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Inflammatory protein elicitation in response to whole-body vibration exposure

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INFLAMMATORY PROTEIN ELICITATION IN RESPONSE TO WHOLE-BODY VIBRATION EXPOSURE

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Approval of Thesis

We, the faculty supervising the work of Nicholas Miller, affirm that the thesis, *Inflammatory Protein Elicitation in Response to Whole-Body Vibration Exposure*, meets the high academic standards for original scholarship and creative work established by the Department of Biomechanics and the College of Health Professions. The work also conforms to the requirements and formatting guidelines of Marshall University. With our signatures, we approve the manuscript for publication.

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Dedication

This paper is dedicated to my parents, Pam and Wayne Miller. Together, we persevered through a harrowing battle with cancer, a pandemic, a move halfway across the country, and what seemed like never-ending research setbacks. Through our collective strength as a family, we prevailed. We are small in number but mighty in heart. Thank you for your enduring support.

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Abstract

This study aimed to assess the effects of whole-body vibration (WBV) on the brain through changes in blood protein concentrations, seat and head accelerations, and symptomatology over time. Subjects were assigned to control, 1-hour, or 8-hour vibration exposure groups. Glial fibrillary acidic protein (GFAP) and S100B concentrations were measured. Root mean square average weighted vibration (A_{ws}), vibration dose value (VDV), and seat-to-head transmissibility (STHT) were calculated. There were no differences in GFAP ($p = 0.79$) or S100B ($p = 0.97$) concentrations between 1-hour and 8-hour subjects ($p = 0.79$). Average weighted head acceleration ($p = 0.566$) and VDV ($p = 0.843$) were not significantly different between the 1-hour and 8-hour groups. The average resultant STHT was not significantly different across time ($p = 0.852$). Similarities in blood biomarker concentrations and head acceleration measures between exposure groups indicate that injury does not occur from singular WBV exposure. This study furthers the knowledge of heavy vehicle operation, demonstrating that individual exposure to WBV likely does not cause neurological injury.

Chapter 1: Introduction

There are 29 million commercial motor vehicle (CMV) workers, such as commercial truck drivers, forklift operators, and machinists, who are at risk of developing musculoskeletal and physiological injury through excessive vibration exposure (Abbate et al., 2004; McBride et al., 2014; Paschold & Sergeev, 2009). The American population is regularly exposed to potentially excessive vibrations through 220.43 billion vehicle trips occurring every day in the United States of America (Transportation, 2017). Vibrations cause muscle activation to stabilize the body, leading to fatigue and subsequent strain injury when vibration exposure is excessive. The extensive vibration dosage that American motor vehicle operators are exposed to potentially puts the population at risk for whole-body vibration (WBV)-related injury. Whole-body vibrations result from an alternating periodic or imbalanced force acting on the body, injuring tissue when the frequency and magnitude of the vibration are large enough to overcome the tissue's damping capabilities (CCOHS, 2017; McBride et al., 2014). The International Organization for Standardization (ISO) has set an exposure action value (EAV) of 0.5 m/s^2 root mean square (r.m.s.) acceleration and 8.5 $m/s^{1.75}$ for vibration dose value (VDV) and an exposure limit value (ELV) of 1.0 m/s^2 r.m.s. acceleration and 17 $m/s^{1.75}$ VDV for triaxial accelerations (ISO, 1997). While these recommendations are commonly known, vehicle operators regularly exceed these limitations to maximize earning potential. Bovenzi (2009) found that WBV exposure exceeding Aws and VDV exposure action values are experienced by 7.8% and 28.9% of professional drivers, respectively. Seated railroad engineers are exposed to VDV values above critical ISO ratios, suggesting they are at risk for harmful levels of shock (Johanning et al., 2006). Milosavljevic et al. (2010) found that farmers riding ATVs for a typical 95.7 minutes per day are exposed to a VDV of 16.6 and exceed the EAV after 8 minutes and the ELV after 220.8

minutes. Whole-body vibration exposure below the EAV presents a minimal risk for musculoskeletal or physiological injury, specifically to the lumbar spine and its connective tissue; however, upon reaching the EAV, caution is necessary as the risk of injury gradually increases until reaching the ELV. The risk of injury is then considered to become more dangerous once the WBV levels reach the ELV and intervention starts to become necessary. Both EAV and ELV levels are regularly surpassed by occupational vehicle operators, potentially leading to an increased risk of injury.

Vibration occurs when a periodic or imbalanced force is applied to an object, causing the object to oscillate about its equilibrium position (CCOHS, 2017). The degree to which the object vibrates depends on the force's frequency and magnitude (CCOHS, 2017). The kinetic energy transferred from a vibrating surface to the human body and its musculoskeletal tissue causes injury through the tissue's inability to absorb and dissipate the transmitted energy. Compositional characteristics such as lean mass and muscular cross-sectional area factor into the absorptive capabilities of the tissue (Mansfield et al., 2006; Smith, 1994). Vibrations at frequencies ideal for localized musculoskeletal tissue composition resonate, amplifying and propagating the mechanical waves (Singh et al., 2016). A mechanical wave's power is related to the energy the wave supplies over a time period. Absorbed power within skeletal muscle tissue increases linearly with vibration frequency until the frequency reaches resonance, beyond which the muscle activation is impeded, and frequency decreases (Mizrahi, 2015). Musculoskeletal tissue is susceptible to resonance at frequencies in the 4-6 Hz and 8-12 Hz ranges, typical to vehicle operation (Fairley & Griffin, 1989; Hinz & Seidel, 1987; Holmlund et al., 2000; Mansfield & Griffin, 2000). Resonance amplifies the vibration magnitude, which as a vibration propagates from the alternating periodic or imbalanced force, leads to higher exposure at the

head than what is seen at the seat (Paddan & Griffin, 1998; Wang et al., 2006). The body presents a biodynamic response to WBV, in which one body segment's response to vibration triggers the reaction of another body segment (Qui & Griffin, 2012). The biodynamic response to WBV is due to the biomechanical and physiological characteristics of the bone, skeletal muscle, and internal organs exposed to the force (Cardinale, 2003). Vibration magnification is also due in part to the coupled motion of the seated body, which results in more significant head motion, causing a whiplash effect that amplifies accelerations at the head (Mandapuram et al., 2012; Paddan & Griffin, 1998; Wang et al., 2006). Kociolek et al. (2018) found that vibration at the head can be 2.19 times higher in the anterior-posterior, 0.91 in the medial-lateral, and 1.37 in the inferior-superior axes than at the seat. Low-frequency vibrations are amplified and transmitted throughout body tissue, damaging the musculature and causing pain and discomfort for vehicle operators. Resonant effects, coupled motion of the body, and smaller muscular cross-sectional area at the neck are factors in higher vibration magnitude at the head, increasing head acceleration, and potential for injury.

The risk for musculoskeletal injury to the lumbar spine and its connective tissue from excessive WBV exposure is well-established; however, less is known about the risk of brain injury. The effects of low-level mechanical forces on the brain have been researched in traumatic brain injury (TBI) populations and present potentially similar- injury mechanisms as WBV. Indirect forms of brain injury, due to mechanical wave propagation, can cause damage similar to direct head impacts depending on the wave frequency and magnitude (Meaney & Smith, 2011; Taber et al., 2006). Mechanical brain injury is caused by the linear and rotational acceleration of the brain within the skull, leading to tissue deformation (Barth et al., 2001; Kleiven, 2013; Rowson et al., 2016). Rotational acceleration poses a greater risk of injury due to the brain being

more resilient to compression than shear strain (Kleiven, 2013). Additionally, repetitive impacts prevent the brain from returning to a resting state and subsequently recovering, posing a greater risk of injury than singular impacts (Broglio et al., 2017; O'Connor et al., 2017). An injury mechanism such as WBV may not generate large tissue deformation per period of vibration, but the cumulative vibration exposure could lead to chronic injury.

The constant brain acceleration due to vibration results in physical injury from the brain colliding with the cranium walls; however, injury also occurs from the brain's physiological response to the external stressor. Physical stress applied to the brain and surrounding vasculature causes decreased oxygen delivery to the brain due to vasoconstriction and increased blood-brain barrier (BBB) permeability (Betz et al., 1989; Curry et al., 2002; Olsen et al., 1985; Unterberg et al., 2004; Yan, Zhang, Agresti, LoGiudice, et al., 2015). The physiological stress caused by vasoconstriction leads to ischemia-reperfusion injury, cellular metabolic flux, and further BBB permeability through edema (Betz et al., 1989; Unterberg et al., 2004). Increased BBB permeability allows for the bi-directional flow of inflammatory-response proteins (Di Battista et al., 2016; Diaz-Arrastia et al., 2014; Kawata et al., 2016; Kawata et al., 2018; Kellermann et al., 2016; Papa et al., 2016; Shahim et al., 2018). Inflammatory-response protein concentrations are commonly used as a benchmark for injury in individuals suspected of suffering a TBI(Papa et al., 2014). Measuring inflammatory-response protein concentrations in the blood could provide a link between high frequency, low magnitude WBV exposure and brain injury.

Several studies indicate cumulative WBV induces physiological adaptions associated with physical brain injury. Yan, Zhang, Agresti, Yan, et al. (2015) determined that decreased nerve conduction velocity, reduced cerebral blood flow, cerebral tissue damage, and neuron necrosis accumulate with continued exposure to WBV. These findings were supported by

Grewal et al. (2017), who suggested that cerebrovascular damage increased with longer exposure to WBV. Additionally, Dubayle et al. (2020) found that singular bouts of low-level vibration do not elicit a change in BBB permeability, but cumulative exposure over time does, indicating that the magnitude and duration of WBV exposure may cause physiological injury. The findings of these studies indicate that physiological adaptions do occur from excessive WBV exposure; however, assessing for inflammatory-response protein concentrations such as glial fibrillary acidic protein (GFAP) and S100 calcium-binding protein B (S100B) could provide further evidence of excessive WBV exposure and a potential brain injury mechanism.

The cognitive effects of brain injury have been thoroughly examined in TBI populations and show similar effects from chronic WBV exposure. Individuals exposed to cumulative WBV exposure have reported increased symptomatology similar to those who have experienced a TBI, such as depression, irritability, lethargy, cognitive deficits, emotional distress, low self-efficacy, anxiety, confusion, anger, hostility, impaired motor control, and emotional isolation (Abbate et al., 2004; Curry et al., 2002; Kociolek et al., 2018; Mino et al., 1991; Willigenburg et al., 2013; Yan, Zhang, Agresti, LoGiudice, et al., 2015). Sherwood and Griffin (1990) determined that vibrations at 1.0 m/s^2 r.m.s. cause cognitive deficits, indicating that low-magnitude vibrations can cause brain injury. While the long-term effects of WBV on cerebral health have not been assessed, the physiological adaptions and symptomatology indicate that those exposed to chronic WBV may be at risk for similar cognitive impairments and disorders as what is witnessed in those with a history of TBI.

Statement of the Problem

The primary focus regarding WBV vibration-related injury has been on the lumbar spine and its connective tissue, while little to no research has looked at the effects of WBV on brain

injury. Chronic WBV exposure could lead to brain injury, which has an adverse impact on the long-term health of vehicle operators. Determining the effect of prolonged WBV on biomarker elicitation indicative of brain injury will further the knowledge of the harmful effects of excessive WBV exposure and help in making recommendations for vehicle manufacturers and operators.

Purpose

The purposes of this study are

1. to determine if prolonged exposure to WBV will elicit a change in GFAP and S100B protein concentrations in the blood,
2. to determine the differences between head acceleration and seat acceleration (STHT) over time, and
3. to determine if WBV exposure leads to symptom responses similar to TBIs.

Research Question(s)

1. Does vibration exposure trigger an elevation in protein concentrations indicative of traumatic brain injury?
2. Does increased exposure to vibration result in postural muscle fatigue, which in turn results in increased vibration exposure at the head?
3. Do individuals who experience prolonged vibration exposure experience symptoms indicative of traumatic brain injury?

Hypothesis 1

Null Hypothesis 1

There will be no increase in GFAP and S100B protein concentrations following prolonged WBV exposure.

Alternative Hypothesis 1

There will be an increase in GFAP and S100B protein concentrations following prolonged WBV exposure.

Hypothesis 2

Null Hypothesis 2

The acceleration at the head will not be higher over time.

Alternative Hypothesis 2

The acceleration at the head will be higher over time due to a decrease in cervical stability over the course of testing.

Hypothesis 3

Null Hypothesis 3

The WBV exposure will not lead to symptoms and accumulated head accelerations similar to those diagnosed with a TBI.

Alternative Hypothesis 3

The WBV exposure will lead to symptoms and accumulated head accelerations similar to those diagnosed with a TBI.

Limitations

Limitations of this study included:

1. Vibration testing is limited to the vertical axis, which may not accurately represent the motion experienced by motor vehicle operators.
2. Motor vehicle operation following completion of the test may impact blood protein concentration sampling 24 hours after testing.
3. Exposure duration may not truly reflect the brain response following longer bouts of motor vehicle operation or from repetitive or chronic exposure.
4. The brain's acceleration within the cranium was not directly measured.
5. Recruitment difficulties that led to a small sample size may not accurately represent the true brain response to whole-body vibration.

Delimitations

Delimitations of this study included:

1. The Lansmont Model 1000 Vibration Test System® (Lansmont Model 1000 Vibration Test System, Monterey, CA), Vicon Blue Trident® (Vicon Blue Trident, Version 2, Denver, CO) inertial measurement units, and DuoSet® Assay kits (R&D Systems, Human DuoSet ELISA, Minneapolis, MN) were used to control and measure vibration exposure's effect on subjects.
2. The inclusion criteria of no history of traumatic brain injuries within the past six months, no current pregnancy, being above 18 years of age, having full mental capacity, and being of sound health were chosen with the consent, health, and safety of subjects in mind.
3. The effects of repetitive WBV exposure were omitted due to study feasibility.
4. Anthopometric effects on head acceleration were omitted due to the individuality of the subject body dimensions and composition.
5. The physiological effect of biological sex on brain response was not considered due to the complexity that would add to the study.

Assumptions

Assumptions of this study included:

1. Vertical vibration testing will be valid since motor vehicle operators experience the greatest motion in the vertical axis, with negligible lateral and fore-aft motion.
2. Motor vehicle operation following completion of the test will not impact blood protein concentration sampling 24 hours after testing since recruited subjects will be local and likely driving minimal distances.
3. Exposure duration may not truly reflect the brain response following longer bouts of motor vehicle operation or from repetitive exposure.
4. It is impossible to measure the brain's acceleration within the cranium directly; however, the motion of the cranium is assumed to be the best possible method.
5. The small sample size was assumed to accurately represent the population for a pilot study and would be expanded for future research.

Operational Definitions

Average weighted vibration exposure ($A_{ws}(8)$) is the average (A) exposure over an eight-hour (8) day and takes into account the magnitude of the vibration and how long you are exposed to it and is calculated from the frequency weighted root mean square (r.m.s.) acceleration measurements, a_{wx}, $a_{wy,}$ and a_{wz} and the measured exposure period T_{exp}. The highest value of $A(8)_x$, $A(8)_y$, or $A(8)_z$ is the Average weighted vibration exposure ($A_{ws}(8)$) (Filho et al., 2019; Kim et al., 2016; Taing, 2020).

Glial fibrillary acidic protein (GFAP) is the main cytoskeletal intermediate filament protein produced by astrocytes and is increasingly expressed when a neural injury occurs, and astrocytes are damaged (Diaz-Arrastia et al., 2014; Kawata et al., 2016). Changes in GFAP are measured

through venous blood sampling and assay done at a baseline and period(s) of time following exposure to the physical stressor.

S100 calcium-binding protein B (S100B) is a **protein** that assists with intracellular calcium-binding, which, when the brain is exposed to a physical stressor, triggers an upregulation of S100B, resulting in a damaging influx of calcium into the cell (Giza & Hovda, 2001; Kawata et al., 2018). Changes in S100B are measured through venous blood sampling and assay done at a baseline and period(s) of time following exposure to the physical stressor.

Seat-to-Head-Transmissibility (STHT) refers to the body's complex frequency domain characteristics that result in the transmission of vibration from the point of contact at the seat to the most distal connection at the head. The ratio of acceleration at the head compared to the acceleration at the **seat** is the Seat-to-Head-Transmissibility (STHT) (Sandover, 1988).

Vibration Dose Value (VDV(8)) is a cumulative measurement of the vibration level received over 8 hours providing an alternative evaluation of vibration exposure that is often used to give a better indication of the risks associated with "shock" or "peak" events. The VDV is a cumulative value that increases with measurement time. The highest value of $VDV_{exp,x}$, $VDV_{exp,y}$, or $VDV_{exp,z}$ is the vibration dose value, VDV (Kim et al., 2016; Taing, 2020).

Chapter 2: Literature Review

The American population is regularly exposed to potentially excessive vibrations through vehicle operation. There are 220.43 billion vehicle trips that occur every day in the United States of America, with 36.57 million trips occurring for work (Transportation, 2017). Twenty-nine million workers in the United States are exposed to occupational whole-body vibration (WBV) annually, leading to musculoskeletal and physiological injuries (Abbate et al., 2004; McBride et al., 2014; Paschold & Sergeev, 2009). A physical injury occurs when WBVs exceed the tissue's absorptive capabilities, leading to tissue damage. Whole-body vibration translates through the seat and back, up to the neck, impacting all tissue within the body (Paddan & Griffin, 1998; Wang et al., 2006). The transmissibility of vibrations results in a significantly higher vibration magnitude at the head than at the seat due to tissue resonance, amplifying the magnitude leading to significant damage within the body (Singh et al., 2016; Wang et al., 2006). Whole-body vibration exposure can easily exceed recommended limits in a short period, depending on the magnitude and frequency of the vibration (Griffin, 2006; Milosavljevic et al., 2010). Whole-body vibration exposure exceeding recommended limits can result in musculoskeletal disorders, localized specifically, in the neck and low back (Johanning et al., 2006; McBride et al., 2014; Milosavljevic et al., 2012; Milosavljevic et al., 2010).

Excessive WBV exposure's effect on the lumbar spine and its connective tissue have been extensively researched; however, less is known about the impact excessive WBV exposure has on the brain. Whole-body vibration exposure can lead to neurophysiological damage through vasoconstriction of cerebral arteries and capillaries, blood-brain barrier (BBB) disruption, metabolic adaptions, and neuronal damage (Grewal et al., 2017; Yan, Zhang, Agresti, LoGiudice, et al., 2015; Yan, Zhang, Agresti, Yan, et al., 2015). While a correlation between

WBV exposure and brain physiology exists, there is little supporting research and a similar need for research on the direct relationship between WBV exposure and cognition. Whole-body vibration damage leads to noticeable symptoms such as depression, confusion, irritability, aggression, lethargy, anxiety, poor memory and cognition, and postural instability (Abbate et al., 2004; Curry et al., 2002; Kociolek et al., 2018; Willigenburg et al., 2013). However, there is a lack of research on evidence of cognitive deficits at the physiological level. The high frequency, low-magnitude forces acting at the head, and the neurocognitive symptoms experienced raise concerns about the risk of brain injury caused by WBV exposure, driving the need for a more in-depth understanding of excessive WBV's effect on the brain.

The lack of research on the effect of excessive WBV on the brain results in the need to review other research areas that focus on physical forces acting on the brain to cause injury, such as traumatic brain injury (TBI). Traumatic brain injuries can be caused by biomechanical forces affecting function, causing temporary cognitive impairments and possible neuropathological changes (McCrory et al., 2017). The viscoelastic brain's acceleration within the cranium leads to mechanical and physiological stress that results in injury. Whole-body vibration and TBI damage similarities are most noticeable when looking at frequent, repetitive mTBI and high-frequency WBV. While singular, high magnitude forces lead to significant health problems, the more significant issue might reside with repetitive, lower magnitude forces due to the brain's inability to recover (Broglio et al., 2017; Di Battista et al., 2016; Tagge et al., 2018). The damage caused by frequent low-level accelerations of the brain could mirror the injury caused by WBVs.

The evidence of neurophysiological adaptions due to WBV indicates a potential link between WBV exposure and chronic brain injury. However, there is limited research looking into the biochemical effects WBV has on the brain, potentially exposing working populations to

long-term health effects associated with these biochemical changes. This literature review aims to build towards determining the link between WBV exposure and a chronic brain injury indicated by biochemical adaptions. The purpose of this Literature Review is to assess the effects of acceleration and vibration on the brain, how this causes physiological changes, and how WBVs and TBIs lead to short- and long-term cognitive effects. This Literature Review will look at the effect of vibration on the body, the mechanical forces behind brain injury, the physiological effects of brain injury, and the long-term health consequences of chronic WBV exposure and TBIs.

Whole-body Vibration

Vibration

Vibration is the oscillation about an objects equilibrium point due to the application of a periodic or imbalanced force, with the extent of vibration dependent on the vibration frequency and magnitude (CCOHS, 2017). The sinusoidal mechanical wave resulting from vibration is separated into elastic power (P_{et}), instantaneous power (P_{Tr}), and absorbed power (P_{Abs}) (Lundstrom et al., 1998). Elastic power is supplied to and removed from the surface during excitation (Lundstrom et al., 1998). Instantaneous power is transmitted to the surface interfaced with the object at any specific point in the wave (Lundstrom et al., 1998). The absorbed power is absorbed by the object from the surface, equating to the energy dissipated through damping, and is proportional to the acceleration squared (Lundstrom et al., 1998). Vibration impacts the body when the forces that generate the vibration are transferred to the body. The vibration magnitude, frequency, direction of action, and stimulus duration affect the vibration severity (ISO, 1998). Absorbed power increases as vibration frequency increases until it peaks at the object's resonant frequency, whereafter it decreases (Lundstrom et al., 1998). The non-linear relationship between

power and frequency indicates that the peak damage is at the resonant frequency. The biodynamic response to WBV, other than absorbed power, typically includes resonance, impedance, and seat-to-head transmissibility (STHT) (Rakheja et al., 2010).

Resonant Frequency

Resonance refers to the natural frequency at which an object vibrates predetermined by its physical characteristics. Objects at their resonant frequency vibrate at a higher magnitude than the applied alternating periodic or imbalanced force (Mayton et al., 2018). While vibrations outside the resonant frequency pass through the entire body, vibrations in the resonant frequency resonate in localized body tissue, amplifying the vibrations and vehicle occupant's discomfort (Singh et al., 2016). The complex oscillatory motion of vibration within the body can result in unique physiological responses between exposed individuals (ISO, 1997). Two distinct resonant peaks at 4-6 Hz and 8-12 Hz for the human body have been proposed (Fairley & Griffin, 1989; Hinz & Seidel, 1987; Holmlund et al., 2000; Mansfield & Griffin, 2000; Milosavljevic et al., 2011; Wang et al., 2006). However, resonant peaks at 4-6 Hz and 8-12 Hz might be too simplified an explanation for the body's response to vibration. Vibration magnitude and frequency, the physical characteristics of the seat (composition, inclination angle, and foot and arm rests), the human body's anthropometrics, and the interplay between tissue and stiffness, all affect the human body's resonance response (Kubo et al., 2001).

Individual characteristics, such as increased muscular stiffness, lead to resonant frequency changes due to decreased body's rotation about the medial-lateral axis, and increased tissue stiffness (Mansfield et al., 2006). The body's neuromechanics stabilize musculature and increase ligament tension, increasing resonant frequency through increased stiffness (Keller et al., 2000). The varying resonance levels in different body tissue regions result in localized

resonant frequencies. Different regional tissue characteristics could injure some tissues but not others due to localized resonant peaks. Whole-body vibrations at the resonant frequency amplify the vibration magnitude, resulting in musculoskeletal injury by increasing activation and subsequent fatigue of postural muscles (Mayton et al., 2018; Milosavljevic et al., 2011). Intrinsic parameters and reflex mechanisms also assist with stabilization through stiffness and damping when exposed to vibration vibration exposure (Fard et al., 2004). However, when the vibration is significant enough, it overcomes stabilization and and the muscles become incapable of activation.

The resonant behavior of the human body depends on vibration magnitude and frequency, as the relationship between frequency and magnitude is non-linear (Smith, 1994). Higher body tissue stiffness emphasizes resonant frequency differences at higher magnitudes, but muscular stiffness decreases as vibration magnitude increases beyond a point (Fairley & Griffin, 1989; Mansfield et al., 2006). If the vibration frequency and magnitude are great enough, the muscle is incapable of activation, leading to a decrease in frequency (Mizrahi, 2015). Mass, stiffness, and damping characteristic differences may explain the human body's non-linear behavior under varying acceleration levels (Smith, 1994). Human body tissue characteristics possibly contribute to the decrease in resonant frequency and absorbed power as vibration magnitude increases beyond musculoskeletal tissue resonance.

Direct measurement of the transmissibility and driving-point response function, apparent mass and impedance, and the vibrations acting on the body are necessary due to an inability to examine biodynamic responses (Dong et al., 2013). The upper extremity's response to vibration is dependent on the lower extremity's response and its interface with the vibratory source. The peak transmissibilities between the seat-to-pelvis and pelvis-to-spine are likely the cause of the

peak in the apparent mass, giving evidence of similar causes of a non-linear response (Mansfield & Griffin, 2000, 2002). The thighs affect the human body's apparent mass by applying a counterforce to the vibrating force acting on the body; this counterforce is dependent on the stiffness of the thighs, the height of the footrest, and the amplitude of vibration (Fairley & Griffin, 1989). A high contact surface causes larger P_{et} and subsequently larger P_{Tr} and P_{abs}, and the lower extremity actions affect the impedance of the vibration acting on the upper body.

Impedance

Vibrational impedance is the ratio of force at the seat to the seat's velocity, whereas apparent mass is the ratio of force at the seat to the acceleration at the seat (Sandover, 1988). The human body dampens vibration through deformation kinematics and resulting dynamics that impede vibration transference (Mizrahi, 2015). Mechanical impedance of vibration within the body can be affected by the frequency and magnitude of the vibration, anthropometrics, and biological sex (Holmlund et al., 2000). Vibration magnitude and impedance are inversely related at lower frequencies, where impedance increases as vibration magnitude decreases until the resonant frequency, beyond which muscles activation is inhibited (Holmlund et al., 2000). Impedance up to the first peak is due to static weight, while the primary source of impedance at the first resonant frequency of the human body is the spine, chest, and shoulders, and the second frequency peak can be attributed to the head, abdomen, and pelvis (Holmlund et al., 2000; Smith, 1994). Males experience a larger, more focused first impedance peak, while females had a larger second peak (Holmlund et al., 2000). The higher body fat percentage in females could explain larger P_{Abs} and damping at lower frequencies than men when normalized for bodyweight due to a decreased stiffness-to-mass-ratio at which lower frequencies resonate (Lundstrom et al., 1998).

Muscle mass and fiber type differences between skeletal muscle groups and biological sexes could also explain the impedance differences and the two frequency peaks.

The structural differences between regions of the body and their surrounding tissue stiffnesses impact localized impedance. The difference in impedance per region of the body can be witnessed in the spine, where the lumbar spine has a higher dynamic impedance and stiffness than the thoracic spine (Keller et al., 2000). The chest and shoulders are the primary sources of impedance in the 5-8 Hz frequency range, and the primary source of impedance in the 12-14 Hz frequency range is dependent on the pelvic motion within the seat (Smith, 1994). Both posture and hand positioning positively affect apparent mass and STHT due to an increase in the upper body's support and stability (Wang et al., 2008). Hand placement on the thighs supports the upper body and prevents displacement. A relaxed, kyphotic seating posture requires a lower frequency for peak P_{Abs} than an erect seated posture (Lundstrom et al., 1998). Subjects seated in a kyphotic posture experience increased apparent mass damping at resonance (Mansfield & Griffin, 2002). Increased apparent mass damping could be due to increased thigh contact area through the pelvis's posterior rotation from the forward-leaning posture (Kitazaki & Griffin, 1998). The larger contact area increases the excitation point of the body and shear deformation of the pelvic area, lowering the natural frequency (Kitazaki & Griffin, 1998). The impact of posture and localized structural differences on impedance emphasizes seat design and postural muscle strength.

Seat-to-Head-Transmissibility

Seat-to-head transmissibility refers to the body's complex frequency domain characteristics that result in the ratio of acceleration at the head to the acceleration at the seat (Sandover, 1988). Vibration stemming from the vehicle-road interface during operation

translates through the seat of the car, up the back, and to the neck and head due to the kinetic chain, resulting in 1.75 times larger at the head than at the seat (Paddan & Griffin, 1998; Wang et al., 2006). The largest STHT acceleration is experienced in the vertical and anterior-posterior directions when exposed to accelerations matching the seated body's primary resonant frequency (Wang et al., 2006). The body has more significant biodynamic responses to triaxial than uniaxial accelerations due to the body's coupled motion, leading to higher vibration transmission (Mandapuram et al., 2012). The head-neck complex has the greatest transmissibility between 4-8 Hz, with vibrations higher than 12 Hz resulting in a noticeable facial vibration sensation (Hagena et al., 1986, as cited in Smith, 1994). Resonant response to vibration in the first frequency peak of WBV exposure amplifies the P_{abs} up the kinetic chain where neck musculature cannot stabilize the head. There is a lag between the accelerations at the head compared to the seat, indicative of STHT, which could explain the whiplash effect of amplified accelerations at the head compared to the seat (Kociolek et al., 2018). A decrease in vibratory impedance and an increase in the head's acceleration magnifies the brain's acceleration within the cranium, leading to more significant brain damage.

WBV Exposure Guidelines and Measurement Practices

Humans develop pathology as a direct result of exposure to WBV. The cumulative exposure to prolonged low-level vibrations, repetitive shocks, singular, high-level shocks, or both low-level shocks and vibrations contribute to injury (Johnson et al., 2015). The cumulative load of vehicular shock and accelerations, as well as the duration of exposure, are likely causes for musculoskeletal pain in drivers (Milosavljevic et al., 2012). Prolonged periods of exposure lead to higher vibration dosage, increasing the risk of musculoskeletal injury and vibrational disease due to excessive maximum and summated vibration levels (Bovenzi, 2009; Solecki,

2012). The degree of vibrational disease can be classified into first, second, or third-degree stages based on the progression of neurovascular dysfunction and polyneuropathy (Seidel, 1993). Chronic exposure to excessive vibration and shock could result in the development and progression of vibrational disease in vehicle operators. The risk of developing vibration exposure-related diseases and disorders has caused governing bodies to create vibration exposure guidelines, most notably the European Union (EU) and the International Organization for Standardization (ISO). Two commonly analyzed vibration parameters are the root mean square average weighted vibration (A_{ws}) and the Vibration Dose Value (VDV). Table 1 reprents a synthesis of vibration exposure testing from prior research.

Table 1

Vibration Exposure Measured for Different Populations

Study	Population	Freq (Hz)	Magnitude	Exposure Duration
(Kociolek et al., 2018)	ATV	1.3-4.9 Hz	Head (2.26 m^2/s^4/Hz) seat (1.00 m^2/s^4/Hz)	30 min
(Du et al., 2018)	CMV	N/A	Active seat 6.5 m/s^1.75 Passive seat 11.2 m/s^1.75	Weighted – 8hr
(Moschioni et al., 2010)	Car	N/A	0.3-0.43 m/s2	2 km drive
(Mandapuram et al., 2012)	Vibration simulator	Random vibration in 0.5-20 Hz range	0.25 and 0.4m/s2 (individual axis) 0.23 and 0.4m/s2 (3-axis)	64 trials over two days, 60 sec each with 2 minutes of rest between trials
(Wang et al., 2006)	Vibration simulator	Random vibration in 0.5-15 Hz range	0.25, 0.5 and 1 m/s2.	Two 56 sec trials
(Wang et al., 2008)	Vibration simulator	Random vibration in 0.5-15 Hz range	0.25, 0.5 and 1 m/s2.	Two 56 sec trials

(Duarte & Melo, 2018)	Car & SUV	N/A	0.02-0.98 m/s2	30 second trial per road condition and vehicle speed
(Fethke et al., 2018)	Heavy utility Vehicle	N/A	0.81 m/s2	Operation during workday (0.58 hr)
(McBride et al., 2014)	Locomotive	N/A	0.28 m/s2 ax, 0.32 m/s2 ay, 0.62 m/s2 az,	5 work shifts (32 hr)
(Johanning et al., 2006)	Locomotive	N/A	Vector sum of 0.14, 0.22, 0.28, and 0.49 m/s^2	Workshift
(Dubayle et al., 2020)	Vibration simulator (mice in centrifuge)	90 Hz	0.5 and 2g	2g singular exposure (900s), 0.5g exposure for 63 days (900s)
(Nawayseh & Griffin, 2005)	Random fore-aft vibration simulator	0.25-10 Hz	0.125, 0.25, 0.625, & 1.25ms^{-2} r.m.s.	60 seconds per exposure
(Singh et al., 2016)	Random Vibration Simulator	5, 8, 12, 16, & 20 Hz	0.5, 1.0 & 1.5 m/s^{-2} r.m.s.	60 seconds per back angle
(Yan, Zhang, Agresti, LoGiudice, et al., 2015)	Vibration Simulator (rats)	30 Hz	0.5g	4 hours/day, 5 days/week for 2, 4, or 8 weeks
(Yan, Zhang, Agresti, Yan, et al., 2015)	Vibration Simulator (rats)	30 Hz	0.5g	4 hours/day, 5 days/week for 2, 4, or 8 weeks
(Grewal et al., 2017)	Vibration Simulator (rats)	30 Hz	0.5g	4 hours/day, 5 days/week for 8 or 12 weeks

Note. A meta-analysis of prior studies shows that studies utilizing vibration simulators typically consist of random frequencies between 0.25-20 Hz, magnitudes between 0.125-1.5 m/s^{-2} r.m.s., for a duration between 30-60 seconds per trial.

Root Mean Square Average Weighted Vibration

The root mean square (r.m.s.) average weighted vibration (c) is the calculated average weighted acceleration for vibration exposure. Average weighted vibration can be calculated as seen in (1) (Taing, 2020):

$$A_{ws} = \left[\frac{1}{T}\int_0^T a_w^2(t)dt\right]^{\frac{1}{2}} \quad (1)$$

The root mean square (r.m.s.) average weighted vibration (A_{ws}) where $a_w(t)$ is the frequency-weighted acceleration at time, *t* and refers to the measurement for the duration in seconds (Taing, 2020).

The r.m.s. average weighted acceleration can be extrapolated to account for average vibration exposure over a typical work period of 8 hours as seen in (2) (Filho et al., 2019):

$$A(8) = A_{ws} * \sqrt{\frac{T}{T_0}} \quad (2)$$

The average frequency weighted acceleration extrapolated over an 8-hour period, where *T* is the effective time, and T_0 is the work period (Filho et al., 2019).

The European Union and International Organization for Standardization have set a lower limit, the exposure action value (EAV), and an upper limit, the exposure limit value (ELV), for permissible vibration exposure. The exposure action value is the limit set for vibration exposure whereafter action is recommended to minimize musculoskeletal injury risk, while the exposure limit value for vibration exposure is the limit set for the maximum tolerable exposure amount in which any higher exposure will increase the risk for musculoskeletal injury. The International Organization for Standardization has set an EAV of 0.5 m/s^2 and an exposure limit value (ELV) of 1.0 m/s^2 for triaxial accelerations (Filho et al., 2019). Table 2 shows tolerance thresholds for vibration exposure magnitude as determined by determined by ISO 2631-1 [Table 1].

Table 2

Vibration Magnitude Comfort Levels

	Acceleration, m/s^2
Comfortable	<0.315
Slightly Comfortable	0.315-0.63
Fairly uncomfortable	0.5-1.0
Uncomfortable	0.8-1.6
Very uncomfortable	1.25-2.5
Extremely Uncomfortable	>2.0

Note. Adapted from "*Mechanical vibration and shock—evaluation of human exposure to whole-body vibration—Part 1: General requirements*," ISO 2631-1, 1997 (2), p. 26. Copyright 1997 by the International Organization for Standardization.

Vibration Dose Value

The vibration dose value (VDV) is the calculated total vibration experienced at the seat (Taing, 2020). Equation (3) can be used to calculate the VDV (Kim et al., 2016; Taing, 2020):

$$VDV = \left[\int_0^T a_{ws}^4(t)dt\right]^{\frac{1}{4}} \quad (3)$$

The vibration dose value can be extrapolated to account for vibration exposure over a typical work period of 8 hours as seen in (4) (Taing, 2020):

$$VDV(8) = VDV * \left[\frac{8\ hr*60\ sec*60\ sec}{T}\right]^{\frac{1}{4}} * \left[\frac{T_0}{T}\right]^{\frac{1}{4}} \quad (4)$$

The International Organization for Standardization has set an EAV of 8.5 $m/s^{1.75}$ and an exposure limit value (ELV) of 17 $m/s^{1.75}$ for triaxial accelerations (Filho et al., 2019). Occupations where employees operate larger vehicles regularly see ISO recommended levels exceeded. Seated railroad engineers are exposed to VDV values above critical ISO ratios, and farmers on ATVs are exposed to a VDV of 16.6 and exceed the EAV after 8 minutes and the ELV after 220.8 minutes (Johanning et al., 2006; Milosavljevic et al., 2010). Vehicle operators are more likely to experience WBV levels that exceed the VDV EAV than the A_{ws} EAV (Fethke

et al., 2018). The higher likelihood of exceeding the VDV EAV is due to increased sensitivity to impulsive vibration with the VDV calculation than the A_{ws} calculation (Blood et al., 2011; Kim et al., 2016). Daily vibration dose is likely more sensitive to impulsive vibrations due to it accounting for the total vibration exposure, whereas A_{ws} is used to calculate average vibration exposure. The decreased sensitivity of the A_{ws} can potentially lead to an underestimation of vibration exposure, making VDV the more accurate vibration exposure calculation (Blood et al., 2011).

Seat-to-Head-Transmissibility

The seat-to-head transmissibility ($STHT_{x,y,z(f)}$) is the ratio between the cross-spectral density of the acceleration at the head to the cross-spectral density of the acceleration at the seat for each of the three axes (5, 6, 7) (Kumar & Saran, 2016):

$$STHT_z(f) = \frac{a_{zhead}(f)}{a_{zseat}(f)} \quad (5)$$

$$STHT_x(f) = \frac{a_{xhea\ \ (f)}}{a_{xseat}(f)} \quad (6)$$

$$STHT_y(f) = \frac{a_{yhead}(f)}{a_{yseat}(f)} \quad (7)$$

The cumulative effects of repetitive low-level vibrations and shocks or single bouts of high-level shock cause vibration-related musculoskeletal injuries in vehicle operators. Whole-body vibration exposure exceeding the A(8) maximum, A(8) summation, and VDV maximum is experienced in 11.4%, 23.8%, and 32.2% of respective industrial vehicle operators (Bovenzi, 2009). The underestimation of vibration exposure using A_{ws} calculations could be resulting in an underestimation in the number of vehicle operators exposed to potentially harmful levels of WBV. Whole-body vibration that regularly exceeds the VDV-base action value is a potential factor for 73.9% and 63.1% of industrial workers experiencing neck and low-back pain,

respectively (McBride et al., 2014). The European Union and ISO have set baseline values for vibration exposure levels that increase the risk of developing musculoskeletal disorders; however, these levels have not been determined for an increased risk of brain injury. Measuring total and average vibration along with shock exposure could allow for an understanding of vibration levels that lead to brain injury.

Mechanical Forces of Brain Injury

Linear and Rotational Acceleration

Traumatic brain injury can be caused by direct forces such as an impact to the skull, where the force acting on the skull causes pressure wave propagation extending from the point of impact (Meaney & Smith, 2011). However, the injury can be caused by indirect forces, such as with vibration, where mechanical wave propagation can lead to damage at or away from the point of contact (Smith et al., 2018; Taber et al., 2006). The brain's acceleration within the cranium increases pressure in the coup region and decreases pressure in the contrecoup region (Mao et al., 2015). The mechanisms that cause a brain injury make it a multifaceted injury. Linear and rotational acceleration, as well as the brain's subsequent deceleration, are the primary causes of traumatic brain injury (Meaney & Smith, 2011). Linear acceleration of the head causes transient intracranial pressure gradients leading to a more focal injury, such as a hematoma or contusion, while rotational acceleration causes shear strain of the brain leading to concussion or swelling of the brain (Rowson et al., 2016). The brain is more resistant to compression from linear acceleration than to shear strain, leading to shear being the primary cause of brain deformation (Kleiven, 2013). Rotational acceleration causes a higher incidence of the brain scraping the inside of the cranium and subsequently increases the amount of tissue alteration (Barth et al., 2001). The larger the impact to the skull, the larger the brain movement, pressure,

and subsequent deformation (Rowson et al., 2016). The brain's acceleration within the cranium leads to mechanical injury through its impact within the rigid cranium; however, the pressure wave propagation is another major source of physical injury.

High Magnitude vs. Repetitive Low-Magnitude TBI

Traumatic brain injury occurs through mechanical and physiological responses to a physical disturbance to the brain. An injury commonly occurs from a high force impact to the head; however, the greatest injury might occur from repetitive, low-level head accelerations. Traumatic brain injury risk does not increase with a series of high magnitude hits, and in fact, the greatest injury risk is associated with an individual impact (O'Connor et al., 2017). An increased injury risk associated with individual impacts is valid as long as there is enough time for the brain to return to homeostasis within the skull (Broglio et al., 2017). If there is not enough time for the brain to return to homeostasis before the next impact occurs, then the chance for TBI increases (Broglio et al., 2017). The brain's needed recovery time depends on the magnitude of the previous hit, so the brain takes longer to recover after a high force impact than it would a low force impact (Broglio et al., 2017). While the brain may recover quicker from low-impact forces, constant vibration may prevent the brain from returning to equilibrium, increasing the risk of injury. The brain's repetitive acceleration decreases the integrity of the inferior fronto-occipital fasciculus, with the degree of degradation relating to the amount of impact exposure (Bahrami et al., 2016). Repetitive acceleration increases variability in the default mode network, which is active during periods of lack of focus, and adaptive increases in cerebral blood flow as a response to the occurrence of impacts over time (Slobounov et al., 2017). The mechanical forces of repetitive brain acceleration lead to physical and physiological injury through the brain's inability to return to homeostasis within the cranium.

Physiological Response

Reduced Cerebral Blood Flow

Repetitive brain accelerations (Baseline CBF mean = 2.5 $mm^2/s \pm 0.1$ mm^2/s, Sham Reduction in Baseline CBF mean = 42% ± 6%; P < .01; rCHI Reduction in Sham CBF mean = 21% ± 4%; P < .001) and WBVs (Normal Carotid Artery Blood Flow mean = 15.9 mL/min ± 1.3 mL/min, 4-Week WBV Carotid Artery Blood Flow mean = 13.3 mL/min ± 1.3 mL/min; Normal Temporal Artery Blood Flow mean = 6.7 mL/min ± .5 mL/min, 4-Week Temporal Artery Blood Flow mean = 4.9 mL/min ± 0.9 mL/min; P < .0005) temporarily slow cerebral blood flow, signifying a delayed physiological response following a brain injury (Buckley et al., 2015; Yan, 2015). Indirect stimulation from vibration (Normal Vasodilation Ratio mean = 0.8 EC/EM ±0.1 EC/EM, 4-Week Vasodilation Ratio mean = 0.6 EC/EM ±0.04EC/EM; P < .01) causes excessive vasoconstriction of arteries, reducing cerebral blood flow, and injuring endothelial cells in the lumen (Yan, Zhang, Agresti, LoGiudice, et al., 2015). The decrease in cerebral blood flow, and a subsequent decrease in oxygen supply to the brain, causes damage due to ischemia (Yan, Zhang, Agresti, Yan, et al., 2015). The return of cerebral blood flow following ischemic injury causes a reperfusion injury from the brain's re-oxygenation resulting in inflammation caused by oxidative stress (Yan, Zhang, Agresti, Yan, et al., 2015). The accumulated effects of acceleration-related cerebral blood flow disruption can lead to negative neural and cerebrovascular health outcomes. Short doses of vibration exposure can lead to vascular damage (Tissue Perfusion Mean Decrease = 37 % ±1%; P < .001), while consistent exposure can potentially lead to more progressive injury, such as extensive endothelial cellular death and eventual vascular occlusion (Curry et al., 2002). Vasoconstriction resulting from short-term vibration exposure causes vacuoles to form in endothelial cells and lumen and can result in cell death from edema, apoptosis, or necrosis if

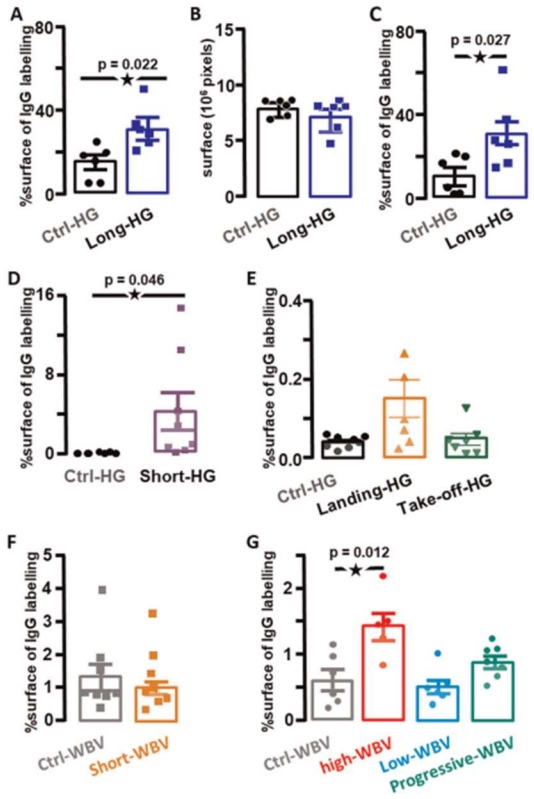
exposure continues (Curry et al., 2002; Grewal et al., 2017). Reduced cerebral blood flow and inhibited neuronal function from repeated WBV exposure potentially explain increased fatigue, decreased judgment, and decreased reaction time that drivers feel during long bouts of vehicle operation (Grewal et al., 2017).

Blood-Brain-Barrier Permeability

Secondary brain injury from a physical injury occurs through increases in neuroinflammatory response and BBB permeability (Vilalta et al., 2008). The division between the neural tissue and blood is constructed of the BBB, the blood CSF barrier, and the arachnoid epithelium, and serves as physical, transport, metabolic, and immunologic barriers to the diffusion of polar solutes (Serlin et al., 2015). The BBB consists of connected endothelial cells, astrocytes, microglia, and pericytes divided by circulating blood from interstitial tissue and maintains homeostasis by limiting the influx of harmful particulates through the function of the neurovascular unit (Lochhead et al., 2010; Sahyouni et al., 2017; Serlin et al., 2015). Occludins-, claudins-, and junctional-associated proteins form tight junctions between endothelial cells regulating BBB permeability (Krueger et al., 2013). Oxygen is perfused across the BBB through surrounding capillaries (Grewal et al., 2017). Consistent exposure to brain acceleration, in conjunction with a high average vibration magnitude, is the primary influencer for BBB leakage [Figure 1] (Dubayle et al., 2020).

Figure 1

Effects of centrifugation and WBV on IgG extravasation in the hippocampus.



Note. a IgG extravasation expressed as the percentage of labelling observed in Long-HG and Ctrl-HG groups for the entire surface of hippocampus. b Comparison of the surfaces of hippocampus in Long-HG and Ctrl-HG groups. c IgG extravasation expressed as the percentage of labelling for the constant area of hippocampus in the LongHG and Ctrl-HG groups. d, e IgG extravasation expressed as the percentage of labelling observed in the Short-HG, landing and take-off groups in comparison with their control. f, g IgG extravasation expressed as the percentage of labelling observed in the WBV groups in comparison with their control. Statistical significant differences are reported. The star indicates $p < 0.05$. From "Effects of centrifugation and whole-body vibrations on blood-brain barrier permeability in mice," by D. Dubayle, A.

Venden-Bossche, M. Beraneck, L. Vico, & J.C. Morel, 2020, *NPJ Microgravity, 6*, p. 3. Copyright 2020 by Nature Research. Reprinted with permission (see Appendix B).

Traumatic brain injury results in multifocal disruption to the BBB, in part, due to direct endothelial damage from brain acceleration (Johnson et al., 2018). Blood-brain barrier disruption can also occur from reductions in cerebral blood flow due to ischemia, disrupting water and electrolyte homeostasis, ionic exchange, and increasing endothelial cellular fluid retention (Betz et al., 1989; Unterberg et al., 2004). The increase in cellular fluid retention disturbs cell function, breaking down the BBB (Betz et al., 1989). Shear stress from the brain's acceleration within the cranium stretches the axons and leads to vascular injury (Sahyouni et al., 2017). Vascular injury leads to the unregulated influx of plasma proteins into the interstitial (ISF) and cerebrospinal fluids (CSF) (Unterberg et al., 2004). Brain injury causes fluid retention, damaging the BBB through swelling and the accumulation of harmful waste. Traumatic brain injury decreases ipsilateral cortex waste clearance by 25% due to reduced paravascular CSF-ISF exchange and interstitial solute removal (increase in P-tau levels identified with anti-pThr205, $P < .05$; increase in P-tau levels identified with anti-pThr231, $P < .05$; increase in P-tau levels identified with pSer396, $P < .01$) (Iliff et al., 2014). Decreased waste removal associated with traumatic brain injury leads to decreased cognitive function and increased neuronal impairment from the chronic accumulation of harmful proteins such as phosphorylated tau (Iliff et al., 2014).

Ischemic injury can lead to the influx of reactive oxygen species that contribute to vasogenic edema and increase blood-brain barrier permeability (Lochhead et al., 2010; Witt et al., 2003). Vasogenic brain edema results from ischemic-reperfusion injury, allowing an influx of plasma proteins into neural cells due to increased BBB permeability (Betz et al., 1989). The interplay between physical disruption from vasogenic edema and metabolic adaption from

endothelial cell activation and calcium instability results in increased BBB permeability for up to 72 hours post-injury (Alluri et al., 2015; Unterberg et al., 2004). Cytotoxic brain edema differs from vasogenic edema due to an intact BBB, and is characterized by ischemic injury resulting in intracellular fluid retention from Na/ K ATPase damage, and subsequent death (Betz et al., 1989). Ischemic injury damages neurons through edema by disrupting cellular homeostasis either through an influx of plasma proteins across a hyperpermeable BBB, or cellular swelling through sodium and water retention.

Repetitive brain injury negatively affects BBB permeability due to adaptions that allow for the influx of inflammatory proteins (serum protein fibrinogen immunoreactivity left hemisphere sham mean = 0.18% ± 0.01%, serum protein fibrinogen immunoreactivity right hemisphere sham mean = 0.29% ± 0.05%; serum protein fibrinogen immunoreactivity left hemisphere 6-hour post-concussion mean = 4.39% ± 2.3%, serum protein fibrinogen immunoreactivity right hemisphere 6-hour post-concussion mean = 3.87% ± 1.88% P = 0.03) (Johnson et al., 2018). Dubayle et al. (2020) found that singular bouts of low-level vibration do not elicit a change in BBB permeability, but cumulative exposure over time does, indicating that physiological injury may be caused by the magnitude and duration of WBV exposure. Repeated brain acceleration from WBV could disrupt the BBB, similar to what is seen in TBIs.

Neurometabolic Cascade

Neuronal deficits following TBI result from ischemic injury that causes a sodium-potassium flux that impairs cellular activity (Giza & Hovda, 2001). A TBI causes mechanical neuronal disruption, resulting in acute and subacute cellular physiological adaptions from an increase in extracellular potassium, depolarizing the neurons (Giza & Hovda, 2001). Rapid depolarization of neurons following a TBI leads to an efflux of potassium and an influx of

calcium into the cell due to mitochondrial dysfunction causing the secretion of glutamate (Pierce et al., 2018). The excessive cytoplasmic calcium pulled into the mitochondria affects membrane potential, leading to inflammatory cascades, apoptosis, and endothelial cellular breakdown (Cornelius et al., 2013; Sahyouni et al., 2017). Oxidative stress resulting from changes in membrane potential following a TBI results in hypometabolism, decreased global neural connectivity, and cerebral blood flow (Giza & Hovda, 2001). Ischemia from the reduced cerebral blood flow prevents the glial cells from taking up excessive extracellular potassium, while the accumulation of intracellular calcium in the mitochondria impairs oxidative metabolism and increases BBB permeability (Giza & Hovda, 2001). Calcium is critical for learning and memory, but long-term elevations in intracellular calcium levels are damaging for cells, decreasing cognitive function due to increased oxidative stress and myelin disruption that increases phosphorylated tau (Deshpande et al., 2008; O'Hare Doig et al., 2017). Increases in ionic flux coinciding with the sodium-potassium pump work to reestablish homeostasis through cellular hypermetabolism deplete energy storage (Barkhoudarian et al., 2016). The rapid period of cellular hypermetabolism to keep up with the energy demand leads to a period of hypometabolism (Barkhoudarian et al., 2016). Lactate, a byproduct of cellular metabolism, accumulates within the cell due to cellular hypermetabolism and decreased lactate metabolism, resulting in cellular dysfunction and increased BBB permeability (Giza & Hovda, 2001). Repetitive exposure to trauma can prolong energy impairments, leading to apoptotic cell death and the accumulation of harmful proteins (Martinez et al., 2010). Brain injury results in inflammatory effects that cause a metabolic cascade exacerbated by repetitive exposure. The high frequency, low magnitude accelerations observed with WBV might trigger a metabolic cascade that leads to chronic injury with prolonged periods of regular exposure.

Biomarkers

Due to the physical effect of vibration and acceleration on the brain, inflammatory proteins produced in the Central Nervous System are transported into the bloodstream (Kawata et al., 2016). Brain-produced proteins potentially enter the bloodstream due to injury to the BBB or the glymphatic system (Kawata et al., 2016). Brain injuries damage the neurons and glia that make up the neurovascular unit, resulting in disrupted neurovascular unit integrity, allowing brain-derived inflammatory proteins to leave the BBB through the glymphatic system (Blyth et al., 2011; Kawata et al., 2016).

The history of TBI does not significantly link to individual inflammatory protein levels, indicating that the high acceleration head impacts might not be the predominant cause for long-lasting damage (Di Battista et al., 2016). Repetitive, low acceleration impacts and gender could be the most significant factors in eliciting a biological response, potentially indicating that consistent low-level disturbances to the brain, such as vibration, could elicit a protein response (Battista, 2016). Two biomarkers commonly analyzed for a TBI that might indicate a response from WBV are glial fibrillary acidic protein (GFAP) and S100 calcium-binding protein B (S100B).

Glial Fibrillary Acidic Protein

Glial fibrillary acidic protein is the main cytoskeletal intermediate filament protein produced by astrocytes and is increasingly expressed when a neural injury occurs, and astrocytes are damaged (Diaz-Arrastia et al., 2014; Kawata et al., 2016). Glial fibrillary acidic protein levels increase ten times that of normal levels following repetitive head impacts (median GFAP level post-injury = 0.112 ng/mL, IQR = 0.030-0.462 ng/mL, range = 0.008-8.078 ng/mL vs median control GFAP level post-injury = 0.008 ng/mL, IQR = 0.008- 0.030 ng/mL, range =

0.008-0.773 ng/mL; P < .001) (Papa et al., 2016). The elevated GFAP levels following a brain injury likely correspond to an increase in the reactive astrocytes (Pham et al., 2019). Glial fibrillary acidic protein levels are significantly elevated for three days in the ipsilateral dentate gyrus ($F_{(2, 29)} = 3.61$; $p < 0.05$) and 4-7 days in the thalamus after brain injury (Kabu et al., 2015; Pham et al., 2019). Glial fibrillary acidic protein levels begin to decrease but remain elevated at a detectable level for up to 90 days post-injury, making it a useful biomarker for tracking recovery (control GFAP median [IQR] = 0.80 [0.8–1.070] pg/mL; day 1 GFAP median [IQR] = 17.60 [3.88–129.6] pg/mL, day 30 GFAP median[IQR] = 1.330 [0.8–2.21] pg/mL, day 90 GFAP median[IQR] = 1.350 [0.8870– 2.280] pg/mL; $p < 0.0001$) (Bogoslovsky et al., 2016). While GFAP levels significantly increase following a TBI, the expression is not significantly elevated when exposed to low-magnitude head accelerations (Non-HHI baseline mean = 32.69 pg/ml ± 9.99 pg/ml, Non-HHI post-game mean = 33.02 pg/ml ± 9.07 pg/ml; $p = 0.6$) (Joseph et al., 2019). The specificity of GFAP to the brain could explain the lower levels of expression under low-magnitude head accelerations since they do not elicit the same short-term effects as high-magnitude head accelerations (Papa et al., 2019). The lack of significant elevation in GFAP levels following low-magnitude head accelerations could make it less useful for detecting an inflammatory response from cumulative WBV exposure.

S100 Calcium-Binding Protein B

S100 calcium-binding protein B primarily assists with intracellular calcium-binding, differentiating glial cell types, and transducing neural signals (Kawata et al., 2018). S100 calcium-binding protein B levels increase following repetitive low-magnitude head accelerations (baseline to post-practice change in S100B concentration level pads off high # of impacts (SE) = 0.06(0.01) μg/l; $p < 0.001$; baseline to post-practice change in S100B concentration level pads on

high # of impacts (SE) = 0.08(0.01) μg/l; $p < 0.001$) (Kawata et al., 2016). Following a TBI, patients saw S100B serum concentrations peak the day of the injury and decrease in the days afterward (S100B peak mean concentration day 1 = 0.18 μg/l, range = 0.12-0.33 μg/l; S100B peak mean concentration day 2 = 0.16 μg/l, range = 0.13-0.23 μg/l; S100B peak mean concentration day 3 = 0.12 μg/l, range = 0.08-0.18 μg/l; S100B peak mean concentration day 4 = 0.09 μg/l, range = 0.06-0.13 μg/l; S100B peak mean concentration day 5 = 0.08 μg/l, range = 0.04-0.09 μg/l; $p < 0.05$) (Kellermann et al., 2016). The observed elevated response from S100B following repetitive low-magnitude head accelerations potentially makes it a strong biomarker for detecting an inflammatory response from cumulative WBV exposure and predicting injury outcomes (Bogoslovsky et al., 2016; Kawata et al., 2018). Individuals with higher S100B concentrations in their blood six months following TBI treatment tend to have worse outcomes, potentially due to the high uptake of S100B in the CSF (high CSF S100B (μg/l ≥30 g/l) concentration level outcome = 30% good, 70% bad; low CSF S100B (μg/l <30 g/l) concentration level outcome = 67% good, 33% bad; OR(95% CI) = 4.15 (1.34–12.84); $p = 0.012$) (Kellermann et al., 2016). Discerning elevated S100B could be a potential tool to distinguish brain injuries resulting from cerebral vascular damage and increased blood pressure at the BBB (Kawata et al., 2017). The distinction between injury modalities would help determine the effects of WBV, which have been previously shown to increase cerebral blood pressure and damage vasculature (Grewal et al., 2017; Yan, Zhang, Agresti, LoGiudice, et al., 2015; Yan, Zhang, Agresti, Yan, et al., 2015).

Justification of a Combined Testing Approach

The multifocal nature of a TBI makes using one biomarker unlikely to accurately reflect the extent of a TBI's damage (Bogoslovsky et al., 2016). Analyzing GFAP and S100B together

could yield information regarding injury mechanisms due to their origins (Diaz-Arrastia et al., 2014). S100B (CT + trauma 0-8 hour mean = 1838.0 ± 3599.6pg/mL, CT + trauma 12-32 hour mean = 569.2 ± 914.2pg/mL; $P < 0.001$) concentrations peak 0-8 hours after injury and then decline, while GFAP concentrations (CT + trauma 0-8 hour mean = 3065.0 ± 7295.2pg/mL, CT + trauma 12-32 hour mean = 10,005.6 ± 15,867.6pg/mL; $P < 0.001$) peak 12-32 hours after injury (Mahan et al., 2019). Glial fibrillary acidic protein has the greater specificity, sensitivity, and accuracy than S100B (Diaz-Arrastia et al., 2014; Gill et al., 2018; Mahan et al., 2019; Papa et al., 2014). However, testing both GFAP and S100B produce more sensitive measures for distinguishing between injured and healthy individuals due to the differences in their elicitation and tissue locations (Mahan et al., 2019).

Symptoms

Traumatic Brain Injury Symptoms

Traumatic brain injuries affect brain function, causing temporary cognitive impairment and possible neuropathological changes (McCrory et al., 2017). Repetitive low-magnitude head impacts affect forebrain and midbrain connections, impairing executive functioning, sight, hearing, and memory (Bahrami et al., 2016; Slobounov et al., 2017). A higher number of TBIs increases the disconnect in the brain leading to a decrease in functional neural efficiency due to the degradation of the frontal white matter integrity (Clark et al., 2018). A neural disconnect between the forebrain and midbrain leads to motor function deficits, learning ability, memory recall, encoding capabilities, and recognition discriminability, with increased dysfunction occurring with larger periods of head acceleration (Lavender et al., 2020; Wright et al., 2020). More frequent exposure to repetitive head accelerations will result in more significant cognitive deficits and emotional irregularity (Oyegbile et al., 2018). A TBI history increases hostility,

depression, and anxiety in the short and long term (Goswami et al., 2016; Guskiewicz et al., 2007; Moore et al., 2016). Kerr et al. (2018) found that athletes sustaining three or more TBIs are 4.2 times as likely to suffer from moderate to severe depression (Kerr et al., 2018). Reger et al. (2012) found that mTBI leads to a heightened fear response to stressful events, similar to what is seen with Post Traumatic Stress Disorder. An increased history of exposure to harmful levels of head acceleration leads to more significant damage to the sections of the brain responsible for motor and cognitive function.

Whole-Body Vibration Symptoms

Excessive WBV exposure results in musculoskeletal disorders (MSD), specifically in the neck and low back (Johanin, 2018; McBride, 2018; Milosavlejevic, 2012; Milosavljevic, 2010). Excessive WBV levels lead to a high incidence of muscular and nerve pain in the neck and upper extremity (Rehn et al., 2002; Rehn et al., 2004). Vehicle operators can experience headaches and neck pain due to the cumulative shock from WBV exposure (Kociolek et al., 2018; Milosavljevic et al., 2012). The cervical injuries and discomfort that individuals exposed to harmful WBV experience indicate that the potential for injury to tissues distal from the vibratory source, specifically the brain. In addition to MSDs, low-level WBV exposure impairs short-term memory and cognitive functions (Sherwood & Griffin, 1990). Individuals exposed to repetitive, low-level WBVs have increased risks of depression, irritability, lethargy, cognitive deficits, emotional distress, low self-efficacy, anxiety, confusion, anger, hostility, and emotional isolation (Abbate et al., 2004). Mino et al. (1991) found that 67.9% of individuals with vibration disease from occupational vibration exposure report having moderate to severe depression. The cumulative effects of WBV exposure led to worsened memory, decision making, slower reflexes, and decreased postural control and stability, which may be important in developing

neurocognitive disorders (Curry et al., 2002; Kociolek et al., 2018; Willigenburg et al., 2013; Yan, Zhang, Agresti, LoGiudice, et al., 2015). Sherwood and Griffin (1990) found that reaction time was significantly impaired when exposed to vibrations of 1.0 m/s^2 r.m.s. Cognitive deficits occurring at 1.0 m/s^2 r.m.s. indicate that low-magnitude accelerations are capable of causing symptoms of brain injury. Increased tau phosphorylation, long-term changes in axonal pathology, and neuroinflammation, caused by cumulative, repetitive head accelerations, are associated with increased anxiety and decreased spatial learning memory (McAteer et al., 2016). The cognitive symptoms experienced by those exposed to repetitive WBV indicate a potential tau accumulation, increasing the chances of developing neurocognitive disorders. Cumulative WBV exposure results in symptoms similar to what is seen from TBI, indicating similar mechanical and physiological responses.

Long-Term Cognitive Effects

Brain injuries can trigger short-term symptomatic responses; however, the cumulative effects can lead to long-term health consequences. Traumatic brain injuries potentially increase the risk of neurodegenerative diseases later in life (Guskiewicz et al., 2005). However, low-threshold brain acceleration can also cause traumatic brain injuries and early signs and neurocognitive disorder complications (Tagge, 2018). Head impacts have also been shown to increase blood flow to the brain, specifically to the somatosensory cortex, and increase white matter integrity alterations three-fold (Bazarian et al., 2012; Slobounov et al., 2017). The neurophysiological damage that cumulative low-threshold accelerations cause from both low-level impacts and WBV has been hypothesized to increase the risk of cerebral diseases such as dementia, Alzheimer's Disease, Parkinson's, and CTE (Grewal et al., 2017; McAllister & McCrea, 2017). While the mechanics might not be the same between chronic low-level impacts

and WBV exposure, similar physiological adaptions that occur could potentially lead to similar poor health outcomes.

Tau

Traumatic brain injuries lead to an increase in hyperphosphorylated tau in the neurons (Di Battista et al., 2016; Shahim et al., 2018). Tau stabilizes axonal microtubules, with this process being regulated by phosphorylation at binding sites (Puvenna et al., 2016) . However, injury causes the hyperphosphorylation of tau, destabilizes the microtubules, and alters axonal transport (Puvenna et al., 2016). Tau hyperphosphorylation causes tau to detach from the microtubules and accumulate in the neuron, where it self-aggregates and polymerizes to form oligomers that are toxic to the cell (Collins-Praino & Corrigan, 2017). Once the injury progresses to neuronal death, tau is released (Neergaard et al., 2018). Elevated t-tau levels lead to worse global functional connectivity of neurons (Di Battista et al., 2016). As oligomers accumulate in the cell, they combine to form neurofibrillary tangles (NFTs), which are observed posthumously in individuals with CTE and Alzheimer's Disease (Collins-Praino & Corrigan, 2017; Neergaard et al., 2018). Chronic traumatic encephalopathy (CTE) is a disease affecting the brain that is believed to be caused by repetitive impacts to the head and is characterized by degeneration of mental cognition, emotional stability, impulse control, mood, executive functioning, and short-term memory (Baugh et al., 2014). Chronic traumatic encephalopathy is a neurodegenerative disease characterized by the accumulation of hyperphosphorylated tau in the form of NFTs in the neurons (McKee et al., 2013). There are four stages of CTE progression, with it originating in the perivasculature, proximal to the sulci of the cerebral cortex, and characterized by NFTs slowly promulgating throughout the brain over time, leading to cerebral atrophy and an increase in the severity of symptoms from headache, depression and shortened attention span in the early stages,

to impaired cognition and memory and increased aggression in the later stages (McKee et al., 2015; McKee et al., 2013). Alarmingly, McKee et al. (2013) found evidence of CTE present in 80% of subjects with a history of repetitive mTBI. A history of repetitive mTBI, potentially from chronic WBV exposure, leads to chronic cell death and the subsequent accumulation of tau leads to neurodegenerative diseases later in life.

Traumatic Brain Injury

Repetitive TBIs and mTBIs have been potentially linked to an increased risk of neurocognitive disorders such as CTE, dementia, and Alzheimer's Disease (Bertrand et al., 2016; McAllister & McCrea, 2017; Tagge et al., 2018). There has been significant evidence that shows a correlation between a history of repetitive head impacts and the development of neurodegenerative diseases. Of patients with CTE, 90% had a history of TBI (McAllister & McCrea, 2017). Retired football players are diagnosed with Alzheimer's Disease at a rate of 1.3% (Guskiewicz et al., 2005). McAllister and McCrea (2017) found an 11.8% incidence of CTE and 16% for Parkinson's Disease in impact exposed brains. Approximately 45% of athletes with CTE develop dementia, which increases to 66% after the age of 60 (Bertrand et al., 2016). Chronic headaches are an issue for 30% of retired athletes, potentially indicating the early stages of CTE (Bertrand et al., 2016; McKee et al., 2013). Repetitive head impacts increase the risk of developing neurodegenerative diseases with age.

A history of TBIs leads to neurocognitive impairments later in life. Mental health is worse for athletes who have previously sustained a TBI than those who have not, with mental health impairments being 2.5 times as likely if they have sustained three or more TBIs (Kerr et al., 2018). While TBI history is associated with CTE, the actual cause might be the repetitive low magnitude head accelerations athletes sustain (Tagge et al., 2018). The potential link between

CTE and chronic low-level brain acceleration could indicate that other low acceleration forces, such as repetitive WBV, could cause neurocognitive disorders.

Whole-Body Vibration

To the knowledge of this review, no research has been conducted on tau accumulation in populations exposed to chronic WBV; however, there is evidence to support that WBV exposure could increase the risk of neurocognitive disorders. Continued daily WBV exposure for one month leads to significant cerebral tissue injuries (Yan, Zhang, Agresti, LoGiudice, et al., 2015). The damage to cerebral tissue results in injury to the neuronal structures of the brain. Increased duration of exposure to WBVs results in an increased accumulation of dark, shrunken neurons and neuronal atrophy due to daily exposure preventing healing (Yan, Zhang, Agresti, Yan, et al., 2015). Yan, Zhang, Agresti, LoGiudice, et al. (2015) found that after two weeks of daily WBV exposure, there were reductions in lumen size, differences in endothelial circumference, decreased length of the elastic membrane, and increased vasoconstriction of the middle cerebral arteries are more constricted. Prolonged WBV exposure causes cerebral vascular spasm that decreases cerebral blood flow from vasoconstriction of the capillaries (Grewal et al., 2017). Whole-body vibration exposure causes the endothelial cells of the cerebral artery wall to form irregular patterns, leading to its degradation (Grewal et al., 2017; Yan, Zhang, Agresti, LoGiudice, et al., 2015). Cerebral artery wall degradation impairs the brain's blood perfusion capability and subsequent function (Grewal et al., 2017; Yan, Zhang, Agresti, LoGiudice, et al., 2015). The impaired blood perfusion decreases the ability of oxygen to enter the brain, causing ischemia. Along with shear, ischemia-reperfusion resulting from daily WBV exposure and nightly rest may factor into the damage done to neuron and peripheral nerves (Yan, Zhang,

Agresti, Yan, et al., 2015). The damage done from chronic WBV exposure causes neuronal damage through vasoconstriction, impaired perfusion, and ischemia, leading to cell death.

Conclusion

The purpose of this literature review was to assess the effects of acceleration and vibration on the brain, how this causes physiological changes, and how the WBVs and TBIs lead to short- and long-term cognitive effects. By analyzing the injury mechanisms of WBV and TBI forces, similarities were seen in each physical stressor's mechanical and physiological responses. Repetitive, lower-level acceleration exposure, such as what is seen with mTBI and WBV exposure, may pose a higher risk for injury compared to a singular, high force TBI due to the magnitude of injury increasing when the brain does not have the time to return to homeostasis (Broglio et al., 2017). The repetitive, high frequency, low-magnitude acceleration of the brain due to WBV could prevent the brain from returning to its homeostatic level, increasing the risk for injury. The increased vibration magnitude at the head compared to the seat indicates an amplification in vibration that could result in more significant mechanical and physiological injury (Abbate et al., 2004; Fairley & Griffin, 1989; Hinz & Seidel, 1987; Holmlund et al., 2000; Mansfield & Griffin, 2000; Milosavljevic et al., 2011; Paddan & Griffin, 1998; Singh et al., 2016; Wang et al., 2006). Brain injury can be caused by an applied force, such as vibration or a head impact, that damages the brain's sulci and neurovascular unit (Smith et al., 2018). A physical stressor such as vibration or a head impact can lead to neurophysiological damage through vasoconstriction of cerebral arteries and capillaries, BBB disruption, and metabolic adaptions that trigger the response of inflammation-causing proteins (Grewal et al., 2017; Kawata et al., 2016; Yan, Zhang, Agresti, LoGiudice, et al., 2015; Yan, Zhang, Agresti, Yan, et al., 2015). Mechanical and physiological injury triggers adaptive mechanisms that result in

harmful conditions later in life. The cumulative effects of low-magnitude head accelerations and low-level WBV exposure lead to similar neurocognitive disorder symptoms (Abbate et al., 2004; Goswami et al., 2016; Moore et al., 2016; Pham et al., 2019; Tsushima et al., 2019). While the mechanics might not be the same between chronic mTBI and WBV exposure, the neurophysiological damage could increase the risk of developing cerebral diseases such as dementia, Alzheimer's, Parkinson's, and CTE (Grewal et al., 2017; Guskiewicz et al., 2005; McAllister & McCrea, 2017). Similarities in physical mechanisms and response outcomes potentially indicate similarities in cerebral injury. Analyzing known inflammatory-response proteins expressed during TBI, such as GFAP and S100B could indicate an injury response in individuals exposed to WBV. There is evidence to support the belief that excessive, chronic WBV exposure can result in brain injury and needs to be further investigated to determine if there is a risk for the development of neurodegenerative diseases.

Chapter 3: Methodology

Subjects

The methodology for this study complies with the testing standards established in ISO 10326-1 and the safety standards established in ISO 13090-1.

This study is a cross-sectional randomized control trial. Subjects were recruited from Virginia Polytechnic Institute and State University (Virginia Tech) and the surrounding Blacksburg, VA area through flyers posted around campus and Blacksburg. Thirty-two subjects, 14 males and 18 females, participated in this study [Table 3]. Subjects were informed of the study purpose, protocol, and safety measures in place to prevent harmful vibration exposure before testing commenced.

Table 3

Test subject physical characteristics

N = 32	Mean (SD)	Minimum	Maximum
Age (years)	35.4 ±16	18	64
Weight (kg)	77.9 ± 20.1	50	149
Height (cm)	169.8 ± 12.0	150	200

Note. Subjects were between 18 to 64 years old, 50 to 149 kg, and 150 to 200 cm.

Subjects were excluded if they had a history of traumatic brain injuries within the past six months, were currently pregnant, were under 18 years of age, did not have full mental capacity, used a prosthesis, recently had a surgical procedure, or had an active disease of the respiratory, gastrointestinal tract, genito-urinary, cardiovascular, musculoskeletal, or nervous system (ISO, 1998).

Subjects were randomly assigned to a control, short-term exposure, or long-term exposure group. Block randomization was used to group subjects into either the control (no exposure), short-term exposure (1 hour exposure), or long-term exposure (8 hours exposure)

group. Block sizes were hidden from the executor and randomly mixed. Nine subjects were in the control group, twelve were in the short-term exposure group, and eleven were in the long-term exposure group. The study was approved by the institutional review board at Marshall University (see Appendix B) after deference from the institutional review board at Virginia Tech (see Appendix C). Informed and written consent was obtained from all subjects (see Appendix D).

Materials

The study used a Lansmont Model 1000 Vibration Test System® (Lansmont Model 1000 Vibration Test System, Monterey, CA) to administer a uniaxial alternating periodic or imbalanced force in only the vertical axis to subjects. The vibration profile was measured for a 26' leaf spring Freightliner M2 106 straight delivery box truck. This vehicle had 26,000 lbs. of gross vehicle weight and 10,000 lbs. of payload capacity. The vehicle was loaded up to 75% of its payload capacity. The truck was traveling between Mocksville, NC, and Blacksburg, VA, on a two-lane asphalt highway. The vibration measurement was conducted using a Lansmont Saver3x90 data logger mounted under the frame of the seat using a magnetic mount (Lansmont Corporation, Monterey, CA, USA) [Table 4].

Table 4

Settings Used for the Vibration Datalogger.

	Timer Triggered
Record time	15s
Sampling Frequency	100 samples/s
Wakeup Interwall	15s
Filter	250Hz
Data Retention	Fill/Stop

Note. The data logger has a 200g maximum range. The data logger was configured to collect data continuously throughout the trip.

Table 5

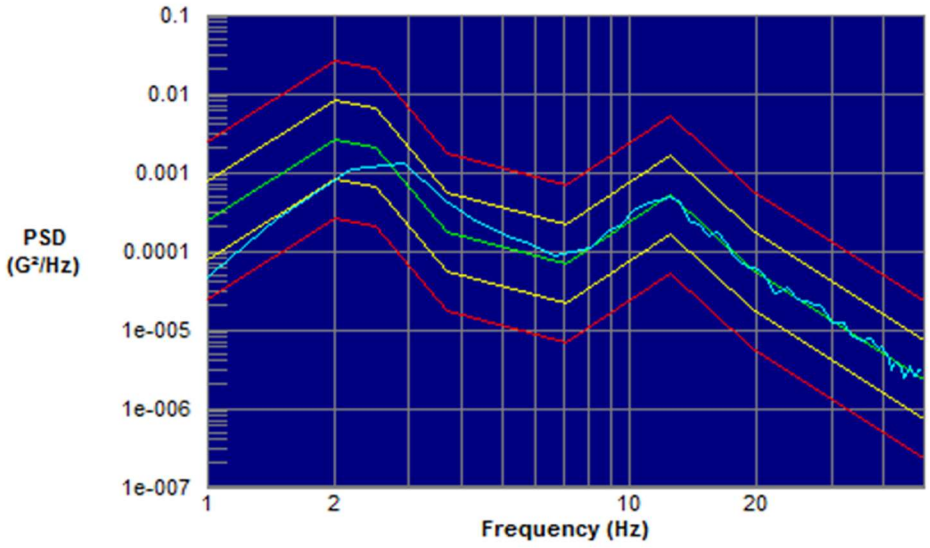
Summary Table of the Used Power Spectral Density Profile for Vibration.

Frequency (Hz)	PSD (G^2/Hz)
1	0.0002387
2	0.0026415
2.5	0.0020159
3.7	0.0001767
7.1	0.0000672
12.5	0.0005267
19.4	0.0000565
49.9	0.0000023

Note. The data collected from the data logger was processed using the SaverX software with a 50 Hz filter (Lansmont Corporation, Monterey, CA, USA). Any recorded events below 0.04g were filtered out.

Figure 2

Vibration Profile Obtained from a Penske Truck



Note. The Gravitational Root Mean Square acceleration of the vibration profile was 0.081, while the profile included frequencies between 1 and 50 Hz.

Two Vicon Blue Trident® (Vicon Blue Trident, Version 2, Denver, CO) inertial measurement units were used to measure vibrations at the lower back and at the head in 2-hour

intervals for the 8-hour exposure group, lasting for 1 minute for each interval. Burland et al. (2020) found high reliability for cumulative impact loading during an acceleration-deceleration task (left limb ICC[95% CI] = 0.88[0.65-0.97], right limb ICC = 0.89[0.68-0.97]).

DuoSet® Assay kits (R&D Systems, Human DuoSet ELISA, Minneapolis, MN) were used to assess GFAP and S100B protein concentrations in the blood.

Modified Rivermead Post Concussion Symptom Questionnaires (RPQ) (King et al., 1995) (see Appendix E) and Whole-Body Vibration Health Screening Questionnaires (WBVHSQ) were given to subjects to gauge head injury symptoms from WBV exposure and vibration history (Pope et al., 2002) (See Appendix F). Rivermead Post Concussion Symptom Questionnaire scores typically range from (0) to (64), with higher scores indicating more severe TBI symptoms (King et al., 1995). The RPQ was chosen due to its good test-retest reliability (0.89 for RPQ-13, 0.72 for RPQ-3, $P < 0.01$) and external construct validity scores (0.83 for RPQ-13, 0.62 for RPQ-3, $P < 0.01$) (Eyres et al., 2005). The WBVHSQ was chosen to assess symptoms of neck and low-back pain due to the significant relationship it has with vibration and shock exposure ($P < 0.05$) for neck pain over a 12-month duration and low-back pain (OR = 1.24, $P = 0.092$) over a (12) month period (Milosavljevic et al., 2011). An hourly discomfort survey was used to gauge local discomfort on an increasing scale from 0-10, where 0 was no discomfort and 10 was maximum discomfort.

Protocol

Subjects arrived at the testing site and consented to participate in the study. Subjects completed a Whole-Body Vibration Health Screening Questionnaire and buckled themselves into the truck seat on the vibration platform. Subjects scored their discomfort every hour, ranging

from no pain (0) to maximum pain (10). At the end of testing, subjects completed a modified Rivermead Post-Concussion Questionnaire.

Data Collection

Subjects were randomly assigned to control, short-term exposure, and long-term exposure groups. The control group experienced no vibration, the short-term exposure group experienced 1 hour of vibration, and the long-term exposure group experienced 8 hours of vibration. Subjects were given the modified WBVHSQ before and the modified RPQ after testing.

Venous blood was sampled before, immediately after, and 24 hours after testing, and sterile tubes that contained an anticoagulant agent were filled (Kawata et al., 2017). The plasma was separated through centrifugation for 10 minutes and stored at -80°C until analysis was conducted (Kawata et al., 2017).

One researcher, positioned between the subject and the Lansmont vibration test system, operated the system and observed the subject. Testing would cease at the subject's request or in case of a system malfunction, with the researcher having the ability to use an emergency stop if required. Test duration was determined by the subject's experimental group. The long-term exposure group subjects were given 1 hour of cumulative breaks throughout testing. Fifteen-minute breaks were assigned after hours two and six of vibration exposure, and a 30-minute break was given after hour four of vibration exposure. Subjects were given the ability to modify break schedules as needed, as long as the cumulative break did not exceed 1 hour before testing was completed.

Vicon Blue Trident® IMUs were fixed to the seat and the head of the subjects, with the +Z axis going to the left side of the subject, the +Y direction pointed behind the subject, and the +X direction pointed upwards [Figure 3]. The IMUs were set up to collect both linear and

rotational accelerations in the Z, Y, and Z directions. The sample rate for the IMUs was set to 1134 Hz, and the collection time was set to 60 seconds. Head and seat accelerations were sampled every 2 hours for the 8-hour subjects and at the beginning and end for the 1-hour group. Localized subject discomfort was gauged every hour, ranging from no pain (0) to maximum pain (10).

Vibration data were obtained in real-time using the Vicon Blue Trident® IMUs and uploaded to Vicon Capture.U (Capture.U 1.3, Version 7).

Figure 3

Test setup

Note. The trials were conducted using a rigid original equipment manufacturer truck seat without armrests and an installed aftermarket seat belt. Subjects were allowed to use devices during testing.

A code was implemented for all subject data to maintain subject anonymity. Data were stored on a flash drive in a locked filing cabinet in a locked office in Gullickson Hall at Marshall University.

Data Processing

Glial fibrillary acidic protein and S100B measurements for the serum samples were performed using enzyme-linked immunosorbent assay (ELISA) kits via manufacturer instructions. Biomarker data were retrieved following plasma analysis.

Raw acceleration data from the Vicon Blue Trident® IMUs fixed to the platform, seat, and subjects' head were processed in Matlab (MATLAB R2022b Version 9.13.0). Table 6 defines the variables used in A_{ws} and VDV calculations.

Table 6

Definitions of Variables Used in Vibration Exposure Calculations.

Symbol	Definition
A_{ws}	r.m.s average weighted acceleration wx=1.4; wy=1.4;wz=1.0
$a_w(t)$	frequency-weighted acceleration at time, t
VDV	vibration dosage value
t	Instantaneous time
T	Effective time or duration of the measurement
T_0	Work period
$STHT_{x,y,z}$	Seat-to-head-transmissibility
$a_{x,y,z}$	acceleration

Note. Definitions for variables used in root mean square average weighted vibration and vibration dose value, two measures for vibration exposure.

The root mean square (r.m.s.) average weighted vibration (A_{ws}) was calculated as seen in (1) and compared to the ISO 2361-1 exposure action value (EAV) of 0.5 m/s^2 and an exposure limit value (ELV) of 1.0 m/s^2 for triaxial accelerations (ISO, 1997; Taing, 2020):

$$A_{ws} = \left[\frac{1}{T}\int_0^T a_w^2(t)dt\right]^{\frac{1}{2}} \quad (1)$$

The r.m.s. average weighted vibration (A_{ws}) where $a_w(t)$ is the frequency-weighted acceleration at time, t. T refers to the measurement for duration in seconds (Taing, 2020).

The r.m.s. average weighted acceleration was extrapolated to account for average vibration exposure over a typical work period of 8 hours, where T is the effective time, and T_0 is the work period, as seen in (2) (Filho et al., 2019):

$$A(8) = A_{ws} * \sqrt{\frac{T}{T_0}} \quad (2)$$

The vibration dose value (VDV) was calculated to determine the total vibration experienced at the seat and compared to the ISO 2361-1 EAV of 8.5 $m/s^{1.75}$ and an ELV of 17 $m/s^{1.75}$ for triaxial accelerations (Taing, 2020). Equation (3) can be used to calculate the VDV (Kim et al., 2016; Taing, 2020):

$$VDV = \left[\int_0^T a_w^4(t)dt\right]^{\frac{1}{4}} \quad (3)$$

The vibration dose value can be extrapolated to account for vibration exposure over a typical work period of 8 hours (4):

$$VDV(8) = VDV * \sqrt{\frac{T}{T_0}} \quad (4)$$

The seat-to-head transmissibility (STHT) for each of the three axes was calculated by dividing the cross-spectral density (CPSD) of the seat and head by the auto-spectral density of the seat (Kumar & Saran, 2016). This was done to look at how the frequency transmits:

$$STHT = \frac{CPSD_{S_X H_k}(f)}{CPSD_{S_X S_X}(f)} \quad (5)$$

H = the transfer function for a given frequency, f = hamming window (1-20 Hz)

The seat-to-head transmissibility ($STHT_{x,y,z}$) for each of the three axes was also calculated by taking the average of the acceleration of the head divided by the average of the seat acceleration (Kumar & Saran, 2016). This was done to look at how the amplitude transmits:

$$STHT = \frac{RMS_{H_k}}{RMS_{S_x}} \quad (6)$$

Statistical Analysis

Questionnaire Responses

Descriptive statistics (maximum, mean, and standard deviation) for the Rivermead Post-concussion Questionnaire were conducted for the short-term exposure and long-term exposure groups. Paired samples t-tests were conducted to compare subject RPQ response data for the short-term exposure and long-term exposure groups.

Descriptive statistics (maximum, mean, and standard deviation) for the Discomfort survey were conducted for the short-term exposure and long-term exposure groups. The percent differences compared to baseline discomfort levels were calculated for each hour of vibration exposure. Kruskal Wallis analysis with a Sidak correction method was used to compare discomfort levels between hours of vibration exposure.

Blood Protein Concentrations

Two-way analysis of variance was used to compare GFAP and S100 B levels before, after, and post-testing. Paired samples t-tests were used to compare normalized GFAP and S100B levels after and post-testing. Statistical significance was set a priori at alpha = 0.05.

Acceleration Calculations

These data were calculated for each subject, and then statistical analysis was conducted. Descriptive statistics (maximum, mean, and standard deviation) were calculated for the subjects' head and seat acceleration data.

Two-way mixed ANOVAs with between-subjects factor of vibration exposure duration and within-subjects factor of time were calculated to assess differences in: average resultant head acceleration, maximum resultant head acceleration, average resultant seat acceleration, maximum resultant seat acceleration, average weighted head acceleration, total vibration dose volume at the head, average weighted seat acceleration, and total vibration dose volume at the seat. Both maximum resultant seat acceleration at 0 hours ($W_{11} = 0.796$, $p = 0.008$) and RMS average weighted seat vibration at 0 hours ($W_{11} = 0.835$, $p = 0.027$) showed positive kurtosis. These variables were not transformed as kurtosis would be expected, given the proximity of the seat accelerometer and vibration source. A three-box-length criterion was used to assess the dataset for outliers. A Shapiro-Wilk test was used to determine whether the variables were normally distributed. The homogeneity of variances was assessed using a Levene's test. Levene's test was found to be violated for average resultant seat acceleration at the last recording ($W_{1,19} = 7.687$, $p = 0.012$), which may affect type I error, so results for average resultant seat acceleration should be interpreted with caution. There was homogeneity of covariances ($p > 0.001$) for all variables, as assessed by Box's M test. Seat-to-head-transmissibility was determined by measuring the vibration magnitude at different frequencies. Average resultant STHT and average resultant STHT at distinct frequency peaks for subject groups were then compared using one-way ANOVA.

Chapter 4: Results

Demographics

Thirty-two (32) total subjects volunteered to participate in this study. Fourteen (14) subjects were male and eighteen (18) were female. There were nine (9) control, twelve (12) 1-hour, and eleven (11) 8-hour exposure subjects [Table 7].

Table 7

Subject Demographics

	Control	1-hour	8-hour
Age (years)	44.44 ±12.99	37.50 ± 17.88	25.64 ± 1.26
Height (cm)	168.22 ± 12.35	171.00 ± 9.96	169.73 ± 14.59
Weight (kg)	80.00 ± 14.05	76.08 ± 19.27)	78.18 ± 26.13
Sex M/F	3M/6F	6M/6F	5M/6F

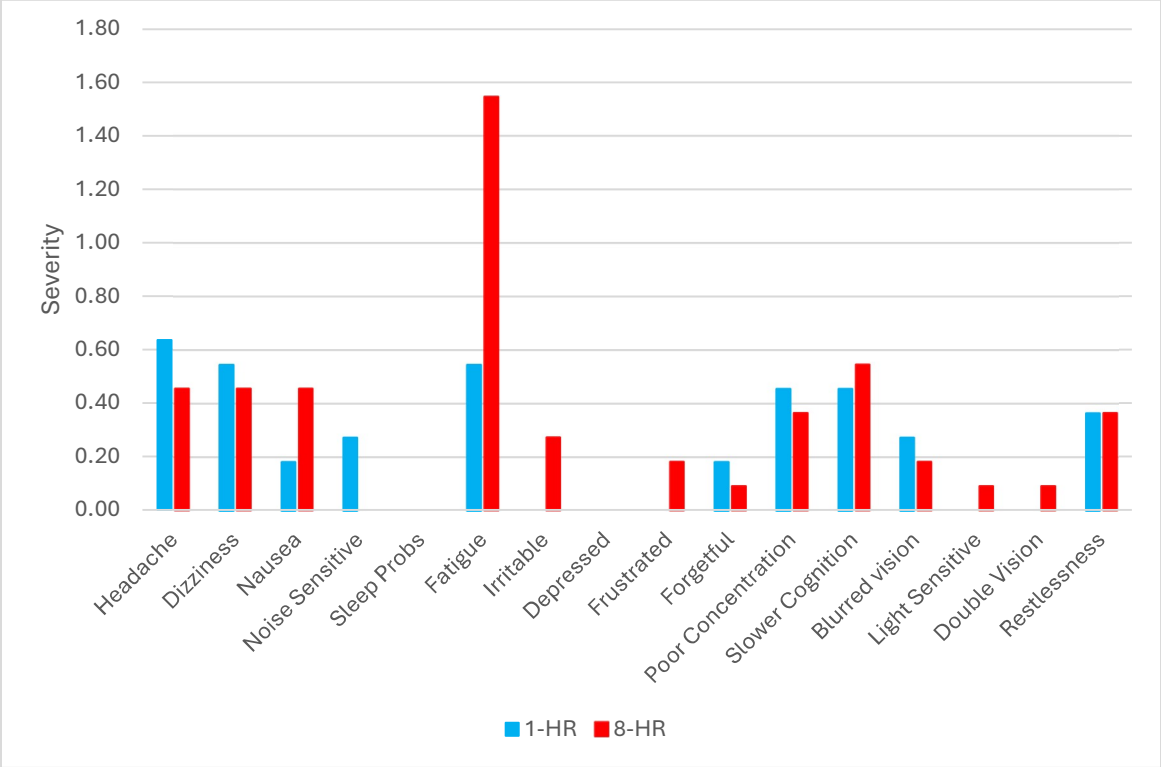
Note. Control subjects had an average body mass index (BMI) of 28.3 kg/m^2, 1-hour exposure subjects had an average BMI of 26.0 kg/m^2, and 8-hour exposure subjects had an average BMI of 27.1 kg/m^2.

Questionnaire Responses

Rivermead Post-concussion Questionnaire

Figure 4

Average Rivermead Post-concussion Questionnaire Responses



Note. The average reported severity score for the reported RPQ symptoms. The average RPQ symptom severity score for overall symptomatology in 1-hour subjects was 3.91 ± 3.73, while the average score for 8-hour subjects was 5.09 ± 4.50.

No significant differences existed in any of the assessed RPQ symptoms between 1-hour and 8-hour vibration exposure subject groups (t= 0.56).

There were no significant differences in average RPQ symptom severity scores for headache symptomatology (1-hour = 0.64 ± 0.81, 8-hour = 0.45 ± 0.52, t= 0.42), nausea (1-hour

= 0.18 ± 0.40, 8-hour = 0.45 ± 0.69, t= 0.33) or noise sensitivity (1-hour = 0.27 ± 0.65, 8-hour = 0.00 ± 0.00, t= 0.31) in the 1-hour and 8-hour vibration exposure groups.

There was a significant difference in average RPQ symptom severity scores for fatigue (1-hour = 0.55 ± 0.69, 8-hour = 1.55 ± 1.44, t = 0.049) but not for restlessness (1-hour = 0.36 ± 0.81, 8-hour = 0.36 ± 0.92, t= 0.93) in the 1-hour and 8-hour vibration exposure groups.

There were no significant differences in average RPQ symptom severity scores for irritability (1-hour = 0.00 ± 0.00, 8-hour = 0.27 ± 0.47, t= 0.08) or frustration (1-hour = 0.00 ± 0.00, 8-hour = 0.18 ± 0.40, t= 0.17) in the 1-hour and 8-hour vibration exposure groups.

There were no significant differences in average RPQ symptom severity scores for forgetfulness (1-hour = 0.18 ± 0.40, 8-hour = 0.09 ± 0.30, t= 0.5), decreased concentration (1-hour = 0.45 ± 0.69, 8-hour = 0.36 ± 0.92, t= 0.71), or decreased cognition (1-hour = 0.45 ± 0.93, 8-hour = 0.55 ± 0.69, t= 0.90) in the 1-hour and 8-hour vibration exposure groups.

There were no significant differences in average RPQ symptom severity scores for blurred vision (1-hour = 0.27 ± 0.65, 8-hour = 0.18 ± 0.60, t= 0.68), light sensitivity (1-hour = 0.00 ± 0.00, 8-hour = 0.09 ± 0.30, t= 0.35), double vision (1-hour = 0.00 ± 0.00, 8-hour = 0.09 ± 0.30, t= 0.35), or dizziness (1-hour = 0.55 ± 0.93, 8-hour = 0.45 ± 0.93, t= 0.91) in 1-hour and 8-hour vibration exposure groups.

Neither of the 1-hour or 8-hour groups experienced symptoms of insomnia or depression.

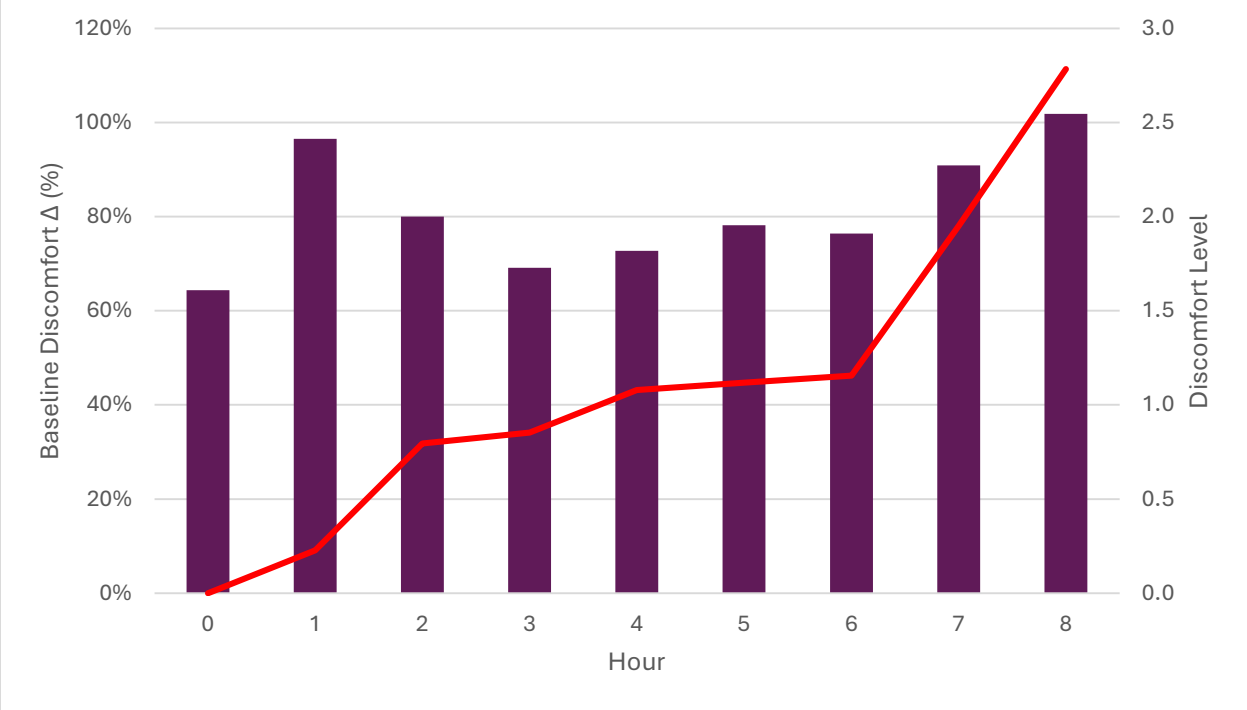
Discomfort Survey

Physical discomfort increased for subjects as the duration of the vibration exposure increased. The average discomfort levels across exposure went as follows: baseline = 1.61 ± 1.23, 1-hour = 2.41 ± 2.17, 2-hour = 2.00 ± 1.47, 3-hour = 1.73 ± 1.10, 4-hour = 1.82 ± 1.08, 5-hour = 1.95 ± 1.46, 6-hour = 1.91 ± 1.38, 7-hour = 2.27 ± 1.49, and 8-hour = 2.55 ± 1.57 [Figure

4]. The average percent increase in discomfort level at each hour of exposure, relative to baseline, went as follows: 1-hour = 9%, 2-hour = 32%, 3-hour = 34%, 4-hour = 43%, 5-hour = 45%, 6-hour = 46%, 7-hour = 78%, and 8-hour = 111% [Figure 5].

Figure 5

Discomfort Level Across Hours of Vibration Exposure



Note. Differences in discomfort were not significant between hours 1-8 of vibration exposure: 1-hour → 2-hour ($\chi^2 = 0.226$, $p = .64$), 2-hour → 3-hour ($\chi^2 = 0.083$, $p = .77$), 3-hour → 4-hour ($\chi^2 = 0.088$, $p = .77$), 4-hour → 5-hour ($\chi^2 = 0.001$, $p = .97$), 5-hour → 6-hour ($\chi^2 = 0.001$, $p = .97$), 6-hour → 7-hour ($\chi^2 = 0.32$, $p = .57$), 7-hour → 8-hour ($\chi^2 = 0.142$, $p = .71$).

However, the change in discomfort across hours of vibration exposure was not seen overall as significant ($\chi^2(8) = 5.19$, $p = .737$). The difference between baseline and 8-hour discomfort was significant ($p = 0.04$), while the differences between baseline and 1-hour discomfort ($p = 0.17$) and 1-hour and 8-hour discomfort ($p = .45$) were not significant.

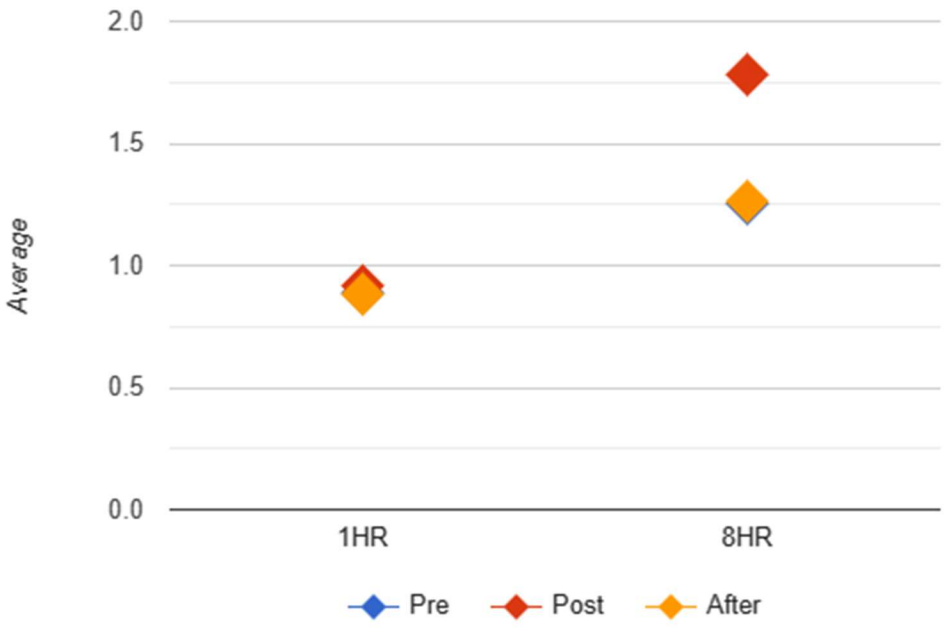
Blood Protein Concentrations

Glial Fibrillary Acidic Protein

Blood concentration levels of GFAP did not significantly change following vibration exposure for either the 1-hour or 8-hour groups [Figure 6]. Glial fibrillary acidic protein concentration levels remained similar for 1-hour subjects before, after, and 24-hour post-testing (Before = 0.89 ± 0.56 ng/mL, After = 0.92 ± 0.43 ng/mL, 24-hour Post = 0.88 ± 0.41 ng/mL, $F_{1,59} = 2.95$, $p = 0.09$, partial $\eta^2 = 0.048$). Similarly, GFAP levels remained similar for 8-hour subjects before, after, and 24-hour post-testing (Before = 1.25 ± 0.64 ng/mL, After = 1.78 ± 2.71 ng/mL, 24-hour Post = 1.26 ± 1.02 ng/mL, $F_{2,59} = 0.40$, $p = 0.68$, partial $\eta^2 = 0.013$).

Figure 6

Glial Fibrillary Acidic Protein Results



Note. There were no significant differences in GFAP concentrations between 1-hour and 8-hour subjects ($F_{2,59} = 0.24$, $p = 0.79$, partial $\eta^2 = 0.008$).

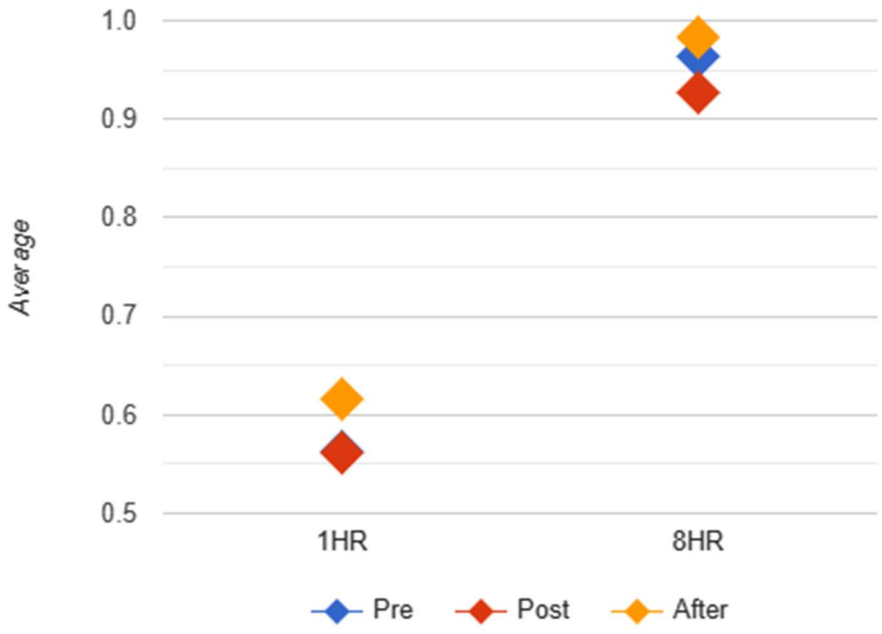
S100 Calcium-Binding Protein B

There were no significant differences in S100B concentrations measured after- and 24-hour post-testing for either 1-hour subjects (t = 0.86) or 8-hour subjects (t = 0.46) [Figure 7].

The 1-hour exposure group experienced a statistically significant change in S100B concentration (Before = 0.56 ± 0.45 ng/mL, After = 0.56 ± 0.48 ng/mL, 24-hour Post = 0.62 ± 0.45 ng/mL, $F_{1,62} = 10.66$, $p < 0.05$, partial $\eta^2 = 0.15$), but this change was not viewed as meaningful by the researchers. Blood concentration levels of S100B did not significantly change following vibration exposure for the 8-hour group (Before = 0.96 ± 0.5 ng/mL, After = 0.93 ± 0.48 ng/mL, 24-hour Post = 0.98 ± 0.49 ng/mL, $F_{2,62} = 0.06$, $p = 0.94$, partial $\eta^2 = 0.002$).

Figure 7

S100 Calcium Binding Protein B Results

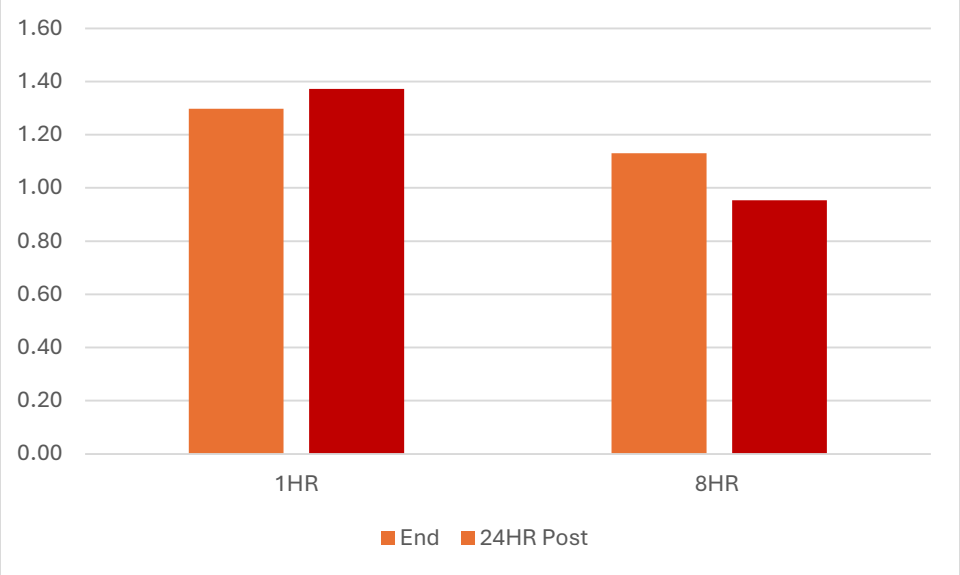


Note. There were no significant differences in S100B levels between 1-hour and 8-hour subjects ($F_{2,62} = 0.03$, $p = 0.97$, partial $\eta^2 = 0.0009$).

There were no significant differences in normalized GFAP concentrations measured after- and 24-hour post-testing for either 1-hour subjects (t = 0.86) or 8-hour subjects (t = 0.46) [Figure 8].

Figure 8

Glial Fibrillary Acidic Protein Normalized Results

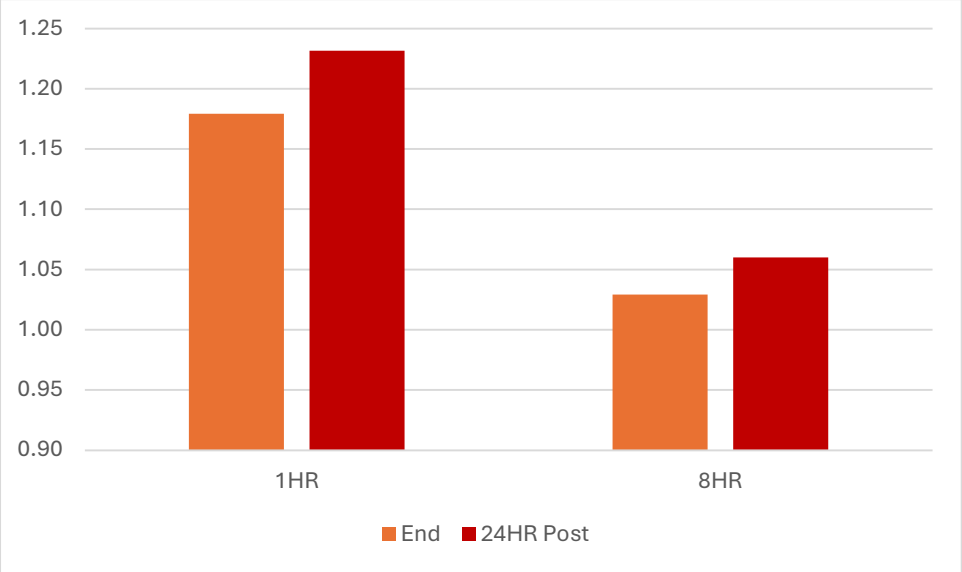


Note. There were no significant differences in GFAP concentrations between 1-hour and 8-hour subjects for blood samples collected after testing (t = 0.63) or 24-hour post-testing (t = 0.25).

There were no significant differences in normalized S100B concentrations measured after- and 24-hour post-testing for either 1-hour subjects (t = 0.89) or 8-hour subjects (t = 0.81) [Figure 9].

Figure 9

S100 Calcium Binding Protein B Normalized Results



Note. There were no significant differences in S100B concentrations between 1-hour and 8-hour subjects for blood samples collected after testing (t = 0.56) or 24-hour post-testing (t = 0.59).

Acceleration Calculations

There was no statistically significant interaction between exposure duration group and time for any study variable: average resultant head acceleration ($F_{1,19} = 0.164$, $p = 0.690$, partial $\eta^2 = 0.009$), maximum resultant head acceleration ($F_{1,19} = 0.017$, $p = 0.896$, partial $\eta^2 = 0.001$), average resultant seat acceleration ($F_{1,19} = 0.771$, $p = 0.391$, partial $\eta^2 = 0.039$), maximum resultant seat acceleration ($F_{1,19} = 1.013$, $p = 0.327$, partial $\eta^2 = 0.051$), average weighted head acceleration ($F_{1,19} = 1.188$, $p = 0.289$, partial $\eta^2 = 0.059$), total vibration dose volume at the head ($F_{1,19} = 0.033$, $p = 0.858$, partial $\eta^2 = 0.002$), average weighted seat acceleration ($F_{1,19} = 0.014$, $p = 0.908$, partial $\eta^2 = 0.001$), and total vibration dose volume at the seat ($F_{1,19} = 0.060$, $p = 0.809$, partial $\eta^2 = 0.003$). Given no significant interactions, follow-up analyses were conducted for main effects.

Resultant Head Acceleration

Average Resultant Head Acceleration

Average resultant head acceleration was significantly greater at the end of a session than at the beginning of a session (beginning = 9.809 m/s^2, end = 9.862 m/s^2, $F_{1,19}$ = 14.689, p = 0.001, partial η^2 = 0.436). Average resultant head acceleration was not significantly different between the 1-hour group and the 8-hour group (1-hour = 9.827 m/s^2, 8-hour = 9.844 m/s^2, $F_{1,19}$ = 0.234, p = 0.634, partial η^2 = 0.012).

Maximum Resultant Head Acceleration

Maximum resultant head acceleration was not significantly different at the end of a session than at the beginning of a session (beginning = 14.665 m/s^2, end = 14.679 m/s^2, $F_{1,19}$ = 0.008, p = 0.929, partial η^2 = 0.000). Maximum resultant head acceleration was not significantly different between the 1-hour group and the 8-hour group (1-hour = 14.576 m/s^2, 8-hour = 14.768 m/s^2, $F_{1,19}$ = 0.644, p = 0.432, partial η^2 = 0.033).

Resultant Seat Acceleration

Average Resultant Seat Acceleration

Average resultant seat acceleration was significantly greater at the end of a session than at the beginning of a session (beginning = 9.814 m/s^2, end = 9.817 m/s^2, $F_{1,19}$ = 6.136, p = 0.023, partial η^2 = 0.244). Average resultant seat acceleration was not significantly different between the 1-hour group and the 8-hour group (1-hour = 9.815 m/s^2, 8-hour = 9.816 m/s^2, $F_{1,19}$ = 0.118, p = 0.735, partial η^2 = 0.006).

Maximum Resultant Seat Acceleration

Maximum resultant seat acceleration was not significantly different at the end of a session than at the beginning of a session (beginning = 13.160 m/s^2, end = 13.228 m/s^2, $F_{1,19}$ =

0.361, $p = 0.555$, partial $\eta^2 = 0.019$). Maximum resultant seat acceleration was not significantly different between the 1-hour group and the 8-hour group (1-hour = 13.135 m/s^2, 8-hour = 13.253 m/s^2, $F_{1,19} = 1.893$, $p = 0.185$, partial $\eta^2 = 0.091$).

Root Mean Square Average Weighted Acceleration

Weighted Head Acceleration

Average weighted head acceleration was not significantly different at the end of a session than at the beginning of a session (beginning = 1.509 m/s^2, end = 1.573 m/s^2, $F_{1,19} = 2.644$, $p = 0.120$, partial $\eta^2 = 0.122$). Average weighted head acceleration was not significantly different between the 1-hour group and the 8-hour group (1-hour = 1.558 m/s^2, 8-hour = 1.525 m/s^2, $F_{1,19} = 0.341$, $p = 0.566$, partial $\eta^2 = 0.018$).

Weighted Seat Acceleration

Average weighted seat acceleration was not significantly different at the end of a session than at the beginning of a session (beginning = 0.975 m/s^2, end = 0.971 m/s^2, $F_{1,19} = 0.269$, $p = 0.610$, partial $\eta^2 = 0.014$). Average weighted seat acceleration was not significantly different between the 1-hour group and the 8-hour group (1-hour = 0.969 m/s^2, 8-hour = 0.977 m/s^2, $F_{1,19} = 1.317$, $p = 0.265$, partial $\eta^2 = 0.065$).

Vibration Dose Value

Vibration Dose Value at the Head

Total vibration dose volume at the head was not significantly different at the end of a session than at the beginning of a session (beginning = 8.396 m/s$^{1.75}$, end = 8.729 m/s$^{1.75}$, $F_{1,19} = 1.301$, $p = 0.268$, partial $\eta^2 = 0.064$). Total vibration dose volume at the head was not significantly different between the 1-hour group and the 8-hour group (1-hour = 8.531 m/s$^{1.75}$, 8-hour = 8.593 m/s$^{1.75}$, $F_{1,19} = 0.041$, $p = 0.843$, partial $\eta^2 = 0.002$).

Vibration Dose Value at the Seat

Total vibration dose volume at the seat was not significantly different at the end of a session than at the beginning of a session (beginning = 8.983 $m/s^{1.75}$, end = 8.754 $m/s^{1.75}$, $F_{1,19}$ = 1.606, p = 0.220, partial η^2 = 0.078). Total vibration dose volume at the seat was not significantly different between the 1-hour group and the 8-hour group (1-hour = 8.761 $m/s^{1.75}$, 8-hour = 8.976 $m/s^{1.75}$, $F_{1,19}$ = 2.067, p = 0.167, partial η^2 = 0.098).

Seat-to-Head Transmissibility

Average resultant seat-to-head transmissibility was not significantly different across time (beginning = 2.03, 1-hour = 2.075, 8-hour = 2.086, $F_{2,57}$ = 0.16, p = 0.852, partial η^2 = 0.0056). Two distinct frequency peaks were found for STHT at 3 Hz and 14 Hz for hours 0, 1, and 8 of vibration exposure. The peak at 3 Hz was insignificantly higher after the first hour of vibration exposure compared to the beginning and eighth hours of exposure (beginning = 1.84, 1-hour = 1.92, 8-hour = 1.84, $F_{2,41}$ = 0.680, p = 0.512, partial η^2 = 0.032). The peak at 14 Hz was insignificantly higher after the eighth hour of vibration exposure compared to the beginning and first hours of exposure (beginning = 2.42, 1-hour = 2.41, 8-hour = 2.50, $F_{2,41}$ = 0.529, p = 0.593, partial η^2 = 0.025).

Figure 10

Seat-to-Head Transmissibility by Frequency Band at Baseline

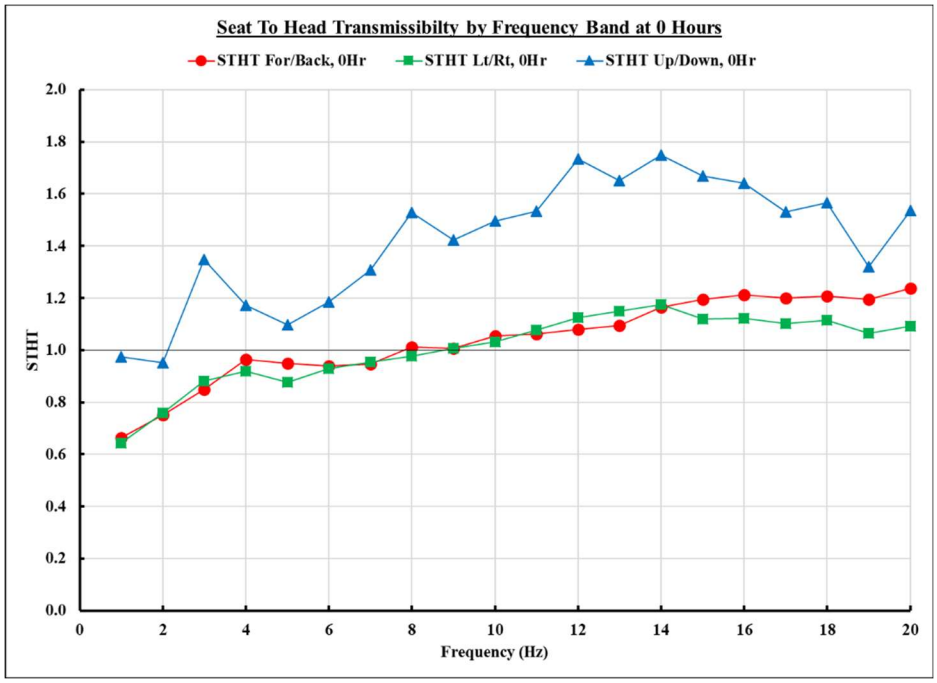


Figure 11

Seat-to-Head Transmissibility by Frequency Band at 1-hour

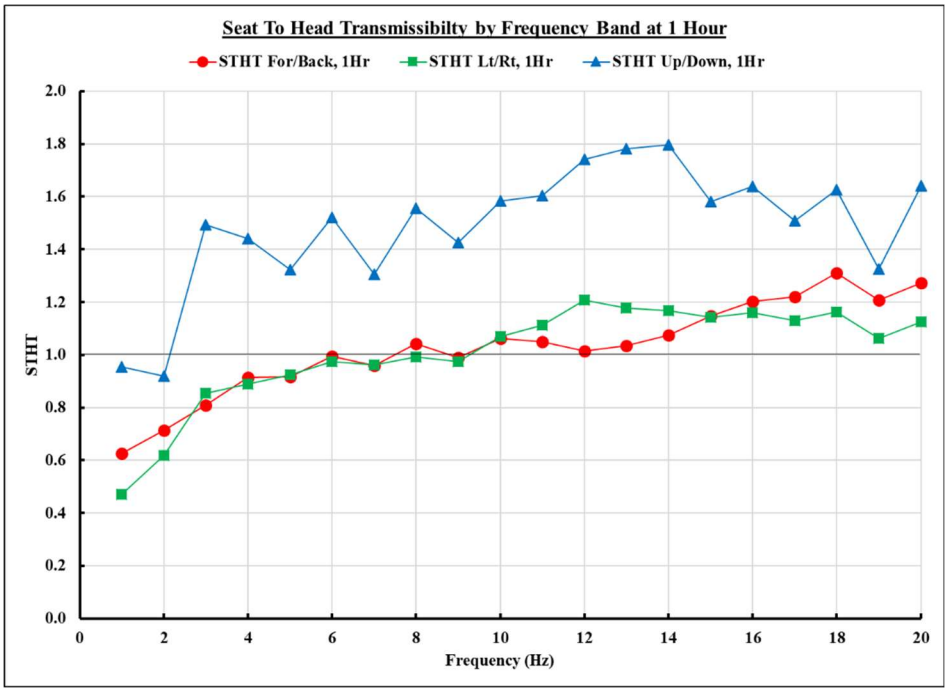
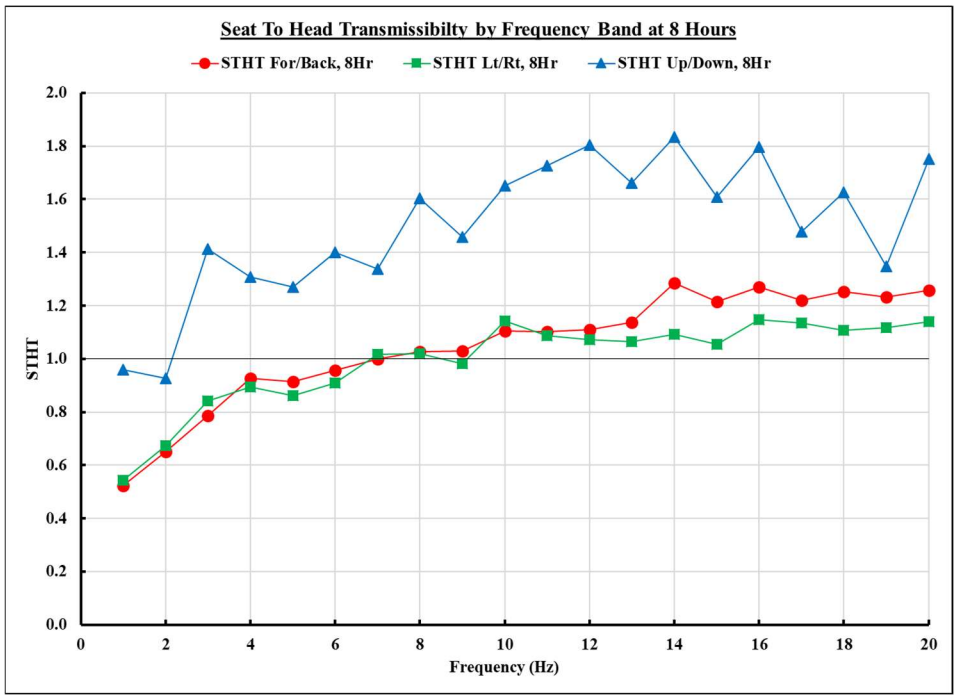


Figure 12

Seat-to-head transmissibility by frequency band at 8-hour



Chapter 5: Discussion

This study aimed to determine the effect of prolonged WBV exposure on GFAP and S100B protein concentrations, STHT, and TBI symptom response. It was believed that WBV exposure would trigger an elevation in protein concentrations, increase vibration at the head due to postural muscle fatigue, and lead to a TBI-like symptom response.

Questionnaire Responses

There was a significant difference between baseline discomfort and discomfort for the 8-hour vibration exposure group; however, there was no significant difference between baseline discomfort and discomfort for the 1-hour vibration exposure group. The difference in discomfort between baseline and after 8 hours of vibration exposure was as expected. However, the lack of difference in discomfort between the 1-hour and 8-hour exposure groups was unexpected, despite the difference in discomfort between baseline and 8 hours of exposure. It is possible that the lack of difference between the 1-hour and 8-hour exposure groups was due to the small number of subjects that experienced vibration exposure beyond 1 hour. Fatigue began to increase at a greater rate beginning in hour six and maintained the increased rate of discomfort until testing ended at hour eight. The increased rate of discomfort raises concern about further exposure, such as for semi-truck drivers who are driving for the Federal Motor Carrier Safety Administration's maximum work period of 11 hours per day and 70 hours per week. Mansfield et al. (2014) found that physical discomfort increases with increased sitting time and is accelerated by WBV exposure. Increases in experienced discomfort across exposure expectedly coincided with increased fatigue following WBV exposure.

There was no significant difference in the RPQ symptoms experienced by the 8-hour exposure group compared to the 1-hour exposure group outside of fatigue, indicating that

exposure duration did not influence symptomatology. Average total RPQ symptomatology scores were below the injury threshold average total symptom scores reported by Zeldovich et al. (2022). Despite being below the injury threshold, fatigue was significantly different between the 1-hour and 8-hour exposure groups. Additionally, irritability was close enough to statistically significant to indicate that a larger sample size might show a difference over time. Prior studies have theorized that the fatigue motorists experience after an extended period of driving could be due to brain dysfunction (Grewal et al., 2017; Yan, Zhang, Agresti, Yan, et al., 2015). Azizan et al. (2018) determined that fatigue increased as vibration amplitude and exposure duration increased. However, this was not supported by this study, as no physiological effect on the brain from WBV exposure was indicated. The significant fatigue and discomfort responses with prolonged exposure could, in part, be due to the sedentary nature of the task. Subjects potentially experienced discomfort from constant postural muscle activation, as well as inactive glutes, causing the hip flexors to tighten and anteriorly rotate the pelvis, leading to back pain. Fatigue could stem from boredom or the rhythmic rocking at low-frequency oscillations (Zhang et al., 2024). Future research could be conducted to test subject fatigue objectively. Future research could also consider the incorporation of cognitive testing pre- and post-vibration exposure.

Blood Protein Concentrations

Vibration exposure did not elicit a change in GFAP or S100B levels for either the 1-hour or 8-hour groups. Glial fibrillary acidic protein concentration levels remained similar before, after, and 24-hour post-testing for 1-hour (Before = 0.89 ± 0.56 ng/mL, After = 0.92 ± 0.43 ng/mL, 24-hour Post = 0.88 ± 0.41 ng/mL) and 8-hour (Before = 1.25 ± 0.64 ng/mL, After = 1.78 ± 2.71 ng/mL, 24-hour Post = 1.26 ± 1.02 ng/mL) subjects. There is no injury threshold value for GFAP concentration levels, but prior research has found that GFAP levels can range from 0.008 to

10.01 ng/mL, depending on injury severity (Mahan et al., 2019; Papa et al., 2016). The witnessed GFAP levels fall within this large, reported range.

S100B concentration levels remained similar before, after, and 24-hour post-testing for 1-hour (Before = 0.56 ± 0.45 ng/mL, After = 0.56 ± 0.48 ng/mL, 24-hour Post = 0.62 ± 0.45 ng/mL) and 8-hour (Before = 0.96 ± 0.5 ng/mL, After = 0.93 ± 0.48 ng/mL, 24-hour Post = 0.98 ± 0.49 ng/mL) subjects. The normal injury threshold for S100B is 0.12 ng/ml (Janigro et al., 2022). Prior research has found that TBI patients can experience a peak concentration of 0.18 ng/ml (Kellermann et al., 2016). The reported injury threshold and injury values are notably lower than the witnessed baseline S100B levels for this study. The significantly greater values witnessed in this study are potentially due to the ELISA kit used. Therefore, these values should not be used in comparison with other research values; instead, they should be used to assess trends across sampling within this study.

The lack of significant change in GFAP levels could be due to its sensitivity to low-magnitude head accelerations (Joseph et al., 2019). However, S100B is more sensitive to low-magnitude head accelerations, and no significant differences in protein levels were detected (Kawata et al., 2016). Due to this, it is likely that the acceleration experienced was not great enough to cause an inflammatory response.

While the experienced individual bouts of vibration exposure did not lead to a pathophysiological adaptation, several studies have indicated that the cumulative effect of daily exposure may cause neurophysiological damage. Dubayle et al. (2020) theorized that duration period was of greater significance than vibration intensity regarding cerebral injury. This theory is supported by Yan, Zhang, Agresti, LoGiudice, et al. (2015), who determined that rats exposed to repetitive bouts of whole-body vibration did not sustain significant neurological injury early

on in exposure, but the cumulative effects of exposure over time led to more harmful injury, such as neuronal damage and death. Additionally, Yan, Zhang, Agresti, LoGiudice, et al. (2015) theorized that commercial motor vehicle operators' daily whole-body vibration exposure and subsequent rest mimics that of ischemic reperfusion injury. Subsequent research by Yan, Zhang, Agresti, Yan, et al. (2015) found that rats exposed to two months of whole-body vibration experienced vasoconstriction of cerebral vasculature. Grewal et al. (2017) also found that cerebral capillaries remained intact early on in exposure; however, capillary damage occurred as vibration exposure accumulated. Repetitive, prolonged WBV exposure may elicit similar disorders in commercial motorists and would need to be assessed over a longer experimental period. Future research may consider including complementary testing, such as computerized tomography (CT), which could be used with blood biomarker testing to better understand the effects of WBV on the brain. Additionally, future research may consider changing the study design to a cohort study to see how vibration exposure affects the brain over a longer duration.

Acceleration Calculations

Vibration exposure, between and within exposure duration groups did not have a notable effect on experienced head acceleration. Follow-up analysis did primarily support this, except regarding average resultant head acceleration. Vibration exposure led to increased average resultant head acceleration levels at the end of exposure compared to the beginning. However, the difference between exposure groups was statistically significant by 0.053 m/s^2, which is of no practical importance due to the marginal difference.

Maximum resultant head acceleration was not significantly different at the end compared to the beginning of the sessions, nor was it significantly different between 1-hour and 8-hour groups. The similarities observed in maximum resultant head acceleration indicate that while

head acceleration trended to increase across exposure, cervical stability did not decrease significantly. The maintenance of cervical stability could be due to the sampled vibration profile lacking "shock" events, as the maximum acceleration experienced was 1.5 g's. Greater whole-body vibration exposure, stemming from a worse road surface, could lead to shock events that increase peak head acceleration and VDV. Additionally, the lack of shock events could be attributed to the utilization of a uniaxial vibration table for testing. The restriction of motion to the vertical axis prevented rapid acceleration exposure from whiplash (sudden forward-backward or side-to-side motion) stemming from braking or turning. Hynes (2008) found that horizontal and vertical head accelerations were similar for mild vibration exposure, but horizontal head acceleration was significantly greater for moderate vibration exposure, showing that peak acceleration is dependent on the direction of the applied force.

Average resultant head acceleration was significantly different between exposure groups, but A_{ws} acceleration was similar. The differences between acceleration measures could explain the difference in outcomes. Average resultant head acceleration was the resultant of the acceleration averaged over the sampling duration, while for A_{ws}, each input signal was weighted by an assigned multiplier due to direction and frequency. The root-mean-square was taken for these weighted signals. While the average resultant acceleration may have changed, accelerations at frequencies of greater weight may not have.

The values of this study (1-hour = 1.558 m/s^2, 8-hour = 1.525 m/s^2) were higher than some prior studies that looked at A_{ws} from heavy vehicle operation (0.39-0.43 m/s^2) (Johnson et al., 2015; Kumar et al., 2021) but were not far exceeding other reported data for heavy trucks or agricultural vehicles with reported peak A_{ws} of 1.22 and 1.88 m/s^2, respectively (Filho et al., 2019; Kociolek et al., 2018). The vibration profile was sampled from a 26' leaf spring box truck

utilizing 75% of its 26,000 lb. payload capacity. The size and weight of the truck, coupled with its installed rigid seat, could potentially explain why the A_{ws} were on the higher end for heavy vehicle operation. These excessive values could highlight injury risks associated with occupations such as movers and large-scale delivery drivers.

Vibration dose value, like max resultant acceleration levels, did not significantly change throughout vibration exposure. This was potentially due to the lack of "shock" events from the sampled vibration profile, as well as postural stability not decreasing to the point that the back and head were vulnerable to higher acceleration levels. Vibration dose value is a measure that is more sensitive to peaks due to its use of the fourth power instead of the second, as for $A_{ws,}$ for acceleration time history. The roadway on which the vibration profile was sampled could have contributed to the lack of shock events. The vibration profile was sampled over an asphalt highway between Mocksville, NC, and Blacksburg, VA, for one hour. The smoother surface of the highway potentially does not represent the type of exposure that an individual may see over prolonged vehicle operation, such as from a residential neighborhood or job site. Additionally, the use of a vertical axis vibration table does not incorporate the vibration magnitude of the x- and y-directions. Vibration dose values were similar to prior studies that examined VDV from heavy vehicles (Du et al., 2018; Johnson et al., 2018; Kumar et al., 2021).

Bovenzi (2009) found that public utility and transport vehicles did not exceed the EAV or ELV for A_{ws} and VDV; however, these findings were in regard to musculoskeletal injury risk when assessing for low-back pain. This study found that A_{ws} and VDV for a similar vehicle exceed the EAV, and in the case of A_{ws}, the ELV for accelerations at the head. The increased acceleration experienced at the head, exceeding the EAV and ELV, furthers the need for established thresholds for brain injury risk.

While seat-to-head transmissibility remained similar across time, there were noticeable peaks at 3 Hz (beginning = 1.84, 1-hour = 1.92, 8-hour = 1.84) and 14 Hz (beginning = 2.42, 1-hour = 2.41, 8-hour = 2.50). The STHT peaks witnessed in this study are similar to what has been found in prior research (Smith, 1994; Wang et al., 2006). Smith (1994) reported that the lower frequency resonant peak was attributable to the motion of the upper torso and head-neck complex; however, this shifted to the increased motion of the lower torso at the higher frequency peak.

Limitations

The first limitation of this study is that the exposure duration was significantly less compared to similar types of studies, which could have contributed to a lack of pathophysiological injury. The shortened exposure duration was due to challenges with using human subjects as opposed to rats. The average life span of a rat is three years (Yan, Zhang, Agresti, Yan, et al., 2015). Therefore, the couple weeks to months of exposure used to test rats is equivalent to one to four and a half years for a human (Yan, Zhang, Agresti, Yan, et al., 2015). Due to study constraints, exposing a human subject to whole-body vibration exposure for that period was not feasible. Secondly, vibration testing was limited to the vertical axis, which may not accurately represent the motion experienced by motor vehicle operators who are accelerating, braking, or turning while driving. Thirdly, subjects may be exposed to varying levels of road-induced vibration following testing, which may affect blood protein concentration sampling 24 hours after testing. Restricting subject vehicle operation following testing was not feasible as subjects could not remain at the facility following vibration exposure. Fourthly, the inability to physically measure the brain's acceleration within the cranium's fluid barrier is another potential limitation. However, it is still possible to reasonably predict the vibration's effect on the brain.

And finally, the small sample size may not accurately represent the brain's WBV response. There is a likelihood that a larger sample size would have improved the statistical accuracy of subject symptomatology. However, it is unlikely that increasing the sample size would have affected blood protein or acceleration results.

Societal Benefits

This study furthers the knowledge of commercial motor vehicle operators and manufacturers as it demonstrates that individual bouts of road-induced vibration exposure likely do not cause neurological injury. Establishing human subject protein response levels to prolonged whole-body vibration is an important step toward determining if WBV exposure from vehicle operation negatively impacts a motorist's health or ability to operate the vehicle. Gauging subjects' head acceleration over the exposure period shows how a motorist's postural stability potentially decreases over time, which could increase the risk of injury. Assessing subject symptomatology shows that there is the potential that fatigue from vibration exposure increases over time, which could increase the risk of traffic accidents. Future research can be done to find the effects of repetitive exposure, over months and years, to long bouts of road-induced whole-body vibrations.

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Appendix A: IRB Approval Letter

MARSHALL UNIVERSITY
www.marshall.edu

Office of Research Integrity
Institutional Review Board
One John Marshall Drive
Huntington, WV 25755

FWA 00002704

IRB1 #00002205
IRB2 #00003206

February 17, 2022

Suzanne Konz, Ph.D.
Biomechanics

RE: IRBNet ID# 1784850-1
At: Marshall University Institutional Review Board #1 (Medical)

Dear Dr. Konz:

Protocol Title:	[1784850-1] Inflammatory protein elicitation in response to whole-body vibration exposure	
Site Location:	MU	
Submission Type:	New Project	APPROVED
Review Type:	Expedited Review	

In accordance with 45CFR46.110(a)(2,4&7), the above study was granted Expedited approval today by the Marshall University Institutional Review Board #1 (Medical) Chair. An annual update will be required on February 17, 2023 for administrative review and approval. The update must include the Annual Update Form and current educational certificates for all investigators involved in the study. All amendments must be submitted for approval by the IRB Chair prior to implementation and a closure request is required upon completion of the study.

If you have any questions, please contact the Marshall University Institutional Review Board #1 (Medical) Coordinator Anna Robinson at (304) 696-2477 or robinsonn1@marshall.edu. Please include your study title and reference number in all correspondence with this office.

Sincerely,

Bruce F. Day, ThD, CIP
Director, Office of Research Integrity

Appendix B: Figure Approval

Re: Data for Fig. 2 F & G

Jean-Luc Morel <jean-luc.morel@u-bordeaux.fr>
Wed 1/27/2021 11:39 AM
To:Miller, Nick <miller1070@live.marshall.edu>

Hello Nick,

If you just use the figures of our papers in your work, it is OK and if you want some other details about it don't hesitate to ask me. It will be nice to interact with you.

if you have a report to write on this subject and you want a proofreading/reviewing from me, I will do my best, you will just have to give me a few days of delay (depending on its size)

You can also read the paper of Laurence Vico's group about effects on bones.

"bon courage" as we said in France

JLuc

Le 27/01/2021 à 18:02, Miller, Nick a écrit :

> Hello Dr. Morel,
>
> My study is still in the early stages, but I am looking at the effects of prolonged WBV exposure on the brain. Findings from your study, as well as some others related to the topic, have led me to believe that prolonged exposure to vibration could lead to harmful pathophysiological adaptions over time.
>
> I am referencing your study in my literature review and would like to include the IgG extravasation means and standard deviations for your five vibration groups. I apologize for any confusion with my original message. Please let me know if you need any more information.
>
> Thank you,
> Nick
>
> Sent from Mail for Windows 10

> **From:** Jean-Luc Morel
> **Sent:** Wednesday, January 27, 2021 8:46 AM
> **To:** Miller, Nick
> **Subject:** Re: Data for Fig. 2 F & G
>
> Hi Nicholas,
>
> Befonre sending you the raw data, I need to know what do want to do with them. What is the tpoci of the work and your hypothesis.

I am completely ready to collaborate with you but I still need to know more about the project.

Thank you for your reply.

Jean-Luc

Le 25/01/2021 à 05:24, Nicholas Miller a écrit :

> Hello,
>
> My name is Nicholas Miller and I am a graduate student at Marshall University in Huntington, WV, USA. I am working on my graduate thesis on WBV and am referencing your study in my literature review. If possible, could you send me the data used for Figure 2F and 2G?
>
> Thank you,
> Nicholas

--
Jean-Luc MOREL
Institut des Maladies Neurodégénératives
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Appendix C: Memorandum

VIRGINIA TECH

Division of Scholarly Integrity and Research Compliance
Institutional Review Board
North End Center, Suite 4120 (MC 0497)
300 Turner Street NW
Blacksburg, Virginia 24061
540/231-3732
irb@vt.edu
http://www.research.vt.edu/sirc/hrpp

MEMORANDUM

DATE: October 29, 2021

TO: Laszlo Horvath

FROM: Virginia Tech Institutional Review Board (FWA00000572)

PROTOCOL TITLE: Effect of long term vibration on human health

IRB NUMBER: **21-939**

The IRB determined that the proposed activity is research involving human subjects as defined within the Federal Policy for the Protections of Human Subjects, but Virginia Tech is not engaged in the research.

IRB review and approval by Virginia Tech is not required. This determination applies only to the activities described in the IRB submission and does not apply should any changes be made. If changes are made and there are questions about whether these activities are research involving human subjects in which the organization is engaged, please submit a new request to the IRB for a determination.

SPECIAL INSTRUCTIONS:

This activity,conducted by Marshall University, does meet the definition of human subjects research as defined within the Federal Policy for the Protections of Human Subjects. However, Virginia Tech will not be engaged in activities involving human subjects or biospecimens. Virginia Tech will be permitting use of its facilities for intervention or interaction with Human Subjects by investigators from another organization. Per determination submission: "We will assisting Marshall University with this project but VT does not take part of the part of the study that involves the human subjects and biospecimen collection. We will collect vibration data from a Penske truck and setup a vibration table in the lab to simulated the measured vibrations. The student from Marshall will operate the table and conduct any other part of the study. We will help them with the description of the methods pertaining for the vibration test in their publication but will not ever see the collected data."

Appendix D: Informed Consent

Informed Consent to Participate in a Research Study
Inflammatory protein elicitation in response to whole-body vibration exposure

Suzanne Konz, PhD, ATC, CSCS, Principal Investigator
Nicholas Miller, Co-Investigator

Introduction

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You may or may not receive any benefit from being part of the study. There may also be risks associated with being part of research studies. If there are any risks involved in this study, then they will be described in this consent. Your participation is voluntary. Please take your time to make your decision and ask your study investigator or research staff to explain any words or information that you do not understand.

Why Is This Study Being Done?

The purposes of this study are:

4. to determine if prolonged exposure to whole-body vibration will elicit a change in stress-released protein concentrations in the blood,
5. to determine the differences between head acceleration and seat acceleration over time, and
6. to determine if whole-body vibration exposure leads to symptom responses similar to traumatic brain injuries.

How Many People Will Take Part In The Study?

Approximately 20-50 individuals from Virginia Tech University and the surrounding Blacksburg, VA community will participate in this study. A total of 50 subjects are the most that would be able to enter the study.

What Is Involved In This Research Study?

- Block randomization will be used to group you into either the control (no exposure), short-term exposure (1-hour exposure), or long-term exposure (8-hour exposure) group. Block sizes will be hidden from the executer and randomly mixed.
- You will be asked to complete two (2) questionnaires, give three (3) blood samples and sit in a chair attached to a vibrating platform for a set duration of either no time, thirty (30) minutes, or one (1) hour.

Before the study begins,

- You will complete a modified whole-body vibration health screening questionnaire to determine your eligibility to participate in the study.
- You will then read and sign the consent form if you are willing to participate in the study.
- The study investigator will answer any questions you have regarding the consent form.

During the study,

- You will be randomly assigned to a control, short-term exposure, or long-term exposure group. The control group will experience no vibration and are free to leave after blood sampling, the short-term exposure group will experience 1-hour of vibration, and the long-term exposure group will experience 8 hours of vibration.
- Your blood will be sampled before testing, immediately after testing, and 24-hours after testing.
- An device that measures acceleration, force, and direction, an IMU (inertial measurement unit), will be applied to your head, behind the right ear using double-faced tape. Coverlet will be placed over the IMU and your skin to further secure the IMU position.
- You will complete one (1) trial of seated vibration exposure, meeting the specifications of your assigned experimental group.
- You will have a blood sample taken following the completion of vibration testing and then complete a modified Rivermead Post-Concussion Symptom Questionnaire.
- You will be free to leave the testing site after completing the blood sampling and questionnaire with the expectation to return 24-hours later for a final blood draw.

How Long Will You Be In The Study?

You will be in the study for approximately two (2) 1.5-hour sessions for control and short-term exposure groups, and one (1) 8.5-hour and one (1) 1.5-hour sessions.

You can decide to stop participating at any time.

The study investigators may stop you from taking part in this study at any time if they believes it is in your best interest; if you do not follow the study rules; or if the study is stopped.

What Are The Risks Of The Study?

Being in this study involves some risk to you. You should discuss the risk of being in this study with the study staff. The risks and side effects related to this study include: nausea (less likely), dizziness (less likely), bruising (less likely), light-headedness (less likely), muscle soreness (less likely), confusion (less likely), fatigue (less likely), drowsiness (less likely)

You should talk to your study investigator about any side effects that you have while taking part in the study.

There may also be other side effects that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions, and other risks.

No funds have been set aside to compensate for any injury sustained while participating in this study.

Are There Benefits To Taking Part In The Study?

If you agree to take part in this study, there may or may not be direct benefit to you. We hope the information learned from this study will benefit other people in the future. The benefits of participating in this study may be: the satisfaction from helping to discover evidence of inflammatory-response protein concentration changes following WBV exposure, helping to determine the vibration magnitude transmitted from the seat to the head, and helping to discover evidence of a potential for chronic injury by comparing inflammatory-response protein concentrations to known concentrations indicative of injury.

What About Confidentiality?

We will do our best to make sure that your personal information is kept confidential. However, we cannot guarantee absolute confidentiality. Federal law states that we must keep your study records private. Nevertheless, certain people other than your researchers may also need to see your study records. By law, anyone who looks at your records must keep them completely confidential. Records will be kept in a locked filing cabinet inside a locked office within the offices of the co-investigators at Marshall University.

Those who may need to see your records are:

- Co-Investigators of the Study

If we publish the information we learn from this study, you will not be identified by name or in any other way.

What Are The Costs Of Taking Part In This Study?

There are no costs to you for taking part in this study. All the study costs, including any study medications and procedures related directly to the study, will be paid for by the study. Costs for your regular medical care, which are not related to this study, will be your own responsibility.

Will You Be Paid For Participating?

A five dollar ($5) Amazon gift card will be given to control subjects after completion of the initial blood draw and a second five dollar ($5) Amazon gift card will be given to control subjects after completion of the blood draw 24-hours after the initial blood draw.

A five dollar ($5) Amazon gift card will be given to short-term exposure subjects after completion of the initial blood draw, a second five dollar ($5) Amazon gift card will be given to short-term exposure subjects after completion of the blood draw following short-term vibration exposure, and a third five dollar ($5) Amazon gift card will be given to short-term exposure subjects after completion of the blood draw 24-hours after the initial blood draw.

A five dollar ($5) Amazon gift card will be given to long-term exposure subjects after completion of the initial blood draw, a one hundred dollar ($100) Amazon gift card will be given to long-term exposure subjects after completion of the blood draw following short-term vibration exposure, and a ten dollar ($10) Amazon gift card will be given to long-term exposure subjects after completion of the blood draw 24-hours after the initial blood draw.

What Are Your Rights As A Research Study Participant?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences.

Whom Do You Call If You Have Questions Or Problems?

For questions about the study or in the event of a research-related injury, contact one of the study's co-investigators, **Dr. Suzanne Konz at (304) 696-2926, Dr. Laszlo Horvath at (540) 231-7673, or Nicholas Miller at (304) 941-4417**. You should also call the investigator if you have a concern or complaint about the research.

For questions about your rights as a research participant, contact the Marshall University IRB#1 Chairman **Dr. Henry Driscoll or ORI at (304) 696-7320**. You may also call this number if:

- You have concerns or complaints about the research.
- The research staff cannot be reached.
- You want to talk to someone other than the research staff.

You will be given a signed and dated copy of this consent form.

SIGNATURES

You agree to take part in this study and confirm that you are 18 years of age or older. You have had a chance to ask questions about being in this study and have had those questions answered. By signing this consent form you are not giving up any legal rights to which you are entitled.

_____

Subject Name (Printed)

_____ _____

Subject Signature Date

_____ _____

Person Obtaining Consent Date

Appendix E: Whole-Body Vibration: Pre-Placement Health Surveillance Questionnaire

Present Job (if any)

1 What is your current occupation?
2 How many years have you spent working in your present job?
3 Did or do you drive any kind of vehicle in your current job? (i.e., car, bus, van, truck, train, tram, helicopter, other)
Yes No

If Yes: Type of vehicle	from _ until	hours/day	days/week	weeks/year
**********	**** ****	hrs ******	days ******	weeks ******
**********	**** ****	hrs ******	days ******	weeks ******
**********	**** ****	hrs ******	days ******	weeks ******
**********	**** ****	hrs ******	days ******	weeks ******

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4. Which postures do you adopt when driving?

Bent Forward	Often	Occasionally	Never
Twisted	Often	Occasionally	Never
Lean Against	Often	Occasionally	Never
Backrest	Often	Occasionally	Never

any other constrained posture?

5. Do you experience discomfort by mechanical vibration or shock in your work?

vertical vibration	Yes	No
fore/aft vibration	Yes	No
side-to-side vibration	Yes	No

6. Did or do you drive on a regular basis any kind of vehicle in your spare time (outside work)? Yes No

If Yes: Type of vehicle	from _ until	hours/day	days/week	weeks/year
**********	*** **	hrs ***	days ***	weeks ****
**********	*** **	hrs ***	days ***	weeks ****
**********	*** **	hrs ***	days ***	weeks ****

	During the last 7 days		During last 12 months	
7. Did you have pain/troubles	(a) never (b) seldom (c) often		(a) never (b) seldom (c) often	
8. What type of troubles did you have? (Circle all applicable alternatives)	(a) not applicable/no pain (b) neck pain only (c) arm pain/symptoms only (d) neck and arm pain/symptoms		(a) not applicable/no pain (b) neck pain only (c) arm pain/symptoms only (d) neck and arm pain/symptoms	
9. How many episodes have you had?	0 1 2-4 More than 4		0 1 2-5 6-10 More than 10	
10. How long did they typically last?	Not applicable Hours 1-2 days Always		Not applicable Hours 1-2 days 3-6 days 1-3 weeks 1-3 months 3-6 months Always	
11. How much time did you have to take off work due to the neck/arm pain?	None 1-2 days 3-5 days More than 5 days		None 1-4 weeks 1-3 months 3-6 months More than 6 months	
12. Has a doctor told you what was wrong with your neck, i.e., given a diagnosis?	No Yes	Namely	No Yes	Namely

13. Have you ever had a trauma to your back that required a medical visit?	No Yes	What kind of trauma?	When did it happen?	
14. What treatment did your doctor prescribe? (Anti-inflammatory drugs, painkillers, physical therapy, surgery, or other?)	None Yes	Namely	None Yes	Namely
15. Is there any movement or activity that causes your pain?	No Yes	Namely	No Yes	Namely
16. Is there any movement or activity which aggravates your pain?	No Yes	Namely	No Yes	Namely
17. Do you usually get neck pain during or shortly after driving a vehicle?	No Yes	Typically for how long?	No Yes	Typically for how long?

M.POPE E: A .

18. How would you rate your back/neck/shoulder pain on a 0-10 scale during the last 7 days where 0 is "no pain" and 10 is "pain as bad as it could be"?

20. In the past 12 months, how intense was your pain rated on a 0-10 scale where 0 is "no pain" and 10 is "pain as bad as it could be"?

	No pain									Pain as bad as it could be
Neck	0	1	2	3	4	5	6	7	8	9 10

19. About how many days in the last 12 months have you been kept from your usual activities (work, school, or housework) because of:

Neck pain	Number of days: 0	1-6	7-14	15-30	31

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21. Annual amount of personal car driving? (km(miles)): less than 8,000 (5000) 24,000 (15,000) more than 24,000(15,000)

22. What kind of transportation do you use to get to and from work?

Car Bus Train Bicycle Walk

23. How long does it take you to get to work?

Less than 20 min 20-40 min 41-60 min More than 1 hour

24. On which type of ground surface do you drive regularly?

asphalt/concrete:

good condition	no	yes	hours/day	type of vehicle
poor condition	no	yes	hours/day	type of vehicle
stelcon-plates	no	yes	hours/day	type of vehicle
paved road (cobbel)	no	yes	hours/day	type of vehicle
track/rail	no	yes	hours/day	type of vehicle
o-road	no	yes	hours/day	type of vehicle
construction road	no	yes	hours/day	type of vehicle
other, namely	no	yes	hours/day	type of vehicle

25. In which environment do you usually drive?

highway	% time	vehicle
country side road	% time	vehicle
city street	% time	vehicle
mixed	% time	vehicle

26. What is your normal style/speed of driving? smooth slow fast accelerating/braking

27. On what kind of driver seat do you sit regularly?

has suspension? Yes No

Type of suspension? mechanical suspension air suspension hydraulic suspension system

Is your seat adjustable? yes no

Do you adjust your seat? yes no not applicable

Did you receive instruction on how to adjust your seat? yes no

Do you use automatic or manual gear? Automatic Manual

28. Does your back rest give good support of your back? yes no

Do you use a separate back support when you drive? yes no

Does your seat have arm rests? yes no

Do you use arm rests when you drive? yes no not applicable

29. Which postures do you adopt when driving?

bent forward	Often	Occasionally	Never
twisted	Often	Occasionally	Never
lean against backrest	Often	Occasionally	Never

any other constrained posture?

30. Do you experience discomfort by mechanical vibration or shock in your work?

vertical vibration yes no

fore/aft vibration yes no

side-to-side vibration yes no

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31. If you drive and lift on the job how often do you lift immediately after driving?

Seldom Occasionally Often

32. Does your job include (on an average working day) any of the following conditions?

Prolonged or recurrent work done with your back:

bent forwards, backwards or sidewards Yes No

twisted Yes No

bent and twisted simultaneously Yes No

any other constrained posture?

33. Does your job include repeated, prolonged, or uncomfortable carrying, pushing or pulling of loads? yes no

34. Are there any other duties required in your job that stress your low back or neck?

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35. How many breaks do you usually take during the workday (this means getting out of your vehicle)?

36. How long are your breaks?

37. What do you do during your breaks? Walk around Sit Stand Other

Appendix F: Modified Rivermead Post-Concussion Symptoms Questionnaire*

After a head injury or accident some people experience symptoms which can cause worry or nuisance. We would like to know if you now suffer from any of the symptoms given below. As many of these symptoms occur normally, we would like you to compare yourself now with before the accident. For each one, please circle the number closest to your answer.

0 = Not experienced at all
1 = No more of a problem
2 = A mild problem
3 = A moderate problem
4 = A severe problem

Compared with before the accident, do you now (i.e., over the last 24 hours) suffer from:

Headaches.....	0	1	2	3	4
Feelings of Dizziness	0	1	2	3	4
Nausea and/or Vomiting	0	1	2	3	4
Noise Sensitivity, easily upset by loud noise	0	1	2	3	4
Sleep Disturbance	0	1	2	3	4
Fatigue, tiring more easily	0	1	2	3	4
Being Irritable, easily angered	0	1	2	3	4
Feeling Depressed or Tearful	0	1	2	3	4
Feeling Frustrated or Impatient	0	1	2	3	4
Forgetfulness, poor memory	0	1	2	3	4
Poor Concentration	0	1	2	3	4
Taking Longer to Think	0	1	2	3	4
Blurred Vision	0	1	2	3	4
Light Sensitivity, Easily upset by bright light	0	1	2	3	4
Double Vision	0	1	2	3	4
Restlessness	0	1	2	3	4

Are you experiencing any other difficulties?

1. _____	0	1	2	3	4
2. _____	0	1	2	3	4

*King, N., Crawford, S., Wenden, F., Moss, N., and Wade, D. (1995) J. Neurology 242: 587-592

Curriculum Vitae

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EXPERIENCE

Accident Reconstructionist Associate (March 2022 - present)
Evans Accident Reconstruction, College Station, TX

- Vehicle inspections (passenger vehicles and tractor trailers)
- Accelerometer equipment (braking and acceleration testing)
- Accident site documentation and measurement (including use of Total Station and aerial photography)
- Night and day visibility measurements and photography
- Perception and reaction time calculations
- Downloads of airbag control modules (vehicle "black boxes")

Ergonomic Specialist Intern (June 2021 – August 2021)
Kenworth Truck Company, Chillicothe, OH

- Conduct ergonomic walkthroughs of the plant
- Develop ergonomic policies and guidelines for the plant
- Assist with the development of a new, pre-hire physical evaluation
- Create an ergonomic evaluation of the plant for safety and human resources managers
- Collaborate with safety staff and mechanical engineers to implement ergonomic interventions

Graduate Assistantship (August 2019 – May 2021)
Marshall University, Huntington, WV
Graduate Assistant

- Instruct two Fitness and Wellness courses per semester
- Assist with concussion research using inertial measurement units (IMUs) and 3D photogrammetry
- Collect and analyze hammer throw data for USA Track & Field
- Conduct insurance physical testing using Cybex Isovelocity Dynamometer
- Mentor undergraduate students with research and equipment usage

EDUCATION

2019 – present Marshall University; Huntington, WV
M.S. in Biomechanics, GPA: 4.00
2015 – 2019 Marshall University; Huntington, WV
B.S. in Biomechanics**,** Magna Cum Laude with High Honors, GPA: 3.75

CERTIFICATES. CERTIFICATIONS, and LICENSES

2022 Advanced Collision Reconstructionist Certificate – Texas A&M Engineering Extension Services
2021 Advanced Occupational Ergonomics Certificate – Colorado State University
2022 HSI Adult First Aid / CPR / AED – American Safety and Health Institute

SPECIALIZED TRAINING

2022 Heavy Vehicle Electronic Control Module Data Use in Crash Reconstruction (40 Hours), Jacksonville, FL
2022 STAPP Car Crash Conference, Denver, CO
2022 TAARS Advanced HVEDR Systems, Austin, TX
2022 CRASHCON22, New Orleans, LA
2022 Bosch CDR Tool Technician (24 Hours), online
2022 Pix4D Mapper In-depth, online
2022 Pix4D Mapper Essential, online
2021 Pedestrian/ Auto Reconstruction (40 Hours), Humble, TX
2021 Collision Reconstruction (80 Hours), Webster, TX
2021 Advanced Collision Investigation (80 Hours), Webster, TX
2021 Tire Forensics Class, Chattanooga, TN
2020 Intermediate Collision Investigation (40 Hours), Garland, TX

SEMINAR AND CONFERENCE PRESENTATIONS

2021 International Society of Biomechanics in Sports Conference (Podium), Canberra, AU, September 2021
2019 Human Movement Science Research Symposium (Poster) Chapel Hill, NC, March 2019

PROFESSIONAL MEMBERSHIPS

2021 – present National Association of Professional Accident Reconstruction Specialists

COMMUNITY INVOLVEMENT

- Vice-President, President of Biomechanics Club Fall 2018 – Spring 2019

PUBLICATIONS

Cumulative biomechanical analysis of a female hammer throw athlete for back-to-back American record years
https://commons.nmu.edu/isbs/vol39/iss1/86

Hammer athletes must optimize performance variables to maximize their official distance. Analysis of key performance variables might explain how the subject improved an American record year in 2018 to another record in 2019. A 3-D analysis was performed on trial videos from 2018 and 2019. Release height, release velocity, release angle, and hip-shoulder separation were compared among years and throws, and their relationship with official distance was assessed. Release height ($p < 0.01$) and release angle ($p < 0.01$) were more consistent in 2019 than 2018. The relationships among official distance, release height ($p = 0.06$), and hip-shoulder separation ($p = 0.04$) were different between years. The efficient use of hip-shoulder separation could be responsible for the increase in official distance between years.

REFERENCES

Available upon request