.[70] Overall these factors limit the SCI individual's ability to perform aerobic exercise which may lead to a sedentary lifestyle and encourage physical de-conditioning in this population.

Functional electrical stimulation (FES) has been introduced as a better way to improve the cardiovascular system as it can activate the large lower extremity muscles. Previous studies

of SCI patients have shown that applying FES to the paralyzed muscles can ameliorate the detrimental effects of cardiac response resulting from SCI;[106,108-109] however FES is potentially painful and can induce adverse responses including autonomic dysreflexia and musculoskeletal injury.[35] Moreover FES is time and labor intensive. Consequently, novel, time and labor effective exercise interventions are needed to reverse myocardial regression and low cardiovascular fitness.

Whole-body vibration (WBV) exercise is emerging as a treatment to improve muscle strength in able-bodied individuals.[24-25] One area of potential benefit that has not been investigated is the effect of WBV exercise on the hemodynamic responses and oxygen consumption in the SCI population. WBV exercise on muscle performance is elicited via reflex muscle activation.[137] This muscle activity has a potential to promote venous return via activation of the skeletal muscle pump. Moreover, the mechanical forces produced by muscle contraction and relaxation acting on the muscle vasculature have been shown to generate a significant increase in muscle[153] and skin blood flow,[23,152] and a decrease in muscle oxygenation.[154] Taken together it is suggested that increases in muscle blood flow may be an attempt to match the increased metabolic demands of the contracting musculature during vibration exercise. Frequencies of 30-50 Hz of WBV exercise have been shown to increase oxygen consumption and muscle blood flow in able-bodied people. However, it is still not clear if there is an optimal physiological response to vibration. Discovery of the frequency that can optimize the physiological responses would aid a clinician in choosing a vibration frequency that can most effectively optimize central and hemodynamic responses to WBV exercise.

WBV exercise may provide a sufficient training stimulus for the cardiovascular system in individuals with SCI as it has been shown to activate paralyzed muscles and increase the skeletal

muscle metabolism. If WBV exercise can be shown as an effective and safe exercise option, it could become an important therapeutic modality to aid in prevention of the serious cardiovascular complications that accompany individuals with SCI. Therefore, the purposes of this study were twofold: 1) to investigate the acute effects of WBV exercise with varying frequencies on central and peripheral hemodynamic responses and oxygen consumption; 2) to compare physiological responses between three WBV frequencies (30, 40, and 50 Hz) in individuals with SCI compared to age and activity matched able-bodied individuals.

Methods

Experimental Design

This study utilized a 2x3x6 repeated measures experimental design. The independent variables were group with 2 levels (SCI and control), treatment with 3 levels (30, 40, and 50 Hz WBV exercise), and time with 6 levels (pre-WBV seated steady-state, pre-WBV standing steady-state, WBV first minute, WBV steady-state, post-WBV standing steady-state, and post-WBV seated steady state). The dependent variables were heart rate, systolic blood pressure, diastolic blood pressure, stroke volume, cardiac output, and oxygen consumption. Additionally, a 2x3x4 repeated measures experimental design was designed for skin temperature analysis. The independent variables were group with 2 levels (SCI and control), treatment with 3 levels (30, 40, and 50 Hz WBV exercise), and time with 4 levels (pre-WBV, immediately post-WBV, 10 minute post-WBV, and 15 minute post-WBV). A schematic representation of a testing session can be found in Figure 7.

Participants

Eleven males with SCI (injury levels: C4-T6; ages: 50.39 ± 8.16) and ten and gender matched able-bodied individuals (ages: 48.17±6.78) completed the study (Demographics of the participants are included in Table 3). SCI participants with motor incomplete or complete, chronic (≥ 1 year post-injury) injuries were eligible to participate in the study. Sedentary able-bodied individuals who exercise less than 3 times a week were eligible to participate as age and gender matched controls. All participants were screened for potential orthopedic or medical conditions that prevented participation in the study. Information of daily use of medications, daily health status (Appendix A) and assistive devices for mobility were recorded for individuals with SCI.

WBV Intervention

Using a randomized crossover design, each participant completed 30, 40, and 50 Hz WBV exercise with a vertical displacement of 2 mm on 3 separate days, at least 1 week apart. The WBV exercise sessions were performed at the same time each day to reduce physiologic changes that might occur from the effects of circadian rhythms. During exercise sessions participants were asked to remove their shirts. Participants stood on the vibration platform (Wave Plate, Wave Manufacturing Inc, Windsor, ON) with their knees flexed at approximately 18-25° from anatomical neutral position. Standing position on the vibration platform was assisted by a standing frame which was incorporated into the platform for both groups (Figure 8).

Preliminary Procedures and Assessments

Qualifying volunteers were scheduled for an initial visit to the Auburn University Neuromechanics Research Laboratory for further screening. Upon arrival, volunteers were provided with and asked to sign an institutionally-approved informed consent document prior to any screening processes (Appendix B & C). Volunteers meeting all of the inclusion criteria then continued with the skinfold measurement with a skinfold caliper (Beta Technology Inc., Cambridge, MA, USA) on the lateral calf and full body Dual-energy X-ray absorptiometry (DEXA) scanning. Body composition results that are provided by DEXA scans were utilized to normalize oxygen consumption values between individuals with SCI and able-bodied individuals.

Experimental Procedures and Assessments

Heart Rate and Blood Pressure: An automatic digital blood pressure monitor (Omron, Model: HEM-705CP, IntelliSense, Woburn, MA, USA) with a measuring range of 20-280 mmHg was used to measure heart rate, systolic and diastolic blood pressures. This automatic monitor has been shown to surpass the accuracy criteria required for British Hypertension Society.[159] The blood pressure cuff was secured on the right arm, 0.5 inches above the elbow over the brachial artery. The participants remained silent and stationary during the measurement. Heart rate and blood pressure were recorded pre-WBV standing steady-state, WBV first minute, WBV steady-state, post-WBV standing steady-state.

Stroke Volume and Cardiac Output: In the present study stroke volume was obtained by the product of aortic valve area and the integral of the aortic velocity[160], then cardiac output was obtained using the product of stroke volume and heart rate. Cardiac output was recorded during pre- WBV standing steady-state, WBV first minute, WBV steady-state, post- WBV standing steady-state.

Aortic Valve Area Measurement: An M-mode echocardiogram (LOGIQ® 5 PRO, GE Medical Systems, Fairfield, CT, USA) at the level of the aortic valve was recorded from a two-dimensional image. When the walls of the aorta appeared to move in a parallel fashion, a recording was made. The distance between the aortic leaflets in early systole was measured at the tip of the valve from the trailing edge of the right coronary cusp to the leading edge of the non-coronary cusp (Figure 9). The area was computed from the formula AVA = ∏ x AVD2/4, where AVA = aortic valve area and AVD = aortic valve leaflet diameter. All recordings were obtained with the patient in a left recumbency position.

Doppler Aortic Blood Flow Velocity Measurements: Flow velocity measurements were made using pulsed wave Doppler (LOGIQ® 5 PRO, GE Medical Systems, Fairfield, CT). Blood flow through the aortic valve was obtained using a 2 MHz transducer (3S Sector Probe, LOGIQ® 5 PRO, GE Medical Systems, Fairfield, CT, USA) positioned at the apex of the heart with the participant standing on the platform. The transducer was angulated until Doppler blood flow velocity signals were acquired. Slight manipulations of the transducer were performed until maximal blood velocity was detected. The maximal velocity signal was detected by listening to

the audio signal and by observing the peak velocity from the tracing visualized on the computer screen. The area under the flow velocity curve (flow velocity integral) was digitally measured using J-image (National Institutes of Health, Bethesda, Maryland, USA). The smooth outer edge was outlined, excluding spikes from the tracing (Figure 10). An average of three maximal velocity measurements was taken.

Oxygen consumption: Oxygen consumption during each WBV exercise condition was measured with an automated metabolic testing system (True Max 2400 Metabolic Testing System, Parvo Medics, Salt Lake City, UT, USA). This system uses a mixed chamber and the dedicated software averages oxygen consumption values over 15 seconds. The oxygen values were recorded during pre-WBV seated state, pre-WBV standing state, pre-WBV standing steady-state, WBV first minute, WBV steady-state, post- WBV standing steady state, and post-WBV seated steady state. Steady state at each position was assumed when four 15 second averages of oxygen consumption values were within 10% of each other.[161]

Near-Infrared spectroscopy (NIRS): Near Infrared Spectroscopy was performed using a commercially available unit (Oxymon Mk III, Artinis Medical Systems, Zeiten, Netherlands). The NIRS optodes were placed over the belly of the lateral gastrocnemius muscle and held in place with a black rubber housing that eliminated external light. This was taped to the skin to maintain constant optode spacing (45mm) and prevent displacement of the probe during WBV exercise. Sampling of the NIRS signal began at the completion of subject setup and continued uninterrupted until the end of testing. Relative changes in oxy-hemoglobin, de-oxyhemoglobin,

and total hemoglobin responses were recorded. These parameters are expressed in arbitrary units (a.u.) as a change from resting values. Physiological calibrations were used to quantify oxy-hemoglobin response to WBV. Each participant underwent a 5 min period of cuff ischemia at the end of each experiment. A thigh blood pressure cuff (OMRON, IntelliSense, Woburn, MA, USA) inflated around the lower thigh (2" above the patella) to perform an arterial occlusion. The physiological range was determined by inducing muscle ischemia to obtain the lowest value (set to 0%) of oxy-hemoglobin, then releasing the cuff and observing the highest value of oxy-hemoglobin in the ensuing reactive hyperemia (set to100%).[162] The oxy-hemoglobin was then normalized to the maximally observed physiological range. The signal output from the Oxymon unit was collected using the OxySoft DAQ 2.1.2 digital recording system (Artinis Medical Systems, Zeiten, Netherlands). Data were sampled at 10 Hz, displayed in real time, and stored on disk for off-line analysis.

Dynamic Infrared Thermography (DIRT): Posterior and lateral thermal images of the lower leg and thigh were taken utilizing a portable infrared camera (FLIR B200, FLIR Systems Inc., Boston, MA, USA) during pre, immediate-post, 10 minute-post and 15 minute post-WBV. The ambient room temperature of 23.58C–25.28C, considered optimal room temperature for comfort, was maintained during WBV exercise sessions. The average, high, low, and standard deviation values of the selected regions were then determined by using FLIR Reporter Software (FLIR Systems Inc., Boston, MA, USA).

Statistical Analysis

Data was entered into a custom database (Microsoft Excel 2007, Microsoft Corp., Redmond, WA, USA), and analyzed using Statistical Package for Social Sciences version 19 (IBM SPSS Statistics 19, IBM Corp., Somers, NY, USA). Descriptive statistics (mean ± standard deviation [SD]) were calculated. A 2 X 3X 6 (group [SCI and able-bodied] X treatment [30, 40, 50 Hz WBV] X time [pre-WBV sitting steady-state, pre-WBV standing steady-state, WBV 1st minute, WBV steady-state, post-WBV standing steady-state, post-WBV sitting steady-state]) repeated measures MANCOVA using pre-WBV seated steady-state baseline measures as covariates was completed for central hemodynamics and muscle oxygenation analysis. A 2 X 3X 4 (group X treatment X time [pre-WBV, immediately post-WBV, 10 minute post-WBV, 15 minute post-WBV]) repeated measures MANCOVA using pre-WBV baseline measures as covariates was competed for skin temperature analysis. Follow up univariate ANCOVAs and *t*-tests were utilized to compare the treatment and control groups on the outcome measures. Additionally one-way repeated measures ANOVAs were utilized to assess effects of each frequency on the outcome measures within groups. Significance level was set *a priori* at $p \leq 0.05$ (2 tailed).

Results

Descriptive statistics and Bonferroni's pairwise comparisons for central and peripheral hemodynamic measures are presented in Tables 4 -7 and Tables 10-29 respectively.

Central hemodynamic measures

Heart rate and blood pressure: Treatment X time charts can be found in Figure 11. No significant treatment X time (Wilks'Λ= 0.91; $F_{16,208}$= 0.56, p= 0.9, η_p^2= 0.04) or treatment X group (Wilks'Λ= 0.72; $F_{4,10}$= 2.23, p= 0.07, η_p^2 = 0.15) interaction occurred for the heart rate measures. Heart rate increased following the standing steady state condition and remained elevated until the end of the WBV steady-state condition for both groups.

Systolic and diastolic blood pressure: Treatment X time charts can be found in Figure 12 and 13 respectively. A significant time X group interaction was evident (Wilks'Λ= 0.22; $F_{6,8}$= 3.54, p = 0.05, η_p^2= 0.78), as was the follow-up time X group univariate ANCOVA of the systolic blood pressure measure ($F_{5,95}$= 5.11, $p\leq$ 0.001, η_p^2= 0.21). Pairwise comparisons did not reveal a significant difference between groups on systolic blood pressure measures (p= 0.85). Systolic blood pressure was greater following WBV compared to pre- and post-WBV conditions in the SCI group. Systolic blood pressure was significantly greater within the SCI group during WBV exercise first minute at 30 (t= 3.07, $p\leq$ 0.05 and 40 (t= 3.71, $p\leq$ 0.04) compared to standing steady-state conditions. Diastolic blood pressure did not change significantly during WBV conditions compared to pre- and post-WBV conditions in both groups. No significant interactions were found between treatment X time (Wilks'Λ= 0.39; $F_{8,9}$= 0.74, p= 0.65, η_p^2= 0.39), treatment X group (Wilks'Λ= 0.92; $F_{2,15}$= 0.62, p= 0.96, η_p^2= 0.77), or time X group (Wilks'Λ= 0.77; $F_{4,13}$= 0.95, p= 0.46, η_p^2= 0.22) in diastolic pressures.

Stroke volume and Cardiac output: Stroke volume and cardiac output treatment X time charts can be found in Figures 14 and 15 respectively. No significant interactions were found between treatment X time (Wilks'Λ= 0.09; $F_{2,2}$= 9.15, p= 0.09, η_p^2= 0.90), treatment X group (Wilks'Λ= 0.96; $F_{2,2}$= 0.03, p= 0.96, η_p^2= 0.59), or time X group (Wilks'Λ= 0.10; $F_{2,2}$= 8.51, p= 0.10, η_p^2= 0.89). It is important to note that Doppler velocity measures could only be successfully completed on 4 individuals in each group due to positional and physiological limitations during testing. Examination of the means suggest that stroke volume increased following WBV exercise in both groups compared to standing steady-state conditions and remained elevated until the end of WBV exercise.

Oxygen consumption (VO_2):

VO_2 treatment X time charts can be found in Figure 16. Bonferroni's all pairwise comparisons with p values and confidence intervals are included in Tables 8-10. A significant time X group interaction was revealed (Wilks'Λ= 0.45; $F_{8,102}$= 6.23, p= 0.01, η_p^2= 0.32). A time X group follow-up univariate ANCOVA of the VO_2 measure was also significant ($F_{4,52}$= 12.53, $p\leq$ 0.001, η_p^2= 0.49). Pairwise comparisons revealed a significant difference ($p\leq 0.001$) between the SCI and the able bodied group on VO_2 response. VO_2 during WBV during the first minute of treatment at 40 Hz (t= 2.58, p= 0.01), at 50 Hz WBV (t= 2.68, p= 0.01) and during WBV-steady state at 40 Hz (t= *2.83*, p= 0.01) and at 50 Hz (t=*3.86*, p= 0.001). The VO_2 values were significantly higher in the SCI group compared to the able-bodied group at these time points. Moreover, VO_2 values were significantly greater within each group during WBV exercise during

the first minute and WBV steady-state conditions compared to pre- and post-WBV standing steady-state conditions (Tables 8-10).

Peripheral hemodynamic measures

Treatment X time plots and pairwise comparisons for oxyhemoglobin, de-oxyhemoglobin and total hemoglobin can be found in Figures17-18 and Tables 13-26 respectively.

Oxyhemoglobin: A significant time X group interaction was revealed (Wilks'Λ= 0.15; $F_{6,8}$= 4.14, p= 0.03, η_p^2= 0.84). A time X group follow-up univariate ANCOVA of the oxyhemoglobin measure was also significant ($F_{4,52}$= 14.84, $p\leq$ 0.001, η_p^2= 0.53). Pairwise comparisons revealed a significant difference (p= 0.04) between the SCI and the able bodied group on the oxyhemoglobin response. One way ANCOVAs between groups at each frequency revealed a significance difference in oxyhemoglobin during post-WBV standing steady-state at 30 Hz ($F_{1,19}$= 4.87, p= 0.04) and 40 Hz ($F_{1,19}$= 5.75, p= 0.02), and post-WBV seated steady-state at only 40 Hz ($F_{1,19}$= 8.11, p= 0.01). Oxyhemoglobin values were significantly higher in the SCI group compared to the able-bodied group at these time points. Moreover, oxyhemoglobin was significantly greater within the SCI group during post-WBV standing and seated steady-state conditions compared to pre-WBV seated and steady-state conditions.

De-oxyhemoglobin: A significant time X group interaction was evident (Wilks'Λ= 0.15; $F_{6,8}$= 4.14, p= 0.03, η_p^2= 0.84). A time X group follow-up univariate ANCOVA of the de-oxyhemoglobin measure was also significant ($F_{4,52}$= 13.72, $p\leq$ 0.001, η_p^2= 0.51). Pairwise comparisons revealed a significant difference ($p\leq$ 0.39) between the SCI and the able bodied

group on the de-oxyhemoglobin response. One way ANCOVAs between groups at each frequency revealed a significance difference in de-oxyhemoglobin during post-WBV standing steady-state ($F_{1,19}$= 9.87, p= 0.005), and during post-WBV seated steady state at 30 Hz ($F_{1,19}$= 7.64, p= 0.01). Significant differences were also found during WBV steady-state ($F_{1,19}$= 6.20, p= 0.02), post-WBV standing steady-state ($F_{1,19}$= 7.96, p= 0.01), and post-WBV seated steady state at 40 Hz ($F_{1,19}$= 12.86, p= 0.001). De-oxyhemoglobin values were significantly higher in the able-bodied group compared to the SCI group at these time points.

Total hemoglobin: A significant interaction occurred between time X group (Wilks'Λ= 0.15; $F_{6,8}$= 4.14, p= 0.03, η_p^2= 0.84). A time X group follow-up univariate ANCOVA of the total hemoglobin measure was also significant ($F_{4,52}$= 5.72, p= 0.04, η_p^2= 0.16). Pairwise comparisons did not reveal a significant difference (p= 0.62) between the SCI and the able bodied group on the total hemoglobin response; however pairwise comparisons within groups revealed significant increases in total hemoglobin during post-WBV conditions compared to pre- and WBV steady-state condition.

Skin temperature: Treatment X time charts can be found in Figure 19. Originally skin temperature measures were collected from right and left lower leg; however there were no significant differences between legs throughout the experiment within each group (p values ranged 0.56 to 0.72). Accordingly the mean of right and left lower leg temperatures were used for statistical analysis. Significant treatment X time X group interactions (Wilks'Λ= 0.52; $F_{82,15}$= 3.60, $p\leq$ 0.05, η_p^2= 0.52) and treatment X group (Wilks'Λ= 0.67; $F_{82,15}$= 15.51, $p\leq$ 0.001, η_p^2= 0.67) were revealed. Treatment X time follow-up univariate ANCOVA of the skin

temperature was significant ($F_{2,32}$= 12.53, $p \leq$ 0.001, η_p^2= 0.39). Skin temperatures were significantly higher following WBV in the SCI group and remained elevated 15 min post-WBV (Tables 27-29). On the contrary no significant differences were revealed in the able-bodied group during post-WBV conditions.

Discussion

The purposes of this study were: 1) to determine the acute effects of WBV exercise on central and peripheral hemodynamics and oxygen consumption; and 2) to compare physiological responses to WBV between three WBV frequencies (30, 40, and 50 Hz) in individuals with SCI and age and activity matched able-bodied individuals. The main findings of this investigation were that an acute bout of WBV elicited small changes on heart rate, diastolic blood pressure, stroke volume and cardiac output in both groups as compared to pre-WBV conditions. Significant differences between groups were found for oxygen consumption, systolic blood pressure, muscle oxygenation and lower leg skin temperature. Individuals with SCI demonstrated larger increases in those measures as compared to the able-bodied group. No specific frequency effect was revealed within or between groups.

Central hemodynamic measures

Heart rate did not significantly increase following WBV in either group. The SCI participants all presented with injuries between spinal levels C5 – T6, which is known to significantly disrupt sympathetic nervous system control on the sympathetic efferent organs (heart, adrenal medulla, arteries and veins).[1] Without sympathetic nervous system control to increase heart rate, vasoconstriction, or adrenalin release, there is limited ability to respond to the

requirements of metabolism induced by exercise. This interruption in the sympathetic efferent outflow is likely to account for the slight increase in heart rate observed in the SCI group.[3] Although cardiac acceleration was limited in the SCI group, our results indicate a slight increase in heart rate response during the first minute of WBV and during the WBV steady-state conditions. A potential mechanism for this increase may be related to a cardiac withdrawal response; which is defined by a reduction in vagus verve activity. At the initiation of exercise, heart rate may be increased by increasing sympathetic outflow to the heart via central influences and by decreasing vagus nerve activity.[2] The vagus nerve is a cranial nerve that is unaffected by SCI. Reduced vagus nerve activity may increase heart rate during exercise in the SCI population. Another possible reason for increased heart rate may be related to the effects of circulating plasma nor-epinephrine, a neurotransmitter which serves to increase heart rate. An increase in plasma nor-epinephrine has been shown during wheel chair exercise in the SCI population.[4] This increase in plasma nor-epinephrine level is thought to be a result of the spillover from postganglionic sympathetic nerve endings. Therefore, increased heart rate during WBV may be due to an increase in plasma nor-epinephrine levels or decreased vagus nerve activity in the SCI group. This warrants further investigation.

Heart rate did not significantly increase in the able-bodied group. The small mean increase in heart rate during and following WBV was approximately 1-2 beats/min. These results are in agreement with previous work[5] investigating the effects of an acute bout of vertical WBV at 45 Hz on cardiovascular responses in able-bodied individuals that demonstrated a very small increase (1-3 beats/min) in heart rate during WBV. The American College of Sports Medicine recommends an intensity of exercise corresponding to 60% to 80% of heart rate reserve to improve cardiovascular fitness in symptom free able-bodied individuals.[6] None of our

participants reached 60% of their heart rate reserve during WBV. Therefore, by solely considering exercise intensity based on heart rate, WBV intensities at 30, 40, and 50 Hz did not elicit any cardiovascular benefits in able-bodied individuals.

Systolic blood pressure was significantly increased during the first minute of WBV and WBV steady-state conditions in the SCI group and remained elevated above pre-WBV in the seated and standing conditions throughout testing. This finding is interesting as blood pressure control is severely disrupted following SCI, particularly in individuals with high level (C5-T6) injuries.[7] Interruption in sympathetic activity,[3] impaired baroreflex activity[8] and lack of skeletal muscle pump activity[9] have been suggested to be responsible for the disruption in blood pressure regulation during exercising in an upright position in the SCI population. Baroreceptors are stretch receptors located in the aortic arch, carotid sinus and coronary arteries that respond to perturbations in arterial pressure and reflexively modulate sympathetic and parasympathetic outflow in order to maintain blood pressure homeostasis.[8] This modulation is absent in high-level injuries due to an interruption of sympathetic connections in the spinal cord.[3] Moreover, venous pooling in the lower extremities due to an absence of the skeletal muscle pump decreases circulating blood volume and results in orthostatic intolerance during upright exercise in this population.[9] Accordingly, we postulate two potential mechanisms for the observed increase in systolic blood pressure response during WBV exercise. During normal standing postural muscles are continually activated in able-bodied individuals. These muscle contractions provide a means of compressing the veins and pumping blood back to the heart, which is well documented to be an important mechanism for maintaining venous return when upright in able-bodied individuals.[10] SCI individuals lack this skeletal muscle pumping effect resulting in a reduced venous return in the upright position. This decrease in venous return may acutely lower stroke

volume, cardiac output, and systolic blood pressure. We hypothesized that WBV may activate paralyzed skeletal muscle via a tonic vibration reflex; hence increased muscle activity may have the potential to promote venous return via activation of the skeletal muscle pump.[11] As a result, we expected heart rate, stroke volume or cardiac output to increase to maintain or increase blood pressure during WBV. Heart rate and stroke volume did not significantly increase following WBV; therefore, it is possible that circulating nor-epinephrine has played a role in the observed increase in systolic blood pressure in the SCI group. Increased plasma nor-epinephrine response to wheelchair exercise has been shown in the SCI population.[4] Nor-epinephrine causes vasoconstriction in the vascular smooth muscle. This vasoconstriction normally results in an increase in total peripheral resistance. Increase in peripheral resistance generally results in an increased systolic blood pressure when the cardiac output does not change significantly. Given that cardiac output did not change significantly during WBV exercise, increased peripheral resistance may be a reason for an increase in systolic blood pressure in the SCI group.

Systolic and diastolic blood pressure did not significantly increase in the healthy group following WBV. These results are in agreement with a previous study[16] which examined the effect of an acute bout of WBV exercise in a semi-squat position (120º knee flexion) to assess change in mean arterial pressure responses in the able-bodied individuals. Their results indicate that WBV did not significantly increase mean arterial blood pressure compared to non-WBV conditions. Although they measured mean arterial pressures; diastolic pressure changes little during exercise in able-bodied individuals. Thus we speculate that a significant change in mean arterial blood pressure is most likely due to change in systolic pressure. As mentioned previously changes in blood pressure are due to changes in stroke volume, cardiac output and peripheral

resistance. In the present study cardiac output did not significantly change so we speculate that peripheral resistance also did not significantly change during WBV in the able-bodied group.

Given the evidence demonstrating skeletal muscle activation during WBV,[12,13] we anticipated that stroke volume and cardiac output would increase during WBV due to increased venous return via activation of the skeletal muscle pump. We did not observe any significant change in stroke volume and cardiac output for either group. Cardiac output was indirectly calculated from the following formula: cardiac output= stroke volume X heart rate. The SCI group demonstrated slight increase in cardiac output during WBV first minute and WBV steady-state conditions. A possible explanation for this may be that the activated skeletal muscle pump was insufficient to increase venous return due to vascular limitations in the paralyzed legs. The effects of autonomic disruption and inactivity on the venous function in the SCI group are well studied.[14] The venous vascular properties in the legs of individuals with SCI are altered following SCI. Venous distensibility and capacity and venous smooth muscle tone have been shown to decrease in the chronic stages of SCI.[15] It is possible that these factors may potentially increase resistance to venous flow; thus this increase in resistance may limit the venous return. Furthermore, our participants stood upright on the platform with slight knee flexion. In an upright position circulating blood is subject to gravity. The combined effects of gravity and venous insufficiency together may have masked the effects of WBV on stroke volume and cardiac output.

Oxygen consumption

Several studies have demonstrated an increase in skeletal muscle activity as measured by electromyography during exposure to WBV.[12,13] Evidence that WBV produces muscular

contractions suggests that there may be an increase in skeletal muscle metabolism, suggesting that WBV may be an effective exercise stimulus for individuals with SCI. In the present study oxygen consumption was increased in both groups during the first minute of WBV and during WBV steady-state as compared to pre-WBV seated and standing conditions. This suggests that WBV elicits muscle activity, resulting in an increase energy expenditure as compared to the energy cost of simple standing. These findings support our hypothesis and agree with previous work investigating able-bodied individuals which found side alternating WBV using 26 Hz-34 Hz at amplitudes of (4-6mm) increased oxygen consumption by 113%[16] and by 104%[17] above the energy cost of simple standing during the last minute of a 3 minute bout of WBV exercise. Our results revealed a mean a 24% increase in the SCI group and 15% increase in the able-bodied group during WBV steady-state. Our results show a smaller increase in oxygen consumption when compared to a previous study[12]. Prior studies used a WBV platform that delivers side-alternating vibrations which has been shown to elicit greater muscle activation (as measured by electromyography) on leg extensor muscles.[12] Furthermore; in the previous study WBV was performed with the knees almost fully extended. This significantly alters the transmission of vibration through the body because the vibration is transferred from one segment to the next (i.e. foot to the calf, calf to thigh, thigh to trunk). The amount of vibration transmitted will depend on muscle stiffness and damping. Axial body stiffness increases with straight limbs.[18] Straight limbs result in higher levels of vibration transferred to the upper extremities, which results in increased muscle contractions to dampen the vibration,[19] requiring greater metabolic activity. Thus, the higher oxygen consumption values found in previous studies are likely due to increased muscle involvement as compared to the current participants.

In the present study participants stood on the platform with knees flexed at 18-25 degrees (Figure 7). This position was chosen to prevent the phenomenon known as a "resonance catastrophe"[18] which may occur during WBV exercise. Muscles and tendons in the body perform like springs that store and release mechanical energy. This spring-like system can accumulate mechanical energy when the frequency of vibration platform matches the frequency of the body's musculoskeletal structures and organs. The accumulation of mechanical energy can lead to a situation in which the vibration amplitude is greater in the body than the vibration platform, which may lead to damage within these structures (resonance catastrophe). Resonance can be prevented during WBV exercise by introducing a damping element (friction). Flexion of the knees has been suggested as a way to prevent resonance during WBV exercise. Vibration transmission has been shown to be reduced by 50% when knee flexion angle is increased from 10 to 30 degrees.[131,134] We believe standing with 18-25 degrees of knee flexion provides a safer mode of exercise; however it may have diminished the amount of muscle activation during WBV exercise.

An increase in oxygen consumption was evident during WBV in both groups; however this response was significantly greater in the SCI individuals as compared to able-bodied controls. This response was consistent with each of the WBV frequencies. We can speculate two potential mechanisms for the difference in oxygen consumption response. The higher oxygen consumption in the SCI group may indicate a higher skeletal muscle activity in the muscles exposed to vibration; thus the higher muscle activity may result in higher oxygen consumption. On the other hand if the muscle activity were matched, for a given adenosine triphosphate demand during WBV there would be a greater oxygen requirement in SCI individuals to generate a sufficient amount of adenosine triphosphate from oxidative phosphorylation as compared to

able-bodied controls. While we did not perform measurements to determine muscle activity and differences in metabolic efficiency, it is possible that differences in mitochondrial function or morhphology[20] due to alterations in skeletal muscle fiber type (conversion from Type I to Type IIX) could play a role. Future studies utilizing 31 phosphate magnetic resonance spectroscopy to look at mitochondrial function may be needed to further investigate this question. In summary, increases in oxygen consumption, combined with little effect on heart rate, stroke volume and cardiac output may suggest an increase in the arteriovenous difference due to an increase in skeletal muscle activity as oxygen consumption is a product of cardiac output and arteriovenous difference.

Peripheral hemodynamic measures

The potential to investigate local muscle metabolism during and after exercise has been enhanced via the use of Near Infrared Spectroscopy (NIRS). NIRS provides information about the concentration changes in oxyhemoglobin, de-oxyhemoglobin, and total hemoglobin in the small vessels such as capillaries and arterioles. These concentration changes represent a dynamic balance between oxygen supply and oxygen consumption in the investigated the tissue. Although we did not take arteriovenous samples in the present study, NIRS measurements may be utilized as means of indirectly reflecting the local skeletal muscle metabolism.

Oxyhemoglobin and total hemoglobin were significantly greater during post-WBV standing steady-state at 30 and 40 Hz and during post-WBV seated steady-state at 40 Hz. De-oxyhemoglobin was significantly lower at post-WBV time points and did not demonstrate a significant increase during WBV in the SCI group. The lack of significant increase in de-oxyhemoglobin and/or decrease in oxyhemoglobin during WBV may indicate that WBV did not

alter local muscle metabolism significantly in the SCI group. A significant increase in total hemoglobin was observed during post-WBV time periods. This increase may suggest that tissue blood flow increased in the gastrocnemius muscle following WBV exercise. Reduced arterial stiffness[21] and vasodilation due to liberation of local metabolites[22] have been suggested to be responsible for the increased muscle blood flow after WBV in able-bodied individuals; however which mechanism is more responsible in increasing the tissue flow warrants further investigation. It is important to note that there was a considerable inter-individual variability within the SCI group in oxyhemoglobin, de-oxyhemoglobin and total hemoglobin concentrations during and after WBV. This difference may be a consequence of differences in the contribution of each of these factors to the changes in oxygenation and muscle blood flow during WBV.

An increase in the total hemoglobin and de-oxyhemoglobin following WBV was also revealed in the able-bodied group; however no significant change was found in oxy-hemoglobin. It is important to note that the increase in de-oxyhemoglobin during WBV steady-state and post-WBV conditions were not significantly different from pre-WBV standing conditions. This suggests that the increase in de-oxyhemoglobin concentrations may have been a result of solely standing; therefore our results suggest that WBV may not significantly increase skeletal muscle metabolism more than standing without vibration. These findings are in agreement with previous studies in which gastrocnemius oxygenation and tissue blood flow was measured following 30, 40 and 50 Hz WBV.[23] Their study showed that WBV exercise with frequencies of 30, 40, and 50 Hz did not affect muscle oxygenation more than a non vibration condition.

Total hemoglobin was increased following WBV in the able bodied group. This result is in agreement with a previous study.[24] An increase in muscle blood flow following one bout of 9-minute WBV was reported. They attributed this increase to widening of the vessels due to

vibration induced vasodilation. Due to different frequency, amplitude and duration of WBV used in the previous study, we cannot make direct comparisons with the previous work. However, given that WBV did not significantly affect muscle metabolism in the present study, we suggest that increase tissue flow in the gastrocnemius muscle may be related to vibration induced vasodilation in the skeletal muscle vessels.

This was the first study to investigate skin temperatures following WBV utilizing dynamic infrared thermography. With this technique quantification of skin temperature can be correlated to qualitative evaluations of skin blood flow.[26] Skin temperatures were significantly higher following WBV in the SCI group and remained elevated up to 15 minutes post-WBV. Significant increases in skin temperature during and following WBV exercise suggest increased skin blood flow in the lower legs. An explanation for this increase may be related to increased skin blood flow from vasodilation in the skin resistance vessels.[25] In general, blood circulation in the skin of the lower limbs can be promoted by submaximal exercise[29] or heat stress[30] if the injury level of spinal cord is below L1; however our participants could not utilize these mechanisms to increase skin blood flow due to their high SCI level (C5-T6). On the other hand vibration-induced shear forces have been suggested as a potential mechanism to stimulate nitric oxide release.[27] Nitric oxide causes vasodilation in the skin resistance vessels which may result in an increase skin blood flow during and following WBV exercise in this population.[28] This warrants further investigation.

Skin temperature did not significantly increase following WBV in the able-bodied group. Skin blood flow has been shown to increase during and following 30 Hz WBV at 6mm amplitude in able-bodied individuals.[27] In the present study we utilized a similar frequency; however our amplitude was relatively low (2mm) as compared to 6mm used in the previous

study. Our WBV intensity parameters may not have provided an adequate stimulus for significantly increasing metabolic activity in the contracting muscles and/or eliciting vasodilation in skin resistance vessels as proposed previously.

In summary, an acute bout of WBV elicited small physiological changes on heart rate, diastolic blood pressure, stroke volume and cardiac output in both groups as compared to pre-WBV conditions. Significant differences between groups were found for oxygen consumption, systolic blood pressure, muscle oxygenation and lower leg skin temperature. Individuals with SCI demonstrated larger increases in those measures as compared to the able-bodied group. A possible explanation for this difference is that WBV may elicit a greater stress for the cardiovascular system in the SCI group. Although the increase in central hemodynamics was higher in the SCI group as compared to the able-bodied group, these changes are comparatively small in relation to cardiovascular changes elicited by aerobic exercise for both groups. This study also demonstrated that WBV increases muscle oxygenation and skin temperatures in the SCI group and increases tissue blood flow in the gastrocnemius muscle in both groups during the post-WBV conditions. Moreover no specific frequency effect was revealed within or between groups.

Future work

At the moment it is not clear whether WBV represents a training stimulus to improve cardiovascular fitness in the SCI populations; hence future studies investigating the effects of different vibration parameters (frequency, amplitude, and duration) on cardiovascular responses are needed.

On the basis of muscle oxygenation, tissue blood flow and skin temperatures observations, one could suspect a possible application of WBV, as a tissue blood flow and/or oxygen saturation enhancer for patients with peripheral blood flow deficiency; such as those with diabetes and SCI. However, much work remains to be carried out to confidently use WBV as means of improving peripheral blood flow. Future studies should investigate the mechanism responsible for the observed increase in peripheral blood flow in response to WBV. Furthermore, the effects of long term WBV training on peripheral blood flow should be investigated. It is still not clear if WBV effect on tissue blood flow and/or oxygenation is long lasting or an immediate response in the SCI as well as able-bodied group. Answering these question will enable to use WBV as a way of enhancing tissue oxygenation and/or blood flow in the special populations.

Study Limitations

In the present study Doppler aortic flow measurements could only be obtained from 8 participants (4 SCI, 4 able-bodied) due to positional (upright stance) and physiological (high % of fat or muscle tissue on the chest) difficulties. Therefore, small sample size may have masked the true effects of WBV exercise on stroke volume and cardiac output measurements. Moreover, dynamic infrared thermography and near infrared spectroscopy are indirect measures of peripheral blood flow. Future studies should utilize more direct methods for measuring peripheral blood flow in the SCI group. Finally we did not perform electromyography measures to confirm muscle activity during WBV due to problems with removing vibration artifacts from the electromyography data. We can only speculate that the muscle activity has increased from our oxygen consumption findings. Therefore, future studies should include electromyography measures in order to more accurately assess muscle activation.

Table 3. Demographics of participants

Participant	Gender	Age (years)	Lean Body Mass (kg)	Injury Level	ASIA classification	Anti-spastic agents
SCI 01	M	49.2	38	C5-C6	B	Baclofen
SCI 02	M	54.1	36	C6-C7	A	None
SCI03	M	52.8	50.3	T5-6	A	None
SCI 04	M	44	43.4	T4	A	None
SCI 05	M	49	52.1	T4-5	B	None
SCI 06	M	64	54.05	C5-C6	B	None
SCI 07	M	55.6	63.04	T5-6	A	None
SCI 08	M	52.5	58	C5-C6	B	Baclofen
SCI 09	M	46.4	52.07	T4	A	None
SCI 10	M	55	45.86	T5-6	B	None
SCI 11	M	31.7	45.91	C5-C6	B	None
AB 01	M	53.5	57.5			
AB 02	M	54.4	58.8			
AB 03	M	49	55.2			
AB 04	M	56	54.59			
AB 05	M	47	68.23			
AB 06	M	48	56.81			
AB 07	M	44	56.52			
AB 08	M	31.7	58..75			
AB 09	M	53.5	70.46			
AB 10	M	44.7	55.74			

Abbreviation: ASIA: American Spinal Injury Association

Table 4. Descriptive statistics for pre- and post-WBV at 30 Hz measures in SCI and able-bodied group

SCI 30 Hz	Pre-WBV sitting steady-state	Pre-WBV Covariate*	Standing steady-state	WBV first minute	WBV steady-state	Post-WBV standing steady-state	Post-WBV seated steady-state
HR (beats/min)	78±6.63	74.47	79.90±8.44	83.54±12.52	84.09±14.28	82.81±16.57	76.27±14.94
SBP (mmHg)	114.36±23.45	123.95	119.45±11.86	138.63±21.79	135.36±22.83	128.54±21.47	129.09±21.06
DBP (mmHg)	80.63±10.67	83.28	78.72±13.63	87.81±10.93	85.00±8.77	81.27±13.03	87.00±13.06
SV (ml/beat)		52.87*	35.37±3.22	41.75±0.75	40.88±3.12	39.26±2.74	
CO (l/min)		3.39*	2.94±0.7	3.58±0.80	3.50±0.10	3.27±0.10	
VO_2 ($ml/kg_{LBM}/min$)	4.69±0.69	4.77	5.17±0.86	6.84±1.12	6.07±1.01	5.06±0.75	4.58±0.71
HbO_2 (a.u.)	-0.35±0.30	0.07	-3.51±12.10	-1.97±13.86	8.02±21.77	24.67±33.63	20.70±32.82
HHb (a.u.)	-3.21±0.4	-1.71	2.70±15.40	-0.10±17.77	-6.64±24.01	-16.77±23.43	-9.33±18.96
THb (a.u.)	-3.56±12.63	-1.69	-0.81±19.66	-2.08±20.91	2.14±15.73	7.90±25.59	11.37±28.01
Able-bodied 30 Hz	**Pre-WBV sitting steady-state**	**Pre-WBV Covariate***	**Standing steady-state**	**WBV first minute**	**WBV steady-state**	**Post-WBV standing steady-state**	**Post-WBV seated steady-state**
HR (beats/min)	70.6±9.31	74.47	74.50±7.60	75.7±9.84	74.8±9.68	74.9±0.65	70.20±8.59
SBP (mmHg)	134.5±11	123.95	123.40±5.39	133.70±15.00	131.10±12.98	137.90±5.48	128.90±6.43
DBP(mmHg)	86.2±6.67	83.28	81.20±7.61	84.00±9.36	85.40±11.82	84.30±7.91	88.9±5.58
SV (ml/beat)		52.87*	70.38±15.42	73.21±22.42	66.37±18.23	65.83±18.61	
CO (l/min)		3.39*	4.91±0.72	4.98±0.78	4.48±0.68	4.48±0.61	
VO_2 ($ml/kg_{LBM}/min$)	4.85±0.73	4.77	4.89±0.67	5.90±0.79	5.65±0.76	5.06±0.68	4.76±0.84
HbO_2 (a.u.)	0.55±0.93	0.07	-0.63±5.17	-1.90±4.50	-0.65±3.68	0.66±7.10	0.73±6.82
HHb (a.u.)	-0.06±0.40	-1.71	6.65±3.91	3.02±6.03	0.13±8.39	7.42±6.74	8.17±6.58
THb (a.u.)	0.37±1.02	-1.69	6.46±4.82	1.11±8.90	4.43±7.10	8.02±3.50	8.83±3.29

Values are reported as mean ± SD

Abbreviations: HR: heart rate; SBP: systolic blood pressure; DBP: diastolic blood pressure; SV: stroke volume; CO: cardiac output; VO_2: oxygen consumption; HbO_2: oxygenated hemoglobin; HHb: de-oxygenated hemoglobin; THb: total hemoglobin. *: Common covariate evaluation point

Note: SV and CO measures were not performed during at steady state and post-WBV seated steady state time points.

Table 5. Descriptive statistics for pre- and post-WBV at 40 Hz measures in SCI and able-bodied group

SCI 40 Hz	Pre-WBV sitting steady-state	Pre-WBV Covariate*	Standing steady-state	WBV first minute	WBV steady-state	Post-WBV standing steady-state	Post-WBV seated steady-state
HR (beats/min)	77±10.55	75.04	79.45±13.04	83.81±13.54	89.72±16.35	79.63±14.39	74.63±14.29
SBP (mmHg)	126.00±18.82	127.76	126.81±16.04	143.00±17.61	135.54±23.37	131.45±23.05	134.54±24.50
DBP(mmHg)	78.81±11.32	82.33	78.09±9.34	83.18±12.08	82.45±8.94	78.9±9.96	82.63±14.81
SV (ml/beat)		48.77*	35.03±4.21	37.89±2.86	37.13±6.29	33.96±5.13	
CO (l/min)		3.37*	2.51±0.68	3.11±0.44	3.44±0.86	2.75±0.77	
VO_2 ($ml/kg_{LBM}/min$)	4.35±0.45	4.55	4.87±0.46	6.85±1.17	6.18±0.61	4.96±0.55	4.54±0.39
HbO_2 (a.u.)	-0.07±0.93	0.16	-1.55±11.35	-4.53±10.67	8.07±22.91	27.26±29.37	0.92±5.07
HHb (a.u.)	0.84±2.05	0.37	11.07±10.79	3.25±11.01	-5.93±13.45	-8.52±16.84	-8.28±13.37
THb (a.u.)	0.76±2.36	0.54	9.52±15.11	-1.28±9.60	1.38±19.89	18.73±24.95	19.29±21.63
Able-bodied 40 Hz	**Pre-WBV sitting steady-state**	**Pre-WBV Covariate***	**Standing steady-state**	**WBV first minute**	**WBV steady-state**	**Post-WBV standing steady-state**	**Post-WBV seated steady-state**
HR (beats/min)	72.90±10.18	75.04	74.20±10.72	76.00±8.65	77.40±12.42	73.50±11.46	69.20±9.51
SBP (mmHg)	129.70±4.32	127.76	127.50±7.77	130.50±15.67	132.00±12.03	123.70±12.61	131.50±13.34
DBP(mmHg)	86.2±11.76	82.33	83.90±13.48	85.60±7.79	84.20±12.49	84.80±11.67	89.00±12.19
SV (ml/beat)		48.77*	62.52±14.76	64.85±21.34	64.33±18.99	60.06±17.61	
CO (l/min)		3.37*	4.22±0.88	4.56±0.92	4.39±0.84	4.08±0.42	
VO_2 ($ml/kg_{LBM}/min$)	4.78±0.62	4.55	4.80±0.83	5.72±0.73	5.38±0.68	4.73±0.49	4.54±0.70
HbO_2 (a.u.)	0.43±0.91	0.16	1.10±6.51	-4.03±7.98	-0.78±5.28	3.80±9.93	0.92±5.07
HHb (a.u.)	-0.13±1.62	0.37	9.79±9.06	9.05±4.75	5.22±4.54	7.70±7.10	8.14±5.75
THb (a.u.)	0.29±1.68	0.54	10.89±11.49	5.02±9.23	-0.71±5.56	11.50±9.88	9.06±5.77

Values are reported as mean ± SD

Abbreviations: HR: heart rate; SBP: systolic blood pressure; DBP: diastolic blood pressure; SV: stroke volume; CO: cardiac output; VO_2: oxygen consumption; HbO_2: oxygenated hemoglobin; HHb: de-oxygenated hemoglobin; THb: total hemoglobin. *: Common covariate evaluation point

Note: SV and CO measures were not performed during at steady state and post-WBV seated steady state time points.

Table 6. Descriptive statistics for pre- and post-WBV at 50 Hz measures in SCI and able-bodied group

SCI 50 Hz	Pre-WBV sitting steady-state	Pre-WBV Covariate*	Standing steady-state	WBV first minute	WBV steady-state	Post-WBV standing steady-state	Post-WBV seated steady-state
HR (beats/min)	77.36±8.15	71.95	82.09±11.78	87.09±18.10	82.54±15.10	77.09±15.80	75.27±15.61
SBP (mmHg)	121.81±23.67	125.66	120.00±29.36	131.45±22.40	130.81±22.25	125.18±21.66	128.90±6.43
DBP(mmHg)	78.9±13.26	81.71	77.27±15.04	85.45±14.06	80.27±11.99	80.81±12.10	86.72±13.71
SV (ml/beat)		49.64*	36.47±5.01	40.39±5.17	39.81±6.45	38.16±5.08	
CO (l/min)		3.71*	3.12±0.90	3.91±0.86	3.77±1.07	3.23±0.75	
VO_2 ($ml/kg_{LBM}/min$)	4.63±0.73	4.52	5.49±0.49	7.48±1.38	6.96±1.19	4.58±0.89	4.44±0.71
HbO_2 (a.u.)	-0.33±0.84	0.36	-0.87±10.29	-1.04±10.57	-2.16±17.32	23.96±42.25	23.14±40.52
HHb (a.u.)	0.47±1.96	1.03	8.33±7.68	7.23±8.22	7.54±11.70	-7.35±17.06	-1.13±16.07
THb (a.u.)	0.13±2.27	1.40	7.45±12.63	6.19±13.44	5.37±18.50	16.61±32.00	22.01±27.95
Able-bodied 50 Hz	**Pre-WBV sitting steady-state**	**Pre-WBV Covariate***	**Standing steady-state**	**WBV first minute**	**WBV steady-state**	**Post-WBV standing steady-state**	**Post-WBV seated steady-state**
HR (beats/min)	66.00±6.63	71.95	71.20±7.65	70.00±6.23	72.9±6.77	72.6±8.26	66.8±6.44
SBP (mmHg)	129.90±6.53	125.66	124.05±6.15	129.40±7.60	127.60±9.25	121.90±9.21	128.90±6.43
DBP(mmHg)	84.80±7.69	81.71	81.60±7.53	83.10±7.40	85.70±7.46	83.8±8.32	88.4±7.53
SV (ml/beat)		49.64*	67.55±20.11	67.55±24.36	62.92±20.04	63.22±19.30	
CO (l/min)		3.71*	4.29±0.45	4.46±0.10	4.41±0.79	4.34±0.52	
VO_2 ($ml/kg_{LBM}/min$)	4.39±0.37	4.52	4.39±0.33	5.51±0.75	5.28±0.70	4.28±0.45	4.24±0.40
HbO_2 (a.u.)	1.40±3.36	0.36	0.70±8.04	-0.23±9.22	0.68±7.98	2.12±12.29	0.68±11.97
HHb (a.u.)	1.64±3.97	1.03	8.16±5.67	11.03±8.16	7.78±9.80	9.16±7.39	10.32±4.66
THb (a.u.)	2.78±4.22	1.40	8.86±11.36	10.79±11.33	8.47±13.85	11.28±12.92	10.41±22.07

Values are reported as mean ± SD

Abbreviations: HR: heart rate; SBP: systolic blood pressure; DBP: diastolic blood pressure; SV: stroke volume; CO: cardiac output; VO_2: oxygen consumption; HbO_2: oxygenated hemoglobin; HHb: de-oxygenated hemoglobin; THb: total hemoglobin. *: Common covariate evaluation point

Note: SV and CO measures were not performed during at steady state and post-WBV seated steady state time points.

Table 7. Skin temperature descriptive statistics for pre- and post-WBV at 30, 40, and 50 Hz in SCI and able-bodied group

Lower Leg Skin Temperature (°C)	Pre-WBV	Pre-WBV Covariate*	Immediately post-WBV	10 minute post-WBV	15 minute post-WBV
SCI 30 Hz	30.29±1.63	31.54	30.80±1.54	31.30±1.25	31.50±1.18
Able-bodied 30 Hz	32.91±0.27	31.54	32.98±0.41	32.80±0.42	32.80±0.53
SCI 40 Hz	31.14±1.09	31.73	31.95±1.34	32.09±1.25	32.29±1.24
Able-bodied 40 Hz	32.37±0.87	31.73	32.25±1.18	32.20±1.13	31.97±1.15
SCI 50 Hz	30.85±1.84	31.76	31.39±1.81	31.68±1.66	31.80±1.59
Able-bodied 50 Hz	32.76±0.71	31.76	32.92±0.67	32.87±0.58	32.76±0.80

. *: Common covariate evaluation point

Table 8. VO_2 Bonferroni's all pairwise comparisons within SCI and able-bodied group at 30 Hz WBV

SCI						
Time		Mean Difference	Lower Bound	Upper Bound	*t*	*p*
Seated steady-state	WBV first minute	-2.15	-2.98	-1.31	-5.73	<0.0001
Seated steady-state	WBV steady-state	-1.38	-2.20	-0.55	-3.74	<0.0001
Standing steady-state	WBV first minute	-1.67	-2.33	-1.00	-5.59	<0.0001
Standing steady-state	WBV steady-state	-0.9	-1.62	-0.17	-2.77	<0.0001
WBV first minute	WBV steady-state	0.77	0.27	1.26	3.44	<0.0001
WBV first minute	Post-WBV standing steady-state	1.77	1.32	2.22	8.72	<0.0001
WBV first minute	Post-WBV seated steady-State	2.26	1.59	2.93	7.53	<0.0001
WBV steady-state	Post-WBV standing steady-state	1.00	0.46	1.54	4.16	0.01
WBV steady-state	Post-WBV seated steady-state	1.49	0.93	2.05	5.97	<0.0001
Able-bodied						
Time		Mean Difference	Lower Bound	Upper Bound	*t*	*p*
Seated steady-state	WBV first minute	-1.04	-1.56	-0.52	-4.56	<0.0001
Seated steady-state	WBV steady-state	-0.79	-1.34	-0.25	-3.31	<0.0001
Standing steady-state	WBV first minute	-1.03	-1.39	-0.63	-6.00	<0.0001
Standing steady-state	WBV steady-state	-0.76	-1.22	-0.30	-3.73	<0.0001
WBV first minute	Post-WBV standing steady-state	0.84	0.28	1.40	3.40	0.01
WBV first minute	Post-WBV seated steady-state	1.14	0.74	1.53	6.52	<0.0001
WBV steady-state	Post-WBV standing steady-state	0.89	0.48	1.30	4.92	<0.0001
WBV steady-state	Post-WBV seated steady-state	0.89	0.48	1.30	4.92	<0.0001

Table 9. VO_2 Bonferroni's pairwise comparisons within SCI and able-bodied group at 40 Hz WBV

SCI						
Time		Mean Difference	Lower Bound	Upper Bound	*t*	*p*
Seated steady-state	WBV first minute	-2.49	-3.09	-1.89	-9.26	<0.0001
Seated steady-state	WBV steady-state	-1.83	-2.10	-1.56	-15.07	<0.0001
Standing steady-state	WBV first minute	-1.97	-2.70	-1.25	-6.09	<0.0001
Standing steady-state	WBV steady-state	-1.31	-1.69	-0.93	-7.78	<0.0001
WBV first minute	WBV steady-state	0.66	-0.02	1.34	2.15	<0.0001
WBV first minute	Post-WBV standing steady-state	1.88	1.15	2.61	5.75	<0.0001
WBV first minute	Post-WBV seated steady-state	2.30	1.65	2.96	7.84	<0.0001
WBV steady-state	Post-WBV standing steady-state	1.22	0.69	1.74	5.17	<0.0001
WBV steady-state	Post-WBV seated steady-state	1.64	1.19	2.09	8.06	<0.0001
Post-WBV standing steady-state	Post-WBV seated steady-state	0.42	0.05	0.79	2.58	0.02
Able-bodied						
Time		Mean Difference	Lower Bound	Upper Bound	*t*	*p*
Seated steady-state	WBV first minute	-0.94	-1.42	-0.46	-4.49	<0.0001
Seated steady-state	WBV steady-state	-0.60	-0.88	-0.31	-4.76	<0.0001
Standing steady-state	WBV first minute	-0.92	-1.44	-0.39	-3.96	<0.0001
Standing steady-state	WBV steady-state	-0.57	-1.03	-0.11	-2.88	<0.0001
WBV first minute	Post-WBV standing steady-state	0.99	0.61	1.36	5.98	<0.0001
WBV first minute	Post-WBV seated steady-State	1.18	0.90	1.45	9.60	<0.0001
WBV steady-state	Post-WBV standing steady-state	0.64	0.34	0.94	4.85	<0.0001
WBV steady-state	Post-WBV seated steady-state	0.83	0.42	1.24	4.61	<0.0001

Table 10. VO_2 Bonferroni's pairwise comparisons within SCI and able-bodied group at 50 Hz WBV

SCI						
Time		Mean Difference	Lower Bound	Upper Bound	*t*	*p*
Seated steady-state	Standing steady-state	-0.85	1.42	-0.28	-3.34	<0.0001
Seated steady-state	WBV first minute	-2.84	-3.59	-2.09	-8.44	<0.0001
Seated steady-state	WBV steady-state	-2.33	-2.89	-1.76	-9.14	<0.0001
Standing steady-state	WBV first minute	-1.98	-2.92	-1.05	-4.74	<0.0001
Standing steady-state	WBV steady-state	-1.47	-2.13	-0.81	-4.99	<0.0001
WBV first minute	WBV steady-state	0.51	0.13	0.88	3.06	0.01
WBV first minute	Post-WBV standing steady-state	2.89	2.20	3.58	9.37	<0.0001
WBV first minute	Post-WBV seated steady-state	3.03	2.18	3.89	7.94	<0.0001
WBV steady-state	Post-WBV standing steady-state	2.37	1.85	2.90	10.08	<0.0001
WBV steady-state	Post-WBV seated steady-state	2.52	1.89	3.14	9.00	<0.0001
Able-bodied						
Time		Mean Difference	Lower Bound	Upper Bound	*t*	*p*
Seated steady-state	WBV first minute	-1.12	-1.48	-0.76	-7.08	<0.0001
Seated steady-state	WBV steady-state	-0.88	-1.26	-0.51	-5.36	<0.0001
Standing steady-state	WBV first minute	-1.12	-1.55	-0.69	-5.98	<0.0001
Standing steady-state	WBV steady-state	-0.89	-1.35	-0.42	-4.36	<0.0001
WBV first minute	Post-WBV standing steady-state	1.22	0.72	1.73	5.48	<0.0001
WBV first minute	Post-WBV seated steady-state	1.26	0.79	1.73	6.10	<0.0001
WBV steady-state	Post-WBV standing steady-state	0.99	0.55	1.42	5.12	0.00
WBV steady-state	Post-WBV seated steady-state	1.03	0.58	1.47	5.26	0.00

Table 11. Systolic blood pressure Bonferroni's all pairwise comparisons within SCI group at 30 Hz WBV

		SCI				
Time		Mean Difference	Lower Bound	Upper Bound	*t*	*p*
Seated steady-state	WBV first minute	-24.27	-43.47	-5.07	3.89	0.004
Standing steady-state	WBV first minute	-19.18	-38.38	0.01	3.07	0.05

Table 12. Systolic blood pressure Bonferroni's all pairwise comparisons within SCI group at 40 Hz WBV

		SCI				
Time		Mean Difference	Lower Bound	Upper Bound	*t*	*p*
Seated steady-state	WBV first minute	-20	-37.72	0.12	3.42	0.05
Standing steady-state	WBV first minute	-16.80	-38.43	-0.02	3.71	0.04

Table 13. Oxyhemoglobin Bonferroni's pairwise comparisons within SCI group at 30 Hz WBV

		SCI				
Time		Mean Difference	Lower Bound	Upper Bound	*t*	*p*
Seated steady-state	WBV steady-state	-25.02	-45.25	-4.80	3.81	0.005
Seated steady-state	Post-WBV seated steady-state	-21.05	-41.28	-0.82	3.20	0.03
Standing steady-state	Post-WBV standing steady-state	-28.19	-48.41	-7.96	4.29	0.001
Standing steady-state	Post-WBV seated steady-state	-24.21	-44.44	-3.99	3.69	0.008
WBV first minute	Post-WBV standing steady-state	-26.65	-42.11	-6.42	4.06	0.002
WBV first minute	Post-WBV seated steady-state	-22.68	-42.90	-2.45	3.45	0.01

Table 14. Oxyhemoglobin Bonferroni's pairwise comparisons within SCI group at 40 Hz WBV

SCI						
Time		Mean Difference	Lower Bound	Upper Bound	*t*	*p*
Seated steady-state	Post-WBV seated steady-state	-27.66	-47.17	-8.14	4.62	0.0004
Standing steady-state	Post-WBV standing steady-state	-28.81	-47.05	-10.57	4.82	0.0002
Standing steady-state	Post-WBV seated steady-state	-29.13	-47.55	-10.71	4.87	0.0002
WBV first minute	Post-WBV standing steady-state	-31.80	-50.22	-13.38	5.32	<0.0001
WBV first minute	Post-WBV seated steady-state	-32.12	-50.54	-13.69	5.37	<0.0001
WBV steady-state	Post-WBV standing steady-state	-19.18	-37.60	-0.76	3.21	0.03
WBV steady-state	Post-WBV seated steady-state	-19.50	-37.92	-1.07	3.26	0.02

Table 15. Oxyhemoglobin Bonferroni's pairwise comparisons within SCI group at 50 Hz WBV

SCI						
Time		Mean Difference	Lower Bound	Upper Bound	*t*	*p*
Seated steady-state	Post-WBV standing steady-state	-24.30	-48.86	0.24	3.05	0.05
Standing steady-state	Post-WBV standing steady-state	-24.84	-49.40	-0.28	3.11	0.04
WBV first minute	Post-WBV standing steady-state	-25.01	-48.25	-0.45	3.14	0.04
WBV first minute	Post-WBV seated steady-state	-24.18	-46.25	0.36	3.03	0.05
WBV steady-state	Post-WBV standing steady-state	-26.13	-50.68	-1.57	3.28	0.02
WBV steady-state	Post-WBV seated steady-state	-25.30	-44.51	-0.75	3.17	0.03

Table 16. De-oxyhemoglobin Bonferroni's pairwise comparisons within SCI group at 30 Hz WBV

		SCI				
Time		Mean Difference	Lower Bound	Upper Bound	*t*	*p*
Seated steady-state	Post-WBV seated steady-state	13.55	0.56	26.54	3.21	0.03
Standing steady-state	Post-WBV seated steady-state	19.48	6.49	32.22	4.62	0.0004
WBV first minute	WBV steady-state	16.66	3.67	29.65	3.95	0.03

Table 17. De- oxyhemoglobin Bonferroni's pairwise comparisons within SCI group at 40 Hz WBV

		SCI				
Time		Mean Difference	Lower Bound	Upper Bound	*t*	*p*
Standing steady-state	WBV steady-state	17.01	3.35	20.66	3.83	0.005
Standing steady-state	Post-WBV standing steady-state	19.60	5.94	33.26	4.42	0.0008
Standing steady-state	Post-WBV seated steady-state	19.36	5.70	33.01	4.37	0.0009

Table 18. De- oxyhemoglobin Bonferroni's pairwise comparisons within SCI group at 50 Hz WBV

		SCI				
Time		Mean Difference	Lower Bound	Upper Bound	*t*	*p*
Standing steady-state	Post-WBV standing steady-state	15.68	1.39	29.97	3.38	0.02
WBV first minute	Post-WBV standing steady-state	14.59	0.94	28.23	3.14	0.04
WBV steady-state	Post-WBV standing steady-state	14.89	0.60	29.18	3.21	0.03

Table 19. Total hemoglobin Bonferroni's pairwise comparisons within SCI group at 30 Hz WBV

SCI						
Time		Mean Difference	Lower Bound	Upper Bound	*t*	*p*
Seated steady-state	Post-WBV seated steady-state	-19.66	-33.95	-5.37	4.24	0.04
Standing steady-state	Post-WBV seated steady-state	-17.13	-31.43	-2.84	3.69	0.008
WBV first minute	Post-WBV seated steady-state	-17.60	-31.89	-3.31	3.79	0.006
WBV steady-state	Post-WBV seated steady-state	-14.76	-29.05	-0.46	3.18	0.03

Table 20. Total hemoglobin Bonferroni's pairwise comparisons within SCI group at 40 Hz WBV

SCI						
Time		Mean Difference	Lower Bound	Upper Bound	*t*	*p*
Seated steady-state	Post-WBV seated steady-state	-18.53	-34.91	-0.56	3.18	0.03
WBV first minute	Post-WBV standing steady-state	-18.94	-38.19	-1.77	3.40	0.01
WBV first minute	Post-WBV seated steady-state	-20.57	-36.86	-3.73	3.75	0.006
WBV steady-state	Post-WBV seated steady-state	-17.15	-37.75	-1.39	3.33	0.02

Table 21. De-oxyhemoglobin Bonferroni's pairwise comparisons within able-bodied group at 30 Hz WBV

		SCI				
Time		Mean Difference	Lower Bound	Upper Bound	*t*	*p*
Seated steady-state	Post-WBV standing steady-state	-7.49	-12.31	-0.09	3.13	0.04
Seated steady-state	Post-WBV seated steady-state	-8.24	-13.02	-0.84	3.45	0.01
WBV steady-state	Post-WBV standing steady-state	-7.29	-14.69	0.10	3.05	0.05
WBV steady-state	Post-WBV seated steady-state	-8.03	-13.02	-0.64	3.37	0.02

Table 22. De-oxyhemoglobin Bonferroni's pairwise comparisons within able-bodied group at 40 Hz WBV

		SCI				
Time		Mean Difference	Lower Bound	Upper Bound	*t*	*p*
Seated steady-state	Standing steady-state	-9.92	-16.02	-3.83	4.60	0.0005
Seated steady-state	WBV first minute	-9.19	-15.99	-2.74	4.26	0.00
Seated steady-state	Post-WBV standing steady-state	-7.84	-12.05	-1.39	3.63	0.008

Table 23. De-oxyhemoglobin Bonferroni's pairwise comparisons within able-bodied group at 50 Hz WBV

		SCI				
Time		Mean Difference	Lower Bound	Upper Bound	*t*	*p*
Seated steady-state	WBV first minute	-9.38	-17.16	-1.16	3.54	0.01
Seated steady-state	Post-WBV seated steady-state	-8.68	-16.89	-0.46	3.27	0.03

Table 24. Total hemoglobin Bonferroni's pairwise comparisons within able-bodied group at 30 Hz WBV

		SCI				
Time		Mean Difference	Lower Bound	Upper Bound	*t*	*p*
Seated steady-state	Post-WBV seated steady-state	-7.65	-10.41	-4.89	3.80	0.006
Seated steady-state	Post-WBV seated steady-state	-8.46	-11.13	-1.41	4.20	0.001
Standing steady-state	WBV steady-state	7.17	0.93	12.90	3.56	0.01
WBV first minute	Post-WBV standing steady-state	-7.71	-13.04	-2.38	-3.27	0.01
WBV first minute	Post-WBV seated steady-state	-6.91	-11.82	-1.99	3.43	0.01
WBV steady-state	Post-WBV standing steady-state	-8.74	-12.52	-4.95	4.34	0.0001
WBV steady-state	Post-WBV seated steady-state	-9.54	-13.35	-5.73	4.74	0.0003

Table 25. Total hemoglobin Bonferroni's pairwise comparisons within able-bodied group at 40 Hz WBV

		SCI				
Time		Mean Difference	Lower Bound	Upper Bound	*t*	*p*
Seated steady-state	Standing steady-state	-10.60	-18.85	-2.34	3.21	0.03
Seated steady-state	Post-WBV standing steady-state	-11.20	-18.18	-4.23	3.39	0.02

Table 26. Total hemoglobin Bonferroni's pairwise comparisons within able-bodied group at 50 Hz WBV

		SCI				
Time		Mean Difference	Lower Bound	Upper Bound	*t*	*p*
Seated steady-state	WBV first minute	-8.00	-16.04	0.03	3.08	0.05
Seated steady-state	Post-WBV standing steady-state	-11.20	-16.53	-0.45	3.27	0.03

Table 27. Skin temperature Bonferroni's pairwise comparisons within SCI group at 30 Hz WBV

SCI						
Time		Mean Difference	Lower Bound	Upper Bound	*t*	*p*
Pre-WBV	10 minute post-WBV	-1.00	-1.75	-0.25	4.00	0.002
Pre-WBV	15 minute post-WBV	-1.21	-2.00	-0.42	4.81	0.002
Immediately post-WBV	15 minute post-WBV	-0.70	-1.41	-0.01	2.78	0.05

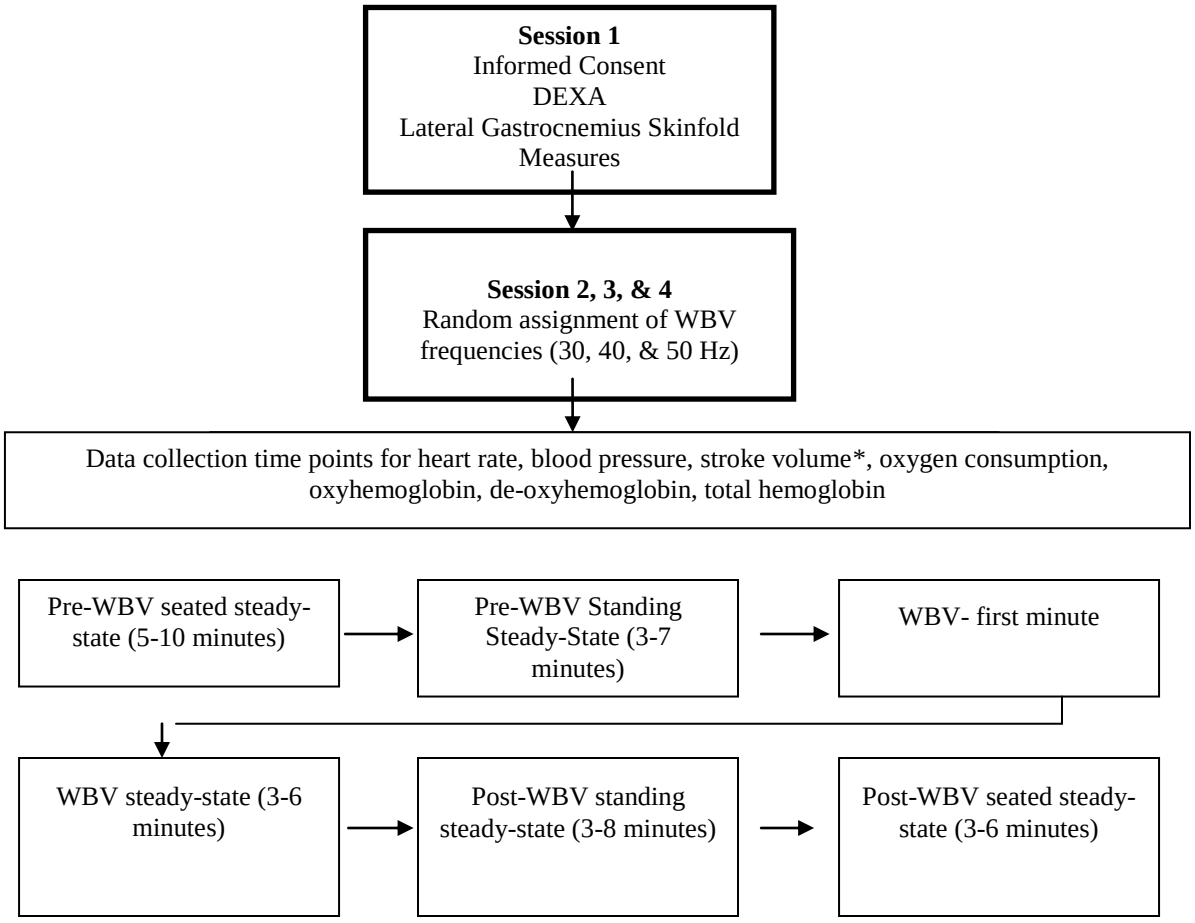
Table 28. Skin temperature pairwise comparisons within SCI group at 40 Hz WBV

SCI						
Time		Mean Difference	Lower Bound	Upper Bound	*t*	*p*
Pre-WBV	Immediately post-WBV	-0.81	-1.28	-0.34	4.39	0.0008
Pre-WBV	10 minute post-WBV	-0.95	-1.42	-0.48	5.14	<0.0001
Pre-WBV	15 minute post-WBV	-1.14	-1.64	-0.64	6.18	<0.0001

Table 29. Skin temperature pairwise comparisons within SCI and able-bodied group at 50 Hz WBV

SCI						
Time		Mean Difference	Lower Bound	Upper Bound	*t*	*p*
Pre-WBV	10 minute post-WBV	-0.82	-1.25	-0.40	4.22	0.001
Pre-WBV	15 minute post-WBV	-0.95	-1.50	-0.39	4.85	0.0002

Figure 7. Schematic diagram of a testing session for central hemodynamics, muscle oxygenation and skin temperature measures



* Stroke volume measurement was not performed at pre-WBV seated state and post-WBV seated state

Schematic diagram of a testing session for skin temperature measures

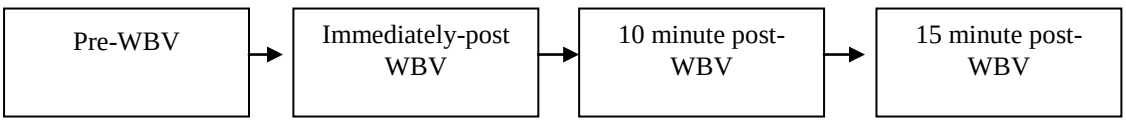


Figure 8. Experimental setting for participants on the vibration platform

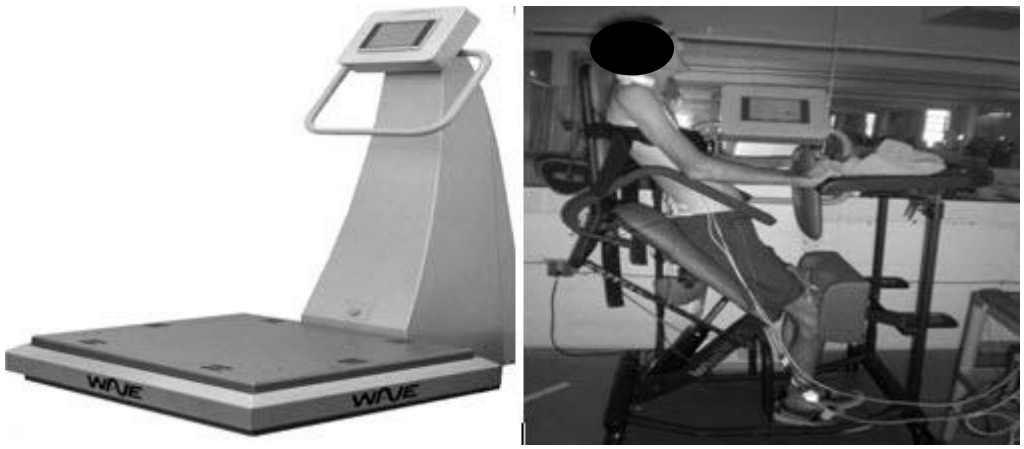
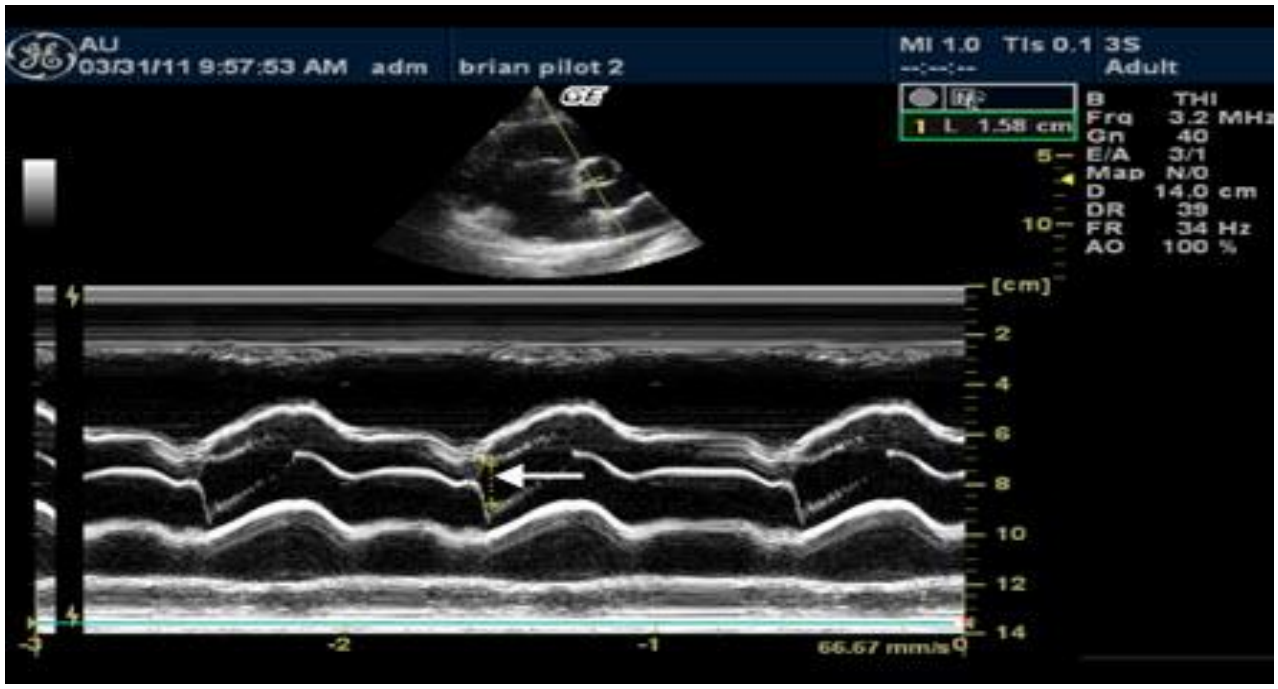
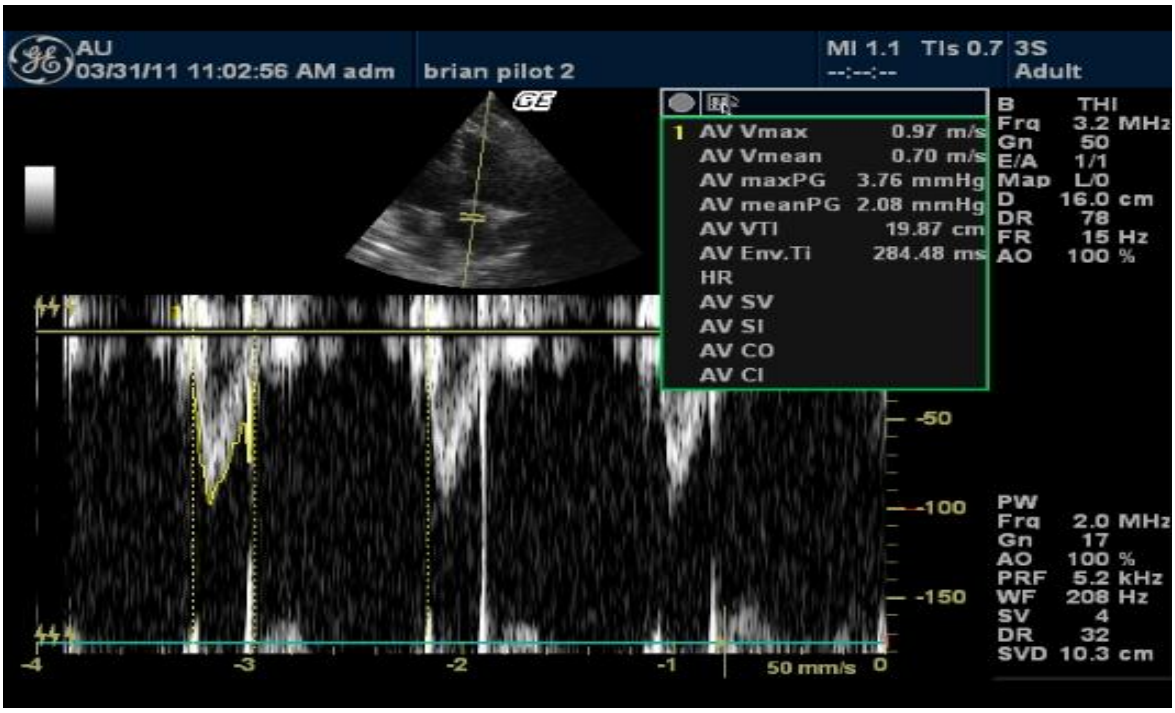


Figure 9. Two dimensional echocardiography image of aortic valve



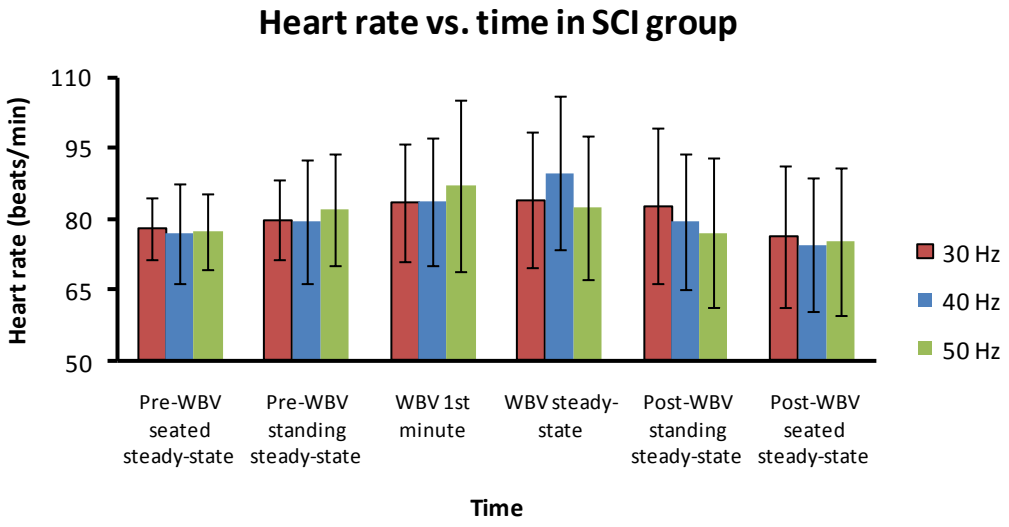
Note: The white arrow indicates where the diameter of the aortic leaflets was measured

Figure 10. Aortic flow velocity obtained by Pulse-Wave-Doppler



Note: Transducer positioned at the apex, the area under the flow velocity curve was digitally measured.

Figure 11. Changes in heart rate over time at 30, 40, and 50 Hz WBV exercise in SCI (a) and able-bodied group (b)
(a)



(b)

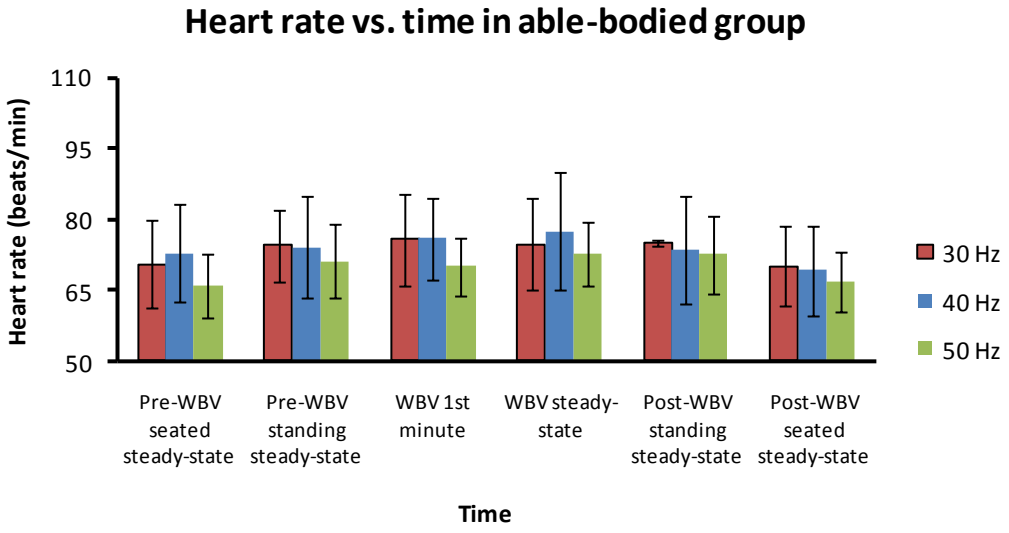
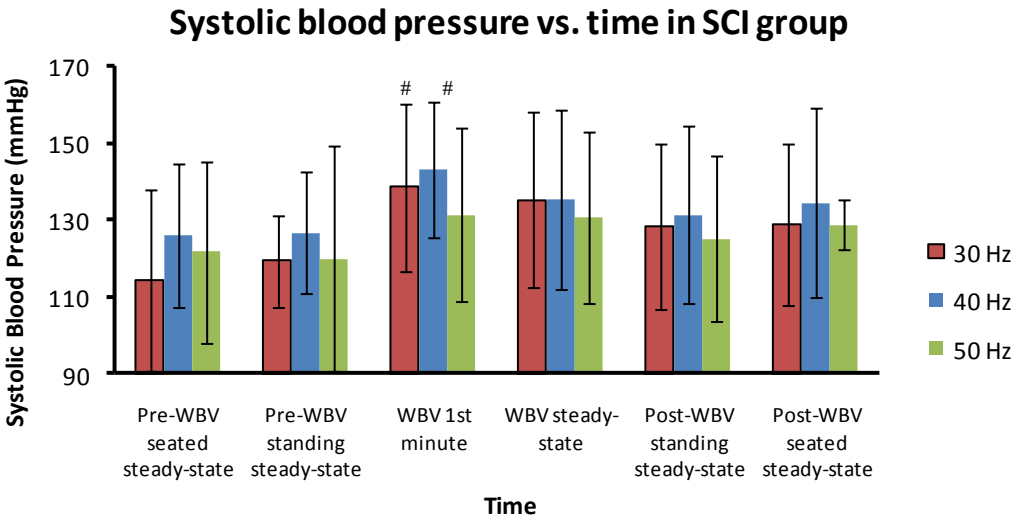


Figure 12. Changes in systolic blood pressure over time at 30, 40, and 50 Hz WBV exercise in SCI (a) and able-bodied group (b)

(a)



Values are reported as mean ± SD. # Significant increase systolic pressure compared to pre-WBV standing steady-state $p \leq 0.05$.

(b)

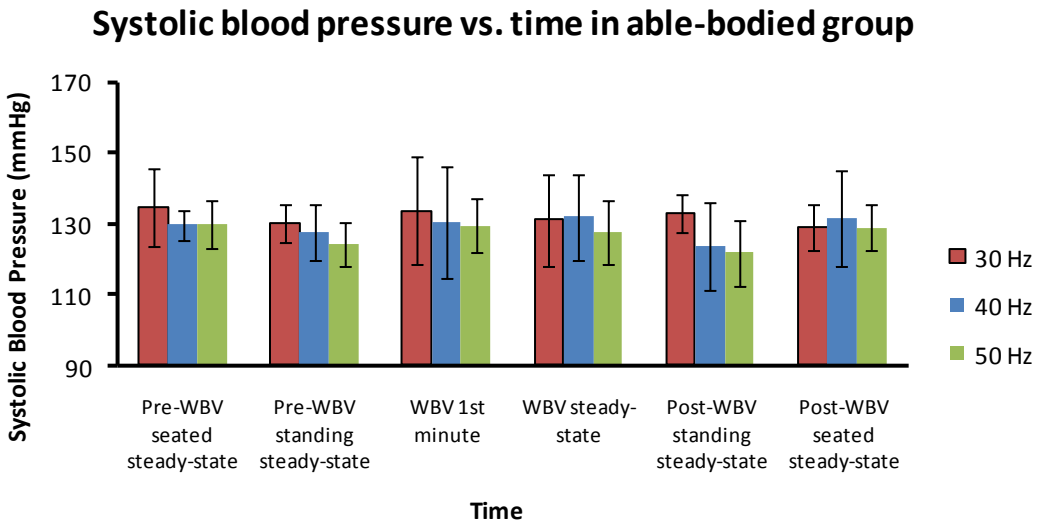
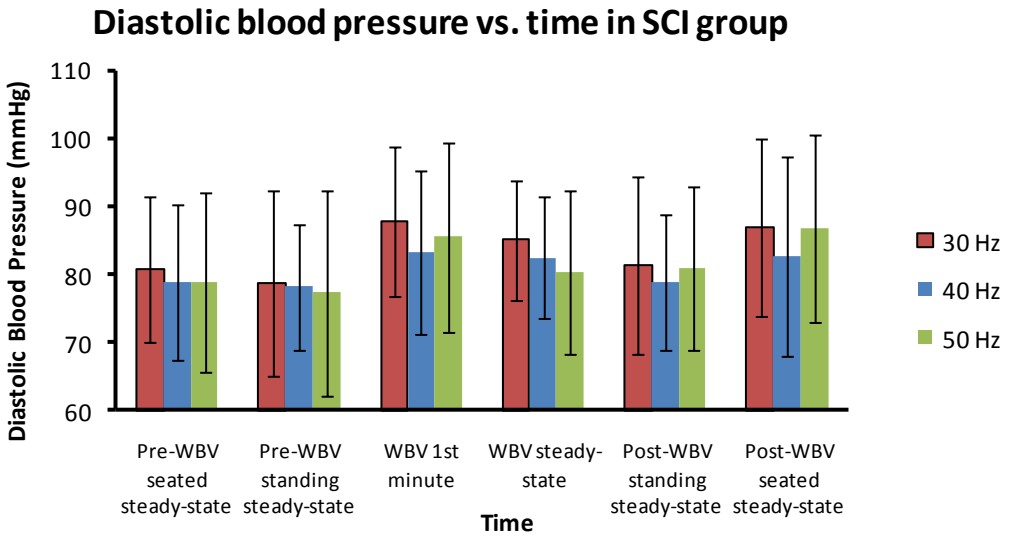


Figure 13. Changes in diastolic blood pressure over time at 30, 40, and 50 Hz WBV exercise in SCI (a) and able-bodied group (b)

(a)



(b)

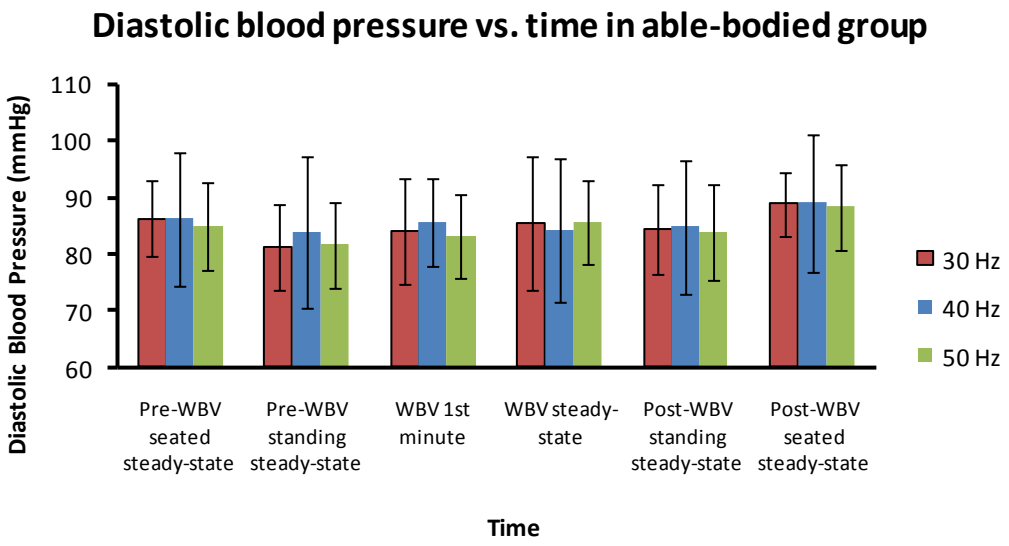
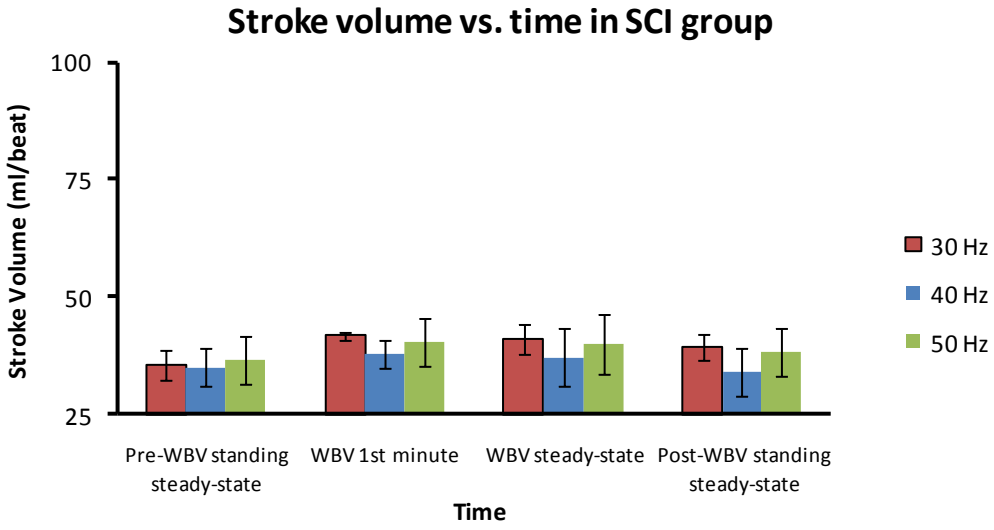


Figure 14. Changes in stroke volume over time at 30, 40, and 50 Hz WBV exercise in SCI (a) and able-bodied group (b)

(a)



(b)

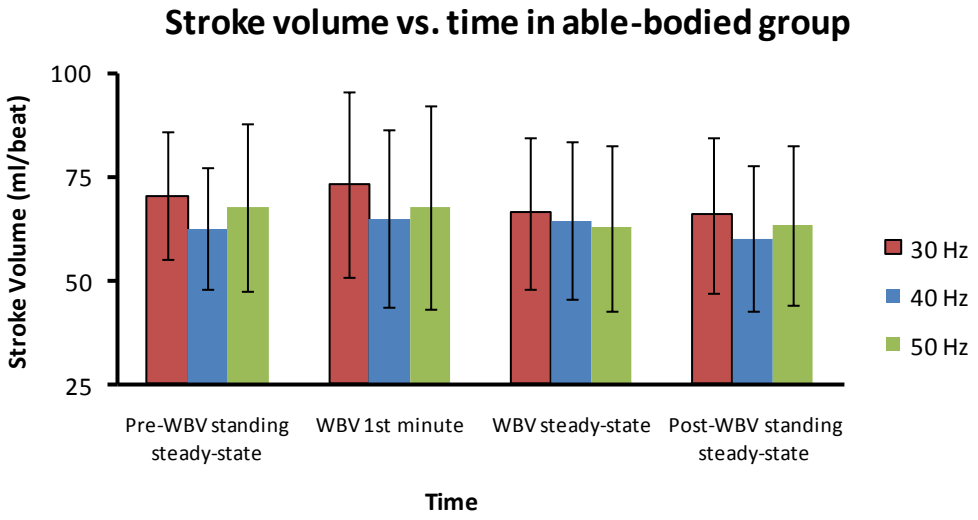
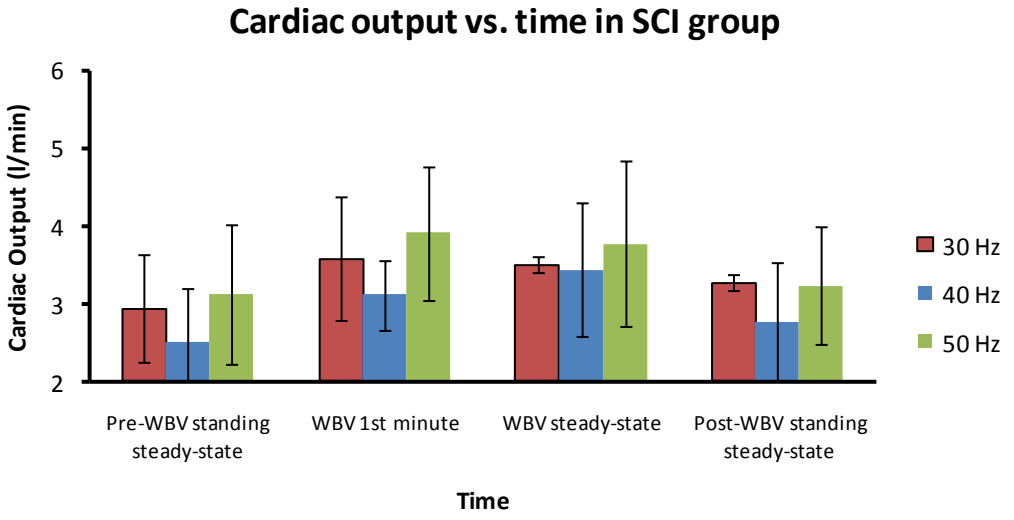


Figure 15. Changes in cardiac output over time at 30, 40, and 50 Hz WBV exercise in SCI (a) and able-bodied group (b)

(a)



(b)

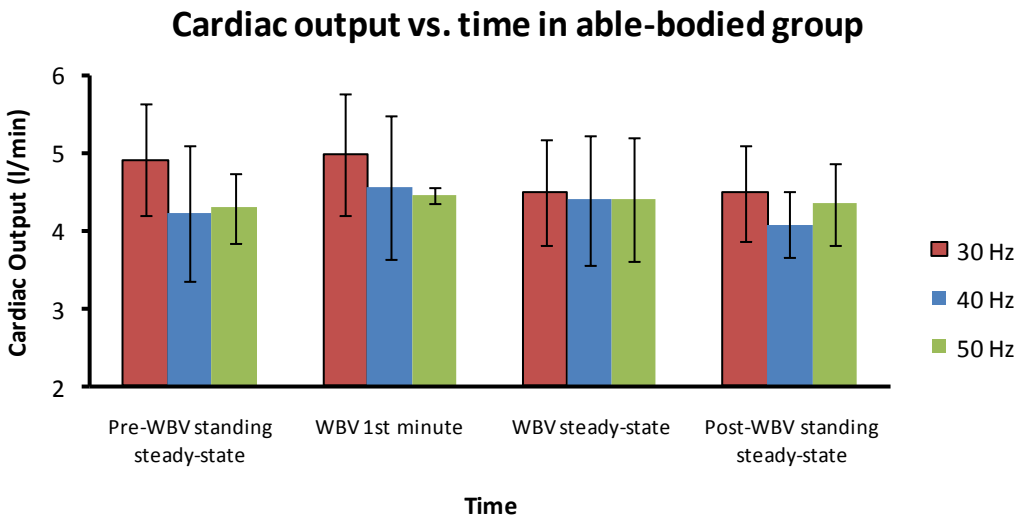
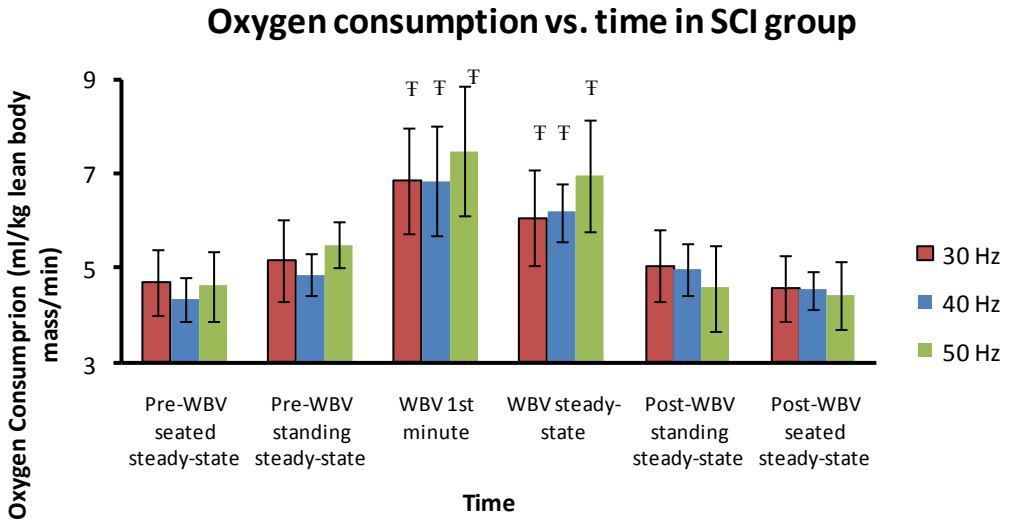


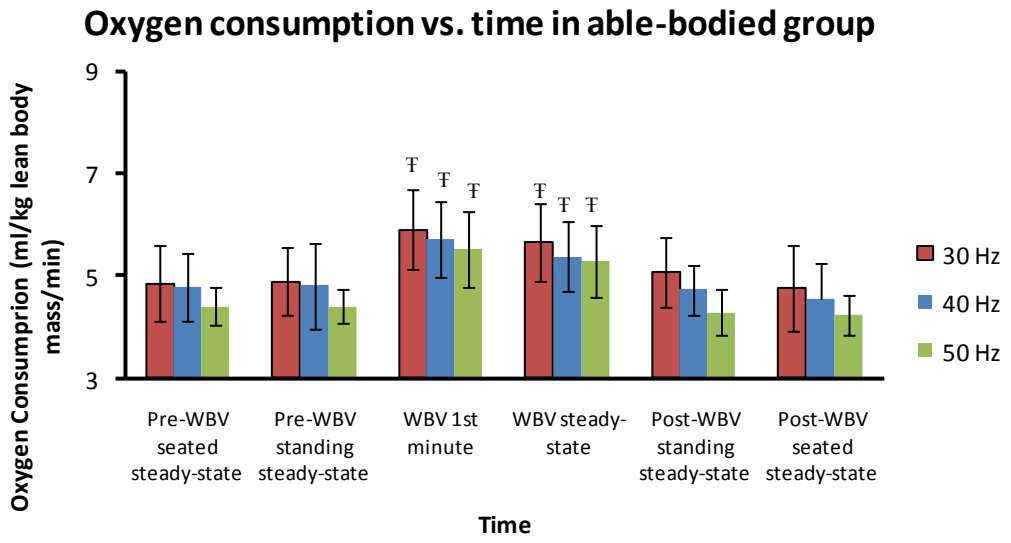
Figure 16. Changes in oxygen consumption over time at 30, 40, and 50 Hz WBV exercise in SCI (a) and able-bodied group (b)

(a)



Values are reported as mean ± SD. Ŧ Significant increase in oxygen consumption compared to pre-WBV standing steady-state, $p \leq 0.0001$.

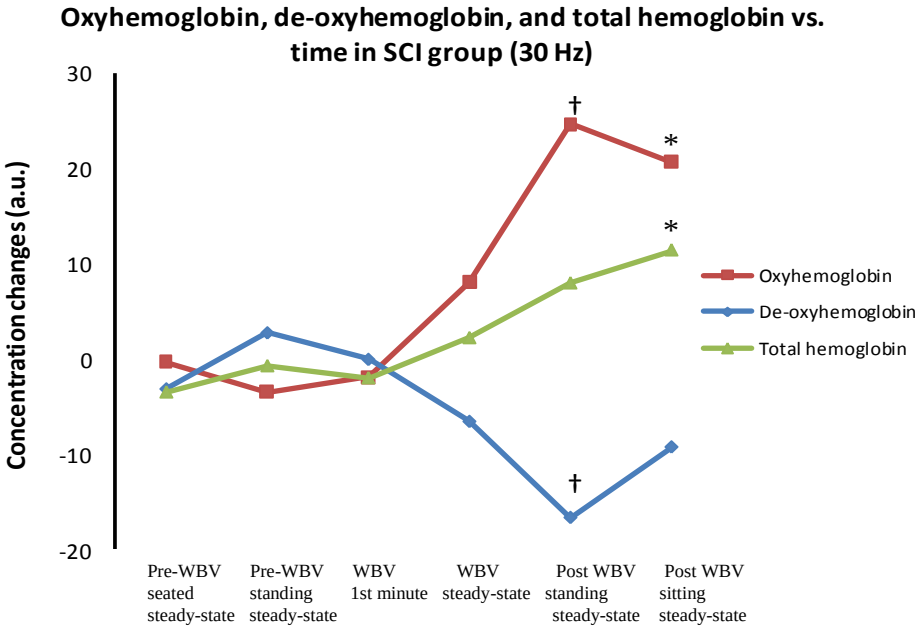
(b)



Values are reported as mean ± SD. Ŧ Significant increase in oxygen consumption compared to pre-WBV standing steady-state, $p \leq 0.0001$.

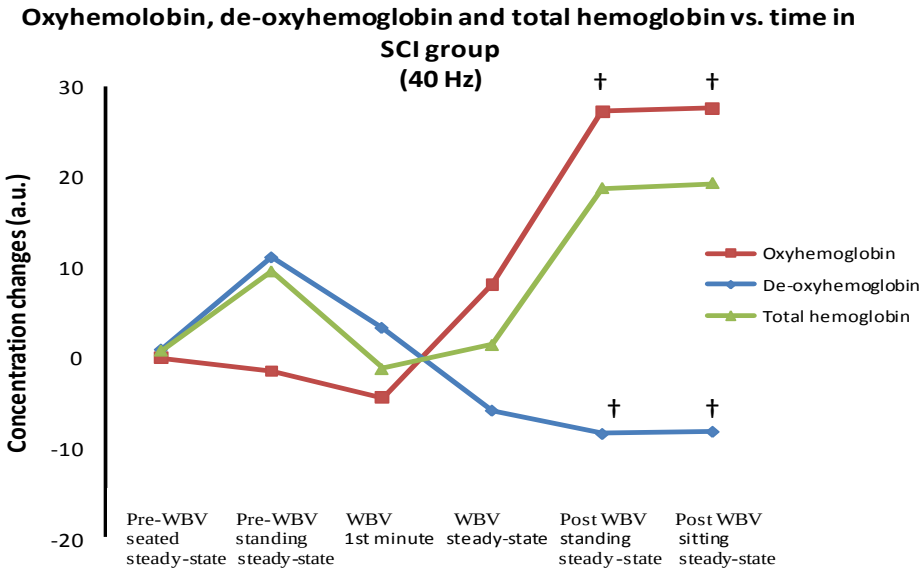
Figure 17. Relative changes in oxyhemoglobin, de-oxyhemoglobin, and total hemoglobin over time at 30 (a), 40 (b) and 50-Hz WBV (c) in SCI group

(a)



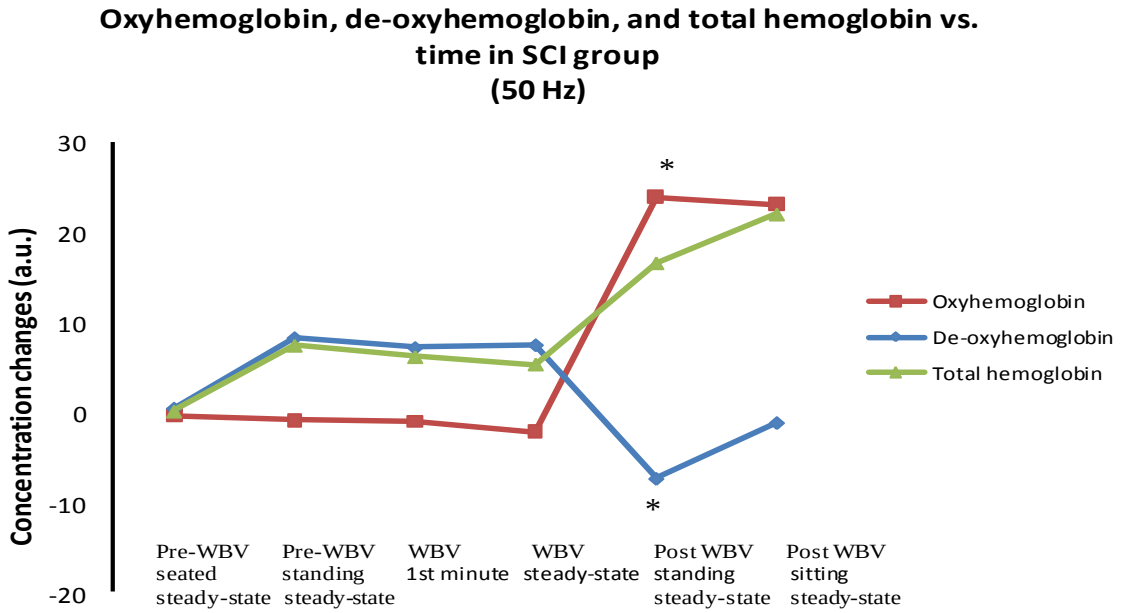
† Significant increase compared to pre-WBV standing steady-state, p ≤0.001, * Significant increase compared to pre-WBV standing steady-state, p ≤0.05

(b)



† Significant increase compared to pre-WBV standing steady-state, p ≤0.001

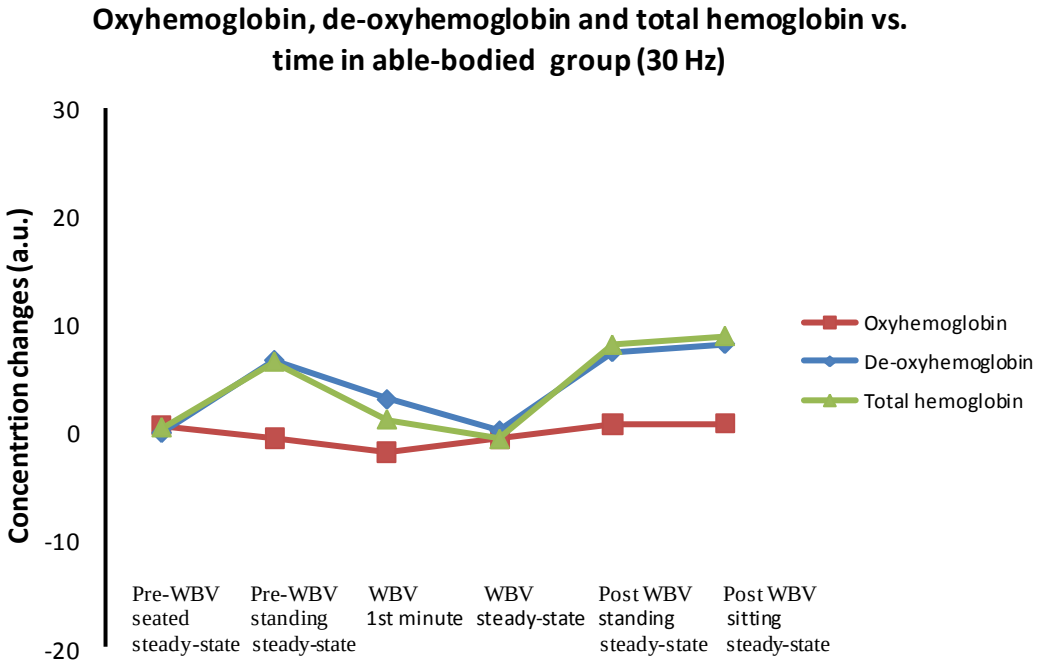
(c)



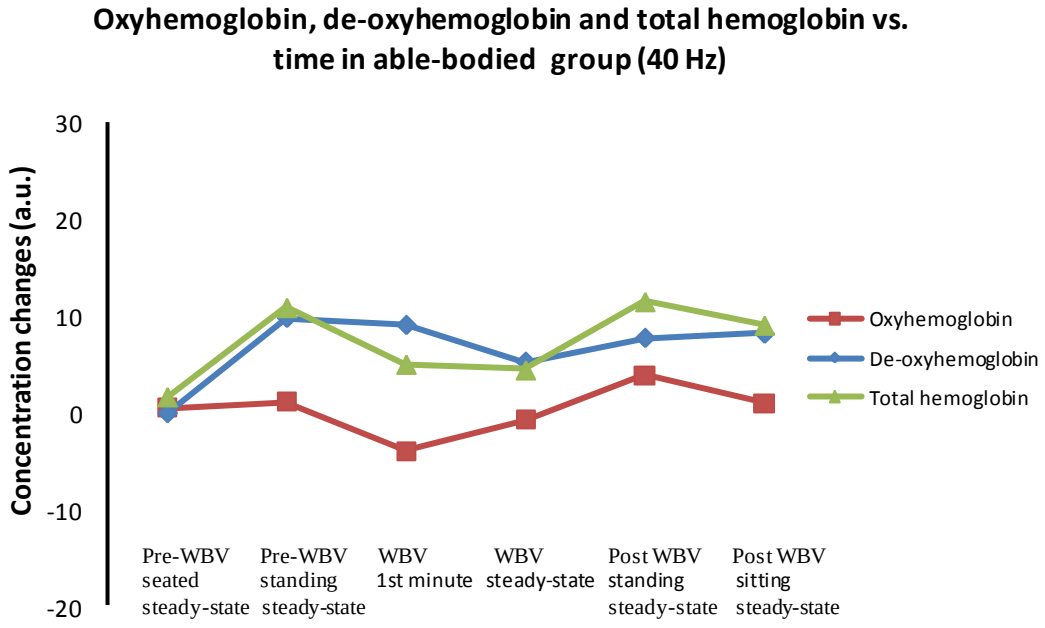
* Significant increase compared to pre-WBV standing steady-state, $p \leq 0.05$

Figure 18. Changes in oxyhemoglobin, de-oxyhemoglobin, and total hemoglobin over time at 30 (a), 40 (b) and 50-HzWBV (c) in able-bodied group

(a)



(b)



(c)

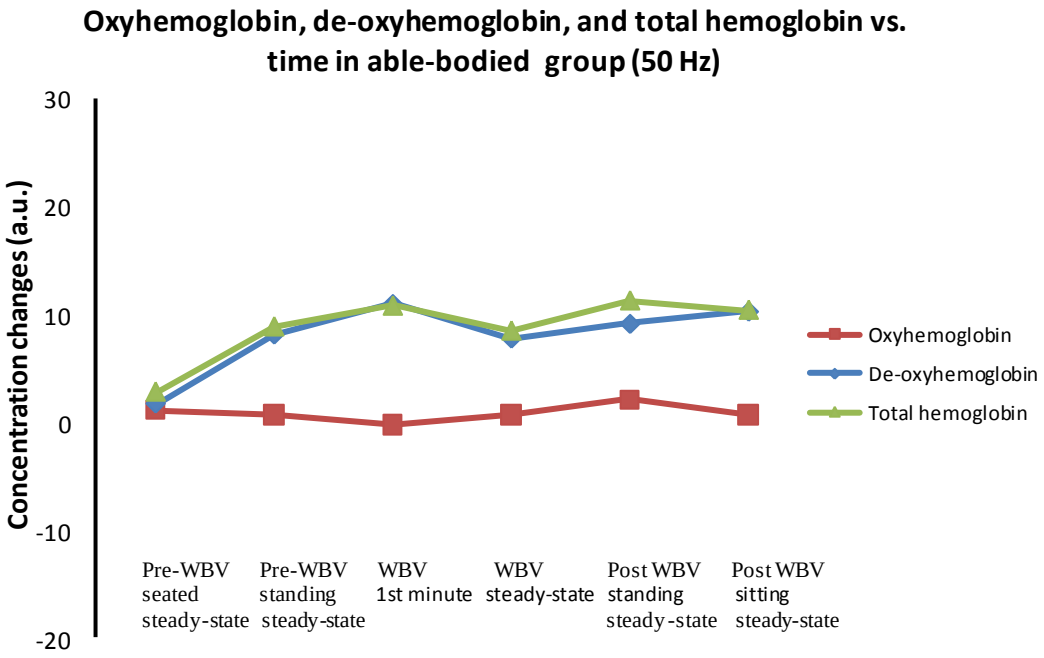
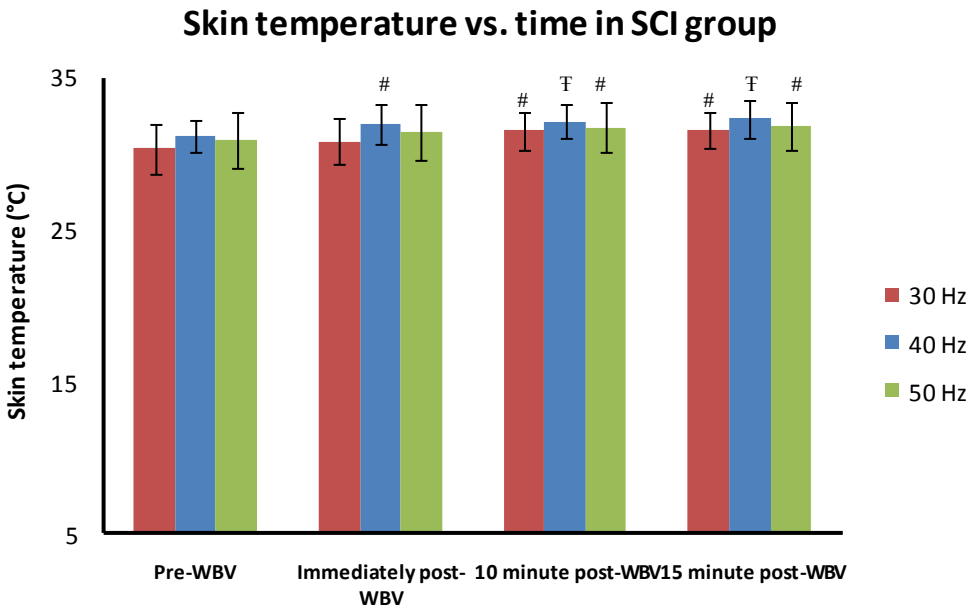

Oxyhemoglobin, de-oxyhemoglobin, and total hemoglobin vs. time in able-bodied group (50 Hz)
Concentration changes (a.u.)
30
20
10
0
-10
-20
Pre-WBV seated steady-state
Pre-WBV standing steady-state
WBV 1st minute
WBV steady-state
Post WBV standing steady-state
Post WBV sitting steady-state
Oxyhemoglobin
De-oxyhemoglobin
Total hemoglobin

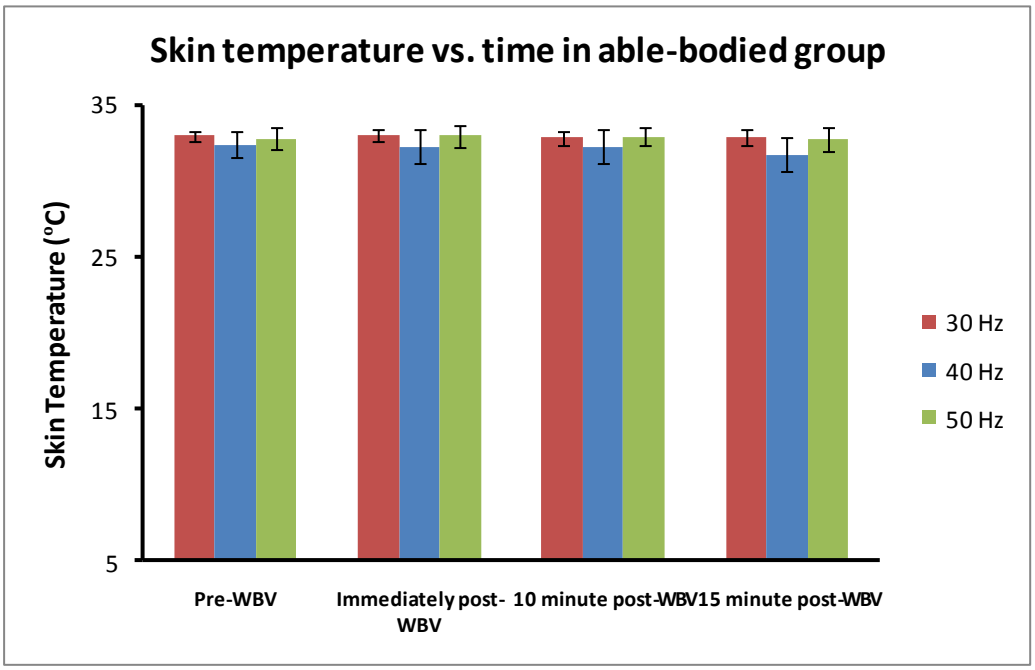
Figure 19. Changes in skin temperatures over time at 30, 40, and 50 Hz WBV exercise in SCI (a) and able-bodied group (b)

(a)



Values are reported as mean ± SD. Ŧ Significant increase in skin temperature compared to pre-WBV, $p \leq 0.0001$, #Significant increase in skin temperature compared to pre-WBV, $p \leq 0.001$

(b)



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APPENDIX A
DAILY SAFETY CHECKLIST

Participant #:
Date:
DAILY SAFETY CHECKLIST
Please circle the correct answer to the following questions:

PART 1

- If you have an indwelling catheter did you empty your leg bag? YES NO
- If you have an indwelling catheter did you check to make sure your tubing is straight each time you change positions? YES NO
- Did you empty your bowels? YES NO
- Have you changed your catheter during past month? YES NO
- Are you wearing comfortable clothes today? YES NO

PART 2

- Are your toenails straight across the top and not too short? YES NO
- Are you having menstrual cramps? YES NO
- Have you recently developed a skin problem? YES NO
- Do you have any infections on/in your body? YES NO

APPENDIX B
INFORMED CONSENT FOR INDIVIDUALS WITH SCI

(NOTE: DO NOT SIGN THIS DOCUMENT UNLESS AN IRB APPROVAL STAMP WITH CURRENT DATES HAS BEEN APPLIED TO THIS DOCUMENT.)

INFORMED CONSENT
for a Research Study entitled

" Effects of Whole Body Vibration Therapy on Cardiovascular Responses in Healthy Individuals and Individuals with Spinal Cord Injury "

You are invited to participate in a research study to examine whole body vibration effects on cardiovascular function in healthy individuals and individuals with spinal cord injury. The study is being conducted by Ceren Yarar, Doctoral Student and Manager of the Neuromechanics Research Laboratory in Auburn University Department of Kinesiology. You were selected as a possible participant because you have a spinal cord injury (SCI), you appear to be between 19-55 years old and have a stable SCI at the levels of C5-T8 (quadriplegia), T1-T6 (paraplegia).

What will be involved if you participate? If you decide to participate in this research study, you will be asked to come to the Neuromechanics Research Laboratory 4 times. During an informational visit, we will provide you this informed consent, the booklets "GUIDE FOR PARTICIPANTION IN RESEARCH INVESTIGATIONS FOR PARTICIPANTS WITH SPINAL CORD INJURY and DEXA EXAMINATION", the Confirmation of Exclusion Form and the Physician Release/Participant Medical Information Release Form. We will show you the equipment, explain the experimental procedures, measure your bone mineral density and body fat levels with Dual Energy Absorptiometry ONLY IF you are interested and answer all your questions. If you wish to participate, you must bring a signed Physician Release/Participant Medical Information Release Form on your next visit, at that time we will answer any further questions and you may sign this form. During each of the remaining visits you will be standing on a vibration plate with feet side by side and bent knees on the vibration plate with the support of standing frame. During the whole body vibration sessions you will be bare foot to eliminate any damping of the vibration caused by the footwear. We will place a small echocardiogram sensor on the left side of your chest to measure your heart rate, blood pressure, cardiac output (the volume of blood you are pumping from your heart each minute), and stroke volume (the volume of blood you are pumping from your heart each beat).

We will also measure your oxygen consumption via a mouth piece or a facemask, your leg blood flow via a small electrode placed on your lower or upper leg, and leg skin temperature via an infrared camera. At the end of the experiment we will put a blood pressure cuff above your knee and inflate it until it feels very tight around your thigh. We will deflate it after 5 minutes. This procedure may increase the chances of an autonomic dysreflexia event. Additionally we will

draw blood either from the arm or the finger ONLY IF you are willing to give your blood to measure myokines in your blood. You will receive 5 minutes of whole body vibration therefore you will be standing for total 5 minutes on the vibration plate. We estimate your total time commitment to be an hour.

Exclusion Criteria

1. SCI patients that have adapted to walking
2. Smokers
3. Individuals with chronic illness such as: cancer, diabetes, renal failure, diabetes type I and II
4. Individuals with heart disease, high blood pressure, or previous stroke
5. Individuals on cardiovascular medications such as: anti-hypertension drugs and/or any drug that effects the strength of contraction of heart muscle
6. Evidence or history of blood vessel disease (narrowing the blood vessels in the legs, abdomen, and the arms causing tissue and cell death or gangrene)
7. Any blood clotting disorders
8. Individuals with active illness such as sepsis (serious medical condition characterized by a half-body inflammatory state caused by infection), pressure sores, common cold or influenza
9. Individuals with uncontrolled spasticity (uncontrolled stiffness or tightness of the muscles)
10. Individuals with muscle contractures (permanent shortening of a muscle or a tendon in upper extremity/lower extremity)
11. Local infection, acute inflammation (occurring on the body surface characterized by redness, increased heat, swelling, and pain), injury, tumors or other malignancy, recent wounds
12. Severe migraine or epilepsy

Are there any risks or discomforts?

Autonomic Dysreflexia and Orthostatic Hypotension are risks associated with spinal cord injury and may occur during the procedures. This study will not increase the incidence of Autonomic Dysreflexia or Orthostatic Hypotension risk but we will plan for their possible occurrence.

1- Autonomic Dysreflexia is a state that is unique to patients after spinal cord injury at T-5 level and above. Autonomic Dysreflexia occurs when an irritating stimulus is introduced to the body below the level of spinal cord injury, such as an overfull bladder.

It is characterized by pounding headache (caused by the elevation in blood pressure), sweating above the level of injury, hypertension, flushed (reddened) face, and decreased heart rate.

2- Orthostatic Hypotension: Orthostatic hypotension is a decrease of blood pressure when standing, due to changes in the blood pressure regulation systems within the body.

You may experience orthostatic hypotension during whole body vibration.

3- Risk of falling

4- You may not like the interventions

5- Breach of confidentiality

6- Fatigue or discomfort

7- Phlebotomy complications (petechiae and excessive bleeding).Petechiae: are small dots appear on the skin that could be a result of tying the tourniquet tight during blood draws.

8- Claustrophobic reaction due to the face mask

9- Allergic reactions due to the gel used in echo-cardiography

10- Unexpected test results from echocardiography
11-Exposure to radiation during DEXA examination
12-Unexpected results from DEXA
13- The cuff above your knee may cause discomfort and may increase the chances of an autonomic dysreflexia event

Precautions
Ceren Yarar is a certified physical therapist in Turkey who has an extensive experience in working with spinal cord patients. She has experienced several autonomic dysreflexia and orthostatic hypotension episodes during rehabilitation sessions with spinal cord patients. She is competent to catheterize the patient in cases of autonomic dysreflexia and/or reposition the patient in cases of orthostatic hypotension.
1- Autonomic dysreflexia: We have created a "daily safety checklist" which includes safety precautions to be completed prior to each study session. If you are not eligible for that day, we will schedule you for another convenient date. Additionally an "Acute Autonomic Dysreflexia Management Plan" has been developed for use in cases of autonomic dysreflexia. Ceren Yarar, the primary investigator of the project, may have to reposition your catheter or recatheterize you in cases of autonomic dysreflexia.
2- Orthostatic Hypotension (OH): You will be secured to the standing table with the velcro tapes around your body to eliminate the risk for falls (you will only be standing during whole body vibration). In the case of OH you will be taken to the treatment table. You will be lying down with your legs elevated to allow blood reach the brain.
3- Risk of falling: During interventions and transportation from wheel chair to the treatment table one physical therapist with sufficient laboratory personnel will be with you to assist you in order to insure your safety.
4- You may not like the intervention or the tests; if that is the case you may stop at any time.
5- Breach of confidentiality: To reduce the risk of breach of confidentiality - all confidential materials and questionnaires will be kept in the office of the primary investigator (PI)'s faculty advisor (JoEllen Sefton), in a locked filing cabinet. The office is in a secure laboratory that is locked when not in use by the researchers. Only those listed in this IRB application will have access to the forms. Each subject will be given a non-identifiable subject code to be used during the study. The PI will be the only one to have the list of subject codes that coordinate subjects to confidential forms. This list will also be kept in a locked filing cabinet separate from all other study data. The subject database will be maintained on the PI's personal computer that is password protected and located in a locked office within a locked laboratory.
Only the project investigators will be given access to the database. This will be backed up daily to a password protected secure folder on the laboratory server. Only the investigators will have access to this information.
6- The test will be terminated immediately if you feel fatigued or discomfort.
7- In order to prevent petechiae the tourniquet will not be on your arm for longer than 1 minute during blood draws. In order to prevent excessive bleeding, the investigator will not leave you until the bleeding has stopped. (normally this is a few minutes)
8- We will provide you an option for using a small and light weight mouth-piece instead of a face mask.
9-Vaseline will be used in order to prevent allergic reaction due to echo gel.
10- You will be encouraged to discuss the test results with your physician.

11- The radiation dose utilized in DEXA is negligible regarding cancer risk.
12- You will be encouraged to discuss the test results with your physician.
13- The test will be terminated immediately if you feel discomfort and we will monitor your blood pressure each minute during 5 min cuff occlusion. If your blood pressure goes up more than 20 mmHg, the cuff will be released and the experiment will be ended for preventing you from a potential autonomic dysreflexia event.

Are there any costs? If you decide to participate, the only cost to you will be transportation to and from the Neuromechanics Laboratories – located on the main campus of Auburn University. You will be provided parking passes for free parking on campus near the laboratory entrance. In the unusual circumstance where you did injure yourself, you are responsible for any costs associated with medical treatment.We have created a special booklet for you discussing the benefits and any concerns or questions you may have.

Are there any monetary compensation? You will receive $25 for each visit except the initial informational visit. Additionally 1 free workout sessions (45 minutes) will be provided to you in "Students with Disabilities Fitness Center" in Memorial Coliseum at Auburn University.

Free workout sessions can only be used during available laboratory/ building hours. In the case of withdrawal from the study, your monetary compensation will be prorated for the sessions you have already participated and you still will be able to receive the remaining free workout session. Additionally, you will receive a copy of your heart rate, blood pressure, cardiac output, stroke volume, oxygen consumption, blood flow, and blood work results. You will also receive a copy of the final manuscript if you would like one.

Your privacy will be protected. Any information obtained in connection with this study will remain confidential. Only the investigators in this project will have access to your information. Your personal information will remain in locked storage at all times. Your identifying information will be destroyed after data analysis is complete. Your identifying information will not be included in the database and there will be no way to connect you with any information you provide us. This consent form will be retained for 3 years and then destroyed.

Information obtained through your participation may be combined with that of other subjects for publication in scientific journals or presentation at scientific conferences. However, your individual data will not be able to be identified. You will receive a copy of this informed consent to keep.

If you change your mind about participating, you can withdraw at any time during the study. Your participation is completely voluntary. If you choose to withdraw, your data can be withdrawn as long as it is identifiable. Your decision about whether or not to participate or to stop participating will not jeopardize your future relations with Auburn University, the Department of Kinesiology, or Ceren Yarar.

If you have questions about your rights as a research participant, you may contact the Auburn University Office of Human Subjects Research or the Institutional Review Board by phone (334)-844-5966 or e-mail at hsubjec@auburn.edu or IRBChair@auburn.edu, and Ceren Yarar

by phone (334)- 844-1694 or e-mail at czy0002@auburn.edu, and JoEllen Sefton by phone (344)-844-1694 or e-mail at jms0018@auburn.edu.

HAVING READ THE INFORMATION PROVIDED, YOU MUST DECIDE WHETHER OR NOT YOU WISH TO PARTICIPATE IN THIS RESEARCH STUDY. YOUR SIGNATURE INDICATES YOUR WILLINGNESS TO PARTICIPATE.

_____

Participant's signature Date

_____

Printed Name

_____

Investigator obtaining consent Date

_____

Printed Name

APPENDIX C
INFORMED CONSENT FOR ABLE-BODIED INDIVIDUALS

(NOTE: DO NOT SIGN THIS DOCUMENT UNLESS AN IRB APPROVAL STAMP WITH CURRENT DATES HAS BEEN APPLIED TO THIS DOCUMENT.)

INFORMED CONSENT
for a Research Study entitled
"Effects of Whole Body Vibration Therapy on Cardiovascular Responses in Healthy Individuals and Individuals with Spinal Cord Injury"

You are invited to participate in a research study to examine whole body vibration effects on cardiovascular function in healthy individuals and individuals with spinal cord injury. The study is being conducted by Ceren Yarar, Doctoral Student and Manager of the Neuromechanics Research Laboratory in Auburn University Department of Kinesiology. You were selected as a possible participant because you appear to be between 19-55 years old and have no circulatory disorders or orthopedic problems.

What will be involved if you participate? If you decide to participate in this research study, you will be asked to come to the Neuromechanics Research Laboratory on 4 occasions. During an informational visit you will fill out a health questionnaire that will ask you questions about your general health to make sure you can participate in the study. We will show you the equipment, explain the experimental procedures, measure your bone mineral density and body fat levels with Dual Energy Absorptiometry (DEXA) ONLY IF you are interested (A booklet including information about DEXA will be provided) and answer all your questions. During experimental procedures you will be standing on a vibration plate with feet side by side and bent knees with the support of standing frame. During the whole body vibration sessions you will be bare foot to eliminate any damping of the vibration caused by the footwear. We will place a small echocardiogram sensor on the left side of your chest to measure your heart rate, blood pressure, cardiac output (the volume of blood you are pumping from your heart each minute), and stroke volume (the volume of blood you are pumping from your heart each beat). We will also measure your oxygen consumption via a mouth piece or a facemask, your leg blood flow via a small electrode placed on your lower or upper leg, and leg skin temperature via an infrared camera. At the end of the experiment we will put a blood pressure cuff above your knee and inflate it until it feels very tight around your thigh. We will deflate it after 5 minutes. This procedure may cause discomfort. Additionally we will draw blood either from the arm or the finger ONLY IF you are willing to give your blood to measure myokines in your blood.You will receive 5 minutes of whole body vibration therefore you will be standing for total 5 minutes on the vibration plate. We estimate your total time commitment to be an hour.

Are there any risks or discomforts?
1- You may not like the interventions
2- Breach of confidentiality
3- Fatigue or discomfort
4- Phlebotomy complications (petechiae and excessive bleeding).Petechiae: are small dots appear on the skin that could be a result of tying the tourniquet tight during blood draws.
5- Claustrophobic reaction due to the face mask
6- Allergic reactions due to the gel used in echo-cardiography
7- Unexpected test results from echocardiography
8-Exposure to radiation during DEXA examination
9-Unexpected results from DEXA
10- The cuff above your knee may cause discomfort

Precautions:
1-You may not like the intervention or the tests; if that is the case you may stop at any time.
2- Breach of confidentiality: To reduce the risk of breach of confidentiality - all confidential materials and questionnaires will be kept in the office of the primary investigator (PI)'s faculty advisor (JoEllen Sefton), in a locked filing cabinet. The office is in a secure laboratory that is locked when not in use by the researchers. Only those listed in this IRB application will have access to the forms. Each subject will be given a non-identifiable subject code to be used during the study. The PI will be the only one to have the list of subject codes that coordinate subjects to confidential forms. This list will also be kept in a locked filing cabinet separate from all other study data. The subject database will be maintained on the PI's personal computer that is password protected and located in a locked office within a locked laboratory. Only the project investigators will be given access to the database. This will be backed up daily to a password protected secure folder on the laboratory server. On the investigators will have access to this information
3- The test will be terminated immediately if you feel fatigued or discomfort.
4- In order to prevent petechiae the tourniquet will not be on for longer than 1 minute. In order to prevent excessive bleeding, the investigator will not leave you until the bleeding has stopped. (normally this is a few minutes)
5- We will provide you an option for using a small and light weight mouth piece instead of a face mask.
6- Vaseline will be used in order to prevent allergic reaction due to the gel.
7- The radiation dose utilized in DEXA is negligible regarding cancer risk.
8- You will be encouraged to discuss the test results with your physician.
9- The test will be terminated immediately if you feel discomfort.

Are there any benefits to yourself or others? There are no psychological, social or physical benefits to be gained from participation in this study. You will have the opportunity see how research is conducted and learn more about your own body. Significant benefit for others can be achieved in trying to understand the how whole body vibration therapy works. The results of this study will have an impact on the understanding treatment programs currently in use, as well as the development of future research programs into whole body vibration therapy.

Will you receive compensation for participating? You will receive $10 for each visit except the initial informational visit. In the case of withdrawal from the study, your monetary compensation will be prorated for the sessions you have already participated. Additionally, you will receive a copy of your heart rate, blood pressure, cardiac output, stroke volume, oxygen consumption, blood flow, and blood work results. You will also receive a copy of the final manuscript if you would like one.

Are there any costs If you decide to participate, the only cost to you will be transportation to and from the Neuromechanics Laboratories – located on the main campus of Auburn University. You will be provided parking passes for free parking on campus near the laboratory entrance. In the unusual circumstance where you did injure yourself, you are responsible for any costs associated with medical treatment.

If you change your mind about participating, you can withdraw at any time during the study. Your participation is completely voluntary. If you choose to withdraw, your data can be withdrawn as long as it is identifiable. Your decision about whether or not to participate or to stop participating will not jeopardize your future relations with Auburn University, the Department of Kinesiology, or Ceren Yarar.

Your privacy will be protected. Any information obtained in connection with this study will remain confidential. Only the investigators in this project will have access to your information. Your personal information will remain in locked storage at all times. Your identifying information will be destroyed after data analysis is complete. Your identifying information will not be included in the database and there will be no way to connect you with any information you provide us. This consent form will be retained for 3 years and then destroyed. Information obtained through your participation may be combined with that of other subjects for publication in scientific journals or presentation at scientific conferences. However, your individual data will not be able to be identified. You will receive a copy of this informed consent to keep.

If you have questions about this study, please ask them now. If you have questions after the study you may contact Ceren Yarar at 334-844-1694 or czy0002@auburn.edu. A copy of this document will be given to you to keep.

If you have questions about your rights as a research participant, you may contact the Auburn University Office of Human Subjects Research or the Institutional Review Board by phone (334)-844-5966 or e-mail at hsubjec@auburn.edu or IRBChair@auburn.edu.

HAVING READ THE INFORMATION PROVIDED, YOU MUST DECIDE WHETHER OR NOT YOU WISH TO PARTICIPATE IN THIS RESEARCH STUDY. YOUR SIGNATURE INDICATES YOUR WILLINGNESS TO PARTICIPATE.

_____

Participant's signature Date

_____

Printed Name

_____

Investigator obtaining consent Date

_____

Printed Name