# ASSOCIATIONS AMONG PERCEIVED STRESS, MINDFULNESS, AND CONCUSSION-RELATED OUTCOMES IN YOUNG ADULTS WITH CONCUSSION HISTORY

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#### ABSTRACT

### Christine Elizabeth Callahan: Associations among Perceived Stress, Mindfulness, and Concussion-Related Outcomes in Young Adults with Concussion History (Under the direction of Johna K. Register-Mihalik)

Concussion causes neurophysiological changes resulting in clinical deficits and psychological changes - presenting those injured with significant physical and psychosocial burden. Increased perceived stress, which is associated with decreased mental, physical health, and quality of life (QOL), may be heightened post-concussion. Furthermore, research suggests higher mindfulness is associated with decreased perceived stress and increased mental and physical health. Despite these connections, no research has identified the associations among perceived stress, mindfulness, and clinical and psychological concussion outcomes - knowledge necessary to inform effective interventions. This dissertation consisted of two studies: 1) a cross-sectional observational study in 80 young adults with a concussion history in which participants completed a single study visit including measures for demographics, concussion history, mental health history, current mindfulness practice, perceived stress, mindfulness, clinical concussion outcomes (concussion symptoms, balance performance, ANS function, vestibular/ocular function, and exertion tolerance), and psychological concussion outcomes (neurocognitive performance, psychological distress, and QOL); and 2) a single arm mindfulness intervention pilot study where 15 participants completed 10-20 minutes of mindfulness exercises/meditations daily for six weeks and were assessed for adherence, acceptability, feasibility, intervention perceptions, and preliminary efficacy (concussion symptoms, perceived stress, and mindfulness). Cross-sectional results suggest that higher perceived stress was significantly associated with higher concussion

symptoms, higher psychological distress, and lower QOL. Additionally, higher mindfulness was significantly associated with lower concussion symptoms, lower psychological distress, and higher QOL. Mindfulness did not moderate the relationship between perceived stress and concussion outcomes. Pilot intervention results suggest positive adherence, acceptability, feasibility, and overall intervention perceptions. Additionally, concussion symptoms significantly decreased pre/post-intervention. Results provide a novel understanding of the association among perceived stress, mindfulness, and clinical and psychological concussion outcomes and the impact of a mindfulness intervention in young adults with a concussion history. This study will inform future interventions aimed to mitigate stress and/or target mindfulness post-concussion.

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### LIST OF ABBREVIATIONS

- 95%CI 95% confidence interval
- AIM Acceptability of Intervention Measure
- ANS Autonomic Nervous System
- BCTT Buffalo Concussion Treadmill Test
- BESS Balance Error Scoring System
- BSI-18 Brief Symptom Investory-18
- COM Center of mass
- FFMQ Five Facet Mindfulness Questionnaire
- FIM Feasibility of Intervention Measure
- fMRI Functional Magnetic Resonance Imaging
- HR Heart rate
- HRV Heart rate variability
- ImPACT Immediate Post-Concussion Assessment and Cognitive Testing
- IMU Inertial Measurement Unit
- LF/HF Low frequency to high frequency power ratio
- MBSR Mindfulness-based stress reduction
- NCAA National Collegiate Athletic Association
- PI Principal investigator
- PROMIS Patient-Reported Outcomes Measurement Information System
- PSS-10 Perceived Stress Scale, 10 question version
- PTSD Post-traumatic stress disorder
- QOL Quality of life

- RPE Rate of perceived exertion
- RPQ Rivermead Post-concussion Symptom Questionnaire
- SD Standard deviation
- TBI Traumatic brain injury
- UNC-CH The University of North Carolina at Chapel Hill
- VOMS Vestibular/Ocular Motor Screening

#### **CHAPTER 1: INTRODUCTION**

### **1.1 Background and Rationale**

Concussive injury causes neurophysiological changes<sup>1</sup> resulting in clinical deficits [e.g., increased concussion symptoms, balance dysfunction, autonomic nervous system (ANS) dysfunction, and exercise intolerance] and psychological changes (e.g., increased irritability, anxiety, depression, cognitive dysfunction) presenting those injured with significant physical and psychosocial burden.<sup>2</sup> For adults, concussion symptoms typically resolve 10-21 days post-injury.<sup>2–4</sup> However, in those with a concussion history, 10-25% experience persistent concussion symptoms beyond typical recovery.<sup>2,3</sup> Neurophysiological changes remain in concussion history patients with persistent concussion symptom expression;<sup>5,6</sup> resulting in continued clinical and psychological dysfunction<sup>7,8</sup> causing those impacted to potentially miss school,<sup>9</sup> work,<sup>10</sup> sport,<sup>11</sup> and have less societal engagement<sup>12</sup> leading to long-term decreased quality of life (QOL).<sup>13</sup> Additionally, student-athletes with a concussion history, regardless of persistent symptom expression, report increased depression and anxiety as well as sleep and QOL disturbances.<sup>14,15</sup> Furthermore, our preliminary work indicates reporting persistent emotional and behavioral concussion-related symptoms is associated with decreased psychosocial, physical, and overall QOL in adolescents.<sup>16</sup>

Increased perceived stress is associated with increased depression,<sup>17</sup> anxiety,<sup>17</sup> and exhaustion<sup>17</sup> as well as decreased physical health,<sup>18</sup> life satisfaction,<sup>19</sup> and QOL.<sup>20</sup> In sport specific research, perceived stress predicts sports injury<sup>21,22</sup> and negatively impacts injury rehabilitation for musculoskeletal injuries.<sup>21</sup> Specifically, in young adults, increased stress symptoms are associated with increased injury risk throughout a competitive soccer season.<sup>23</sup> Additionally, perceived

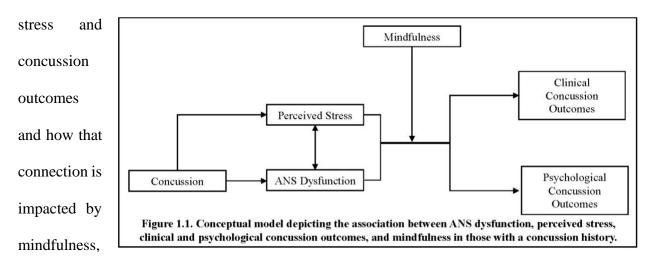
negative life event stress increased the risk of overuse injuries in elite female soccer players<sup>24</sup> and negative life event stress and high levels of life-related stress predicted injury rates in adolescent and young adult soccer players.<sup>25</sup> Despite the prior connections between stress and injury, limited data suggests perceived stress is heightened acutely post-concussion<sup>13</sup> with much of the work making these connections being focused in those with a concussion history. Specifically, in those with a concussion history, exposure to a high stress condition (mental arithmetic) increased perceived stress and heart rate (autonomic stress) compared to uninjured controls.<sup>26</sup> Additionally, in individuals with a concussion history experiencing persistent concussion symptoms, exposure to the high stress condition exacerbated post-concussion symptoms, decreased information processing speed, and decreased memory performance.<sup>26</sup> Building upon this work, research suggests perceived stress may also play a role in predicting long-term post-concussion impairments.<sup>27</sup> However, research has not indicated a connection between perceived stress and commonly used post-concussion assessments.

Supplementing data associating perceived stress's association with injury and concussion history, extensive research in military populations identified associations between concussion history and increased likelihood of reporting post-traumatic stress disorder (PTSD) symptoms, a psychological condition related to an exposure to a traumatic event and its associated stress.<sup>28,29</sup> Various factors are associated with the presentation of PTSD including increased pre-injury perceived stress.<sup>28</sup> Additionally, soldiers reporting a concussion history and PTSD diagnosis often have decreased cognitive performance, increased psychological distress, and decreased ability to manage post-injury life stressors, identifying a continued connection between stress and concussion outcomes.<sup>28,30</sup> In non-military populations, limited research suggests perceived stress acutely post-concussion meditates the relationship between concussion symptom scores at two

weeks post-concussion and PTSD symptom scores at three months post-injury.<sup>31</sup> Despite evidence suggesting perceived stress may play a role in an individual's concussion recovery, identifying a potential mechanism to inform comprehensive interventions, the association between perceived stress and concussion outcomes is largely unknown.

Intersecting data concerning perceived stress and concussion are studies indicating higher mindfulness levels are associated with decreased perceived stress<sup>32-34</sup> and increased mental health,<sup>35</sup> physical health,<sup>36</sup> and subjective psychological well-being.<sup>33</sup> In healthy populations, mindfulness-based interventions (i.e., meditation and yoga) improve mindfulness and perceived stress.<sup>36–40</sup> In athletic populations, mindfulness-based yoga has shown to mitigate stress and fatigue related to sports injury.<sup>41</sup> To our knowledge, no mindfulness-based studies have been completed in a concussion history-specific population. However, recent pilot data in persistent concussion symptom patients suggests mindfulness-based stress reduction improves QOL.<sup>42</sup> But, this study did not investigate associations between mindfulness and comprehensive clinical and psychological concussion outcomes, findings necessary to design effective concussion interventions. In patients with other forms of brain injury (i.e., moderate traumatic brain injury and stroke) and particularly those also experiencing PTSD, engaging in mindfulness techniques (meditation, breathing exercises, guided visualization, and body-scanning) significantly improved QOL.<sup>43–45</sup> However, these techniques: 1) have not been connected to concussion-related outcomes such as clinical assessments for concussion symptoms, balance performance, ANS function, vestibular/ocular function, and exercise tolerance and psychological post-concussion assessments outside of QOL such as neurocognition and psychological distress; and 2) have not typically focused on concussion history patients.

Building upon the presented perceived stress, mindfulness, and brain injury literature, we believe increased perceived stress has the potential to result in negative post-concussion outcomes. As such, utilizing mindfulness techniques to improve perceived stress may improve overall post-concussion outcomes. However, no research has identified the connection between perceived

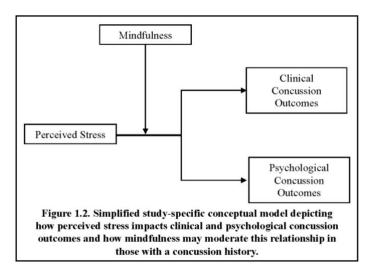


particularly in those with a concussion history where perceived stress may be higher. Based on this literature surrounding concussion, perceived stress, mindfulness, and concussion outcomes, we identify a conceptual model (Figure 1.1) indicating: 1) concussion causes ANS dysfunction and perceived stress; 2) these deficits negatively impact clinical and psychological concussion outcomes; and 3) improving mindfulness may decrease post-concussion outcome impairments.

#### **1.2 Statement of the Problem**

There is a gap in understanding how perceived stress and mindfulness impact clinical and psychological concussion outcomes in those with a concussion history. Based on the concussion, perceived stress, and mindfulness literature as well as the big picture conceptual model described above (Figure 1.1), we identify a simplified study-specific conceptual model (Figure 1.2) indicating increased perceived stress may negatively impact clinical and psychological concussion outcomes and improving mindfulness may decrease post-concussion outcome impairments.

Specifically, we hypothesize perceived stress negatively impacts clinical and psychological concussion outcomes and that this relationship is moderated by mindfulness. Clinically, this means if an individual who suffers a concussion has increased perceived stress, he/she will show greater deficits in clinical and



psychological concussion outcomes. As such, if one improves mindfulness to decrease perceived stress, clinical and psychological concussion outcomes will also improve. Understanding the association among perceived stress, mindfulness, and concussion outcomes in those with a concussion history may provide evidence supporting stress reduction and/or mindfulness-based interventions during concussion rehabilitation to facilitate concussion recovery and mitigate prolonged effects.

#### **1.3 Specific Aims and Hypotheses**

- Aim 1. Estimate the associations among perceived stress, mindfulness, and clinical concussion outcomes (concussion symptoms, balance performance, ANS function, vestibular/ocular system function, and exertion tolerance) in young adults with a concussion history.
- Hypothesis: (1a) Participants with higher perceived stress will have worse clinical concussion outcomes indicated by higher concussion symptom burden, lower balance performance, higher ANS dysfunction, higher vestibular/ocular symptom provocation, and lower exertion tolerance when controlling for number of

concussions, sex, and most recent concussion mechanism. (1b) Participants with higher mindfulness will have better clinical concussion outcomes indicated by lower concussion symptom burden, higher balance performance, lower ANS dysfunction, lower vestibular/ocular symptom provocation, and higher exertion tolerance when controlling for number of concussions, sex, and most recent concussion mechanism. (1c) The association among perceived stress and clinical concussion deficits identified in (1a) will be moderated by mindfulness levels. Specifically, mindfulness will buffer the relationship between perceived stress and clinical concussion outcomes.

- Aim 2. Estimate the associations among perceived stress, mindfulness, and psychological concussion outcomes (neurocognitive performance, psychological distress, and QOL) in young adults with a concussion history.
- Hypothesis: (1a) Participants with higher perceived stress will have worse psychological concussion outcomes indicated by lower neurocognitive performance, higher psychological distress, and lower QOL when controlling for number of concussions, sex, and most recent concussion mechanism. (1b) Participants with higher mindfulness will have better psychological concussion outcomes indicated by higher neurocognitive performance, lower psychological distress, and higher QOL when controlling for number of concussions, sex, and most recent concussions, sex, and most recent concussion outcomes indicated by higher neurocognitive performance, lower psychological distress, and higher QOL when controlling for number of concussions, sex, and most recent concussion mechanism. (1c) The association among perceived stress and psychological concussion deficits identified in (1a) will be moderated by mindfulness levels. Specifically, mindfulness will buffer the relationship between perceived stress and psychological concussion outcomes.

- Aim 3.Determine the acceptability, feasibility, usability, and preliminary efficacy of an<br/>online mindfulness intervention in young adults with a concussion history.
- Hypothesis: Participants who participate in the mindfulness intervention will report high adherence (complete five days of the mindfulness/meditation exercises per week), positive acceptability, positive feasibility, and positive intervention perceptions. Additionally, after completing the intervention, participants will report decreased concussion symptoms, decreased perceived stress, and increased mindfulness compared to before the intervention.

Expected main and interaction effects for Aims 1 and 2 are outlined in Appendix 1.

# **1.4 Independent Variables**

# 1.4.1 Aims 1 and 2

- Perceived stress [Perceived Stress Scale (PSS-10) total score]
- Mindfulness [Five Facet Mindfulness Questionnaire (FFMQ) total score]
- Mindfulness (FFMQ total score) and perceived stress (PSS-10 total score) interaction term

# 1.4.2 Covariates for Aims 1 and 2

- Number of previous concussions reported (1-5+)
- Sex (male or female)
- Most recent concussion mechanism (sport-related or non-sport-related)

### 1.4.3 Exploratory Aim 3

• Time (pre/post-intervention, used in the preliminary efficacy outcomes t-tests)

### **1.5 Dependent Variables**

### 1.5.1 Aim 1

- Concussion symptoms [Rivermead Post-Concussion Symptom Questionnaire (RPQ) total symptom severity and total concussion symptoms worse than before injury]
- Balance performance [Balance Error Scoring System (BESS) total errors and center of mass (COM) standard deviation (SD) of acceleration in the anterior/poster and medial/lateral planes, eyes open and eyes closed trials)
- ANS function [heart rate variability (HRV) low to high frequency (LF/HF) power ratio and average heart rate (HR)]
- Vestibular/ocular function [change in total symptom score (pre- vs. post-test) for each Vestibular/Ocular Motor Screening (VOMS) assessment: smooth pursuits, horizontal and vertical saccades, near-point convergence, vestibular ocular reflex, and visual motion sensitivity.]
- Exertion tolerance [step test number of steps, post-test Rate of Perceived Exertion (RPE)]

# 1.5.2 Aim 2

- Neurocognitive performance (CNS Vital Signs scores for verbal memory, visual memory, psychomotor speed, cognitive flexibility, complex attention, processing speed, reaction time, and executive functioning)
- Psychological distress [Brief Symptom Inventory-18 (BSI-18) total score]
- QOL [Patient Reported Outcomes Measurement Information System (PROMIS) scores for physical function, anxiety, depression, fatigue, sleep disturbances, ability to participate in social roles and activities, pain interference, and pain intensity scores]

### 1.5.3 Exploratory Aim 3

- Adherence (number of mindfulness exercises/meditations completed per week)
- Acceptability [Acceptability of Intervention (AIM) total score and individual items]
- Feasibility [Feasibility of Intervention (FIM) total score and individual items]
- Intervention perceptions (intervention facilitators, barriers, changes, usability, and helpfulness questions, qualitative and quantitative)
- Concussion symptoms (RPQ total concussion symptom severity and total concussion symptoms worse than before injury)
- Perceived stress (PSS-10 total score)
- Mindfulness (FFMQ total score)

### **1.6 Operational Definitions**

- <u>Concussion</u>: mild traumatic brain injury that is caused by either a direct blow to the head, face, neck, or elsewhere on the body with an impulsive force transmitted to the body resulting in the rapid onset of short-lived impairment of neurological function that resolves spontaneously<sup>2</sup>
- <u>Concussion History</u>: self-report experiencing a concussive injury within the past five years, but not within the past month, based on the following provided definition, "A change in brain function following a force to the head, which may be accompanied by temporary loss of consciousness and is identified in awake individuals with measures of neurologic and cognitive dysfunction. Common concussion symptoms include headache, feeling slowed down, difficulty concentrating or focusing, dizziness, balance problems/loss of balance, fatigue/loss of energy, feeling in a fog, irritability, drowsiness, nausea, memory loss, sensitivity to light/noise, and blurred vision."<sup>2</sup>

- <u>Mindfulness</u>: a technique which focuses on attention (bringing your awareness and experiences to focus on the present moment) and acceptance (observing any feelings or sensations without judgment and letting them go without reaction).<sup>46</sup> Mindfulness will be measured in this study using the FFMQ.
- <u>Current Mindfulness Practice:</u> self-reported currently engaging in a mindfulness practice (i.e., yoga or meditation) at least one day per week.
- <u>Perceived Stress:</u> feelings or thoughts that an individual has about how much stress they are under at a given point in time or over a given time period, how an individual feels about the general stressfulness of their life and their ability to handle such stress.<sup>47</sup> Perceived stress will be measured using the PSS-10.

# **1.7 Assumptions**

- Participants answered all questionnaire components honestly.
- Participants completed clinical assessments to the best of their ability.
- Participants completed assessments and questionnaires according to the provided directions.

# **1.8 Delimitations**

- All participants were young adults aged 18-30.
- Participants with health histories that put them at greater than minimal risk for assessments were excluded.
- Participants who are still under care for a concussion at the time of study enrollment were excluded.

#### **1.9 Limitations**

- Participants who chose to participate in this study may have only done so due to preexisting interest in the topic of the study.
- All questionnaires were self-reported, presenting the possibility of response bias.
- Participants were recruited at the University of North Carolina at Chapel Hill (UNC-CH) and surrounding community, presenting the possibility of selection bias.

### 1.10 Significance of the Proposed Study

There is a gap in understanding how perceived stress and mindfulness impact clinical and psychological concussion outcomes in those with a concussion history. Understanding the association among perceived stress, mindfulness, and concussion outcomes in those with a concussion history may provide evidence that intervening on perceived stress and/or improving mindfulness during concussion rehabilitation is pertinent to achieving a full recovery. Therefore, this novel study aims to understand the association among perceived stress, mindfulness, and clinical and psychological concussion outcomes, mechanisms necessary to inform effective, comprehensive interventions.

Our central hypothesis is that increased perceived stress negatively impacts clinical and psychological concussion outcomes and that this relationship is moderated by mindfulness. Individuals with a concussion history show increased depression and anxiety as well as sleep and QOL disturbances.<sup>14,15</sup> Additionally, individuals with a concussion history, specifically those who have persistent concussion symptoms, experience continued injury-related deficits beyond the typical recovery period,<sup>2,3,5,6,8,9,48</sup> presenting a societal burden in time missed from school<sup>10</sup> and work<sup>11</sup> as well as a personal physical and psychosocial burden with decreased QOL.<sup>14</sup>

Findings from this study are significant as they provide evidence necessary to inform

comprehensive interventions aimed to mitigate post-concussion clinical and psychological impairments and improve QOL after injury. Additionally, findings will provide the necessary foundation for future studies of comprehensive interventions aimed to directly address perceived stress and/or utilize mindfulness post-injury to further improve post-concussion clinical and psychological outcomes.

#### **CHAPTER 2: LITERATURE REVIEW**

### **2.1 Introduction**

Concussive injury causes neurophysiological changes<sup>1</sup> resulting in clinical deficits [e.g., increased concussion symptoms, balance dysfunction, exercise intolerance, autonomic nervous system (ANS) dysfunction] and psychological changes (e.g., increased irritability, anxiety, depression, cognitive dysfunction) presenting those injured with major physical and psychosocial burden.<sup>2</sup> Increased perceived stress is associated with increased depression,<sup>17</sup> anxiety,<sup>17</sup> and exhaustion<sup>17</sup> as well as decreased physical health,<sup>18</sup> life satisfaction,<sup>19</sup> and quality of life (QOL).<sup>20</sup> Limited data suggests perceived stress is heightened acutely post-concussion,<sup>13</sup> in those with a concussion history,<sup>26</sup> and in those with continued persistent concussion symptoms.<sup>26</sup> Additionally, further research indicates that perceived stress may play a role in predicting long-term postconcussion impairments,<sup>27</sup> indicating a potential mechanism for intervention as a way to improve concussion outcomes. Higher mindfulness levels are associated with decreased perceived stress<sup>32-</sup> <sup>34</sup> and increased mental health,<sup>35</sup> physical health,<sup>35</sup> and subjective psychological well-being.<sup>33</sup> In healthy populations, mindfulness-based interventions such as meditation and yoga improve mindfulness and perceived stress.<sup>36-40</sup> Additionally, minimal research has identified that mindfulness-based stress reduction improves QOL in persistent concussion symptom patients<sup>42</sup> and engaging in various mindfulness techniques (meditation, breathing exercises, guided visualization, and body-scanning) improves QOL in individuals with additional forms of brain injury.<sup>43,44</sup> However, these techniques have not been connected to concussion-related outcomes outside of QOL and studies have not focused on concussion history patients. As such, it is

necessary to understand the association among perceived stress, mindfulness, and concussion outcomes, specifically related to those with a concussion history. This review will identify and review current literature surrounding concussion, post-concussion rehabilitation intervention implementation, perceived stress, and mindfulness, tying findings to the development of the current study's conceptual framework and specific aims.

### **2.2 Concussion**

#### 2.2.1 Definition

The Concussion in Sport Group<sup>2</sup> defines concussion as a mild traumatic brain injury that is caused by a direct blow to the head, face, neck, or elsewhere on the body with an impulsive force transmitted to the body; resulting in the rapid onset of short-lived impairment of neurological function that resolves spontaneously.<sup>2</sup> Concussion is a structural injury, resulting in neuropathological changes which present a range of clinical and psychological deficits.<sup>2</sup> Clinical deficits include increased concussion symptoms, balance dysfunction, sleep/wake disturbance, and exercise intolerance.<sup>2</sup> Psychological changes include increased irritability, anxiety, depression, and cognitive dysfunction.<sup>2</sup>

### 2.2.2 Incidence

The rate of concussion has risen,<sup>49,50</sup> with one to two million sport- or recreation-related concussions reported in the United States each year.<sup>51</sup> Adolescent athletes report a concussion injury rate of 4.17 per 10,000 athlete-exposures<sup>52</sup> and young adult National Collegiate Athletic Association (NCAA) student-athletes report a concussion injury rate of 4.47 per 10,000 athlete-exposures.<sup>53</sup> In non-athletic specific populations, the incidence of concussion-related visits in United States emergency departments was reported as 239 visits per 100,000 person years.<sup>50</sup> The increased prevalence of concussive injury in athletic and general populations highlights the notion

that concussion greatly impacts a wide range of individuals, leaving them susceptible to resulting physical and psychosocial burden.

### 2.3 Concussion Pathophysiology

### 2.3.1 Neurometabolic Cascade

Concussion occurs when biomechanical forces are imparted on the brain.<sup>1</sup> It is a microstructural (i.e., impairments cannot be seen using common, basic neuroimaging techniques) and a functional neuronal injury (i.e., the injury results in changes to neurophysiological structures of the brain).<sup>1</sup> The acute neurophysiology of concussion has been described as a neurometabolic cascade which includes an ionic flux, neural energy crisis, axonal injury, and impaired neurotransmission.<sup>1</sup> Acutely post-concussion, there is an influx of sodium and calcium and efflux of potassium in the neuron, resulting in rapid depolarization of neurons. As a result, a neuronal energy crisis ensues. Specifically, ATP-requiring gated channels in neurons are kicked into overdrive to respond to the rapid depolarization with the goal of bringing neurons back to their homeostatic state. This activity leads to an increase in glucose metabolism, decrease in cerebral blood flow, mitochondrial dysfunction, and decrease in neuronal energy availability. Additionally, concussion causes axonal injury. Increased calcium, as a result of the ionic flux, causes phosphorylation of neurofilaments, leading to axonal structural integrity impairment. Also, biomechanical forces cause microfilament damage, impacting neurotransmission. As a result, neurotransmission is impaired, causing a decrease in cellular communication throughout the brain. This neurometabolic cascade leads to the various clinical and physiological deficits individuals experience after incurring a concussion.<sup>1</sup>

### 2.3.2 Autonomic Nervous System Dysfunction

The ANS plays a key role in balancing the sympathetic and parasympathetic nervous systems to maintain homeostasis; a body regulation imperative for maintaining healthy levels of physiological and psychological stress.<sup>54</sup> In healthy individuals, the parasympathetic nervous system is active when at rest and the sympathetic nervous system is active when engaging in physical, cognitive, or emotionally stressful activities (i.e., exercise/physical activity, concentration/critical thinking, and/or anxiety inducing situations).<sup>54</sup> To maintain balance between the two systems, the ANS induces vagal nerve withdrawal to provoke the sympathetic nervous system in stressful situations and, oppositely, increases vagal nerve activity to bring the body back to using the parasympathetic nervous system during restful times (homeostasis).<sup>54</sup>

As described in detail above, post-concussion neurophysiological changes include increased depolarization of neurons, resulting in an increase in neuronal glucose metabolism as a means to maintain homeostasis.<sup>1</sup> These changes result in a decrease in cerebral blood flow, mitochondrial dysfunction, and decreased neural energy availability.<sup>1</sup> Specifically, these neurophysiological changes lead to ANS dysfunction that is present both at the acute phase of injury<sup>1,55,56</sup> and in athletes who are asymptomatic and cleared for returning to play.<sup>56–58</sup> Post-concussion ANS dysfunction has been attributed to damage to the ANS control center in the brainstem<sup>59</sup> and/or uncoupling of connections between the central ANS, arterial baroreceptors, and heart.<sup>60</sup> Accordingly, previous work illustrates that ANS dysfunction impacts cardiac functioning and overall recovery after concussion.<sup>5,58,61,62</sup>

With ANS dysfunction post-concussion, an individual's balance between the parasympathetic and sympathetic nervous systems is impaired.<sup>56</sup> Meaning that they may be more likely to maintain use of the sympathetic nervous system even in restful states, causing them to

experience more physical, cognitive, and psychological stress.<sup>56</sup> ANS dysfunction post-concussion is expressed clinically as the following symptoms: headache, dizziness, nausea, fogginess, difficulty concentrating, cognitive impairment, mood disturbances, anxiety, depression, increased irritability, and exercise intolerance.<sup>48</sup> Additionally, patients will experience an exacerbation of symptoms when engaging in physical, cognitive, or psychological stressful activities.<sup>48</sup>

### 2.3.3 Concussion Pathophysiology and Concussion Outcomes

The neurometabolic cascade experienced acutely post-concussion leads to commonly experienced clinical and psychological concussion outcomes.<sup>1,2</sup> Specifically, the post-concussion ionic flux described above results in somatic symptoms such as headache and sensitivity to light and sound.<sup>1</sup> Additionally, the energy crisis that occurs as a result of the ionic flux puts an individual at higher risk of second injury.<sup>1</sup> Axonal injury and impaired neurotransmission lead to impaired cognition, slowed processing, and slowed reaction time.<sup>1</sup> Finally, altered cytoskeletal proteins and eventual cell death leads to chronic neural atrophy and development of persistent symptoms.<sup>1</sup>

In addition to the clinical and psychological concussion outcomes outlined in the neurometabolic cascade, research has identified system dysfunctions, specifically ANS (described above), vestibular/ocular system, and cervical spine dysfunctions, that occur post-concussion as a result of the neurometabolic cascade. Post-concussion vestibular/ocular dysfunction may be attributed to a biomechanical injury to the vestibular/ocular system housed in the inner ear and/or uncoupling of the connection between the vestibular/ocular system in the inner ear and the central nervous system.<sup>63–65</sup> The vestibular/ocular system plays a key role in balance, spatial orientation, and gaze movements. The bony labyrinth housed in the inner ear detects changes in head movements and relays that information to the central nervous system to inform decisions of balance and movement. Additionally, this system plays a key role in gaze movements, specifically

seen in the vestibular ocular reflex, and helps to inform decisions about ocular muscle activation. As such, vestibular/ocular dysfunction post-concussion may result in headache, eye strain, blurred vision, dizziness, fogginess, difficulty concentrating, and postural balance impairment.<sup>63–65</sup> Post-concussion cervical spine dysfunction, not seen in all patients post-injury, may be attributed to a biomechanical injury to the cervical spine.<sup>66–68</sup> The cervical spine plays a key role in providing structure for the neck, protecting the skull, and protecting the spinal cord. As such, if one experiences cervical spine dysfunction post-concussion, he/she would clinically express the following symptoms: occipital-specific headache, neck pain, neck stiffness, decreased range of motion rotating the head, eye strain, blurred vision, dizziness, fogginess, difficulty concentrating, and postural balance impairment.<sup>66–68</sup> It should be noted that many of the symptoms associated with vestibular/ocular and cervical spine dysfunction overlap. The cranial nerves, many of which are associated with vision performance and spatial awareness, are housed in the cervical spine. Therefore, damage to the cervical spine may cause vestibular/ocular dysfunction post-concussion.<sup>48</sup>

Neuroimaging concussion research has built upon theory connecting the neurometabolic cascade to clinical and psychological concussion outcomes. Specifically, Lu and colleagues<sup>69</sup> compared resting state functional magnetic resonance imaging (fMRI) in concussion history patients with and without post-traumatic headache. Results suggest evidence of disrupted hypothalamic-based resting state functional connectivity in those with post-traumatic headache and that abnormal functional connectivity was correlated with headache symptom measurement.<sup>69</sup> Additional fMRI research acutely post-concussion compared those with vestibular dysfunction to non-injured controls. Results suggest that those with post-concussion vestibular dysfunction had increased resting state connectivity of visual input, multisensory processing, and spatial memory.<sup>70</sup>

Furthermore, resting state fMRI spatial memory connectivity was correlated with increased symptom provocation during the Vestibular/Ocular-Motor Screening (VOMS) clinical assessment.<sup>70</sup> Additionally, studies in those with acute concussion suggest impaired resting state cerebral blood flow<sup>69</sup> and impaired network centrality and causal connectivity<sup>21</sup> were associated with deficits in cognitive performance. Finally, the neurometabolic cascade identifies that concussion results in axonal injury (i.e., white matter disturbances).<sup>1</sup> As such, research in youths with a concussion history used diffusion tensor imaging to identify that abnormalities in superficial white matter fibers were associated with decreased processing speed.<sup>71</sup> Neuroimaging concussion research is a growing field of research. As such, future research is necessary to build upon current studies to provide further evidence to support the connection between post-concussion neurophysiological disturbances and post-concussion clinical and psychological outcomes.

# 2.3.4 Persistent Concussion Symptom and Concussion History Pathophysiology

The neurophysiological underpinnings surrounding concussion history and persistent concussion symptoms are not fully understood. Research has identified various characteristics which may predict the expression of persistent concussion symptoms. Specifically, old age, female sex, pre-injury mental health history, cognitive bias, migraine headache, increased anxiety, and belief that the symptoms will last a long time and have catastrophic life consequences.<sup>48,72–74</sup> The neurometabolic cascade of concussion identifies that multiple, concurrent concussions result in continued metabolic changes (i.e., continued ionic flux and an energy crisis, described above).<sup>1</sup> Additionally, it identifies that research using diffusion tensor imaging shows axonal injury and impaired neurotransmission in patients with a concussion history and those with persistent symptom expression.<sup>1,71</sup> King and colleagues<sup>75</sup> identified decreased cortical inhibition in adolescents with persistent concussion symptoms. As noted in the neurometabolic cascade of acute

concussion, continued expression of ionic flux, an energy crisis, axonal injury, and impaired neurotransmission may result in eventual neuronal death.<sup>1</sup> Concussion history pathophysiology is not fully understood, and research has identified mixed results regarding clinical and physiological deficits that remain present in individuals with a concussion history. Specifically, research has shown no difference in neurocognition,<sup>76</sup> static and dynamic balance,<sup>77</sup> and vestibular/ocular performance<sup>78</sup> between those with and without a concussion history. However, additional research has identified that reporting a concussion history is associated with increased concussion symptom reporting<sup>15,79</sup> increased postural control deficits,<sup>80</sup> decreased dynamic balance performance,<sup>65</sup> decreased cognitive functioning,<sup>81</sup> and decreased QOL.<sup>15</sup> As such, it is possible that some neurophysiological underpinnings of concussion may still be present in those with a concussion history. We pose that post-concussion ANS dysfunction leads to increased perceived stress leading to post-concussion impairments. This deficit may remain present in those with a concussion history, leading to continued impairments.

## 2.4 Psychological Concussion Considerations

Emotional and behavioral concussion-related symptoms such as irritability, depression, anxiety, and frustration are identified as clinical domains which may present after an individual incurs a concussion.<sup>2</sup> As such, these symptoms are included in concussion symptom questionnaires used acutely post-concussion and throughout the recovery process. Hammer and colleagues<sup>82</sup> identified that depressive-related symptoms worsened from pre-injury baseline to 24 hours, 72 hours, and seven days post-concussion. Additionally, in collegiate athletes, depressive symptoms remained elevated at one day and one-week post-concussion, with improvements in symptoms at one-month post-concussion.<sup>83</sup> Furthermore, concussed athletes, when compared to controls, had significantly different emotional processing connectivity regions one day after concussion.<sup>83</sup>

Emotional and behavioral concussion-related symptoms identified acutely post-concussion may continue to impact an individual persistently after his/her injury and may predict the expression of continued, persistent concussion symptoms beyond the typical recovery timeframe. Specifically, pre-injury mental health history, increased anxiety, and belief that the symptoms will last a long time and have catastrophic life consequences are all predictors of persistent concussion symptoms.<sup>73,74</sup> Additionally, research has identified that emotional and behavioral concussion-related symptoms associated with concussion may onset later post-injury and persist longer than somatic and physical deficits.<sup>84</sup> The overall expression of emotional and behavioral-related concussion symptoms greatly impacts an individual as it may lead to more time lost from school, sport, work, and social engagements - overall impacting QOL.

Sandel and colleagues<sup>73</sup> outlined mechanistic support for the development of emotional and behavioral concussion-related symptoms and for the connection between emotional and behavioral-related and persistent concussion symptoms, attributing it to: 1) pre-injury characteristics; 2) neurophysiological changes; and 3) psychological and clinical response to injury. Specifically, females are more likely to report emotional and behavioral-related symptoms post-concussion and are more likely to have a pre-injury mental health diagnosis.<sup>85,86</sup> Additionally, both female sex and pre-injury mental health diagnoses are predictors of persistent concussion symptoms.<sup>87</sup> Post-concussion neurophysiological changes in serotonin levels, and decreased frontal lobe activity.<sup>1</sup> Finally, psychological response to injury may predict emotional and behavioral-related and/or persistent concussion symptom expression. Specifically, if one believes symptoms will continue long past injury and will have catastrophic life consequences, he/she is more likely to see

symptoms persist.<sup>74</sup> Emotional regulation also plays a key role in emotional and behavioral-related and persistent concussion symptom expression. Specifically, those with increased resilience are more likely to report decreased post-concussion anxiety and depression and are less likely to develop persistent symptoms.<sup>73,88</sup> Finally, clinical concussion management plays a large role in the development of emotional and behavioral-related and persistent concussion symptoms. Specifically, using strict rest compared to an active form of rehabilitation saw an increase in days to recovery post-concussion and an increase in emotional and behavioral concussion-related symptoms.<sup>89–91</sup> Also, lack of concussion knowledge and access to care is associated with continued, persistent symptoms and emotional and behavioral-related symptoms.<sup>92</sup> Additionally, it should be noted that, patients who experience persistent concussion symptoms have more time lost from school, sport, work, and social engagements. This social isolation and missed participation may contribute to the expression of emotional and behavioral-related concussion symptoms. Current knowledge regarding the expression of emotional and behavioral concussionrelated symptoms, specifically in those with a concussion history (those with and without persistent concussion symptoms) provides evidence to support the current study's notion that intervening on perceived stress may improve overall concussion outcomes.

### 2.5 Post-Concussion Treatment and Rehabilitation

Neurophysiological underpinnings of concussion at the acute and persistent phases have informed current post-concussion treatment and rehabilitation paradigms. Additionally, findings from the current study will provide evidence to inform future comprehensive interventions aimed to mitigate concussion-related burden. Current guidelines from the Concussion in Sport Group recommend a 24 to 48 hour rest period before engaging a graduated return to sport strategy.<sup>2</sup> This graduated strategy consists of the following progression: 1) symptom-limited activity (daily

activities that do not provoke symptoms); 2) light aerobic exercise (walking/cycling at a slow to medium pace with no resistance training); 3) sport-specific exercise (running/skating drills, no head impact activities); 4) non-contact training drills (harder training drills, may start progressive resistance training); 5) full contact practice (following medical clearance, participation in normal training activities); and 6) return to sport (normal game play).<sup>2</sup> There should be at least 24 hours for each progression step and if symptoms worsen at any stage the athlete should return to the previous step. This progression, while helpful, has been implemented as a part of acute concussion rehabilitation paradigms; however, it does not provide rehabilitation guidance related to individualized symptom expression or consider individuals who experience persistent concussion symptoms. Various intervention approaches have been used to supplement the current return to sport strategy and implement multifaceted and targeted interventions.

# 2.5.1 Physical and Cognitive Rest

Before the current guidelines, physical and cognitive rest until symptom free was recommended.<sup>93</sup> The purpose of physical and cognitive rest post-concussion was: 1) to ease discomfort during the acute recovery period by mitigating post-concussion symptom expression and exacerbation; and 2) that rest may promote recovery by minimizing brain energy demands following concussion (i.e., rest during the period when the brain is most neurophysiologically vulnerable).<sup>93</sup> Current research suggests strict rest until asymptomatic may be detrimental to post-concussion outcomes.<sup>89–91</sup> Specifically, adolescents who engaged in five days of strict rest compared to the recommended 24-48 hours of rest followed by a stepwise return to activity reported more daily post-concussion symptoms and slower symptom resolution.<sup>89</sup> Sufrinko and colleagues<sup>90</sup> identified that patients who presented to the emergency department acutely post-injury and were prescribed rest were more likely to report symptoms up to eight days post-injury

compared to those prescribed usual care (stepwise return to activity). In addition to symptomrelated and physical conditioning limitations to strict rest post-concussion, an individual's mental health may be impacted by this approach. Long periods of inactivity and time away from sport, school, work, and/or social engagements may lead to isolation resulting in depression and anxietyrelated symptoms. DiFazio and colleagues<sup>91</sup> identify this as an activity restriction cascade, potentially contributing to the development of persistent concussion symptoms (specifically emotional and behavioral-related concussion symptoms). As such, research and clinical practice have transitioned to focus on paradigms as outlined by the current Concussion in Sport Group guidelines<sup>2</sup> and in additional paradigms more recently proposed in the literature including aerobic exercise, multimodal rehabilitations, and targeted interventions.

# 2.5.2 Aerobic Exercise

Recent research supports the notion that sub-symptom threshold aerobic exercise during concussion rehabilitation may improve post-injury outcomes and inform clinicians on intervention techniques.<sup>94–105</sup> The pivotal paper, *Exercise is Medicine for Concussion*, outlines mechanistic support for the use of aerobic exercise for concussion rehabilitation.<sup>94</sup> Specifically, aerobic exercise improves ANS dysfunction, cerebral blood flow control, brain neuroplasticity, attenuates cognitive impairment, and improves emotional and behavioral concussion-related symptoms (specifically anxiety and depression).<sup>94</sup>

Initial research investigating aerobic exercise for concussion rehabilitation focused on patients with persistent concussion symptoms, finding evidence that it improves post-concussion outcomes.<sup>98–100</sup> Specifically, Kurowski and colleagues<sup>98</sup> enrolled adolescents with persistent concussion symptoms into an at home six-week randomized control trial. Subjects were randomized to complete aerobic exercise at 80% of their achieved heart rate during the

baseline exercise tolerance assessment for 20 minutes, 5-6 days/week or a prescribed stretching protocol for the same days and time. Results showed a group by time interaction, indicating an increased recovery rate in subjects in the exercise group. Gladstone and colleagues<sup>99</sup> reported the secondary outcomes, identifying pre-post differences in fluid and crystallized cognition in the aerobic exercise group. Additionally, pre-post differences in self- and parent reported QOL were identified in both the aerobic exercise and stretching groups. Using a modified version of the protocol described by Kurowski and colleagues, Chrisman and colleagues<sup>100</sup> found that subject-reported concussion symptoms improved more rapidly in the aerobic exercise compared to stretching control group (adolescents with symptoms 3-6 weeks post-concussion). In this study, subjects started daily activity participation at 5-10 minutes and worked toward a goal of 60 minutes per day (different than Kurowski et al. where subjects completed 20 minutes of activity per day throughout the entire study period). These findings show that aerobic exercise protocols can be individually modified and used in populations not ready for participation in high intensity or long duration physical activity post-concussion. Additionally, increases in QOL and fear avoidance of pain were reported in both groups.<sup>100</sup>

Current research suggests engaging in aerobic exercise-based rehabilitation acutely postconcussion is safe<sup>101</sup> and results in faster return to asymptomatic.<sup>97,102–104</sup> Specifically, in acutely concussed adolescents, Leddy and colleagues have completed two studies comparing how aerobic exercise compared to prescribed stretching improves concussion recovery.<sup>97,102</sup> In both studies, the aerobic exercise group was instructed to perform daily at-home aerobic exercise on a stationary bike or treadmill for at least 20 minutes per day. During exercise, the subject's intensity goal was to achieve 80% in the initial study and 90% in the more recent study of the heart rate achieved during their baseline exercise tolerance assessment, the Buffalo Concussion Treadmill Test (BCTT).<sup>90</sup> The BCTT, a validated safe protocol used to assess exercise tolerance in concussion patients, is a 20-minute protocol in which subjects walk on a treadmill as intensity increases and concussion symptoms are monitored each minute.<sup>101,102</sup> Results from the initial study showed that subjects who participated in the aerobic exercise group recovered (symptom resolution to normal confirmed by a physical examination and ability to complete the BCTT without symptom exacerbation) sooner than those randomized to the stretching protocol (median recovery of 13 vs. 17 days respectively).<sup>102</sup> Results from a more recent Leddy and colleagues study indicate that aerobic exercise had a significant effect on clinical recovery within the first four weeks post-concussion, with a 48% reduction in persistent post-concussion symptoms risk.<sup>97</sup>

In adolescents and young adults with acute concussion, Howell and colleagues<sup>103</sup> compared symptom severity in those randomized to complete eight weeks of aerobic exercise five times per week for 20 minutes at an individualized target heart rate compared with standard of care. Overall, there were no significant symptom severity differences between groups at the initial, one month, or two-month study visits. Additionally, exercise volume (minutes per week) did not differ between groups, a finding that could have impacted the symptom severity analyses. Regardless of group, subjects who reported <100 minutes of exercise per week reported significantly higher symptom severity at the one-month study visit than subjects who reported  $\geq$ 100 minutes. Furthermore,  $\geq$ 160 minutes of exercise per week discriminated between those with and without symptoms at the one-month study visit, a finding which may inform future post-concussion exercise protocols.

Furthering work investigating the use of aerobic exercise for acute concussion in adolescents, Dobney and colleagues<sup>104</sup> assessed the feasibility of a comprehensive active

rehabilitation protocol beginning two weeks post-concussion compared to four weeks postinjury (control group of usual care for active rehabilitation). The active rehabilitation protocol consisted of aerobic exercise (15 minutes at 60% of the age-predicted maximum heart rate); coordination and skill practice (10 minutes, individualized for sport preference); visualization (5-10 minutes, individualized for sport preference), and education (information about recovery, coping with symptoms, and returning to school/sport). Results indicate an acceptability from physicians and positive safety, adherence, and efficacy of the intervention protocol. Overall, post-concussion symptoms improved over time for both groups. Future research via a largescale clinical trial is necessary to determine the overall impact of utilizing active rehabilitation strategies in acutely post-concussion.

Varner and colleagues<sup>105</sup> have completed the only acute concussion aerobic exercise intervention in a general adult population. Adults presenting to the emergency department within 48 hours of concussion were prescribed 30 minutes per day of light aerobic exercise (intervention) or treatment as usual (follow the gradual return to exercise following symptom resolution). Overall, the proportion of subjects with persistent concussion symptoms at 30 days, median pre/post change in concussion symptoms, visits to a healthcare provider, missed school/workdays, and unplanned emergency department visits did not differ between groups. Subjects in the intervention group were not asked to reach a target heart rate during activity. As such, subjects may not have reached an exertion level intensity impactful enough to target postconcussion neurophysiological dysfunction.

Minimal research has investigated the use of aerobic exercise in individuals with a concussion history. Larson-Dupuis and colleagues<sup>96</sup> completed a 12-week aerobic exercise intervention in which subjects with a concussion history engaged in either aerobic exercise on

a cycle ergometer or whole body stretching (control) for 20-40 minutes three times weekly. Results indicated improved physical fitness (i.e.,  $VO_{2max}$ ) for subjects in the exercise group compared to those in the stretching control group. No differences were identified in neuropsychological performance. Of note, subjects for this study were sedentary, healthy asymptomatic individuals with a concussion history ages 50-70. As such, improvements in physical fitness may have been a result of the increased physical activity compared to the subject's pre-intervention levels.

In addition to the primary original research outlined above, recent systematic reviews suggest moderate to large effects of aerobic exercise for post-concussion rehabilitation. Specifically, in adolescent populations, Langevin and colleagues<sup>106</sup> identified three aerobic exercised-based studies in adolescents with acute sport-related concussion as having a significant beneficial impact on concussion symptom recovery and Powell and colleagues<sup>107</sup> identified five studies in adolescents with both acute and persistent concussion in which aerobic exercise improved recovery and decreased concussion symptom severity. When looking at the effect of physical exercise post-concussion, Lal and colleagues<sup>108</sup> identified 14 studies showing exercise significantly decreased concussion symptoms and days of work missed compared to controls. Finally, Carter and colleagues<sup>109</sup> reviewed the use of various forms of physical activity of concussion recovery, finding a large, positive effect size of physical activity on concussion recovery. Specifically identifying the largest effect sizes for sub-symptom threshold aerobic exercise (g=1.71) and multimodal interventions (g=0.70).

Although research indicates use of aerobic exercise for concussion rehabilitation is beneficial, gaps in the literature exist. Most research has been completed in adolescent populations. Therefore, results may not be generalizable to young or older adults. Although studies in healthy

populations identify that aerobic exercise residually improves cognitive function and emotional and behavioral-related concussion symptoms,<sup>110</sup> majority of aerobic exercise post-concussion studies did not measure results associated with those post-concussion deficits. Similarly, mechanistic support for the use of aerobic exercise hinges upon improvement of ANS balance, yet majority of studies do not directly report physiological outcomes. Finally, limitations exist with the use of aerobic exercise in those with pre-injury orthopedic injuries, cardiovascular impairments, or any medical condition which puts them at risk during aerobic exercise. To address these limitations, future research should investigate the use of additional exercise modalities. Moreover, future studies investigating the combined use of aerobic exercise and mindfulness would aim to intervene on physiological and psychological stress deficits incurred as a result of ANS dysfunction post-concussion.

# 2.5.3 Cognitive Training

To address post-concussion cognitive dysfunction, research has investigated the use of cognitive training to improve post-concussion outcomes. As cognitive training focuses on a single domain of post-concussion deficits, limited studies have been conducted and no cognitive training gold standard protocol exists. However, multiple manuscripts have reported results of a novel cognitive training-based concussion rehabilitation program, the CogSMART compensatory cognitive training protocol. CogSMART is a 12-week cognitive training intervention aimed to improve positive habit learning and compensatory strategies in prospective memory, attention, learning, memory, and executive functioning.<sup>111–114</sup> Specific strategies for each domain include psychoeducation and mindfulness-based stress reduction to improve post-concussion for prospective memory, conversational and task vigilance skills for attention and vigilance, encoding and retrieval strategies for learning and

memory, and problem solving for executive functioning. The initial pilot study observed veterans assigned to CogSMART reported significant reductions in post-concussion symptoms and improvements in prospective memory functioning.<sup>111</sup> Following the initial pilot study, a one-year longitudinal study investigating veterans who participated in either a CogSMART protocol in addition to weekly employment support visits compared to those who participated in just employment support visits found CogSMART-associated reductions in post-concussion symptoms, improvements in prospective memory, and enhanced QOL.<sup>112</sup> Additionally, in Cog-SMART interventions, baseline mental health symptoms were not associated with improvements in concussion symptoms<sup>113</sup> and did not moderate cognitive improvements.<sup>114</sup> CogSMART studies included veterans with mild to moderate traumatic brain injury. Future research should investigate how the protocol differed in veterans with mild compared to moderate injuries and how the intervention could be utilized for additional populations.

Additional cognitive training studies in the military setting have also found positive intervention-related outcomes. Specifically, veterans who completed a 10 week cognitive training intervention reported significantly fewer cognitive and memory difficulties and showed greater use of higher cognitive function as well as improvements in attention, learning, and executive function compared to a usual care group.<sup>115</sup> Similar veteran-focused cognitive research incorporated a cognitive rehabilitation protocol (meeting one-on-one with a cognitive rehabilitation specialist where subjects were taught strategies to help manage cognitive difficulties in the workplace and skills to recognize, control unhelpful behaviors at work, and build positive relationships with coworkers) into a usual vocational rehabilitation care.<sup>116</sup> This study found increased employment rates and overall intervention satisfaction in those randomized to the cognitive training and vocational training group, providing initial evidence

which supports further investigation of this cognitive-focused protocol on a larger scale.<sup>116</sup>

Unfortunately, limited data exists investigating cognitive training interventions in nonmilitary populations. However, these limited studies suggest engaging in cognitive training postinjury can improve cognition. Specifically, research suggests that engaging in an online training for stress management, problem solving, self-regulation, communication, and social skills improved executive function and externalizing behaviors in adolescents from less advantaged households.<sup>117</sup> This study involved adolescents with anywhere from mild to severe brain injuries; therefore, results do not directly translate to concussion-specific rehabilitation. Additional research identified adults who sustained a mild/moderate traumatic brain injury eight to twelve weeks before study onset and randomized subjects to complete ten weeks of compensatory cognitive training combined with supported employment or treatment as usual.<sup>118</sup> Subjects in the intervention group attended weekly sessions with a clinical psychologist and physicians who taught strategies aimed to alleviate cognitive concussion symptoms. Overall, a significantly higher proportion of subjects in the intervention group had returned to stable employment at three months; however, there were no group differences at the six- and twelve-month follow-ups.<sup>118</sup> Despite the intervention description identifying a focus on cognitive concussion symptoms, no concussion-specific outcomes were reported.

Despite positive findings from current cognitive training studies, limitations exist. First, current cognitive training-based interventions focused on individuals either with or at risk for persistent post-concussion symptoms. Furthermore, most studies utilized a military population. Therefore, information gained from these studies is not generalizable. Future research should investigate how cognitive training could impact acute concussion rehabilitation (when post-concussion neurophysiological changes are at their peak) and its effectiveness for different

populations such as athletes and individuals of all ages. Additionally, current interventions incorporate cognitive training techniques that require large amounts of time and access to psychotherapeutic resources that did not coincide with physical rehabilitation, making it clinically and/or financially challenging for some rehabilitation centers or athletic departments. Although the current study does not incorporate cognitive training techniques, research suggests mindfulness-based interventions improve cognition.<sup>119</sup> Specifically, a recent meta-analysis identified 33 randomized control trials investigating the use of mindfulness-based interventions in healthy youth in which those receiving mindfulness had significantly improved executive functioning.<sup>119</sup> Additionally, in a pilot study examining the effects of mindfulness-based stress reduction on persistent concussion symptoms, clinically meaningful, significant improvements were identified in working memory and attention regulation.<sup>42</sup> In patients with other forms of brain injury (i.e., moderate traumatic brain injury and stroke) those who completed mindfulnessbased stress reduction for eight weeks saw significant improvements in Digit Symbol Coding, a measure of processing speed, working memory, visuospatial processing, and attention, and the Trail Making Test measures for dual task.<sup>44</sup> As such, findings from the current study may inform future cognitive-focused intervention protocols.

# 2.5.4 Vestibular Therapy

In addition to other domains, concussion impacts the functional components of the vestibular system which together play a role in balance, gaze, stabilization, and visual/spatial orientation. As such, common post-concussion clinical domains include dizziness and headache symptoms as well as balance impairments. Vestibular therapy is typically individualized to the patient based on his/her post-concussion deficits and may include repositioning maneuvers to address vertigo, habituation exercises to address motion sensitivity, gaze stability and substitution

exercises to address eye movement central programming, and exercises to improve balance impairments.<sup>120</sup> Additionally, due to the neurophysiologic nature of experiencing vestibular system dysfunction post-concussion, majority of studies using vestibular therapeutic exercises incorporated them in a multimodal design (combined with additional modalities such as manual therapy, strength training, occupational tasks, counseling, and medication).<sup>120</sup>

Studies in this area highlight vestibular rehabilitation may improve dizziness and balance impairment post-concussion. Specifically, adults identified via retrospective chart review with dizziness and balance impairment post-concussion who were prescribed vestibular therapy saw improvements in balance performance after completion.<sup>121</sup> Additionally, in a four subject case series, individuals with post-concussion dizziness and balance problems completed an eight-week vestibular rehabilitation intervention. Majority (3/4) reported reduced self-perceived disability because of dizziness, diminished frequency and severity of dizziness, improved QOL, reduced psychological distress, and improved balance performance.<sup>122</sup>

Few randomized control trials have been completed to determine the use and utility of vestibular therapy post-concussion. In a single-blind randomized control trial, 65 subjects were randomized to complete treatment as usual (multidisciplinary outpatient rehabilitation aimed to strengthen self-efficacy and return to activities of daily living and work) or treatment as usual combined with vestibular rehabilitation (exercises to reduce dizziness-related disability, including adaptation, habituation/compensation, and balance/gait, twice a week facilitated by a physiotherapist). Primary analyses indicated intervention-related improvements in dizziness symptoms, vertigo symptoms, concussion symptoms, anxiety symptoms, depression symptoms, and balance performance.<sup>123</sup> Additional analyses indicated that predictors of change in QOL post-concussion were receiving vestibular rehabilitation, baseline psychological distress, and change in

concussion symptom score throughout recovery.<sup>123,124</sup> In a double-blind randomized control trial in adolescents with vestibular symptoms and impairment post-concussion, subjects were enrolled in either treatment as usual (behavioral management including physical activity, sleep, hydration, nutrition, and stress management) or vestibular rehabilitation (30 minutes of at home vestibular exercises daily).<sup>125</sup> Subjects who completed the vestibular rehabilitation saw significant improvements in horizontal and vertical vestibular-ocular reflex, but not in visual motion sensitivity.<sup>125</sup>

As noted, vestibular therapy post-concussion is frequently used in a multimodal intervention design. Schndeider and colleagues completed a randomized control trial combining cervical and vestibular rehabilitation post-concussion in subjects experiencing dizziness, neck pain, and/or headaches post-concussion.<sup>126</sup> Overall 73% of subjects in the treatment group were medical cleared after completing eight weeks of rehabilitation compared to only 7% in the control group. Additionally, individuals in the treatment group were 3.91 times more likely to be medically cleared after eight weeks.<sup>126</sup>

Current research identifies the impact that vestibular rehabilitation may have on individuals with vestibular-related post-concussion symptoms and deficits. However, minimal studies incorporated large samples. Additionally, although some studies have used vestibular rehabilitation techniques in conjunction with other forms of post-concussion rehabilitation, more research is needed to investigate the most impactful use of vestibular rehabilitation as a piece of a multimodal paradigm. Specifically, results from the current study may be informative for future multimodal interventions incorporating both mindfulness and vestibular therapy.

# 2.5.5 Psychotherapy

As described above, research identifies mechanistic support for the development of emotional and behavioral-related and persistent concussion symptoms (i.e., mechanistic support for the use of psychotherapy for concussion rehabilitation as this tool targets emotional and behavioral-related and persistent concussion symptoms).<sup>73</sup> Research indicates that psychotherapy improves symptoms related to various psychiatric disorders including depression and anxiety.<sup>127</sup> In addition, psychotherapy improves ongoing anger, stress, and physical health, specifically showing a decrease in blood pressure.<sup>128</sup> Furthermore, the use of psychotherapy shows long-term benefits, showing less relapse in psychological symptom expression than the use of psychiatric medications alone.<sup>128</sup> The American Psychological Association identifies five broad categories of psychotherapy including psychoanalysis, behavioral therapy (including cognitive behavioral therapy), cognitive therapy, humanistic therapy, and integrative therapy.<sup>129</sup> The use of one/more of these therapy types is therapist and client dependent, with cognitive behavioral therapy being to most widely used approach and the most beneficial to improving anxiety and depression, the most reported mental health struggles in the United States.<sup>130</sup>

Psychotherapy post-concussion is not widely used.<sup>131</sup> However, as persistent concussion symptoms and emotional and behavioral-related concussion related greatly overlap, research identifies that psychotherapy may be an impactful tool for individuals with persistent symptoms.<sup>72</sup> Specifically, a recent systematic review and meta-analysis identified 24 studies investigating the use of cognitive behavioral therapy and persistent concussion symptoms, identifying therapy-related improvements in depression, anxiety, and QOL. However, no significant effects were identified for concussion symptom severity, fatigue, executive function, and problem solving.<sup>72</sup> These results provide evidence that utilizing psychotherapy post-concussion may be beneficial,

specifically in those experiencing persistent concussion symptoms. However, the lack of significant findings related to post-concussion symptoms beyond those that are emotional and behavioral related indicate a need for continued research to identify therapy modalities and tools that may be most beneficial. Furthermore, it should be noted that studies in this meta-analysis were not strictly therapy-specific interventions, as cognitive behavioral therapy techniques were integrated into additional rehabilitation techniques such as cognitive training, vocational training, or usual care. As such, therapy-specific research is necessary to determine the impact such interventions may have on concussion outcomes.

As noted above, minimal research utilizes psychotherapy-specific interventions postconcussion. Silverberg and colleagues<sup>74</sup> provide initial support for the use of psychotherapy postconcussion, identifying that cognitive behavioral therapy provides tools for patients to change their beliefs and actions surrounding concussion-related mental health symptoms and disorders. As such, they completed a randomized control trial where subjects who were at risk for developing persistent concussion symptoms (i.e., believed concussion symptoms would persistent beyond the acute phase and that they would have catastrophic life consequences) and randomized them to complete cognitive behavioral therapy or treatment as usual for six weeks. Results showed that those who completed therapy were less likely to be diagnosed with persistent concussion syndrome post-intervention.<sup>58</sup>

Despite its potential benefit, especially in those with persistent concussion symptoms, limited research investigates the use of psychotherapy post-concussion. Furthermore, there are gaps in the current literature. First, it should be noted, our preliminary work investigating mental health and psychotherapy stigma in those with a concussion history indicates that, although 45.15% reported worsening mental health symptoms post-concussion, only 43.24% of those

individuals reported seeking mental health treatment post-concussion.<sup>132</sup> These results highlight the need for psychotherapeutic-based concussion research to further identify biases associated with seeking mental health treatment post-concussion and how those biases may impact the use and utility of interventions. Additionally, although psychotherapy targets emotional and behavioral-related concussion symptoms, it does not address physical impairments seen post-concussion (i.e., exercise intolerance, balance impairments, vestibular/ocular impairments). As such, research investigating the use of psychotherapy in conjunction with exercise could be impactful for post-concussion patients. Additionally, current research focuses on the use of cognitive behavioral therapy. Although this is a popular form of psychotherapy, investigating into the use of additional forms of therapy (e.g., dialectical behavioral therapy, motivational interviewing, mindfulness-based therapies) may be beneficial. Results from the current study will provide evidence to support the use of mindfulness-based therapy techniques to improve post-concussion outcomes.

# 2.5.6 Yoga

Yoga aims to intervene directly on ANS dysfunction (improve ANS balance to minimize physiological and psychological stress), vestibular/ocular dysfunction (improve balance and spatial orientation), and cervical spine dysfunction (improve balance and neck pain and mobility). As such, yoga interventions may be extremely impactful to improve outcomes post-concussion. Despite this evidence, minimal research exists investigating the use of yoga post-concussion. Paniccia and colleagues<sup>133</sup> completed a study looking at the use of yoga and mindfulness in adolescents with persistent concussion symptoms. Subjects were asked to complete eight group yoga and mindfulness sessions. After completion of the sessions, results suggest decreases in concussion symptoms and increases in QOL.<sup>133</sup> Additionally, using visualization of heart rate variability (HRV) metrics, results suggest an increase in parasympathetic nervous system

activity.<sup>133</sup> Stephens and colleagues<sup>134</sup> completed a study looking at the use of yoga in those with mild and moderate traumatic brain injury. Results showed an increase in balance and mobility after engaging in the eight-week yoga program.<sup>134</sup> Donnelly and colleagues<sup>135</sup> completed a study investigating the LoveYourBrain yoga program, a six-week yoga, meditation, and psychoeducation program in patients with mild and moderate traumatic brain injury. During this program, individuals engaged in six weeks of weekly group classes which included breathing exercises, gentle yoga, guided meditation, and facilitated discussion and psychoeducation. Results showed post-intervention improvements in resilience, QOL, and well-being.<sup>135</sup> Research has identified successful use of the LoveYourBrain yoga program as an in-person intervention for people with traumatic brain injury. Due to the COVID-19 pandemic, LoveYourBrain has transitioned their yoga programming online to the LoveYourBrain Mindset program. As a part of this program, participants are sent weekly yoga and meditation videos to complete and have a weekly group yoga, meditation, and discussion/psychoeducation session that takes place via video conferencing (in lieu of the in-person class). This novel programming indicates positive acceptability, feasibility, and usability as well as post-intervention improvements in QOL, emotional and behavioral dysregulation, cognition, positive affect, and resilience.<sup>136,137</sup>

Despite its potential benefit, minimal research exists investigating the use of yoga postconcussion. Furthermore, there are gaps in the current literature. Majority of the work utilizes mild and moderate traumatic brain injury populations with no results comparing injury severity group differences. Additionally, only one study reported physiological measures as a part of its results. Mindfulness meditation and yoga are deeply intertwined, with purposefully connecting awareness, breath, and movement being an integral part of the yoga practice. Knowing this connection, current yoga and concussion research has used a mindfulness meditation combined with yoga approach to investigate its impact on outcomes.<sup>135,138</sup> As such, the current study's outcomes are imperative to provide more support toward using yoga and mindfulness meditation post-concussion.

#### 2.5.7 Mindfulness

Mechanistic support for the use of mindfulness post-concussion hinges upon ANS restoration, specifically intervening on the balance between the parasympathetic and sympathetic nervous systems to mitigate physiological, cognitive, and perceived stress. Despite this connection, minimal mindfulness-based concussion studies have been conducted. Azulay and colleagues<sup>42</sup> completed a prospective study using mindfulness-based stress reduction in patients with a concussion history. Subjects were asked to attend weekly group-based sessions for 10 weeks where they engaged in mindfulness-based stress reduction techniques (i.e., deep breathing, visualization, and meditation). Results showed a pre- to post-intervention decrease in concussion symptoms and increase in QOL.<sup>42</sup> Bedard and colleagues<sup>43</sup> completed a randomized control trial in subjects with a mild and moderate traumatic brain injury history. For 12 weeks, subjects in the mindfulness group-based stress reduction techniques and those in the control group completed treatment as usual. Results showed that those in the mindfulness group reported significant increases in attention and QOL.<sup>43</sup>

Various gaps exist in the mindfulness-based literature. First, no studies have investigated the impact that mindfulness meditation has on commonly used post-concussion outcomes, questions which will be investigated in the current study. Majority of research is done in populations consisting of mild and moderate traumatic brain injuries, without comparing injury severity groups. Additionally, majority of studies investigating the use of mindfulness and yoga for concussion rehabilitation utilize mindfulness-based stress reduction.<sup>139</sup> As such, future research is necessary to investigate the use of various types of mindfulness techniques and their ability to

impact post-concussion outcomes. Finally, although mindfulness techniques address postconcussion ANS dysfunction, they do not address all physiological and physical post-concussion impairments. As such, research investigating the use of mindfulness in conjunction with exercise could be impactful for post-concussion patients. Results from the current study will not only provide continued evidence to support mindfulness meditation post-concussion, but also how to integrate paradigms into current clinical practices.

# 2.5.8 Post-Concussion Rehabilitation Summary and Future Research

Overall, current intervention paradigms focus on improving time to recovery, symptom expression, and clinical concussion deficits. Despite the evidence identified by current interventions as outlined above, few studies have examined how psychosocial factors and interventions mitigate negative post-concussion outcomes. Understanding such factors is imperative to inform the most effective interventions to improve post-concussion outcomes. As such, this study aims to identify an association between perceived stress, mindfulness, and clinical and psychological concussion outcomes. Further understanding of factors such as perceived stress and additional studies of mindfulness are needed to bridge the current gaps and improve future interventions.

#### **2.6 Perceived Stress**

Perceived stress is defined as, "The feelings or thoughts that an individual has about how much stress they are under at a given point in time or over a given time. It measures how an individual feels about the general stressfulness of their life and their ability to handle such stress."<sup>47</sup> An individual's perceived stress fluctuates based on life events and/or his/her environment. Specific events, such as a major life changes including injury (i.e., concussion), may result in increased perceived stress. Concurrently, an individual's ability to manage stress may also impact

their reactions to stressful life events, potentially increasing stress further. As such, research has identified various social, personality, and behavioral factors which may predict increased perceived stress including socioeconomic status (specifically lower education access and income),<sup>140</sup> female sex,<sup>140</sup> increased anxiety,<sup>141</sup> low levels of physical activity,<sup>141</sup> low emotional intelligence,<sup>142</sup> and low self-acceptance.<sup>143</sup>

Increased perceived stress is associated with a wide range of negative health outcomes including increased depression,<sup>17</sup> anxiety,<sup>17</sup> and exhaustion<sup>17</sup> as well as decreased physical health,<sup>18</sup> life satisfaction,<sup>19</sup> and QOL.<sup>20</sup> To mitigate negative health outcomes associated with increased perceived stress, research has identified interventions which may decrease perceived stress. Specifically, mindfulness meditation,<sup>40,144,145</sup> yoga,<sup>40,135,146</sup> mindfulness-based cognitive therapy,<sup>147</sup> physical activity (including aerobic and anerobic exercise),<sup>148–150</sup> and psychoeducation.<sup>151</sup> Additionally, research has identified that group-based, community and social interventions such as group fitness classes may decrease perceived stress.<sup>135,146,148,151</sup>

## 2.6.1 Perceived Stress, Injury, and Concussion

Athletes, especially those at a high level, are exposed to increased physical and mental demands compared to their non-athlete counterparts and high expectations to consistently perform well and improve, potentially leading to increased perceived stress. As such, research has identified that, in athletes, fear of failure may lead to perceived stress and result in sport burnout.<sup>152</sup> Additionally, research has identified that increased practice and game load leads to increased perceived stress and decreased overall wellness.<sup>153</sup> In sport specific research, perceived stress predicts sports injury.<sup>21,22</sup> Specifically, in young adults, increased reported stress symptoms were related to increased injury risk throughout a competitive soccer season.<sup>23</sup> Additionally, perceived negative life event stress from an athlete's coach increased the risk of overuse injuries in elite

female soccer players<sup>24</sup> and negative life event stress and high levels of life-related stress predicted injury rates in adolescent and young adult soccer players.<sup>25</sup> The presence of perceived stress in athletes not only impacts their mental and physical health, as outlined above, but also leads to decreased sport performance.<sup>154</sup>

Limited data suggests perceived stress is heightened in individuals acutely postconcussion.<sup>13</sup> Specifically, Hutchinson and colleagues<sup>155</sup> identified that perceived stress increased acutely post-concussion but was significantly better at return to play when compared to a control, non-concussed group. Further research indicates that perceived stress may play a role in predicting persistent concussion symptoms,<sup>27</sup> indicating a potential mechanism for intervention to decrease long-term injury. In persistent concussion symptom patients, exposure to a high stress condition (mental arithmetic) exacerbated post-concussion symptoms, decreased information processing speed, and decreased memory performance;<sup>19</sup> findings which indicate the potential impact stress may have on concussion outcomes.

In addition to perceived stress's association with injury and concussion history, extensive research in military populations has identified that reporting a concussion history is significantly associated with an increased likelihood of reporting post-traumatic stress disorder (PTSD) symptoms, a psychological condition related to an exposure to a traumatic event.<sup>28,29</sup> Various factors have been associated with the presentation of PTSD including increased pre-injury perceived stress.<sup>28</sup> Additionally, soldiers reporting a concussion history and PTSD diagnosis showed decreased cognitive performance, increased psychological distress, and decreased ability to manage post-injury life stressors, identifying a continued connection between stress and concussion outcomes.<sup>28,30</sup> In non-military populations, minimal research has identified that perceived stress acutely post-concussion meditated the relationship between concussion symptom

scores at two weeks post-concussion and PTSD symptom scores at three months post-injury.<sup>31</sup> Despite the evidence that perceived stress may play a role in an individual's concussion recovery, the association between perceived stress and concussion outcomes, a mechanism necessary to inform comprehensive interventions, is largely unknown.

# 2.6.2 Mechanistic Support for Perceived Stress in the Proposed Study

Perceived stress is multifaceted as it is impacted by and impacts various psychological and physiological factors. Specifically, as outlined, we recognize that life events as well as social, personality, and behavioral factors may predict increased perceived stress including socioeconomic status (specifically lower education access and income),<sup>140</sup> female sex,<sup>140</sup> increased anxiety,<sup>141</sup> low levels of physical activity,<sup>141</sup> low emotional intelligence,<sup>142</sup> and low selfacceptance.<sup>143</sup> These factors may play a role in instigating perceived stress as well as increasing its intensity throughout one's life. Perceived stress also has physiologic implications. Specifically, the ANS engages the "fight or flight" sympathetic nervous system, causing increased heart rate, blood flow, and breath rate.<sup>54</sup> As identified, concussion causes ANS dysfunction, leading those impacted to have an impaired balance between the parasympathetic and sympathetic nervous systems (specifically increasing sympathetic nervous system activation, this is seen postconcussion as increased heart rate and heart rate variability).<sup>5,54</sup> As such, although we recognize that many factors play a role in causing and increasing perceived stress (factors which also impact concussion), for the proposed study we chose to focus on the physiologic underpinnings connecting perceived stress and concussion outcomes. Specifically, the mechanistic pathway between the ANS, perceived stress, and concussion outcomes.

# 2.7 Mindfulness

Mindfulness is a technique which focuses on attention (bringing your awareness and experiences to focus on the present moment) and acceptance (observing any feelings or sensations without judgment and letting them go without reaction).<sup>46</sup> The neurophysiologic underpinnings of mindfulness hinge upon the notion that mindfulness changes neural structure and connectivity in regions associated with attention and emotional regulation.<sup>156</sup> Specifically, enhanced activation of the anterior cingulate cortex, prefrontal cortex, posterior cingulate cortex, insula, and striatum – all leading to improved attention, emotion, and self-awareness.<sup>156</sup> Additionally, studies have shown mindfulness-related decreased activation of the amygdala, leading to positive emotional processing.<sup>156</sup>

Higher mindfulness levels are associated with decreased perceived stress<sup>32-34</sup> and improved mental health,<sup>35</sup> physical health,<sup>35</sup> and subjective psychological well-being.<sup>33</sup> In healthy populations, mindfulness-based interventions (i.e., meditation and yoga) improve mindfulness and perceived stress.<sup>36-40</sup> In athletic populations, mindfulness-based yoga has shown to mitigate stress and fatigue related to sports injury<sup>41</sup> and mindfulness training has shown to improve performance and mental health in athletes.<sup>157,158</sup> Specifically, athletes who completed six-week of mindfulness training including skills for non-judging, awareness, acceptance, breathwork, and mindful movement (yoga and walking) reported higher mindfulness levels, cognitive function, and overall athletic performance.<sup>157</sup> Athletes who engaged in eight weeks of mindfulness-based stress reduction reported an increased positive mood and decreased stress and anxiety.<sup>158</sup> In addition to improving mindfulness and mental health, mindfulness-based interventions have shown to improve physiologic performance (i.e., resting heart rate, cortisol levels, oxygen uptake, and

immune response).<sup>159</sup> As concussion results in psychological as well as physiologic disturbances, such findings provide evidence that mindfulness training may be impactful post-concussion.

Research suggests that low levels of mindfulness may predict PTSD symptoms.<sup>160</sup> As such, mindfulness-based interventions have been used in military populations, specifically connected to PTSD.<sup>161</sup> Additionally, studies suggest that mindfulness training improves PTSD-related symptoms and impairments. In a recent randomized control trial in 48 veterans with PTSD, subjects were randomized to either complete socio-therapeutic group sessions (control) or mindfulness-based stress reduction sessions (intervention) weekly for eight weeks.<sup>162</sup> Results suggest intervention-related reductions in PTSD symptoms, depression, anxiety, and stress.<sup>162</sup> In another study in veterans with PTSD, subjects participated in a weekly military adapted mindfulness-based yoga program for six weeks with results suggesting post-yoga improvements in PTSD symptoms, mindfulness, insomnia, depression, and anxiety.<sup>163</sup> Furthermore, also in soldiers, research suggests perceived stress partially mediates the relationship between mindfulness and QOL, findings which support the current study and the use of mindfulness post-concussion.<sup>164</sup>

Research suggests mindfulness-based stress reduction improves QOL in persistent concussion symptom patients.<sup>42</sup> However, this pilot study did not investigate associations between mindfulness and comprehensive clinical and psychological concussion outcomes. Such findings are necessary to design effective concussion interventions. In patients with other forms of brain injury (i.e., moderate traumatic brain injury and stroke) engaging in mindfulness techniques (meditation, breathing exercises, guided visualization, and body-scanning) significantly improved QOL.<sup>43,44</sup> However, these techniques have not been connected to concussion-related outcomes outside of QOL and have not been investigated in those with a history of concussion. Additionally,

mindfulness-based traumatic brain injury rehabilitation literature primarily utilizes military populations and those with more severe traumatic brain injuries making it unclear: 1) the connection between mindfulness and concussion-specific outcomes; and 2) how impactful mindfulness techniques may be in those with a concussion history. As such, the current study aims to identify the association among perceived stress and clinical and psychological concussion outcomes in those with a concussion history to inform future interventions.

## 2.8 Theory-Based Conceptual Model

The conceptual model and theoretical framework for the proposed study was built using established public health, mental health, and injury-related conceptual models. The sections below detail the frameworks used to develop the current study methods, identifying connections to concussion, perceived stress, and mindfulness and, finally, outlining the current study's conceptual model.

## 2.8.1 The Biopsychosocial Model

The biopsychosocial model indicates medical conditions are made up of biological, psychological, and social components.<sup>165</sup> This model has been successfully implemented to improve treatment for chronic pain, spinal cord injury, PTSD, and depression.<sup>166</sup> Related to concussion, current research indicates how post-concussion rehabilitation interventions may benefit from adopting the biopsychosocial model.<sup>167–169</sup> Concussion-related symptoms and impairments are associated with each component of the biopsychosocial model. Specifically: 1) biological post-injury considerations include the neurometabolic cascade, ANS dysfunction, vestibular/ocular dysfunction, cervical spine dysfunction, headache, nausea, fatigue; 2) psychological post-injury considerations include increased irritability, anxiety, depression, mood changes, and perceived stress; 3) social post-injury considerations include access to care,

rehabilitation as a social activity, and missed school, work, sport, or social engagements postconcussion. Concussion intervention design and consideration should target key biopsychosocial model components to achieve complete post-concussion recovery. As such, the current study's perceived stress and mindfulness foundation aims to provide evidence supporting the use of mindfulness as a post-concussion intervention, an approach targeting the biological, psychological, and social components of concussion.

## 2.8.2 Keyes Mental Health Continuum

The Keyes Mental Health Continuum focuses on the psychological components of one's health, specifically mental illness and mental health. Mental illness is a diagnosed mental, behavioral, or emotional disorder<sup>170</sup> whereas mental health is a state of well-being related to one's psychological and emotional health.<sup>171</sup> Mental health has individual and community levels, with psychological well-being made up of self-acceptance, life purpose, relationships with others, and personal growth and social well-being encompassing social coherence, acceptance, contribution, and integration.<sup>171</sup> The Keyes Mental Health Continuum operationalizes mental health as a syndrome of positive feelings and positive functioning in life using a dimensional scale of mental health and mental illness.<sup>172</sup> This dual continuum model identifies that those in good mental health, with both yes and no mental illness status, are flourishing (i.e., high functioning, an optimal level of psychological and social functioning) and those in poor mental health are languishing (i.e., low functioning).<sup>172</sup> Within this model, the goal is to reach the flourishing state of optimal mental health regardless of mental illness status. The Keyes Mental Health Continuum highlights the necessity for concussion rehabilitation modalities to target emotional and behavioral-related symptoms at the individual and group (i.e., team, community) levels. This study's conceptual model depicting the impact perceived stress has on concussion outcomes utilizes Keyes's theory that those in poor

mental health status are languishing, playing a role in negative concussion outcomes. Additionally, the current study's investigation into mindfulness's relationship to improve perceived stress and overall concussion outcomes targets mental health-related post-concussion deficits to ultimately improve overall outcomes, with the goal of bringing individuals into the flourishing state.

## 2.8.3 Cognitive Appraisal Model

Continuing to focus on psychological well-being, the Cognitive Appraisal Model provides theory behind psychological consequences and outcomes surrounding injury. Specifically, personal and situational factors influence cognitive appraisal which determine emotional and behavioral responses to injury and recovery, all of which contribute to physical and psychological recovery outcomes.<sup>173</sup> Personal factors include injury-related factors such as history, severity, type, cause, and recovery status as well as individual differences such as demographics (sex, age, ethnicity, sport experience), physical health status, and psychological differences (selfperceptions, personality, motivational orientation, pain tolerance, athletic identity, coping skills, psychological skills, history of stressors, mood states). Situational factors include sport (type, level of competition, time in season, playing status, practice/game, scholarship status), social (teammate influences, coach influences, family dynamics, sports medicine team, social support, sport ethics), and environmental (rehabilitation environment and access).<sup>173</sup> Emotional responses to injury include the fear of the unknown; tension, anger, and depression; frustration/boredom; positive attitude; grief; and emotional coping.<sup>173</sup> Behavioral responses to injury include adherence to rehabilitation, use of social support, risk tasking behaviors, effort, and behavioral coping. Positive personal and situational factors play a role in positive cognitive appraisal surrounding injury, leading to positive physical and psychological injury outcomes.<sup>173</sup> Furthermore, in patients with severe traumatic brain injury, cognitive appraisal was associated with positive changes in selfefficacy and self-discrepancy.<sup>174</sup> The Cognitive Appraisal Model uses theory that one's stress response after injury plays a role in injury response and outcomes. This study's investigation into the association between perceived stress and concussion outcomes will provide evidence to support intervention on perceived stress post-concussion, providing injured individuals with tools to improve stress response and overall injury outcomes.

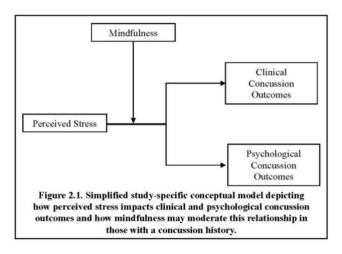
# 2.8.4 Stress and Injury Model

The Stress and Injury Model builds upon Cognitive Appraisal Model to identify that personality, history of stressors, and coping resources all contribute to one's response to psychological and physiological stress after a stressful athletic situation.<sup>175</sup> This interaction impacts overall injury outcomes. As such, intervention on the stress response would impact injury outcomes. Specifically, research utilizing the Stress and Injury model suggests increases in stressful, negative life events increases the probability of sustaining an athletic injury.<sup>176,177</sup> Although the Stress and Injury Model has not been used in concussion-related research, it is a crucial model for concussion rehabilitation intervention design, as perceived stress and physiological stress are impacted after injury. Therefore, utilizing the theory behind this model to intervene on stress responses may improve overall concussion outcomes. Our conceptual model builds from the Stress and Injury Model to show that perceived stress impacts clinical and psychological concussion outcomes. Also building from the Stress and Injury Model, we identify that mindfulness will moderate this relationship, presenting mechanistic support to intervene on perceived stress to improve concussion outcomes.

### 2.8.5 Conceptual Model

Based on the models presented above and literature surrounding concussion, perceived stress, mindfulness, and concussion outcomes, we propose the following conceptual model (Figure

2.1). Specifically, the notion that perceived stress impacts clinical and psychological concussion outcomes, a relationship believed to be moderated by mindfulness. If an individual who suffers a concussion has increased perceived stress, he/she will show greater deficits in clinical and psychological



concussion outcomes. By improving mindfulness to decrease perceived stress, clinical and psychological concussion outcomes will improve (i.e., we expect the moderation of mindfulness to buffer the relationship between perceived stress and concussion outcomes).

#### **2.9 Methodological Considerations for the Current Study**

The sections below outline methodological considerations for the current study necessary to meet the study's aims. Current literature providing support for each key methodological consideration are summarized below. Methodological considerations for the exploratory Aim 3 are discussed separately at the end of this section.

#### 2.9.1 Study Design and Participants

To date no research has identified the impact perceived stress and mindfulness have on clinical or psychological concussion outcomes. As such, a cross-sectional study design was chosen for Aims 1 and 2 to identify initial associations among variables. Results provide evidence to support future mindfulness-based concussion interventions.

The participant age range and concussion history delineation were chosen to contribute to a meaningful analysis relative to the study purpose. Specifically, those aged 18-30 were chosen to: 1) represent the age of individuals with a relatively high concussion risk;<sup>178</sup> 2) remain consistent

with previous literature in the concussion history and concussion outcomes space;<sup>2,18,19,179</sup> 3) ensure subjects will be able to complete all study assessments on their own merit; and 4) maximize recruitment to ensure that the proposed sample size is met.

# 2.9.2 Perceived Stress Considerations

Perceived stress was measured using the Perceived Stress Scale (PSS-10) as it is the most widely used psychological instrument for measuring perceived stress.<sup>180</sup> Furthermore, the PSS-10 is well validated and has been utilized in connection to mindfulness<sup>32–34,37,40</sup> and in brain injury populations.<sup>43</sup> The scale has three versions (PSS-14, PSS-10, and PSS-4, consisting of 14, 10 and four items respectively). The original 14-item scale was developed to assess how individuals perceive their life to be related to stress (specifically as unpredictable, uncontrollable, and overloading).<sup>181</sup> However, research identified four items from the original sale (items 4, 5, 12, and 13) with low factor loadings, resulting in the shorter 10-item scale.<sup>181</sup> Research identified similar to greater reliability and validity for the 10-item compared to the 14-item version.<sup>182–184</sup> As such, the current study utilized the PSS-10. Minimal research has used the four-item version, with results identifying worse reliability and validity compared the 14- and 10-item scales;<sup>182</sup> therefore, we did not consider its use in this study.

### 2.9.3 Mindfulness Considerations

Mindfulness was measured using the Five Facet Mindfulness Questionnaire (FFMQ) as it is the most widely used, valid survey to measure mindfulness<sup>185</sup> and has been researched extensively connected to perceived stress.<sup>34–36</sup> The FFMQ asks 39-questions related to five facets of mindfulness: 1) observing, noticing, and attending to sensations, perceptions, thoughts, and feelings; 2) describing/labeling one's experience with words; 3) acting with awareness; 4) nonjudging; and 5) non-reactivity to inner experience.<sup>186</sup> A shorter, 15-item version was created to minimize participant burden.<sup>187</sup> Research has identified similar reliability and validity for both the long and short versions of the FFMQ.<sup>186,187</sup> Accurately identifying mindfulness levels is a critical component to answering this study's research questions and informing future mindfulness-based concussion research. Furthermore, research suggests the use of the shorter version of the FFMQ only as an alternative measure when briefer forms are needed.<sup>188</sup> As such, we chose to utilize the full 39-item FFMQ to comprehensively capture mindfulness in our participants.

# 2.9.4 Clinical Concussion Outcomes Considerations

All clinical concussion outcomes for this study are commonly used in clinical and research settings and were chosen to ensure results from the current study are directly translatable to clinical practice and future interventions. Described below are specific considerations for each measure.

Concussion symptoms was measured using the Rivermead Post-Concussion Symptom Questionnaire (RPQ),<sup>189</sup> a valid measure frequently used in the proposed study population.<sup>190,191</sup> The RPQ was chosen over other concussion symptom scales as it is the most widely used for persistent concussion symptom patients, specifically in those with no baseline/pre-injury data for concussion symptoms, and factor analyses identified that the RPQ maintains a relatively stable structure up to one year post-concussion.<sup>192,193</sup> Outcomes for concussion symptoms were total symptoms and total symptom severity.

<u>Balance performance</u> was measured using the Balance Error Scoring System (BESS) and center of mass (COM) assessment. The BESS is a validated clinical measure for static postural balance commonly used in concussed patients.<sup>194,195</sup> The BESS is a clinical assessment, making the results from this study directly translatable to clinical practice and informative to future concussion intervention studies in which mindfulness is incorporated and balance is a factor (i.e., exercise, yoga). The outcome for balance performance was total errors on the BESS.<sup>194,195</sup> Since the BESS is a measure of static balance, we also included a COM assessment to measure balance performance. During this assessment, participants completed two one-minute trials, one with eyes open and one with eyes closed, where they were instructed to stand as still as possible with both feet touching. Throughout the assessment, an Inertial Measurement Unit (IMU, Delsys, Inc., United States) was affixed to the participant's trunk to measure center of mass. The Delsys, Inc. IMU was chosen to be used for this study as it is easily portable and accessible to clinical sports settings. This COM assessment is reliable<sup>196</sup> and has been used in the study population.<sup>197,198</sup> For each one minute trial (eyes open and closed), the COM outcomes were standard deviation (SD) of acceleration in the anterior/posterior and medial/lateral planes.

<u>ANS function</u> was measured using HRV during three intervals: 1) seated (parasympathetic domain); 2) standing (sympathetic domain); and 3) seated (recovery) conditions, a protocol used to collect HRV in individuals across all stages of concussion recovery (i.e., acute, persistent concussion symptoms and concussion history).<sup>58</sup> Our data collection and processing technique was chosen as it is consistent with previous concussion literature.<sup>199</sup> As detailed above in the review of ANS dysfunction post-concussion, the balance between the sympathetic and parasympathetic nervous systems is disrupted post-concussion. Therefore, our outcomes were high frequency power to low frequency (HF/LF) power ratio, a measure indicative of sympathetic and parasympathetic nervous system balance, and average heart rate, a measure indicative of sympathetic cardiac activation.<sup>200,201</sup>

<u>Vestibular/ocular function</u> was assessed using the VOMS assessment,<sup>202</sup> a valid and reliable clinical assessment<sup>195,203</sup> commonly used in concussed populations.<sup>202</sup> Similar to the BESS, the VOMS is a clinical assessment, making the results from this study directly translatable to clinical practice and informative to future mindfulness-based concussion interventions in which vestibular/ocular function is a factor (i.e., exercise, yoga). Consistent with previous literature, the outcomes for the VOMS were the change in total symptom score (pre- vs. post-test) for each VOMS assessment.<sup>202,204,205</sup>

Exertion tolerance was assessed using a two-minute step test. Although this assessment has not been used in a concussion-specific population, various forms have been used in additional research to measure exertion tolerance and prescribe exercise.<sup>206</sup> As our population were not acutely injured and participants with health conditions that put them at greater than minimal risk for physical activity will be excluded, this study utilized a modified version of the step test in which participants completed as many steps as possible within the two-minute timeframe. This protocol allowed us to get clear outcomes [number of steps and Rate of Perceived Exertion (RPE)] in which to assess their relationship to perceived stress and mindfulness.<sup>207</sup>

### 2.9.5 Psychological Concussion Outcomes Considerations

All psychological concussion outcomes for this study are commonly used in clinical and research settings and were chosen to ensure results from the current study are directly translatable to clinical practice and future interventions surrounding concussion. Described below are specific considerations for each measure.

<u>Neurocognitive performance</u> was assessed using CNS Vital Signs, a validated, reliable computer based neurocognitive assessment commonly used in concussed populations.<sup>208,209</sup> Additional neurocognitive performance assessments used in concussion research, such as the Immediate Post-Concussion Assessment and Cognitive Test (ImPACT) and King-Devick, were not chosen due to accessibility and the study population not being acutely post-concussion. Minimal research has used the CNS Vital Signs neurocognition index (i.e., the composite score). Therefore, to ensure we are capturing neurocognitive performance, our outcomes included CNS Vital Signs domains identified in previous concussion-related research (verbal memory, visual memory, psychomotor speed, cognitive flexibility, complex attention, processing speed, reaction time, and executive functioning).<sup>210</sup>

Psychological distress was assessed using the Brief Symptom Inventory-18 (BSI-18), a valid, reliable survey used to assess psychological distress in brain injury<sup>211</sup> and concussed<sup>212,213</sup> populations. The BSI-18 asks participants to rate their psychological distress specific to somatization, anxiety, and depression, all of which are related to concussion, perceived stress, and mindfulness.<sup>2,83</sup> Therefore, it is imperative to identify the connection between the BSI-18 and perceived stress and mindfulness in our study sample. The BSI-18 asks sensitive information; specifically question 17 refers to harming oneself (i.e., "Thoughts of ending your life"). Per survey instructions, the PI, Christine Callahan, reviewed the response to Question 17 after each participant completed the BSI-18. If a participant responded to Question 17 with moderately (2), quite a bit (3) or extremely (4), the PI talked to the participant to determine risk. If it was determined there is not a risk, the participant was provided with resources and was allowed to leave the testing session. If it was determined there was a risk, the participant was referred to a health care professional for additional care and the PI's mentor, Johna Register-Mihalik, was notified. If imminent danger was apparent, the PI called 911.<sup>212,213</sup>

<u>QOL</u> was measured using the Patient-Reported Outcomes Measurement Information System (PROMIS<sup>®</sup>); specifically, the PROMIS<sup>®</sup>-29 v2.1 adult measure. The PROMIS-29 is a valid, reliable assessment<sup>214</sup> used in concussion history populations<sup>215</sup> to assess QOL. To capture a comprehensive picture of QOL, our outcomes included the following short form domains: 1) physical function; 2) anxiety; 3) depression; 4) fatigue; 5) sleep disturbances; 6) ability to participate in social roles and activities; 7) pain interference; and 8) pain intensity.<sup>215</sup> The PROMIS<sup>®</sup> contains very detailed questions related to QOL, some of which would not pertain to a healthy, young adult population (i.e., physical functioning, pain intensity). Therefore, separating out the short form domains instead of using a total, composite score provides the current study with QOL data pertinent to the study sample.<sup>215</sup>

## 2.9.6 Statistical Approach Considerations

We recognize that many of the clinical and psychological concussion assessments used in the proposed study overlap. As such, we chose specific, unique outcomes from each assessment. Additionally, standardized  $\beta$  values were used to interpret the difference between measures by determining the magnitude of the difference between perceived stress, mindfulness, and each clinical concussion outcome. Furthermore, following previous literature and to mitigate the change of type 2 error, no adjustment for multiple comparisons was made.<sup>216,217</sup>

## 2.9.7 Exploratory Aim 3 Considerations

Aim 3 is an exploratory pilot study to further understand mindfulness-based interventions in concussion research applications. To address the exploratory third aim, we completed a pilot intervention study in which we recruited 15 participants from the larger study pool to complete a six-week mindfulness intervention. The prospective study design and six-week timeframe was chosen in accordance with previous research investigating the use of mindfulness-based interventions in healthy and brain injury populations.<sup>42–44</sup> Outcomes for this aim were adherence (mindfulness exercises/meditations completed per week), acceptability [Acceptability of Intervention Measure (AIM) scores], feasibility [Feasibility of Intervention Measure (FIM) scores], intervention perceptions, and pre/post changes in concussion symptoms, perceived stress, and mindfulness. As this is a novel intervention looking at the impact of mindfulness in a population of those with a concussion history, it is imperative to understand the use and utility of

the intervention to inform future protocols. As such, our outcomes focused on quantifying and describing the overall use, utility, acceptance, feasibility, and perceptions of the intervention.

Mindfulness exercises and meditations for the pilot study were completed using the LoveYourBrain Foundation Meditation Library. The LoveYourBrain Foundation's yoga program is a well-researched and implemented group-based yoga, meditation, and psychoeducation program for individuals with traumatic brain injuries, their caregivers, and clinicians treating traumatic brain injury patients.<sup>138</sup> The six week program, which has been successfully implemented in-person and online, follows a scientifically backed curriculum including gentle, modified yoga; guided meditation; and psychoeducation with group discussion aimed to mitigate traumatic brain injury-related symptoms, educate participants and injury-related outcomes, and create community surrounding traumatic brain injury.<sup>135,136,138</sup> The LoveYourBrain Meditation Library is a free, online resource containing traumatic brain injury-focused mindfulness-based exercises and meditations created by the LoveYourBrain Foundation based on the researched backed yoga program and its participant feedback.<sup>218</sup> The meditations included in LoveYourBrain's in-person and online yoga programs have been researched and shown to improve resilience, QOL, emotional and behavioral dysregulation, cognition, positive affect, and wellbeing.<sup>135,136,138</sup> However, the Meditation Library itself has not been researched in a concussionspecific population. Therefore, this study is novel in the use of an accessible online meditation resource tailored to those with traumatic brain injury. The Meditation Library was chosen as it is easily accessible to participants via phone, tablet, or computer and contains mindfulness-based exercises and meditations of various lengths that are tailored to individuals who have experienced traumatic brain injury.

## **2.10 Conclusions**

There is a gap in understanding how perceived stress and mindfulness impact clinical and psychological concussion outcomes in those with concussion history. Understanding the association among perceived stress, mindfulness, and concussion outcomes may provide evidence that intervening on perceived stress and/or improving mindfulness during concussion rehabilitation is pertinent to achieving a full recovery. Therefore, this novel study estimated the association among perceived stress, mindfulness, and clinical and psychological concussion outcomes in those with a concussion history, mechanisms necessary to inform effective interventions.

#### **CHAPTER 3: METHODS**

## 3.1 Study Overview

This study's <u>overall objective</u> was to determine the association among perceived stress, mindfulness, and clinical and psychological concussion outcomes. Results from this study will inform future comprehensive post-concussion interventions aimed to mitigate perceived stress and utilize mindfulness techniques to improve post-concussion clinical and psychologic deficits. Our <u>central hypothesis</u> was that increased perceived stress would negatively impact clinical and psychological concussion outcomes and that this relationship would be moderated by mindfulness. Additionally, for our exploratory Aim 3, we hypothesized participants participating in the mindfulness intervention would report high adherence, acceptability, feasibility, and intervention perceptions as well as decreased concussion symptoms, decreased perceived stress, and increased mindfulness post-intervention.

#### **3.2 Specific Aims 1 and 2 Methods**

#### 3.2.1 Study Design and Participants

We conducted a cross-sectional observational study in 80 young adults aged 18-30 with a concussion history aimed to determine the association between perceived stress, mindfulness, and clinical and psychological concussion outcomes. Based on previous literature, this study <u>included</u> participants with a concussion history who were not currently under medical care for their concussion (defined as experiencing a concussive injury within the past five years, but not within the past month). This age range and concussion history delineation were chosen to contribute to a meaningful analysis relative to the study purpose. Specifically, those aged 18-30 were chosen to:

1) represent the age of individuals with a relatively high concussion risk;<sup>178</sup> 2) remain consistent with previous literature in the concussion history and concussion outcomes space;<sup>2,18,19,179</sup> 3) ensure that participants will be able to complete all study assessments on their own merit; and 4) maximize recruitment to ensure that the proposed sample size is met. Participants were <u>excluded</u> for any history of moderate and/or severe traumatic brain injury, if they were currently under provider care for a concussion/traumatic brain injury, and/or health risks (heart conditions, respiratory disorders, and/or neurological disorders) that put them at greater than minimal risk during the concussion outcomes assessments. There was no exclusion based on self-report sex, race, ethnicity, or mental health history.

Various <u>recruitment</u> strategies that have been successfully implemented in previous concussion-related studies<sup>132,219</sup> were utilized to ensure the sample size of 80 participants was met. Specifically, participants were recruited via the University of North Carolina at Chapel Hill's (UNC-CH) undergraduate and graduate student body through student listservs; flyers on UNC-CH's campus; Matthew Gfeller Center, UNC-CH Exercise and Sport Science, and UNC-CH Human Movement Science social media channels; speaking in undergraduate and graduate courses; broadly through community social media pages and listservs; and word of mouth. Recruitment materials contained the Principal Investigator's (PI) email address and telephone number, allowing interested and eligible participants to contact study personnel to schedule a visit or ask questions.

## 3.2.2 Sample Size and Power

We included 80 (alpha=0.05, power=0.8, effect size  $R^2$ =0.09) 18–30-year-old young adults with a concussion history. The projected sample size of 80 was derived from previous literature investigating the association between concussion symptoms and perceived stress in a healthy population,<sup>220</sup> given the limited data for our proposed measures among those with a concussion history. Initial power analyses indicated a sample of n=71 (alpha=0.05, power=0.8, effect size  $R^2$ =0.10). However, to account for possible missing data and a potential improved effect size, we overrecruited to 80 participants.

#### 3.2.2 Measures and Procedures

## 3.2.2.1 Inclusion/Exclusion Screening

Before enrollment, potential participants completed an inclusion/exclusion criteria screening (Appendix 2). Potential participants were directed to the online inclusion/exclusion screener via QR code or study link provided on the recruitment materials. The questionnaire asked potential participants questions concerning all inclusion/exclusion criteria outlined above.

# 3.2.2.2 Demographics, Concussion History, Mental Health History, and Current Mindfulness Practice Information

Participants were asked demographic, concussion history, mental health history, and current mindfulness practice information to describe the study sample. All demographic, concussion history, mental health history, and current mindfulness practice questions were self-report. Demographic questions included age, height, weight, sex, race, ethnicity, highest education level, marital status, employment status, school level (if applicable), COVID-19 history, sleep, caffeine use, alcohol use, sport participation (if applicable), physical activity levels, and menstrual cycle history (if applicable). Concussion history questions included number of concussions incurred; how many were disclosed at the time of injury; and, for each concussion incurred, how long ago the injury was, how long it took for symptoms to subside, and injury mechanism. Mental health history questions included mental health-related symptoms and diagnoses and mental health treatment usage. Current mindfulness practice questions included if participants currently have a

mindfulness practice and, if so, technique use. The demographics, concussion history, mental health history, and current mindfulness practice questionnaires are provided in Appendices 3, 4, 5, and 6 respectively.

#### 3.2.2.3 Perceived Stress

Perceived stress was measured using the Perceived Stress Scale 10 question version (PSS-10, Appendix 7), the most widely used psychological instrument for measuring perceived stress.<sup>180</sup> The PSS-10 is well validated and had been used in connection to mindfulness<sup>32–34,37,40</sup> and in brain injury populations.<sup>43</sup> The PSS-10 consists of 10 questions on a five-point scale (0=never to 4=very often) about how often a participant has felt or thought a certain way relative to their perceived stress in the past month. Final scores were obtained by reversing responses to the four positively stated items and then summing all 10 scale items. The outcome from the PSS-10 for our analyses was the total score (range=0-40). Higher scores indicated higher perceived stress.<sup>181</sup>

## 3.2.2.4 Mindfulness

Mindfulness was measured using the Five Facet Mindfulness Questionnaire (FFMQ, Appendix 8). This widely used, valid survey to measure mindfulness<sup>185</sup> has been researched extensively connected to perceived stress.<sup>34–36</sup> Participants were asked 39 questions on a five-point scale (1=never/very rarely true to 5=very often/always true) related to general mindfulness tendencies in daily life. Questions are focused on five facets of mindfulness which include: 1) observing, noticing, and attending to sensations, perceptions, thoughts, and feelings; 2) describing/labeling one's experience with words; 3) acting with awareness; 4) non-judging; and 5) non-reactivity to inner experience. Each facet makes up a sub-score of the FFMQ and were reported as a part of the demographic values. Total scores were obtained by reversing responses

to the 19 reverse scored questions and then summing all 39 items. The outcome for our analyses was the FFMQ total score (range=39-195). Higher scores indicated greater mindfulness levels.<sup>186</sup>

## 3.2.2.5 Clinical Concussion Outcomes

Clinical concussion outcomes are outlined in Table 3.1. <u>Concussion symptoms</u> were measured using the Rivermead Post-Concussion Symptom Questionnaire (RPQ),<sup>189</sup> a validated

measure<sup>192,193</sup> which asks participants to report the presence and severity (0-4) of 18 concussion-related symptoms compared with before their concussion (Appendix 9). The RPQ has been frequently used in the proposed study population.<sup>190,191</sup> Outcomes for the RPQ were total symptom severity (range=0-72) and total number of symptoms reported as worse than before injury (reporting symptoms as >1 on the severity scale is an indication that symptoms are present at

Table 3.1. Clinical concussion outcomes domains,         assessments, and outcomes.						
Domain	Assessment	Outcomes				
Concussion Symptoms	RPQ	<ul> <li>Total symptom severity</li> <li>Total number of symptoms worse than before injury</li> </ul>				
Balance Performance	BESS COM	<ul> <li>BESS total errors</li> <li>COM anterior/poster plane SD of acceleration (eyes open and closed trials)</li> <li>COM medial/lateral plane SD of acceleration (eyes open and closed trials)</li> </ul>				
ANS Function	HRV	<ul><li>LF/HF power ratio</li><li>Average heart rate</li></ul>				
Vestibular/Ocular Function	VOMS	• Change in total symptom score (pre- vs. post-test) for each VOMS assessment				
Exertion Tolerance	Two Minute Step Test	<ul><li>Number of steps</li><li>Post-test RPE rating</li></ul>				
Abbreviations: RPQ=Rivermead Post-Concussion Questionnaire, BESS=Balance Error Scoring System, COM=center of mass, SD=standard deviation, ANS=autonomic nervous system, HRV=heart rate variability, LF/HF=low frequency/high frequency, VOMS=Vestibular/Ocular Motor Screening, RPE=rate of perceived exertion.						

levels worse than before the subject's injury, range=0-18). Higher scores indicate more concussion symptoms severity and presence.

Balance performance was measured using the Balance Error Scoring System (BESS) and by completing a center of mass (COM) assessment. The BESS is a validated clinical measure for static postural balance commonly used in concussed patients.<sup>194,195</sup> Participants completed three stances on a firm and foam surface for 20 seconds with their eyes closed: 1) double-leg (hands on the hips and feet together); 2) single-leg stance (standing on the nondominant leg with hands on the hips); and 3) tandem (nondominant foot behind the dominant foot in a heel-to-toe arrangement). Study personnel counted errors throughout each stance. An error was defined as opening eyes, lifting hands off the hips, stepping or falling out of position, lifting the forefoot or heel, abducting the hip  $>30^\circ$ , or failing to return to the test position in more than five seconds. The outcome for the BESS was total errors (range=0-60) with higher scores indicating worse balance performance. Administration and scoring instructions for the BESS are provided in Appendix 10. The COM assessment was indexed via a portable Inertial Measurement Unit (IMU) worn on the posterior trunk, a relaible<sup>196</sup> COM assessment used in the study population.<sup>197,198</sup> Participants completed two double-leg stance one-minute trials, one with eyes open and one with eyes closed. Throughout the assessment, an IMU (Delsys, Inc., United States) was affixed to the participant's posterior trunk to measure COM. Results were post-processed by our custom Unity 3D-based data Kapture platform (Unity Technologies, San Francisco, CA). Specifically, data for both trials (eyes open and closed) in the anterior/poster (x) and medial/lateral (z) planes were processing using the following procedure: 1) data from the first and final second of the trials were removed; 2) absolute values of each data point were calculated; 3) standard deviation (SD) of acceleration values were calculated for the anterior/posterior and medial/lateral planes of the eyes open and eyes closed

trials; and 4) outcomes were converted from g to cm/s<sup>2</sup>. The COM assessment outcomes were SD of acceleration in the anterior/posterior and medial/lateral planes for the eyes open and closed trials.<sup>221,222</sup> Administration instructions for the center of mass assessment are provided in Appendix 11.

ANS function was measured using heart rate variability (HRV) during three intervals: 1) seated (parasympathetic domain); 2) standing (sympathetic domain); and 3) a repeated seated condition (recovery), a protocol used to collect HRV in individuals across all stages of concussion recovery (i.e., acute, persistent concussion symptoms, and concussion history).<sup>58</sup> During each interval, HRV data was collected via a Polar H10 heart rate monitor for six minutes with the middle five minutes used for final data analyses.<sup>58</sup> The following data processing was completed using a protocol previously reported in the concussion literature:<sup>199</sup> 1) raw R-R data were processed using Kubios HRV (version 3.5.0, Biosignal Analysis and Imaging Group, Kuopio, Finland); 2) Kubios's automatic beat correction was utilized in accordance with their validated algorithm;<sup>223</sup> and 3) manual inspection was completed with outliers and ectopic beats removed when necessary.<sup>224</sup> The HRV assessment outcomes were average heart rate (time domain), a measure indicative of sympathetic cardiac activation, and the low frequency power to high frequency power (LF/HF) ratio (frequency domain), a measure indicative of sympathetic and parasympathetic nervous system balance, for each trial (seated 1, standing, and seated 2). Protocol for the HRV assessment and data processing is provided in Appendix 12.

<u>Vestibular/ocular function</u> was assed using the Vestibular/Ocular Motor Screening (VOMS) assessment.<sup>202</sup> Participants were asked to rate the severity of four symptoms (headache, dizziness, nausea, and fogginess) from 0-10 before (pre-test) and after (post-test) completing clinical tests for smooth pursuits, horizontal and vertical saccades, near-point convergence,

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vestibular ocular reflex, and visual motion sensitivity. The VOMS is a valid and reliable clinical assessment<sup>195,203</sup> commonly used in concussed populations.<sup>202</sup> The outcome for the VOMS was the change in symptom score (pre- vs. post-test) for each VOMS assessment.<sup>202,204,205</sup> Specifically, symptom total scores (sum of all symptom ratings) were calculated for baseline and each VOMS clinical assessment. Change scores were then calculated for each VOMS clinical test by subtracting the total symptom score at baseline from the post-test score. Change scores that were negative (i.e., when the participant reported higher/worse symptoms at baseline compared to with the post-test) were coded as zero to indicate no provocation of symptoms.<sup>202,204,205</sup> Administration and scoring instructions for the VOMS are provided in Appendix 13.

Exertion tolerance was assessed using the two-minute step test (a modification of the Chester Step Test). Participants were asked to complete as many steps as possible in two minutes. A 30 second rest period began the assessment followed by the two-minute step test and a 30 second (or more) rest period following. The step used was a standardized, 20-centimeter step in accordance with previous literature.<sup>225</sup> Participants were instructed to place both of their feet fully on the step and then fully back down on the ground. Stepping up fully on the step and then back down to the ground counted as one step. Participants wore a pedometer on their shoe to validate the steps completed and counted by study personnel. After completing the step test, participants were asked to rate their perceived exertion using the Borg Rating of Perceived Exertion (RPE; a scale which asks subjects to rank their perceived exertion from zero to maximal exertion). This study used the modified Borg scale, in which participants rated their RPE on a scale from 0 (no exertion) to 10 (maximal exertion).<sup>226</sup> Outcomes for this assessment included number of steps completed and the participant's post-test RPE. Administration instructions for the step test are provided in Appendix 14.

## 3.2.2.6 Psychological Concussion Outcomes

Psychological concussion outcomes are outlined in Table 3.2. <u>Neurocognitive performance</u> was assessed using CNS Vital Signs (Appendix 15), a valid, reliable computer based

neurocognitive	Table 3.2. Psychological concussion outcomes domains, assessments, and outcomes.		
assessment commonly	Domain	Assessment	Outcomes
used in concussed populations. <sup>208,209</sup> Outcomes for CNS Vital signs included standard scores (scores with a mean	Neurocognitive Performance	CNS Vital Signs	<ul> <li>Verbal memory</li> <li>Visual memory</li> <li>Psychomotor speed</li> <li>Cognitive flexibility</li> <li>Complex attention</li> <li>Processing speed</li> <li>Reaction time</li> <li>Executive functioning</li> </ul>
of 100 and SD of 15 based on a normative dataset	Psychological Distress	BSI-18	• Total score
that matches participants by age) for the following domains: verbal memory, visual memory,	QOL	PROMIS <sup>®</sup> -29 v2.1	<ul> <li>Physical function</li> <li>Anxiety</li> <li>Depression</li> <li>Fatigue</li> <li>Sleep disturbances</li> <li>Ability to participate in social roles and activities</li> <li>Pain interference</li> </ul>
<ul><li>psychomotor speed,</li><li>cognitive flexibility,</li><li>complex attention,</li></ul>		ient Reported Outcome	• Pain intensity rentory, QOL=quality of es Measurement

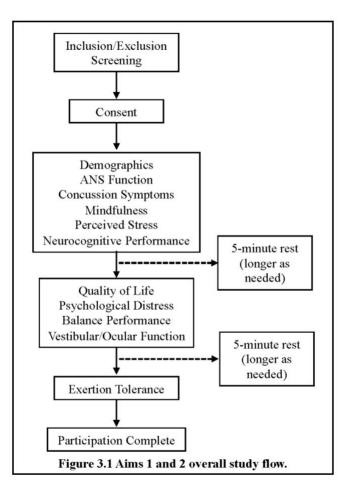
processing speed, reaction time, and executive functioning.<sup>210</sup> Any outcome scores deemed invalid by CNS Vital Signs criteria were removed from analysis.<sup>210,227</sup>

Psychological distress was assessed using the Brief Symptom Inventory-18 (BSI-18, Appendix 16), a validated, reliable survey used to assess psychological distress in brain injury<sup>211</sup> and concussion<sup>212,213</sup> populations. Participants answered 18 questions related to their psychological distress specific to somatization, anxiety, and depression over the past seven days on a five-point scale (0=not at all to 4=extremely). The outcome for the BSI-18 was the global severity index (total score, range=0-72, higher scores indicate more psychological distress). The BSI-18 asks sensitive information; specifically question 17 refers to harming oneself (i.e., "Thoughts of ending your life"). Per survey instructions, the PI, Christine Callahan, reviewed the response to Question 17 after each participant completed the BSI-18. If a participant responded to determine risk. If it was determined there is not a risk, the participant was provided with resources and allowed to leave the testing session. If it was determined there was a risk, the participant was referred to a health care professional for additional care and the PI's mentor, Johna Register-Mihalik, was notified. If imminent danger was apparent, the PI called 911 (Appendix 16).

<u>Quality of life</u> (QOL) was measured using the Patient-Reported Outcomes Measurement Information System (PROMIS<sup>®</sup>). Specifically, the PROMIS<sup>®</sup>-29 v2.1 adult measure (Appendix 17). The PROMIS<sup>®</sup>-29 is a comprehensive QOL assessment made up of the following short forms: 1) physical function (four questions on a five-point scale, 1=unable to do to 5=without any difficulty); 2) anxiety (four questions on a five point scale, 1=never to 5=always); 3) depression (four questions on a five point scale, 1=never to 5=always); 4) fatigue (four questions on a five point scale, 1=not at all to 5=very much); 5) sleep disturbances (one question on a five point scale, 1=very good to 5=very poor and three questions on a five point scale, 1=very much to 5=not at all); 6) ability to participate in social roles and activities (four questions on a five point scale, 1=always to 5=never); 7) pain interference (four questions on a five point scale, 1=not at all to 5=very much); and 8) pain intensity (one question rated from 0=no pain to 10=worst pain imaginable). Raw scores for each short form were summed and converted to t-scores (Appendix 18).<sup>82,214</sup> Higher t-scores indicated more of each short form construct (i.e., higher/better physical functioning, higher/worse anxiety, higher/worse depression, higher/worse fatigue, higher/worse sleep disturbances, higher/better ability to participate in social roles and activities, higher/worse pain interference, and higher/worse pain intensity). The PROMIS-29 is a valid, reliable assessment<sup>214</sup> used in concussion history populations<sup>215</sup> to assess QOL. Outcomes for the PROMIS-29 included t-scores for all eight short form domains.

## 3.2.3 Procedural Study Flow

Participants completed a single study visit at the Matthew Gfeller Center and STAR Heel Performance Laboratory. As described above, the testing session included measures for: 1) demographic, concussion history, mental health history, and current mindfulness practice; 2) perceived stress; 3) mindfulness; 4) clinical concussion outcomes (concussion symptoms, balance performance, ANS function, vestibular/ocular function, and exertion tolerance); and 4) psychological



concussion outcomes (neurocognitive performance, psychological distress, and QOL). The

assessments were chosen as they represent a complete clinical and psychological post-concussion profile and are commonly used in current research and clinical practice. The overall study flow, outlined in Figure 3.1, was chosen to maximize participant safety and minimize the influence of exertion on neurocognitive, ANS, and balance testing. Institutional Review Board approval was obtained for the study and all participants completed informed consent (IRB#22-0235).

## 3.2.4 Data Analysis and Statistical Plan

The data analysis plan for Aims 1 and 2 is outlined in Table 3.3. Descriptive statistics were computed for all variables of interest. To describe the sample, means, SD, and 95% confidence intervals (95% CI) were computed for age, height, weight, physical activity levels, sleep, caffeine use, alcohol use, and time since concussion. Additionally, frequencies and percentages were computed for sex, race, ethnicity, school level (if applicable), sport participation (if applicable), concussion history, COVID-19 history, current mindfulness technique use, mental health diagnoses, and mental health treatment usage. Means, SDs, and 95%CIs were computed for perceived stress (total score) and mindfulness (sub-scores and total score) as well as all clinical and psychological concussion outcomes (clinical outcomes identified in Table 3.1, psychological outcomes identified in Table 3.2). Bivariate correlations were computed between all clinical and psychological concussion outcomes and perceived stress, mindfulness, and regression model covariates (concussion number, sex, and concussion mechanism). Additionally, bivariate correlations were computed between the HRV outcomes and demographic variables that may influence those data (hours slept the previous night, cups of caffeine consumed that day, alcoholic drinks consumed in the past 24 hours, and COVID-19 history). After completing a linearity check between variables, results informed the use of Pearson or Spearman correlations. Spearman

Aim	Dependent Variables	Independent Variables	Analyses
Estimate the associations among perceived stress, mindfulness, and clinical concussion outcomes.	<ul> <li>Concussion symptoms</li> <li>Balance performance</li> <li>ANS function</li> <li>Vestibular ocular system function</li> <li>Exertion tolerance</li> </ul>	<ul> <li>1a: Perceived stress</li> <li>1b: Mindfulness</li> <li>1c: Mindfulness and perceived stress interaction term</li> </ul>	Separate multivariable linear regression models (controlled for concussion number, sex, and most recent concussion mechanism)
Estimate the associations among perceived stress, mindfulness, and psychological concussion outcomes.	<ul> <li>Neurocognitive performance</li> <li>Psychological distress</li> <li>QOL</li> </ul>	<ul> <li>2a: Perceived stress</li> <li>2b: Mindfulness</li> <li>2c: Mindfulness and perceived stress interaction term</li> </ul>	Separate multivariable linear regression models (controlled for concussion number, sex, and most recen concussion mechanism)

correlations were utilized for categorical variables (sex, concussion mechanism, and COVID-19

history). All correlations reported magnitude and directional associations.

Multivariable regression analyses were conducted to assess Aim 1. First, separate multivariable linear regression models were used to determine the association among perceived stress and each clinical concussion outcome (concussion symptoms, balance performance, ANS function, vestibular/ocular system function, and exertion tolerance). All models controlled for number of concussions (1-5+),<sup>228,229</sup> sex (male/female),<sup>87,230</sup> and most recent concussion mechanism (sport/non-sport related).<sup>231–233</sup> Second, separate multivariable linear regression models were used to determine the association among mindfulness and each clinical concussion outcome (concussion symptoms, balance performance, ANS function, vestibular/ocular system

function, and exertion tolerance). All models controlled for number of concussions (1-5+),<sup>228,229</sup> sex (male/female),<sup>87,230</sup> and most recent concussion mechanism (sport/non-sport related).<sup>231–233</sup> Third, consistent with best practices,<sup>234</sup> an interaction term of perceived stress and mindfulness was included to test the potential moderation effect of mindfulness on our outcomes (a separate model for each dependent variable was utilized). All models controlled for number of concussions (1-5+),<sup>228,229</sup> sex (male/female),<sup>87,230</sup> and most recent concussion mechanism (sport/non-sport related).<sup>231–233</sup> Parameter estimate  $\beta$ , standardized  $\beta$ , standardized 95%CI, estimate p-value, and model adjusted R<sup>2</sup> were reported with p<0.05 identified as significant for each parameter. Following previous literature and to mitigate the change of type 2 error, no adjustment for multiple comparisons was made.<sup>216,217</sup>

Multivariable regression analyses were also be conducted to assess Aim 2. First, separate multivariable linear regression models were used to determine the association among perceived stress and psychological concussion outcomes (neurocognitive performance, psychological distress, and QOL). All models controlled for number of concussions (1-5+),<sup>228,229</sup> sex (male/female),<sup>87,230</sup> and most recent concussion mechanism (sport/non-sport related).<sup>231–233</sup> Second, separate multivariable linear regression models were used to determine the association among mindfulness and each psychological concussion outcome (neurocognitive performance, psychological distress, and QOL). All models controlled for number of concussions (1-5+),<sup>228,229</sup> sex (male/female),<sup>87,230</sup> and most recent concussion mechanism (sport/non-sport related).<sup>231–233</sup> Second, separate multivariable linear regression models were used to determine the association among mindfulness and each psychological concussion outcome (neurocognitive performance, psychological distress, and QOL). All models controlled for number of concussions (1-5+),<sup>228,229</sup> sex (male/female),<sup>87,230</sup> and most recent concussion mechanism (sport/non-sport related).<sup>231–233</sup> Third, consistent with best practices,<sup>234</sup> an interaction term of perceived stress and mindfulness was included to test the potential moderation effect of mindfulness on our outcomes (a separate model for each dependent variable will be utilized). All models controlled for number of concussion (1-5+),<sup>228,229</sup> sex (male/female),<sup>87,230</sup> and most recent concussion mechanism (sport/non-sport related).<sup>231–233</sup>

(sport/non-sport related).<sup>231–233</sup> Parameter estimate  $\beta$ , standardized  $\beta$ , standardized 95%CI, estimate p-value, and model adjusted R<sup>2</sup> were reported with p<0.05 identified as significant for each parameter. Following previous literature and to mitigate the change of type 2 error, no adjustment for multiple comparisons was made.<sup>216,217</sup> Data was presented visually using tables and, if significant, interaction plots were reported utilizing the categorical cuts in data for perceived stress<sup>182</sup> and mindfulness.<sup>185</sup>

## 3.3 Exploratory Aim 3 Methods

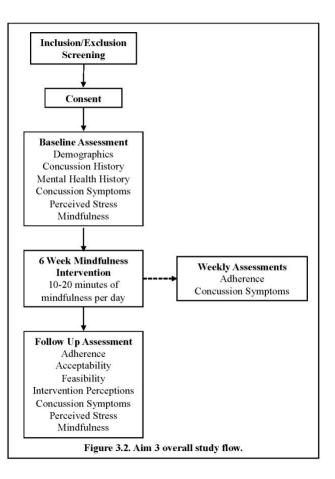
## 3.3.1 Study Design and Participants

To address the exploratory Aim 3, we completed a pilot prospective, intervention study (NCT05399849) in which we recruited 15 participants from the larger study pool to complete a

mindfulness intervention. six-week **Participants** recruited for this were exploratory aim on a first come first serve basis until 15 participants were enrolled. Participants ineligible from were participating in this pilot study if they currently engaged in a mindfulness practice (defined as engaging in a mindfulness practice, meditation or yoga, once per week).

## 3.3.2 Measures and Procedures

The overall flow for this pilot study is outlined in Figure 3.2. Institutional Review Board approval was obtained for the study



and all participants completed informed consent (IRB#22-0732). The initial visit participants completed for Aims 1 and 2 was used as the baseline assessment for this intervention. For the sixweek intervention, participants were instructed to complete 10-20 minutes of mindfulness-focused exercises and meditations each day. Mindfulness exercises were completed online, independently using the LoveYourBrain Foundation Meditation Library.<sup>218</sup> The LoveYourBrain Foundation's Yoga program is a well-researched and implemented group-based yoga, meditation, and psychoeducation program for individuals with traumatic brain injuries, their caregivers, and clinicians treating traumatic brain injury patients.<sup>135,136,138</sup> The six-week program, which has been successfully implemented in-person and online, follows a scientifically backed curriculum including gentle, modified yoga; guided meditation; and psychoeducation with group discussion aimed to mitigate traumatic brain injury-related symptoms, educate participants and injury-related outcomes, and create community surrounding traumatic brain injury. The LoveYourBrain Meditation Library is a free, online resource containing traumatic brain injury-focused mindfulness-focused exercises and meditations. This library was created by the LoveYourBrain Foundation based on the researched backed yoga program and its participant feedback. The meditations included in LoveYourBrain's in-person and online yoga programs have been researched and shown to improve resilience, QOL, emotional and behavioral dysregulation, cognition, positive affect, and well-being.<sup>135,136</sup> Mindfulness-based exercises and meditations completed were chosen by study personnel based on tools utilized in mindfulness-based stress reduction programs that are provided on the LoveYourBrain Meditation Library.<sup>42-44,218</sup> Specific mindfulness-based exercises and meditations included body scan, acceptance, awareness, and breathing.<sup>44,218</sup> The specific mindfulness-based exercises and meditations and their completion timeline are identified in Appendix 19.

At intervention enrollment participants were presented with a detailed manual providing them with beginner mindfulness tips and instructions as well as details on the purpose for the intervention (Appendix 20). Before beginning the exercises and after being presented the manual, participants were asked by study personnel if they have any questions or concerns regarding the intervention. Throughout the six-week intervention, study personnel prompted participants via email at the beginning of each week with the specific exercises/meditations to be completed each day for that week. Participants were prompted via email and text at the end of each week to complete a questionnaire to assess adherence and track concussion symptoms. Participants had one day to complete the weekly assessment. If it was not completed on that day, study personnel prompted the participant via email and text for three days. If the assessment was not completed in three days, study personnel called participants to complete the assessment. At three weeks (halfway through the intervention), study personnel called participants to complete the weekly assessment and check in on participation. Upon completion of the six-week trial, participants were prompted via email and text to complete a final assessment including questions regarding adherence, acceptability, feasibility, intervention perceptions, concussion symptoms, perceived stress, and mindfulness. Participants had one day to complete the final assessment. If they had not completed the final assessment at that time, study personnel prompted the participant via email and text for three days. If it was not completed after three days, study personnel called the participant to complete the assessment over the phone.

## 3.3.2.1 Adherence

Throughout the intervention participants were prompted to complete a weekly questionnaire to assess adherence. Subjects were asked which mindfulness exercises/meditations they completed for that week and their enjoyment level for each completed exercise/meditation.

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The outcome for adherence was the number of mindfulness-based exercises/meditations completed per week. The weekly questionnaire is provided in Appendix 21.

#### *3.3.2.2 Acceptability*

Acceptability was assessed during the post-study assessment using the Acceptability of Intervention Measure (AIM, Appendix 22). The AIM is a four-item validated measure assessing associations with an intervention.<sup>235</sup> It is assessed on a five-point scale from 1=completely disagree to 5=completely agree. A total score was computed by summing the responses for all four items (higher scores indicating more positive acceptance). The outcome for acceptability was the mean, SD, and 95%CI of the total score and frequencies and percentages for each individual AIM item. Higher scores indicate higher acceptability.

## 3.3.2.3 Feasibility

Feasibility was measured during the post-study assessment using the Feasibility of Intervention Measure (FIM), a four-item validated measure assessing intervention feasibility (Appendix 23).<sup>235</sup> The FIM is assessed on a five-point scale from 1=completely disagree to 5=completely agree. A total score was computed by summing the responses for all four items (higher scores indicating more positive feasibility). The outcome for feasibility was the mean, SD, and 95% CI of the total score and frequencies and percentages for each individual FIM item. Higher scores indicate higher feasibility.

#### 3.3.2.4 Intervention Perceptions

Intervention perceptions were measured during the post-study assessment. Participants were asked questions regarding facilitators and barriers to participation, potential changes to be made, usability of the LoveYourBrain Meditation library, and overall if participants felt the exercises/meditations were helpful. Outcomes for intervention perceptions were frequencies and

percentages of all scale items and summary of text for all open-ended responses. Intervention perception questions are outlined in Appendix 24.

#### 3.3.2.5 Concussion Symptoms

Concussion symptoms were measured using the RPQ,<sup>189</sup> a validated measure<sup>192,193</sup> which asks participants to report the presence and severity (0-4) of 18 concussion-related symptoms compared with before their concussion (Appendix 9). The RPQ has been frequently used in the proposed study population.<sup>190,191</sup> Outcomes for the RPQ included total symptom severity and total symptoms reported as worse than before injury with higher scores indicating more concussion symptom severity and presence. Concussion symptoms were collected weekly to monitor safety. RPQ scores collected during the pre- and post-study assessments were utilized for preliminary efficacy analyzes.

## 3.3.2.6 Perceived Stress

Perceived stress was measured using the PSS-10 (Appendix 7), the most widely used psychological instrument for measuring perceived stress.<sup>180</sup> The PSS-10 is well validated and had been used in connection to mindfulness<sup>32–34,37,40</sup> and in brain injury populations.<sup>43</sup> The PSS-10 consists of 10 questions on a five-point scale (0=never to 4=very often) about how often a participant has felt or thought a certain way relative to their perceived stress in the past month. Final scores were obtained by reversing responses to the four positively stated items and then summing all 10 scale items. Higher scores indicated higher perceived stress.<sup>181</sup>

## 3.3.2.7 Mindfulness

Mindfulness was measured using the FFMQ (Appendix 8). This widely used, valid survey to measure mindfulness<sup>185</sup> has been researched extensively connected to perceived stress.<sup>34–36</sup> Participants were asked 39 questions on a five-point scale (1=never/very rarely true to 5=very

often/always true) related to general mindfulness tendencies in daily life. Questions are focused on five facets of mindfulness which include: 1) observing, noticing, and attending to sensations, perceptions, thoughts, and feelings; 2) describing/labeling one's experience with words; 3) acting with awareness; 4) non-judging; and 5) non-reactivity to inner experience. Each facet makes up a sub-score of the FFMQ. Final scores were obtained by reversing responses to the 19 reverse scored questions and then summing all 39 items. Higher scores indicated greater mindfulness levels.<sup>186</sup>

## 3.3.3 Data Analysis and Statistical Plan

Descriptive statistics described above for Aims 1 and 2 were computed for the sub-sample who complete the exploratory pilot intervention. Descriptive statistics were used to determine intervention adherence, acceptability, feasibility, and intervention perceptions. Specifically, means, SDs, and 95%CIs were computed for adherence (days per week completed), acceptability (AIM total score), feasibility (FIM total score), and intervention perception scale items. Frequencies and percentages were computed for the AIM and FIM items. Summary of text using key words was used to report open-ended intervention perception questions. To assess the intervention's preliminary efficacy, paired sample t-tests were used to determine pre/post-intervention changes in concussion symptoms, perceived stress, and mindfulness, with p<0.05 identified as statistically significant.

#### **CHAPTER 4: MANUSCRIPT AIM 1**

## 4.1 Background

Concussion is a significant public health and patient level problem with one to two million sport- or recreation-related concussions reported in the United States each year.<sup>51</sup> In non-athletic populations, the incidence of concussion-related visits in United States emergency departments is 239 visits per 100,000 person years.<sup>50</sup> Concussion causes neurophysiological changes<sup>1</sup> resulting in clinical deficits including increased concussion symptoms, balance dysfunction, autonomic nervous system (ANS) dysfunction, and exercise intolerance as well as psychological changes such as increased irritability, anxiety, depression, and decreased quality of life (QOL).<sup>2</sup> For adults, concussion symptoms typically resolve 10-21 days post-injury.<sup>2–4</sup> However, in those with a concussion history, up to 25% experience persistent concussion symptoms and deficits beyond typical recovery.<sup>2,3</sup> Furthermore, neurophysiological changes remain in concussion history patients with persistent concussion symptom expression;<sup>5,6</sup> resulting in continued clinical and psychological dysfunction.<sup>7,8</sup>

Increased perceived stress is associated with decreased mental health,<sup>17</sup> physical health,<sup>18</sup> and overall QOL.<sup>20</sup> Specifically, in healthy populations research suggests higher perceived stress may negatively impact heart rate variability (HRV)<sup>236</sup> and balance performance<sup>237</sup> – common post-concussion clinical deficits. In sport specific research, perceived stress predicts sports injury<sup>21,22</sup> and negatively impacts injury rehabilitation for musculoskeletal injuries.<sup>21</sup> Specifically, in young adults, increased stress symptoms are associated with increased injury risk throughout a competitive soccer season.<sup>23</sup> Additionally, perceived negative life event stress increased the risk

of overuse injuries in elite female soccer players<sup>24</sup> and negative life event stress and high levels of life-related stress predicted injury rates in adolescent and young adult soccer players.<sup>25</sup> Despite prior connections between stress and injury, limited work has investigated the connection between perceived stress and concussion, with initial data suggesting perceived stress is heightened acutely post-concussion<sup>13</sup> Additionally, in individuals with a concussion history, exposure to a high stress condition (mental arithmetic) increased perceived stress, exacerbated post-concussion symptoms, and elevated heart rate (HR) – results which suggest a connection between increased stress and negative post-concussion outcomes.<sup>26</sup> Building upon this work, additional research suggests perceived stress may also play a role in predicting long-term post-concussion impairments.<sup>27</sup> However, the connection among perceived stress and commonly used clinical post-concussion assessments in concussion populations remains unknown.

Research indicates a connection between perceived stress and mindfulness, specifically indicating higher mindfulness levels are associated with decreased perceived stress<sup>32–34</sup> and increased mental<sup>35</sup> and physical health.<sup>36</sup> In healthy populations, mindfulness-based interventions (i.e., meditation and yoga) improve mindfulness and perceived stress<sup>36–40</sup> as well as HRV<sup>238</sup> and balance control<sup>239</sup> – common clinical concussion impairments. However, there is limited study of mindfulness-based interventions in concussion populations, with preliminary results suggesting intervention-related improvements in QOL,<sup>42,43</sup> attention,<sup>44</sup> mental fatigue,<sup>44</sup> anxiety,<sup>44</sup> and depression.<sup>44</sup> Furthermore, these studies have not investigated the impact of the interventions on mindfulness measures and perceived stress and do not incorporate typical clinical concussion outcomes, findings necessary to understand intervention mechanisms and the impact of the interventions on clinical concussion deficits.

Despite the evidence suggesting negative impacts of perceived stress on post-concussion outcomes and preliminary evidence that mindfulness may mitigate these negative impacts, research has not investigated these connections in young adults with a concussion history. Therefore, this study estimated the associations among perceived stress, mindfulness, and clinical concussion outcomes (concussion symptoms, balance performance, ANS function. vestibular/ocular system function, and exertion tolerance) in young adults with a concussion history. We hypothesized that participants with: 1) higher perceived stress would have worse clinical concussion outcomes [higher concussion symptom burden, lower balance performance, higher ANS dysfunction, higher vestibular/ocular symptom provocation, and lower exertion tolerance]; 2) higher mindfulness would have better clinical concussion outcomes; and 3) the association among perceived stress and clinical concussion deficits would be moderated by mindfulness levels (specifically mindfulness would buffer the relationship between perceived stress and clinical concussion outcomes). Understanding the associations among perceived stress, mindfulness, and concussion outcomes in those with a concussion history may provide evidence supporting the need for stress reduction and/or mindfulness-based interventions during concussion rehabilitation to facilitate concussion recovery and mitigate prolonged effects.

## 4.2 Methods

## 4.2.1 Study Design

This was a cross-sectional observational study in 80 young adults (a priori power: alpha=0.05, power=0.8, effect size  $R^2=0.09$ )<sup>220</sup> aged 18-30 with a concussion history aimed to determine the association among perceived stress, mindfulness, and clinical and psychological concussion outcomes. Institutional Review Board approval was obtained for the study and all participants completed informed consent. Participants completed a single study visit including the

following measures used for these analyses: 1) demographic, concussion history, and current mindfulness practice information; 2) perceived stress; 3) mindfulness; and 4) clinical concussion outcomes (concussion symptoms, balance performance, ANS function, vestibular/ocular function, and exertion tolerance). These assessments were chosen as they represent a complete clinical post-concussion profile and are commonly used in current research and clinical practice. Data were collected at a large state university between May and September 2022.

## 4.2.2 Participants

This study included young adults (aged 18-30) with a concussion history (defined as experiencing a concussive injury within the past five years, but not within the past month). Participants were excluded for any history of moderate and/or severe traumatic brain injury, if they were currently under provider care for a concussion/traumatic brain injury, and/or health risks (heart conditions, respiratory disorders, and/or neurological disorders) that put them at greater than minimal risk during the concussion outcomes assessments. There was no exclusion based on self-report sex, race, ethnicity, or mental health history.

## 4.2.3 Measures and Assessments

Participants self-reported demographic, concussion history, and current mindfulness practice information to describe the study sample. Demographic questions included age, sex, race, and ethnicity. Concussion history questions included number of concussions incurred and, for each concussion incurred, how long ago the injury was and concussion mechanism (categorized binarily as sport-related vs. non-sport-related). Current mindfulness practice questions asked participants if they currently engage in a mindfulness practice and, if so, the techniques they use (yoga and/or meditation).

The independent variables for this study were perceived stress and mindfulness. Perceived stress was measured using the Perceived Stress Scale 10 question version (PSS-10), the most widely used psychological instrument for measuring perceived stress.<sup>180</sup> The PSS-10 is well validated and had been used in connection to mindfulness<sup>32–34,37,40</sup> and in brain injury populations.<sup>43</sup> The PSS-10 consists of 10 questions on a five-point scale (0=never to 4=very often) about how often a participant has felt or thought a certain way relative to their perceived stress in the past month. Final scores were obtained by reversing responses to the four positively stated items and then summing all 10 scale items. These analyses utilized the PSS-10 total score (range=0-40) with higher scores indicating higher perceived stress.<sup>181</sup> Mindfulness was measured using the Five Facet Mindfulness Questionnaire (FFMQ). This widely used, valid survey to measure mindfulness<sup>185</sup> has been researched extensively connected to perceived stress.<sup>34–36</sup> Participants were asked 39 questions on a five-point scale (1=never/very rarely true to 5=very often/always true) related to general mindfulness tendencies in daily life. Questions are focused on five facets of mindfulness which include: 1) observing, noticing, and attending to sensations, perceptions, thoughts, and feelings; 2) describing/labeling one's experience with words; 3) acting with awareness; 4) non-judging; and 5) non-reactivity to inner experience. Each facet makes up a sub-score of the FFMQ. Total scores were obtained by reversing responses to the 19 reverse scored questions and then summing all 39 items. These analyses utilized the FFMQ total score (range=39-195) with higher scores indicating greater mindfulness levels.<sup>186</sup>

Clinical concussion outcomes included assessments measuring concussion symptoms, balance performance, ANS function, vestibular/ocular function, and exertion tolerance. <u>Concussion symptoms</u> were measured using the Rivermead Post-Concussion Symptom Questionnaire (RPQ),<sup>189</sup> a validated measure<sup>192,193</sup> which asks participants to report the presence and severity (0-4) of 18 concussion-related symptoms compared with before their concussion. The RPQ has been frequently used in the proposed study population.<sup>190,191</sup> Outcomes for the RPQ were total symptom severity (range=0-72) and total number of symptoms reported as worse than before injury (symptoms reported as >1 on the severity scale is an indication that symptoms are present at levels worse than before the participant's injury, range=0-18). Higher scores indicate higher concussion symptom severity and presence.

Balance performance was measured using the Balance Error Scoring System (BESS) and by completing a center of mass (COM) assessment. The BESS is a validated clinical measure for static postural balance commonly used in concussed patients.<sup>194,195</sup> Participants completed three stances on a firm and foam surface for 20 seconds with their eyes closed: 1) double-leg (hands on the hips and feet together); 2) single-leg stance (standing on the nondominant leg with hands on the hips); and 3) tandem (nondominant foot behind the dominant foot in a heel-to-toe arrangement). Study personnel counted errors throughout each stance. An error was defined as opening eyes, lifting hands off the hips, stepping or falling out of position, lifting the forefoot or heel, abducting the hip  $>30^\circ$ , or failing to return to the test position in more than five seconds. The outcome for the BESS was total errors (range=0-60) with more errors indicating worse balance performance. The COM assessment was indexed via a portable Inertial Measurement Unit (IMU) worn on the posterior trunk and sampled at 370 samples/second: a relaible<sup>196</sup> COM assessment that has been previously used in the study population.<sup>197,198</sup> Participants completed two double-leg stance one-minute trials, one with eyes open and one with eyes closed. Throughout the assessment, an IMU (Delsys, Inc., United States) was affixed to the participant's posterior trunk to measure COM. Results were post-processed by a custom Unity 3D-based data ingestion and analysis platform (Unity Technologies, San Francisco, CA). Specifically, data for both trials (eyes open

and closed) in the anterior/poster (x) and medial/lateral (z) planes were processed using the following procedure: 1) data from the first and final second of the trials were removed (i.e., 740 samples); 2) absolute values of each data point were calculated; 3) standard deviation (SD) of acceleration values were calculated for the anterior/posterior and medial/lateral planes of the eyes open and eyes closed trials; and 4) outcomes were converted from g forces to cm/s<sup>2</sup>. The COM assessment outcomes were SD of acceleration in the anterior/posterior and medial/lateral planes for the eyes open and closed trials.<sup>221,222,240</sup>

ANS function was measured using HRV during three intervals: 1) seated (parasympathetic domain); 2) standing (sympathetic domain); and 3) a repeated seated condition (recovery), a protocol used to collect HRV in individuals across all stages of concussion recovery (i.e., acute, persistent concussion symptoms, and concussion history).<sup>58</sup> During each interval, HRV data was collected via a Polar H10 (130 Hz sampling rate) heart rate monitor for six minutes with the middle five minutes used for final data analyses.<sup>58</sup> The following data processing was completed using a protocol previously reported in the concussion literature:<sup>199</sup> 1) raw R-R data were processed using Kubios HRV (version 3.5.0, Biosignal Analysis and Imaging Group, Kuopio, Finland); 2) Kubios's automatic beat correction was utilized in accordance with their validated algorithm;<sup>223</sup> and 3) manual inspection was completed with outliers and ectopic beats removed when necessary.<sup>224</sup> The HRV assessment outcomes were average HR (time domain), a measure indicative of sympathetic cardiac activation, and the low frequency power to high frequency power (LF/HF) ratio (frequency domain), a measure indicative of sympathetic and parasympathetic nervous system balance, for each trial (seated 1, standing, and seated 2).

<u>Vestibular/ocular function</u> was assed using the Vestibular/Ocular Motor Screening (VOMS) assessment,<sup>202</sup> a valid and reliable clinical assessment<sup>195,203</sup> commonly used in concussed

populations.<sup>202</sup> Participants were asked to rate the severity of four symptoms (headache, dizziness, nausea, and fogginess) from 0-10 before (pre-test) and after (post-test) completing clinical assessments for smooth pursuits, horizontal and vertical saccades, near-point convergence, vestibular ocular reflex, and visual motion sensitivity. To calculate symptom change scores, symptom total scores (sum of all symptom ratings) were calculated for baseline (prior to the assessment) and each VOMS clinical assessment. Change scores were then calculated for each VOMS clinical test by subtracting the total symptom score at baseline from the post-test score. Change scores that were negative (i.e., when the participant reported higher/worse symptoms at baseline compared to with the post-test) were coded as zero to indicate no provocation of symptoms.<sup>202,204,205</sup> The outcome for the VOMS was the symptom change score (pre- vs. post-test) for each VOMS clinical assessment.<sup>202,204,205</sup>

Exertion tolerance was assessed using the two-minute step test (a modification of the Chester Step Test). Participants were asked to complete as many steps as possible in two minutes. A 30 second rest period began the assessment followed by the two-minute step test and a 30 second (or more) rest period following. The step used was a standardized, 20-centimeter step in accordance with previous literature.<sup>225</sup> Participants were instructed to place both of their feet fully on the step and then fully back down on the ground with stepping up fully on the step and then back down to the ground counting as one step. Participants wore a pedometer on their shoe to validate the steps counted by study personnel. After completing the step test, participants were asked to rate their perceived exertion using the Borg Rating of Perceived Exertion (RPE; a scale which asks subjects to rank their perceived exertion from zero to maximal exertion). This study used the modified Borg scale, in which participants rated their RPE on a scale from 0 (no exertion)

to 10 (maximal exertion).<sup>226</sup> Outcomes for this assessment included number of steps completed and the participant's post-test RPE.

#### 4.2.4 Statistical Analyses

Descriptive statistics were computed for all variables of interest. To describe the sample, means, SD, and 95% confidence intervals (95%CI) were computed for age, number of concussions, and time since most recent concussion. Additionally, frequencies and percentages were computed for sex, ethnicity, race, number of concussions, most recent concussion mechanism, and current mindfulness practice. Means, SDs, and 95%CIs were computed for perceived stress, mindfulness, and all clinical concussion outcomes.

Multivariable regression analyses assessed the association among perceived stress, mindfulness, and clinical concussion outcomes. First, separate multivariable linear regression models were used to determine the association among perceived stress and each clinical concussion outcome. Second, separate multivariable linear regression models were used to determine the association among mindfulness and each clinical concussion outcome. Third, consistent with best practices,<sup>234</sup> an interaction term of perceived stress and mindfulness was included to test the potential moderation effect of mindfulness on our outcomes (a separate model for each dependent variable was utilized). All models controlled for number of concussions (1-5+),<sup>228,229</sup> sex (male/female),<sup>87,230</sup> and most recent concussion mechanism (sport/non-sport related).<sup>231–233</sup> Parameter estimate  $\beta$ , standardized  $\beta$ , standardized 95%CI, estimate p-value, and model adjusted R<sup>2</sup> were reported with p<0.05 identified as significant for each parameter. Following previous literature and to mitigate the change of type 2 error, no adjustment for multiple comparisons was made.<sup>216,217</sup>

## 4.3 Results

## 4.3.1 Demographics and General Descriptives

The study sample's demographic information is reported in Table 4.1. A total of 80 participants completed this study with 24 (30.00%) reporting a current mindfulness practice [12 (50.00%) indicating they use meditation and 18 (75.00%) use yoga]. Descriptive statistics for this study's independent and dependent variables are reported in Table 4.2. Overall, the study sample's mean PSS-10 total fell within moderate levels of perceived stress and was two points higher than young adults norm values<sup>241</sup> and the mean FFMQ total was similar to young adult norm values.<sup>185</sup> Cronbach's  $\alpha$  values indicated good internal consistency for the PSS-10 ( $\alpha$ =0.89) and excellent internal consistency for the FFMQ ( $\alpha$ =0.91) and RPQ ( $\alpha$ =0.92).

Table 4.1. Demographic information for the study same (n=80).				
	Mean±SD	95%CI		
Age (Years)	21.39±2.59	20.78, 22.00		
Number of Concussions	2.50±1.50	2.17, 2.83		
Time Since Most Recent Concussion (Months)	24.18±17.75	20.23, 28.13		
	Frequency	Percent		
Sex				
Female	62	77.50		
Male	18	22.50		
Ethnicity <sup>a</sup>				
Non-Hispanic/Latino	74	93.67		
Hispanic/Latino	5	6.33		
Race				
White	62	77.50		
Non-White	18	22.50		
Number of Concussions				
1	29	36.25		
2	17	21.25		
3	14	17.50		
4	5	6.25		
5+	15	18.75		
Most Recent Concussion Mechanis	m			
Sport-Related	41	51.25		
Non-Sport-Related	39	48.75		
Current Mindfulness Practice				
Yes	24	30.00		
No	56	70.00		
<sup>a</sup> Self-reported ethnicity data missin				
Abbreviations: SD=standard devia	tion, 95%CI=95% confidence	ce interval.		

(n=80).	Mean	SD	95%CI	Median	25% Quartile	75% Quartile
Perceived Stress (PSS-10)					C	
Total	19.53	6.75	18.02, 21.03	19.00	14.50	25.00
Mindfulness (FFMQ)						
Total	122.88	19.22	118.60, 127.15	123.00	109.00	136.00
Concussion Symptoms (R	PQ)					
Total Symptom Severity	22.26	12.43	19.50, 25.03	21.00	13.50	30.50
Total Symptoms Worse than Before Injury	6.80	4.83	5.72, 7.88	6.00	3.00	11.00
Balance Performance (BE	SS)					
Total Errors	10.45	3.84	9.60, 11.30	10.00	8.00	13.00
Balance Performance (CO	M)					
Eyes Open Trial						
Anterior/Posterior Plane SD of	6.86	3.82	5.99, 7.72	5.35	4.38	7.64
Acceleration <sup>a</sup> Medial/Lateral Plane SD of Acceleration <sup>a</sup>	12.35	8.43	10.44, 14.25	9.51	6.66	15.11
Eyes Closed Trial			14.23			
Anterior/Posterior						
Plane SD of	6.53	3.15	5.82,	5.94	4.39	7.21
Acceleration <sup>a</sup>			7.24			
Medial/Lateral Plane SD of Acceleration <sup>a</sup>	12.72	7.72	10.98, 14.47	10.93	8.53	14.17
ANS Function (HRV)						
Seated 1 HR <sup>b</sup>	76.12	12.04	73.44, 78.80	74.05	65.98	84.08
Seated 1 LF/HF Ratio	2.02	2.37	1.49, 2.55	1.22	0.78	2.27
Standing HR <sup>b</sup>	89.37	12.91	86.50, 92.24	88.76	79.66	98.38
Standing LF/HF Ratio	5.78	6.54	4.33, 7.24	3.61	2.17	7.17
Seated 2 HR <sup>b</sup>	76.42	12.13	73.72, 79.12	75.16	66.49	83.23
Seated 2 LF/HF Ratio	1.98	1.81	1.57, 2.38	1.54	0.81	2.47

Smooth Pursuits	0.38	1.06	0.14, 0.61	0.00	0.00	0.00
Horizontal Saccades	0.89	2.03	0.44, 1.34	0.00	0.00	1.00
Vertical Saccades	1.00	2.06	0.54, 1.46	0.00	0.00	1.00
Near Point Convergence	1.20	2.77	0.58, 1.82	0.00	0.00	1.00
Horizontal VOR	2.20	3.64	1.39, 3.01	1.00	0.00	3.00
Vertical VOR	2.15	3.71	1.32, 2.98	1.00	0.00	2.50
VMS	2.44	4.35	1.47, 3.40	0.50	0.00	3.00
Exertion Tolerance (Step	Test)					
Number of Steps	62.78	10.49	60.44, 65.11	61.00	55.00	69.50
RPE	3.02	1.64	2.65, 3.38	3.00	2.00	3.00

<sup>a</sup>Units=cm/s<sup>2</sup>.

<sup>b</sup>Units=beats/minute.

<sup>c</sup>VOMS data reported as change in total symptom scores from baseline for each assessment. **Possible scale ranges:** PSS-10 total=0-40 (higher=more perceived stress), FFMQ total=39-195 (higher=more mindfulness), RPQ total concussion symptom severity=0-72 (higher=more total concussion symptom severity), RPQ total concussion symptoms worse than before injury=0-18 (higher=more symptoms worse than before injury), BESS total errors=0-60 (higher=worse balance performance), VOMS change scores=0-40 (higher=more symptom provocation), step test RPE=0-10 (higher=more perceived exertion). **Abbreviations:** SD=standard deviation, 95%CI=95% confidence interval, PSS-10=Perceived Stress Scale, FFMQ=Five Facet Mindfulness Questionnaire, RPQ=Rivermead Post-Concussion Questionnaire, BESS=Balance Error Scoring System, COM=center of mass, ANS=autonomic nervous system, HRV=heart rate variability, HR=heart rate, LF/HF=low frequency/high frequency, VOMS=Vestibular/Ocular Motor Screening, VOR=vestibular/ocular reflex, VMS=visual motion sensitivity, RPE=rate of perceived exertion.

#### 4.3.2 Perceived Stress and Clinical Concussion Outcomes

Results from the separate multivariable linear regression models with perceived stress and each of the clinical concussion outcomes (each model controlling for number of concussions, sex, and most recent concussion mechanism) are reported in Table 4.3. Higher perceived stress was significantly associated with higher total concussion symptom severity (p<0.001) and higher total number of concussion symptoms reported as worse than before injury (p<0.001). No other significant associations were identified.

# 4.3.3 Mindfulness and Clinical Concussion Outcomes and Perceived Stress Mindfulness Interaction

Multivariable linear regression model results with mindfulness and clinical concussion outcomes (each model controlling for number of concussions, sex, and most recent concussion mechanism) are reported in Table 4.3. Higher mindfulness was associated with lower concussion symptom severity (p<0.001) and lower total number of concussion symptoms reported as worse than before injury (p=0.002). No other significant associations were identified. There were no overall significant models where the interaction effect was also significant, despite the BESS parameter estimate showing significance in the interaction model (Table 4.3).

Table 4.3. Separate multivariable linear regression models estimating the association among perceived stress (PSS-10 total), mindfulness (FFMQ total), and the interaction between perceived stress and mindfulness interaction with clinical concussion outcomes. All models control for concussion number (1-5+), sex (male/female), and concussion mechanism (sport/non-sport).

		Param	eter Estimates		Model
	β	Standardized β	Standardized 95%CI	p Value	Adjusted R <sup>2</sup>
<b>Concussion Sympt</b>	oms (RPQ)				
<b>Total Symptom Se</b>	verity				
Perceived Stress	0.83	0.45	0.25, 0.64	< 0.001*	0.30
Mindfulness	-0.25	-0.38	-0.58, -0.18	< 0.001*	0.25
Interaction	0.002	0.09	-0.78, 0.97	0.83	0.29
<b>Total Symptoms W</b>	Vorse Than	<b>Before Injury</b>			
Perceived Stress	0.31	0.43	0.24, 0.63	< 0.001*	0.29
Mindfulness	-0.08	-0.34	-0.54, -0.13	0.002*	0.22
Interaction	0.0004	0.05	-0.84, 0.94	0.91	0.27
<b>Balance Performan</b>	nce (BESS)				
Total Errors					
Perceived Stress	0.05	0.10	-0.13, 0.32	0.41	0.02
Mindfulness	-0.01	-0.05	-0.28, 0.18	0.66	0.01
Interaction	0.009	1.38	0.39, 2.37	0.01*	0.09
<b>Balance Performan</b>	nce (COM)				
<b>Eyes Open Trial A</b>	nterior/Pos	sterior Plane SD	of Acceleration		
Perceived Stress	0.01	0.02	-0.22, 0.26	0.85	-0.02
Mindfulness	-0.03	-0.13	-0.36, 0.10	0.27	-0.003
Interaction	0.01	0.66	-0.38, 1.73	0.21	0.002
<b>Eyes Open Trial M</b>	Iedial/Late	ral Plane SD of A	Acceleration		
Perceived Stress	0.01	0.01	-0.23, 0.23	0.99	0.04
Mindfulness	-0.04	-0.10	-0.32, 0.13	0.41	0.05
Interaction	0.01	0.39	-0.64, 1.43	0.45	0.04
Eyes Closed Trial	Anterior/P	osterior Plane SI	) of Acceleration		
Perceived Stress	0.02	0.04	-0.19, 0.27	0.73	0.03
Mindfulness	-0.02	-0.13	-0.36, 0.09	0.25	0.05
Interaction	0.01	0.67	-0.36, 1.70	0.20	0.05
Eyes Closed Trial	Medial/Lat	eral Plane SD of	Acceleration		
Perceived Stress	0.05	0.04	-0.18, 0.27	0.69	0.08
Mindfulness	-0.04	-0.11	-0.33, 0.11	0.32	0.09
Interaction	0.01	0.60	-0.41, 1.61	0.24	0.09
<b>ANS Function (HR</b>	RV)				
Seated 1 HR					
Perceived Stress	0.28	0.16	-0.07, 0.38	0.18	0.02
Mindfulness	-0.05	-0.07	-0.30, 0.16	0.53	-0.0002
Interaction	-0.003	-0.19	-1.23, 0.85	0.71	-0.003
Seated 1 LF/HF Ra	atio				
Perceived Stress	0.05	0.15	-0.09, 0.38	0.21	-0.03

Mindfulness	-0.02	-0.13	-0.37, 0.10	0.25	-0.03
Interaction	-0.003	-0.78	-1.83, 0.27	0.14	-0.02
Standing HR					
Perceived Stress	0.16	0.09	-0.15, 0.32	0.47	-0.02
Mindfulness	0.00002	0.00002	-0.23, 0.23	0.99	-0.03
Interaction	-0.002	-0.09	-1.14, 0.97	0.87	-0.04
Standing LF/HF R	Ratio				
Perceived Stress	-0.01	-0.01	-0.24, 0.22	0.94	-0.02
Mindfulness	0.02	0.06	-0.17, 0.29	0.60	-0.02
Interaction	0.002	0.20	-0.85, 1.26	0.70	-0.04
Seated 2 HR					
Perceived Stress	0.34	0.19	-0.04, 0.42	0.10	0.04
Mindfulness	-0.07	-0.10	-0.33, 0.12	0.40	0.01
Interaction	-0.001	-0.06	-1.09, 0.97	0.91	0.01
Seated 2 LF/HF R	atio		,		
Perceived Stress	0.03	0.10	-0.14, 0.33	0.42	-0.03
Mindfulness	-0.004	-0.05	-0.28, 0.19	0.70	-0.04
Interaction	-0.0006	-0.22	-1.28, 0.85	0.69	-0.05
Vestibular/Ocular					
Smooth Pursuits					
Perceived Stress	0.01	0.05	-0.18, 0.28	0.66	0.04
Mindfulness	-0.007	-0.12	-0.34, 0.10	0.29	0.05
Interaction	-0.0004	-0.24	-1.26, 0.78	0.64	0.03
Horizontal Saccad		0.2.	1.20, 01/0		0.00
Perceived Stress	0.0002	0.0006	-0.23, 0.23	0.99	0.02
Mindfulness	-0.01	-0.08	-0.30, 0.15	0.51	0.02
Interaction	-0.001	-0.34	-1.14, 0.69	0.51	0.01
Vertical Saccades	0.001	0.51	1.11, 0.09	0.01	0.01
Perceived Stress	0.01	0.05	-0.19, 0.28	0.69	-0.01
Mindfulness	-0.01	-0.09	-0.32, 0.14	0.45	-0.01
Interaction	-0.001	-0.36	-1.40, 0.69	0.50	-0.03
Near Point Conver		0.50	1.10, 0.09	0.50	0.05
Perceived Stress	0.01	0.01	-0.21, 0.24	0.89	0.06
Mindfulness	-0.01	-0.04	-0.26, 0.18	0.72	0.06
Interaction	-0.001	-0.24	-1.25, 0.78	0.64	0.04
Horizontal VOR	-0.001	-0.24	-1.23, 0.76	0.04	0.04
Perceived Stress	0.01	0.03	-0.19, 0.25	0.81	0.08
Mindfulness	-0.02	-0.10	-0.32, 0.12	0.35	0.08
Interaction	-0.02	-0.10	-1.10, 0.89	0.83	0.09
Vertical VOR	-0.0000	-0.10	-1.10, 0.89	0.85	0.07
Perceived Stress	0.06	0.10	0 12 0 22	0.36	0.09
	-0.03	-0.15	-0.12, 0.32 -0.37, 0.07	0.36	0.09
Mindfulness Interaction			,		
Interaction	-0.002	-0.27	-1.26, 0.73	0.59	0.08
VMS	0.02	0.05	0 17 0 29	0.65	0.05
Perceived Stress	0.03	0.05	-0.17, 0.28	0.65	0.05
Mindfulness	-0.02	-0.08	-0.30, 0.15	0.50	0.05

Interaction	-0.001	-0.21	-1.23, 0.81	0.68	0.03
Exertion Toleranc		0.21	1.20, 0.01	0.00	0102
Number of Steps					
Perceived Stress	0.01	0.003	-0.23, 0.23	0.98	0.001
Mindfulness	-0.01	-0.02	-0.25, 0.21	0.84	0.001
Interaction	-0.01	-0.76	-1.79, 0.28	0.15	0.003
RPE					
Perceived Stress	-0.05	-0.19	-0.41, 0.03	0.09	0.08
Mindfulness	0.01	0.10	-0.13, 0.32	0.39	0.05
Interaction	-0.001	-0.42	-1.43, 0.58	0.40	0.06
* .0.05					

\*p<0.05

Abbreviations: PSS=Perceived Stress Scale, FFMQ=Five Facet Mindfulness Questionnaire,

95%CI=95% confidence interval, RPQ=Rivermead Post-Concussion Questionnaire,

BESS=Balance Error Scoring System, COM=center of mass, ANS=autonomic nervous system, HRV=heart rate variability, HR=heart rate, LF/HF=low frequency/high frequency,

VOMS=Vestibular/Ocular Motor Screening, VOR=vestibular/ocular reflex, VMS=visual motion sensitivity, RPE=rate of perceived exertion.

#### 4.4 Discussion

This study estimated the associations among perceived stress, mindfulness, and clinical concussion outcomes (concussion symptoms, balance performance, ANS function, vestibular/ocular system function, and exertion tolerance) in young adults with a concussion history. Our findings suggest higher perceived stress was significantly associated with greater concussion symptom burden. Additionally, results suggest higher mindfulness levels were associated with lower concussion symptom burden. Overall results suggest similar outcomes for the perceived stress and mindfulness models, and we note that our sample's PSS-10 and FFMQ total scores were highly correlated (R=-0.73, p<0.001). As such, similar perceived stress and mindfulness results may have been driven by the inherence connection between the two scales.

# 4.4.1 Perceived Stress, Mindfulness, and Concussion Symptoms

The current study findings indicate higher perceived stress is associated with higher concussion symptoms (greater burden) – a novel finding in the concussion literature that is consistent with our original hypothesis. Research suggests perceived stress is increased acutely post-concussion,<sup>155</sup> and this potentially prolongs recovery given the association found in the current study among increased perceived stress and concussion symptoms in those with concussion history. Also, supporting this notion is a recent meta-analysis suggesting that negative emotional factors may increase time to return to sport post-concussion.<sup>242</sup> Although none of the analyzed studies utilized specific, validated perceived stress questionnaires, qualitative data suggest that perceived stress may be a key emotional factor that impacts return to play.<sup>242</sup> As such, current perceived stress and concussion symptoms are a key marker for tracking recovery and returning to play/school/life post-concussion. Causality cannot be determined with this cross-sectional study, and we

acknowledge the overlap in the perceived stress and concussion symptoms questionnaires. Specific overlapping symptoms include being irritable/easily angered, feeling nervous/stressed, and reduced tolerance to stress.<sup>184,189</sup> However, the mean number of concussion symptoms reported as worse than before injury was 6.80 – more than the overlapping number of symptoms.

Additionally in line with our hypotheses, the current study suggests higher mindfulness is significantly associated with lower concussion symptom burden. Although the current study is the first to investigate the cross-sectional association among mindfulness and concussion symptoms, research in healthy populations suggest an association between mindfulness and anxiety and depression<sup>243</sup> - emotional post-concussion symptoms that are included in the RPQ and other concussion symptom questionnaires. Additionally, mindfulness interventions post-concussion are minimally researched in the current literature, suggesting promising results at improving overall injury outcomes and QOL.<sup>139,244</sup> Despite this, no studies include objective measures for mindfulness to better understand intervention mechanisms. Furthermore, most post-concussion mindfulness interventions also include other severities of traumatic brain injury (i.e., moderate and severe) within the study sample and, as such, concussion symptoms are rarely measured as an outcome.<sup>139,245</sup> Studies including concussion symptoms as an outcome have found mixed results with some reporting no pre/post-intervention change in concussion symptoms<sup>246,247</sup> and others suggesting significant intervention-related improvements in concussion symptoms.<sup>139</sup> In summary, the current study supports overall mindfulness associations found in the literature and provides concussion-specific evidence connecting mindfulness and concussion symptoms.

### 4.4.2 Perceived Stress, Mindfulness, and Additional Clinical Concussion Outcomes

Contrary to our hypothesis, no other significant associations were identified among perceived stress, mindfulness, and the additional clinical concussion outcomes. However, most previous work connecting perceived stress, mindfulness, and these outcomes have been in healthy populations not accounting for concussion history. Therefore, current study results in those with concussion history present a novel understanding of the associations among perceived stress and mindfulness and balance performance, ANS dysfunction, vestibular/ocular function, and exercise tolerance. Additionally, these results present interesting data to inform future research.

While no significant association of perceived stress or mindfulness with balance was observed in the current study, there are methodological and historical considerations for these findings. Research in healthy young adults suggest perceived stress negatively affects postural control measured using five stances (feet together, slightly apart, further apart, right foot forward, and left foot forward) on a force platform, and these results were magnified in the eyes closed trials.<sup>237,248</sup> Conversely, the current study data showed similar descriptive values for the eyes open and eyes closed trials SD of acceleration in both the anterior/posterior and medial/lateral planes. Previous work outside of concussion assessing the use of IMUs to measure postural control incorporated more challenging balancing protocols than the double leg stance used in the current study.<sup>237,248</sup> In addition to the five stance protocol discussed above, studies have followed a similar protocol to the BESS (double leg, single leg, and tandem stances in eyes open and closed trials) – with results suggesting worse balance performance as stances and trials increased in difficulty (i.e., tandem stance eyes closed trial had the worse outcome).<sup>240</sup> Completing the full BESS protocol while wearing an IMU may provide more evidence to determine the impact of a more comprehensive measure of balance performance post-concussion; however, no influence of perceived stress or mindfulness on the relatively simple balance task was observed in the current study.

Overall, no significant associations were observed for mindfulness, perceived stress, and HRV findings inconsistent with a recent meta-analysis suggesting that exposure to stress is associated with impaired HRV (most often seen as a higher LF/HF ratio).<sup>249,250</sup> Although initial evidence suggests HRV is impaired at symptomatic and asymptomatic stages post-concussion,<sup>155</sup> HRV remains a novel clinical outcome in concussion research - requiring more research to understand its impact and clinical meaningfulness. Additionally, our participants were at various stages removed from the proximity of concussion, which may impact the relationship between perceived stress and HRV. We also recognize that a significant proportion of our sample had COVID-19 in recent months to study participation (n=49, 61.25%), which may have impacted HRV outcomes. However, post-hoc correlations between the HRV outcomes and COVID-19 diagnosis (yes/no) suggest no correlation (p>0.05). Descriptively the current study data suggest an increase mean HR and LF/HF ratio in the standing versus seated trials - results consistent with HRV concussion studies showing an increase in HR and LF/HF during exercise or position change.<sup>251</sup> Additionally, the mean HR and LF/HF ratio in the seated 1 and 2 trials were almost identical, suggesting the participants, regardless of perceived stress or mindfulness levels, returned to their baseline resting HRV after the six-minute standing/exertional trial. Despite the lack of significant findings of the current study in relation to perceived stress, future research is necessary to further understand the association among perceived stress and HRV post-concussion as a potential factor impacting recovery.

Additionally, no significant associations were identified among perceived stress, mindfulness, and vestibular/ocular function in the current study. Previous research suggests that elevated stress levels can lead to vestibular dysfunction;<sup>252,253</sup> however, research in this space has largely focused on animal studies and small, preliminary human trials with no robust clinical data

and/or use of comprehensive vestibular/ocular performance assessments. Furthermore, although literature suggests higher VOMS symptom scores in those with a concussion history compared to those without,<sup>254</sup> overall our data showed small, non-significant changes across the VOMS assessments. These findings may be supported by research suggesting vestibular dysfunction post-concussion resolves within the typical adult recovery timeframe (10-21 days) for 80-90% of patients.<sup>255</sup> Our sample being on average two and a half years from their most recent concussion may have played a role in the small VOMS symptom scores. Furthermore, small BESS errors and similar COM results in the eyes open versus closed balance trials present additional evidence to suggest the current sample may have minimal long-term overall vestibular dysfunction after their concussion.

There was also no significant association among perceived stress, mindfulness, and exertion tolerance (number of steps completed and post-test RPE). Concussion research in acute, symptomatic patients provides evidence that RPE is increased after an exertional, treadmill test when compared to non-concussion controls<sup>256</sup> and an asymptomatic recovery timepoint.<sup>207</sup> Contrary, subjects in the current study sample reported an average post-step test RPE of 3 (moderate). Again, our sample's various post-concussion stages may have contributed to the perceived stress, mindfulness and exercise tolerance findings. Additionally, current study participants completed a two-minute step task compared to a treadmill-based test used in most prior studies.<sup>101,102,257,258</sup> Additionally, most concussion exercise studies have focused on the impact of exercise on concussion symptoms in acute and persistent symptom patients<sup>258</sup> and mechanistic understanding of exercise interventions is not fully understood.

## 4.4.3 Perceived Stress and Mindfulness Interaction

Initial interaction findings suggest a significant moderation effect for the BESS total error; however, the overall model for the BESS was not significant. Additionally, the BESS interaction model only accounted for  $\beta$ =0.009 BESS total errors, a finding deemed not clinically meaningful based on established minimal detectable change scores (6-10 points).<sup>259,260</sup> As such, our data suggest no significant moderation effect of mindfulness on the association among perceived stress and our clinical concussion outcomes. Although limited evidence suggests higher mindfulness is associated with lower perceived stress, an understanding of how much mindfulness Is needed to Impact perceived stress Is unknown. Specifically, no research has identified the length of mindfulness practice/intervention needed to see intervention-related benefits – seen in the traumatic brain injury literature with the inconsistency of mindfulness intervention lengths.<sup>139</sup>

Additionally, FFMQ scoring does not include cut points suggesting lower versus higher levels of mindfulness as the tool was meant to assess a spectrum of mindfulness. Further, understanding how levels of mindfulness are related to mindfulness intervention-related improvements, specifically perceived stress, may provide evidence to understand if a certain mindfulness threshold presents more impact on perceived stress– knowledge which may influence these moderation effects. Furthermore, 70.00% of the current study sample are mindfulness practice naïve – a limitation which may have impacted the FFMQ results, especially as to pertains to understanding impactful threshold of trait mindfulness necessary to influence perceived stress.

### 4.4.4 Strengths, Limitations, and Future Research

This study has several strengths and limitations. The cross-sectional study design limits the ability to determine causality. Future research should expand the study design to a longitudinal cohort study, including multiple timepoints and stages of concussion recovery. Additionally, this

study's sample was majority female, white, and college aged young adults. Future studies should widen the sample to deepen the generalizability of the study results. Despite these limitations, this study included many strengths. To our knowledge, this was the first study to investigate the associations among perceived stress, mindfulness, and clinical concussion outcomes. Additionally, this study utilized a wide range of clinical concussion assessments (questionnaires and physiologic), providing data on many aspects of concussion recovery. Future research should build upon the findings from this study to further understand mechanisms by which mindfulness interventions may impact concussion outcomes.

## **4.5 Conclusions**

This was a novel study estimating the associations among perceived stress, mindfulness, and clinical concussion outcomes in young adults with a concussion history. Results suggest higher perceived stress is associated with higher concussion symptoms and higher mindfulness is associated with lower concussion symptoms and both factors had no associations with other more physically based clinical concussion outcomes. Future research is necessary to build upon these findings to further understand mechanisms impacting post-concussion intervention aimed to improve outcomes.

#### **CHAPTER 5: MANUSCRIPT AIM 2**

## 5.1 Background

Concussion is a mild traumatic brain injury (TBI) resulting in both clinical and psychological deficits (i.e., increased irritability, anxiety, depression, and cognitive dysfunction).<sup>2</sup> Despite research indicating adult's concussion symptoms typically resolve 10-21 days postinjury,<sup>2-4</sup> 10-25% of those with a concussion history experience persistent concussion symptoms beyond typical recovery.<sup>2,3</sup> Furthermore, neurophysiological changes remain in concussion history patients with persistent concussion symptom expression;<sup>5,6</sup> resulting in continued clinical and psychological dysfunction<sup>7,8</sup> causing those impacted to potentially miss school,<sup>9</sup> work,<sup>10</sup> sport,<sup>11</sup> and have less societal engagement<sup>12</sup> leading to long-term decreased quality of life (QOL).<sup>13</sup> Additionally, student-athletes with a concussion history, regardless of persistent symptom expression, report increased depression and anxiety as well as sleep and QOL disturbances.<sup>14,15</sup>

Increased perceived stress is associated with increased depression,<sup>17</sup> anxiety,<sup>17</sup> and exhaustion<sup>17</sup> as well as decreased physical health,<sup>18</sup> life satisfaction,<sup>19</sup> and QOL.<sup>20</sup> Additionally, limited data suggests perceived stress is heightened acutely post-concussion<sup>13</sup> and further research suggests perceived stress may play a role in predicting persistent concussion impairments.<sup>27</sup> Despite these preliminary connections, there is limited research on the impact of perceived stress in a concussion history population or on psychological concussion outcomes, information needed to interpret these outcomes and inform necessary interventions. Interventions targeting perceived stress, <sup>32–34</sup> but also increased mental health,<sup>35</sup> physical health,<sup>36</sup> and subjective psychological well-being.<sup>33</sup>

Furthermore, in healthy populations, research suggests that mindfulness-based interventions (i.e., meditation and yoga) improve mindfulness and perceived stress.<sup>36-40</sup> Mindfulness-based techniques have been minimally used as a rehabilitation mechanism in TBI/concussion populations with preliminary results indicating post-mindfulness intervention improvements in QOL,<sup>42,43</sup> attention,<sup>44</sup> mental fatigue, <sup>44</sup> anxiety, <sup>44</sup> and depression. <sup>44</sup> However, these studies did not investigate the associations among perceived stress, mindfulness, and comprehensive psychological concussion outcomes, findings necessary to design effective concussion interventions.

Despite evidence indicating perceived stress may negatively impact post-concussion outcomes and mindfulness may improve that relationship, research has not investigated those connections in young adults with a concussion history. Therefore, this study estimated the associations among perceived stress, mindfulness, and psychological concussion outcomes (neurocognitive performance, psychological distress, and QOL) in young adults with a concussion history. We hypothesized participants with: 1) higher perceived stress would have worse psychological concussion outcomes (lower neurocognitive performance, higher psychological distress, and lower QOL); 2) higher mindfulness would have better psychological concussion outcomes; and 3) the association among perceived stress and psychological concussion deficits would be moderated by mindfulness levels (specifically mindfulness will buffer the relationship between perceived stress, and psychological concussion outcomes). Understanding the association among perceived stress, and concussion outcomes in those with a concussion history can provide evidence supporting stress reduction and/or mindfulness-based interventions during concussion rehabilitation to facilitate concussion recovery and mitigate prolonged effects.

## 5.2 Methods

#### 5.2.1 Study Design

This study was a cross-sectional observational study in 80 (a priori power: alpha=0.05, power=0.8, effect size  $R^2=0.09$ )<sup>220</sup> young adults aged 18-30 with a concussion history aimed to determine the association among perceived stress, mindfulness, and clinical and psychological concussion outcomes. Institutional Review Board approval was obtained for the study and all participants completed informed consent. Participants completed a single study visit including the following measures used for these analyses: 1) demographic, concussion history, mental health history, and current mindfulness practice information; 2) perceived stress; 3) mindfulness; and 4) psychological concussion outcomes (neurocognitive performance, psychological distress, and QOL). Data were collected at a large state university between May and September 2022.

# 5.2.2 Participants

Participants were young adults (aged 18-30) with a concussion history (defined as experiencing a concussive injury within the past five years, but not within the past month). Participants were excluded for any history of moderate and/or severe TBI, if they were currently under provider care for a concussion/TBI, and/or health risks (heart conditions, respiratory disorders, and/or neurological disorders) that put them at greater than minimal risk during the concussion outcomes assessments. There was no exclusion based on self-report sex, race, ethnicity, or mental health history.

## 5.2.3 Measures and Assessments

Participants self-reported demographic, concussion history, mental health history, and current mindfulness practice information to describe the study sample. Demographic questions included age, sex, race, and ethnicity. Concussion history questions included number of concussions incurred and, for each concussion, time since the concussion and concussion mechanism (categorized binarily as sport-related vs. non-sport-related). Mental health history questions included mental health-related symptoms and diagnoses and mental health treatment usage. Current mindfulness practice questions asked participants if they currently engage in a mindfulness practice and, if so, technique use.

The independent variables for this study were perceived stress and mindfulness. Perceived stress was measured using the Perceived Stress Scale 10 question version (PSS-10), the most widely used psychological instrument for measuring perceived stress.<sup>180</sup> The PSS-10 is well validated and had been used in connection to mindfulness<sup>32–34,37,40</sup> and in brain injury populations.<sup>43</sup> The PSS-10 consists of 10 questions on a five-point scale (0=never to 4=very often) about how often a participant has felt or thought a certain way relative to their perceived stress in the past month. Final scores were obtained by reversing responses to the four positively stated items and then summing all 10 scale items. These analyses utilized the PSS-10 total score (range=0-40) with higher scores indicating higher perceived stress.<sup>181</sup> Mindfulness was measured using the Five Facet Mindfulness Questionnaire (FFMQ). This widely used, valid survey to measure mindfulness<sup>185</sup> has been researched extensively connected to perceived stress.<sup>34–36</sup> Participants were asked 39 questions on a five-point scale (1=never/very rarely true to 5=very often/always true) related to general mindfulness tendencies in daily life. Questions are focused on five facets of mindfulness which included: 1) observing, noticing, and attending to sensations, perceptions, thoughts, and feelings; 2) describing/labeling one's experience with words; 3) acting with awareness; 4) non-judging; and 5) non-reactivity to inner experience. Each facet makes up a sub-score of the FFMQ. Total scores were obtained by reversing responses to the 19 reverse scored

questions and then summing all 39 items. These analyses utilized the FFMQ total score (range=39-195) with higher scores indicating greater mindfulness levels.<sup>186</sup>

Dependent variables for these analyses were the psychological concussion outcomes of neurocognitive performance, psychological distress, and QOL. <u>Neurocognitive performance</u> was assessed using CNS Vital Signs (CNS Vital Signs, Morrisville, NC), a valid, reliable computer based neurocognitive assessment commonly used in concussed populations.<sup>208,209</sup> Outcomes for CNS Vital Signs included standard scores (scores with a mean of 100 and SD of 15 based on a normative dataset that matches participants by age) for the following domains: verbal memory, visual memory, psychomotor speed, cognitive flexibility, complex attention, processing speed, reaction time, and executive functioning.<sup>210</sup> Any outcome scores deemed invalid by CNS Vital Signs criteria were removed from analysis.<sup>210,227</sup>

<u>Psychological distress</u> was assessed using the Brief Symptom Inventory-18 (BSI-18), a validated, reliable survey used to assess psychological distress in brain injury<sup>211</sup> and concussion<sup>212,213</sup> populations. Participants answered 18 questions related to their psychological distress specific to somatization, anxiety, and depression over the past seven days on a five-point scale (0=not at all to 4=extremely). The outcome for the BSI-18 was the global severity index (total score, range=0-72).

<u>Quality of life</u> was measured using the Patient-Reported Outcomes Measurement Information System (PROMIS<sup>®</sup>) v2.1 adult measure, a valid, reliable assessment<sup>214</sup> used in concussion history populations<sup>215</sup> to assess QOL. The PROMIS<sup>®</sup>-29 is a comprehensive QOL assessment made up of the following short forms: 1) physical function (four questions on a fivepoint scale, 1=unable to do to 5=without any difficulty); 2) anxiety (four questions on a five point scale, 1=never to 5=always); 3) depression (four questions on a five point scale, 1=never to 5=always); 4) fatigue (four questions on a five point scale, 1=not at all to 5=very much); 5) sleep disturbances (one question on a five point scale, 1=very good to 5=very poor and three questions on a five point scale, 1=very much to 5=not at all); 6) ability to participate in social roles and activities (four questions on a five point scale, 1=always to 5=never); 7) pain interference (four questions on a five point scale, 1=not at all to 5=very much); and 8) pain intensity (one question rated from 0=no pain to 10=worst pain imaginable). Raw scores for each short form were summed and converted to t-scores.<sup>82,214</sup> Higher t-scores indicated more of each short form construct (i.e., higher/better physical functioning, more/worse anxiety, more/worse depression, more/worse fatigue, more/worse sleep disturbances, higher/better ability to participate in social roles and activities, more/worse pain interference, and more/worse pain intensity). Outcomes for the PROMIS-29 included t-scores for all eight short form domains.<sup>261</sup>

## 5.2.4 Statistical Analysis

Descriptive statistics were computed for all variables of interest. To describe the sample, means, SD, and 95% confidence intervals (95%CI) were computed for age, number of concussions, and time since most recent concussion. Additionally, frequencies and percentages were computed for sex; ethnicity; race; number of concussions; most recent concussion mechanism; current mindfulness practice; and mental health symptoms, diagnoses, and treatment use. Means, SDs, and 95%CIs were computed for perceived stress, mindfulness, and all psychological concussion outcomes.

Multivariable regression analyses assessed the association among perceived stress, mindfulness, and psychological concussion outcomes. First, separate multivariable linear regression models were used to determine the association among perceived stress and each psychological concussion outcome. Second, separate multivariable linear regression models were used to determine the association among mindfulness and each psychological concussion outcome. Third, consistent with best practices,<sup>234</sup> an interaction term of perceived stress and mindfulness was included to test the potential moderation effect of mindfulness on our outcomes (a separate model for each dependent variable was utilized). All models controlled for number of concussions (1-5+),<sup>228,229</sup> sex (male/female),<sup>87,230</sup> and most recent concussion mechanism (sport/non-sport related).<sup>231–233</sup> Parameter estimate  $\beta$ , standardized  $\beta$ , standardized 95%CI, estimate p-value, and model adjusted R<sup>2</sup> were reported with p<0.05 identified as significant for each parameter. Following previous literature and to mitigate the change of type 2 error, no adjustment for multiple comparisons was made.<sup>216,217</sup>

## **5.3 Results**

## 5.3.1 Demographics and General Descriptives

A total of 80 participants completed this study with a mean age of  $21.39\pm2.59$  years, 77.50% female, 93.67% non-Hispanic/Latino, and 77.50% white (Table 5.1). Overall, 24 (30.00%) reported a current mindfulness practice with 12 (50.00%) indicating they use meditation and 18 (75.00%) use yoga. When reporting mental health history, 65 (81.25%) indicated having previously experienced any mental health-related symptom(s) with 59 (90.77%) reporting experiencing anxiety and 40 (61.54%) depression symptoms. Additionally, 33 (41.25%) reported receiving a mental health diagnosis where 28 (84.85%) reported an anxiety diagnosis and 18 (54.55%) a depression diagnosis. Overall, 43 (67.19%) of those reporting either mental health-related symptoms and/or a diagnosis indicated their symptoms worsened after their concussion. Descriptive data for this study's independent and dependent variables are reported in Table 5.2. Overall, the study sample's mean PSS-10 total fell within moderate levels of perceived stress and was two points higher than young adults norm values<sup>241</sup> and the mean FFMQ total was similar to

young adult norm values.<sup>185</sup> The BSI-18 total score was similar to a previous study with a large concussion history young adult sample.<sup>209</sup> QOL t-scores for physical function, depression, social participation, pain interference, and pain intensity fell within normal ranges for young adults and t-scores for anxiety and fatigue indicated mild levels for young adults.<sup>214</sup> Cronbach's  $\alpha$  values indicated good internal consistency for the PSS-10 ( $\alpha$ =0.89) and excellent internal consistency for the FFMQ ( $\alpha$ =0.91) and BSI-18 ( $\alpha$ =0.91). QOL Cronbach's  $\alpha$  values indicated poor internal consistency for physical function ( $\alpha$ =0.60) and excellent internal consistency for anxiety ( $\alpha$ =0.90), depression ( $\alpha$ =0.95), fatigue ( $\alpha$ =0.92), sleep disturbance ( $\alpha$ =0.98), social participation ( $\alpha$ =0.89), and pain interference ( $\alpha$ =0.91).

	Mean±SD	95%CI
Age (Years)	21.39±2.59	20.78, 22.00
Number of Concussions	2.50±1.50	2.17, 2.83
Time Since Most Recent	24 10 17 75	20.22.29.12
Concussion (Months)	24.18±17.75	20.23, 28.13
	Frequency	Percent
Sex		
Female	62	77.50
Male	18	22.50
Ethnicity <sup>a</sup>		
Non-Hispanic/Latino	74	93.67
Hispanic/Latino	5	6.33
Race		
White	62	77.50
Non-White	18	22.50
Number of Concussions		
1	29	36.25
2	17	21.25
3	14	17.50
4	5	6.25
5+	15	18.75
Aost Recent Concussion Mechan	iism	
Sport-Related	41	51.25
Non-Sport-Related	39	48.75
Current Mindfulness Practice		
Yes	24	30.00
No	56	70.00
Experience Any Mental Health-R	elated Symptoms	
Yes	65	81.25
No	15	18.75
Any Mental Health-Related Diag	noses	
Yes	33	41.25
No	47	58.75
Did Mental Health-Related Symp	otoms Worsen Post-Concuss	bion <sup>b</sup>
Yes	43	67.19
No	21	32.81
Receive Mental Health Treatmen	t <sup>c</sup>	
Yes	36	55.38
No	29	44.62

<sup>b</sup>Question asked only to those who reported any mental health symptoms and/or diagnoses and missing n=1 response (n=64).

<sup>c</sup>Question asked only to those who reported any mental health symptoms and/or diagnoses (n=65).

Abbreviations: SD=standard deviation, 95%CI=95% confidence interval.

#### 5.3.2. Perceived Stress and Psychological Concussion Outcomes

Higher perceived stress was significantly associated with higher psychological distress (p<0.001). QOL regression results indicated higher perceived stress was also significantly associated with lower physical function (p=0.01), higher anxiety (p<0.001), higher depression (p<0.001), higher fatigue (p<0.001), lower social participation (p<0.001), higher pain interference (p=0.01), and higher pain intensity (p=0.01). No other significant associations were identified (Table 5.3).

# 5.3.3 Mindfulness, Interaction, and Psychological Concussion Outcomes

Results from the separate multivariable linear regression models with mindfulness and psychological concussion outcomes are reported in Table 5.3. Higher mindfulness was significantly associated with lower psychological distress (p<0.001). QOL regression results indicated higher mindfulness was significantly associated with higher physical function (p=0.02), lower anxiety (p<0.001), lower depression (p<0.001), lower fatigue (p=0.001), higher social participation (p<0.001), and lower pain intensity (p=0.04). No other significant associations were identified. No statistically significant moderation effects of mindfulness were identified (Table 5.3).

	n	Mean	SD	95%CI	Median	25%	75%
	11	Mean	50	95%CI	Median	Quartile	Quartile
Perceived Stress (PSS-10	))						
Total	80	19.53	6.75	18.02, 21.03	19.00	14.50	25.00
Mindfulness (FFMQ)							
Total	80	122.88	19.22	118.60, 127.15	123.00	109.00	136.00
Neurocognitive Performa	ance (C	NS Vital S	igns) <sup>a</sup>				
Verbal Memory	80	103.51	14.48	100.29, 106.73	104.00	94.00	114.00
Visual Memory	80	102.51	14.38	99.31, 105.71	104.50	93.00	113.00
Psychomotor Speed	79	100.04	12.77	97.18, 102.90	100.00	92.00	109.00
Cognitive Flexibility	77	91.88	17.90	87.82, 95.95	94.00	80.00	105.00
Complex Attention	72	92.31	16.33	88.47, 96.14	93.50	83.00	103.50
Processing Speed	80	104.96	13.49	101.96, 107.96	104.00	97.00	112.00
Reaction Time	78	98.22	13.63	95.15, 101.29	101.00	91.00	106.00
Executive Function	79	93.20	17.09	89.38, 97.03	95.00	84.00	106.00
Psychological Distress (I	3SI-18)	)					
Total	80	11.39	9.49	9.27, 13.50	8.00	5.00	16.50
QOL (PROMIS-29)							
Physical Function <sup>b</sup>	80	55.09	4.15	54.17, 56.01	57.00	57.00	57.00
Anxiety <sup>b</sup>	80	57.15	9.34	55.07, 59.23	57.70	52.45	63.40
Depression <sup>b</sup>	80	50.10	9.47	48.00, 52.21	49.00	41.00	56.50
Fatigue <sup>b</sup>	80	57.58	8.64	55.35, 59.20	57.00	51.00	64.60
Sleep Disturbance <sup>b</sup>	80	56.43	3.33	55.69, 57.17	56.10	54.30	59.80
Social Participation <sup>b</sup>	80	53.58	7.83	51.84, 55.32	53.70	47.15	58.30
Pain Interference <sup>b</sup>	80	47.09	7.18	45.48, 48.70	41.60	41.60	53.90
Pain Intensity	80	1.78	1.86	1.36, 2.19	1.00	0	3.00

<sup>a</sup>CNS Vital signs results are standard scores normalized by age to a mean of 100 and SD of 15. Any outcome scores deemed invalid by CNS Vital Signs criteria were removed from analysis resulting in the final n values.<sup>210,227</sup>

<sup>b</sup>PROMIS-29 scales reported as t-scores.<sup>261</sup>

**Scale ranges:** PSS-10 total=0-40 (higher=more perceived stress); FFMQ total=0-40 (higher=more mindfulness); BSI-19 total=0-72 (higher=more psychiatric distress); PROMIS-29 physical function t-score=22.5-57.0 (higher=better physical functioning), anxiety t-score=40.3-81.6

(higher=more/worse anxiety), depression t-score=41.0-79.4 (higher=more/worse depression),

fatigue t-score=33.7-75.8 (higher=more/worse fatigue), sleep disturbance t-score=32.0-73.3

(higher=more/worse sleep disturbance), social participation t-score=27.5-64.2 (higher=more/better social participation), pain interference t-score=41.6-75.6 (higher=more/worse pain interference), pain intensity=0-10 (higher=more/worse pain intensity).

**Abbreviations:** SD=standard deviation, 95%CI=95% confidence interval, PSS-10=Perceived Stress Scale, FFMQ=Five Facet Mindfulness Questionnaire, BSI=Brief Symptom Inventory, QOL=quality of life, PROMIS=Patient Reported Outcomes Measurement Information System.

Table 5.3. Separate multivariable linear regression models estimating the association among perceived stress (PSS-10 total), mindfulness (FFMQ total), and the interaction between perceived stress and mindfulness interaction with psychological concussion outcomes. All models control for concussion number (1-5+), sex (male/female), and concussion mechanism (sport/non-sport).

		Paramet	er Estimates		Model
-	0	Standardize	Standardize	- 17	
	β	dβ	d 95%CI	p Value	Adjusted R <sup>2</sup>
Neurocognitive Pe	rformance (C				
Verbal Memory	· · · ·				
Perceived Stress	-0.43	-0.20	-0.43, 0.03	0.09	-0.02
Mindfulness	0.10	0.14	-0.10, 0.37	0.25	-0.02
Interaction	-0.01	-0.10	-1.15, 0.95	0.85	-0.03
Visual Memory					
Perceived Stress	0.32	0.15	-0.08, 0.38	0.20	0.03
Mindfulness	-0.01	-0.02	-0.24, 0.21	0.89	0.01
Interaction	-0.02	-0.72	-1.73, 0.29	0.16	0.05
<b>Psychomotor Spee</b>	ed				
Perceived Stress	-0.37	-0.20	-0.42, 0.03	0.09	0.03
Mindfulness	0.11	0.17	-0.06, 0.40	0.14	0.21
Interaction	-0.01	-0.51	-1.54, 0.52	0.33	0.02
<b>Cognitive Flexibili</b>	ity				
Perceived Stress	-0.22	-0.09	-0.32, 0.15	0.47	-0.01
Mindfulness	0.10	0.11	-0.12, 0.34	0.34	-0.01
Interaction	-0.01	-0.33	-1.40, 0.74	0.54	-0.03
<b>Complex Attention</b>	n				
Perceived Stress	-0.21	-0.09	-0.32, 0.15	0.46	0.01
Mindfulness	0.08	0.09	-0.14, 0.33	0.44	0.01
Interaction	-0.02	-0.68	-1.73, 0.41	0.22	0.0004
Processing Speed					
Perceived Stress	-0.39	-0.20	-0.43, 0.04	0.10	-0.01
Mindfulness	0.09	0.12	-0.11, 0.36	0.30	-0.03
Interaction	-0.01	-0.49	-1.54, 0.56	0.35	-0.02
<b>Reaction Time</b>					
Perceived Stress	-0.17	-0.08	-0.31, 0.15	0.48	0.01
Mindfulness	0.11	0.15	-0.08, 0.38	0.19	0.03
Interaction	-0.00004	-0.002	-1.33, 1.47	0.99	0.01
<b>Executive Function</b>	n				
Perceived Stress	-0.19	-0.07	-0.31, 0.16	0.51	-0.02
Mindfulness	0.11	0.13	-0.10, 0.36	0.27	-0.01
Interaction	-0.01	-0.32	-1.38, 0.74	0.55	-0.03
<b>Psychological Dist</b>	ress (BSI-18)				
BSI-18 Total					
Perceived Stress	0.83	0.59	0.41, 0.77	< 0.001*	0.40
Mindfulness	-0.23	-0.46	-0.65, -0.26	< 0.001*	0.26
Interaction	-0.01	-0.39	-1.20, 0.41	0.34	0.39

Physical Function					
Perceived Stress	-0.18	-0.30	-0.51, -0.08	0.01*	0.12
Mindfulness	0.06	0.26	0.05, 0.48	0.02*	0.10
Interaction	0.0003	0.05	-0.93, 1.03	0.92	0.10
Anxiety					
Perceived Stress	0.98	0.71	0.55, 0.87	< 0.001*	0.52
Mindfulness	-0.30	-0.61	-0.79, 0.43	< 0.001*	0.40
Interaction	0.005	0.30	-0.40, 1.01	0.39	0.54
Depression					
Perceived Stress	0.90	0.64	0.46, 0.82	< 0.001*	0.42
Mindfulness	-0.25	-0.51	-0.71, 0.32	< 0.001*	0.28
Interaction	-0.01	-0.78	-1.55, -0.01	0.05	0.44
Fatigue			·		
Perceived Stress	0.66	0.51	0.31, 0.70	< 0.001*	0.27
Mindfulness	-0.16	-0.35	-0.56, -0.13	0.001*	0.13
Interaction	-0.002	-0.18	-1.07, 0.72	0.70	0.25
Sleep Disturbance					
Perceived Stress	-0.02	-0.04	-0.27, 0.20	0.76	-0.02
Mindfulness	-0.01	-0.04	-0.27, 0.19	0.72	-0.02
Interaction	0.001	0.28	-0.78, 1.33	0.60	-0.04
Social Participation	n				
Perceived Stress	-0.70	-0.60	-0.79, -0.42	< 0.001*	0.37
Mindfulness	0.21	0.53	0.33, 0.72	< 0.001*	0.29
Interaction	-0.002	-0.22	-1.04, 0.60	0.60	0.37
Pain Interference					
Perceived Stress	0.34	0.32	0.11, 0.54	0.01*	0.13
Mindfulness	-0.08	-0.22	-0.44, 0.01	0.05	0.08
Interaction	-0.003	-0.23	-1.21, 0.75	0.64	0.11
Pain Intensity					
Perceived Stress	0.09	0.32	0.11, 0.54	0.01*	0.13
Mindfulness	-0.02	-0.23	-0.45, -0.01	0.04*	0.08
Interaction	-0.0003	-0.10	-1.08, 0.88	0.84	0.10
*p value<0.05					

Appreviations: PSS=Perceived Stress Scale, FFMQ=Five Facet Mindfulness Questionnaire, BSI=Brief Symptom Inventory, PROMIS=Patient Reported Outcomes Measurement Information System.

#### **5.4 Discussion**

This study estimated associations among perceived stress, mindfulness, and psychological concussion outcomes (neurocognitive performance, psychological distress, and QOL) in young adults with a concussion history. Our findings suggest higher perceived stress was associated with higher psychological distress and lower QOL. Additionally, higher mindfulness was associated with lower psychological distress and higher QOL.

## 5.4.1 Neurocognitive Performance

The current study did not find any significant associations among perceived stress and neurocognitive performance - results inconsistent with current literature. The impact of stress on cognition has been extensively researched in healthy populations, with results suggesting that increased stress is associated with impairments in memory,<sup>262</sup> decision making,<sup>263</sup> concentration,<sup>263</sup> and judgment speed.<sup>264,265</sup> However, many of these prior studies do not utilize subjective measures of stress, but implement experimental stressful conditions and there is a wide range of cognitive assessments used in this literature (i.e., computer versus pencil and paper, verbal versus visual, questionnaire versus experimental conditions).<sup>262</sup> Results from the current study as well as previous stress and cognitive function literature may have been impacted by differences in assessments of stress (i.e., previous literature focusing on acute responses to stress whereas the current study is investigating one's perceived stress over a month long period) and cognitive function. Common psychosocial factors associated with increased stress - such as depression, anxiety, and exhaustion – have also been identified as factors that negatively influence cognitive performance.<sup>266–268</sup> Similarly, increased anxiety before concussion may lead to a greater decrease in cognitive performance acutely post-concussion.<sup>87,269</sup> Cognitive symptoms [forgetfulness, poor concentration, and slowed reaction time (with thoughts and actions)]<sup>131,189</sup> are commonly seen

acutely post-concussion; however, the presence of long-term cognitive impairment postconcussion is inconsistently identified in the literature.<sup>270</sup> Data from the current sample, who are on average two and a half years from their concussion, did not indicate significant associations among perceived stress and neurocognitive performance. These findings may be due to the current study sample, cross sectional study design, and/or the battery of tests utilized in the current study compared to previous studies.

Similarly, our results did not identify any significant associations among mindfulness and neurocognitive performance. Although most research in this space focuses on the impact of mindfulness interventions on cognitive performance, minimal cross-sectional data suggests mindfulness, measured via subjective questionnaire, is associated with increased memory,<sup>271</sup> attention,<sup>272</sup> reaction time,<sup>272</sup> and executive function.<sup>273</sup> Additionally, interventions in healthy populations have identified mindfulness-related improvements in overall cognition,<sup>274,275</sup> working memory, and executive function.<sup>275</sup> Research in TBI/concussion populations have found similar results. A recent meta-analysis identified cognitive function, sudjective suggest mindfulness intervention-related improvements in general cognition, attention, working memory, executive function, and problem solving.<sup>245</sup> However, this meta-analysis included studies with all severities of TBI which may have impacted the cognitive performance results. Furthermore, as previously discussed, long-term cognitive impairment post-concussion is inconsistently identified in the literature<sup>270</sup> – results suggestive of the current study outcome.

### 5.4.2 Psychological Distress

Results suggest a significant association among perceived stress and psychological distress measured via the BSI-18. Inherent connections between perceived stress and psychological distress exist due to the overlap in symptoms between the two scales to measure these constructs. However, the PSS-10 focuses on global perceived stress whereas the BSI-18 focuses on somatization, anxiety, and depression symptoms related to psychological distress. Overall, on average the current sample reported a high BSI-18 global severity score, results consistent with young adult<sup>276</sup> and concussion history research.<sup>277</sup> Specifically, in a recent large-scale, multi-site concussion study (n=29,934), results suggest collegiate student-athletes with a concussion history reported significantly higher BSI-18 scores than those with no concussion history.<sup>277</sup> Current study results build upon these findings, identifying a connection between perceived stress and psychological distress in individuals with a more recent concussion history (on average two and a half years) - providing additional evidence supporting the requirement of measuring psychological concussion impairments throughout the concussion recovery process. Due to the current study's cross-sectional design, causality cannot be determined; however, initial evidence of this association may help to inform future interventions for those with psychological distress post-concussion.

Mindfulness and psychological distress results from the current study coincide with research in healthy young adults,<sup>278</sup> providing evidence to suggest that higher mindfulness is associated with lower psychological distress in young adults with a concussion history. Although the BSI-18 is not commonly used as an outcome for mindfulness intervention studies, recent work in healthy adults found that subjects reported significantly lower BSI-18 scores after completing a three-month yoga and meditation retreat.<sup>279</sup> As previously discussed, collegiate student-athletes with a concussion history reported significantly higher BSI-18 scores than those with no concussion history.<sup>277</sup> Mechanistically, our results suggest improving mindfulness may lower

psychological distress – knowledge that may help to inform target interventions for those reporting higher psychological distress post-concussion.

# 5.4.3 Quality of Life

Additionally and consistent with current research,<sup>20</sup> QOL results identified higher perceived stress was associated with lower physical function, higher anxiety, higher depression, higher fatigue, lower social participation, higher pain interference, and higher pain intensity. However, comparing our sample's means to the established normal/mild/severe PROMIS® cut-off values,<sup>280</sup> on average our sample reported normal levels of physical function, depression, sleep disturbance, social participation, and pain interference and mild levels of anxiety and fatigue. Despite most QOL constructs falling within the normal range, significant regression model results suggest that perceived stress worsens these QOL outcomes even at normal levels - further emphasizing the need for more comprehensive psychological post-concussion assessments. Although inconsistent with recent literature, our results suggest no significant association among perceived stress and sleep disturbance. Subjects reported an average of seven hours of sleep per night, within the normal range of recommended sleep for young adults;<sup>281,282</sup> however, our sample reported mild levels of sleep disturbance – a measure indicative of perceptions of sleep difficulties and adequacy and satisfaction with sleep.<sup>261</sup> The PROMIS<sup>®</sup>'s sleep disturbance questions focus on overall disturbance, with one question asking the participant to rate their sleep quality. Approximately 60% of college students experience poor sleep quality,<sup>283</sup> which has been previously connected to perceived stress.<sup>281</sup> With the majority of our subjects identifying as a student (71.25%), a more in-depth measure of sleep quality may have provided evidence to better understand the connection between perceived stress and sleep.

Mindfulness followed similar trends to perceived stress in the current study. Research in healthy and TBI/concussion populations widely suggest a positive association among mindfulness and QOL<sup>245</sup> – consistent with the current study's results. However, most of this work focuses on mindfulness interventions and utilizes global measures of QOL<sup>245</sup> whereas the current study provides results from QOL sub domains – presenting more detailed evidence to inform mindfulness intervention programming. Similar to the perceived stress results, no significant association was identified among mindfulness and the QOL measure of sleep disturbance, a result inconsistent with recent literature.<sup>284,285</sup> Again, studies connecting mindfulness and sleep have focused on intervention-related changes and sleep quality not disturbance.<sup>284,285</sup> Future research is necessary to determine the long-term impacts of subjective measures of QOL post-concussion.

Our results suggest no significant moderation effects of mindfulness on the association among perceived stress and psychological concussion outcomes. However, the QOL depression scale interaction model presented results worth noting (p=0.05) – data consistent with work identifying the buffering effect of mindfulness on perceived stress and depression.<sup>286</sup> The specific understanding of how different levels of mindfulness (i.e., low, moderate, or high) may impact perceived stress remains unknown. This knowledge may benefit intervention-related research by providing evidence to understand if mindfulness impacting perceived stress requires a certain threshold/exposure of mindfulness – knowledge which may influence these moderation effects. Only 30.00% of subjects in the current study reported a current mindfulness practice and, as such, majority have minimal mindfulness exposure. This inherent study limitation may have led to lower FFMQ scores, potentially impacting the moderation effect between perceived stress and our psychological concussion outcomes.

#### 5.4.4 Strengths, Limitations, and Future Research

This study has several strengths and limitations. This study's sample was majority female, white, young adult students – limiting generalizability. Future studies with larger, more diverse samples are necessary to understand how findings can be more generalizable. Additionally, this study's cross-sectional design does not allow us to determine causality. Future research should expand the study design to a longitudinal cohort study, including multiple timepoints and stages of concussion recovery. Despite these limitations, this study included many strengths. To our knowledge, this was the first study to investigate the associations among perceived stress, mindfulness, and psychological concussion outcomes. Additionally, this study included multiple measures for post-concussion psychologic outcomes, allowing a wider understanding of the impact of perceived stress and mindfulness post-concussion. Future research should build upon the findings from this study to further understand mechanisms by which mindfulness interventions may impact concussion outcomes.

#### **5.5 Conclusions**

This novel study estimated the associations among perceived stress, mindfulness, and psychological concussion outcomes in young adults with a concussion history. Results suggest higher perceived stress was significantly associated with higher psychological distress and lower QOL. Additionally, results suggest higher mindfulness was significantly associated with lower psychological distress and higher QOL. Future research is necessary to build upon these findings to further understand mechanisms impacting post-concussion interventions aimed to improve outcomes and life post-concussion.

#### **CHAPTER 6: MANUSCRIPT AIM 3**

# 6.1 Background

Traumatic brain injury (TBI) is a leading cause of death and disability in the United States with injury-related symptoms and impairments that greatly impact one's physical and mental health and well-being.<sup>287</sup> Approximately 75% of TBIs are diagnosed as mild, or a concussion.<sup>288</sup> Specifically, one to two million sport- or recreation-related concussions are reported in the United States each year.<sup>51</sup> Concussion causes neurophysiological changes<sup>1</sup> resulting in clinical deficits (e.g., increased concussion symptoms) and psychological changes (e.g., increased irritability, anxiety, depression) presenting those injured with major physical and psychosocial burden.<sup>2</sup> Furthermore, 10-25% of individuals with a concussion history experience persistent concussion symptoms beyond typical recovery<sup>2,3</sup> resulting in continued clinical and psychological dysfunction<sup>7,8</sup> causing those impacted to potentially miss school,<sup>9</sup> work,<sup>10</sup> sport,<sup>11</sup> and have less societal engagement<sup>12</sup> leading to long-term decreased quality of life (OOL).<sup>13</sup> Additionally, a subset of student-athletes with a concussion history, regardless of persistent symptom expression, reported increased depression and anxiety as well as sleep and QOL disturbances.<sup>14,15</sup> Overall continued deficits experienced by those with a concussion history may present as negative mental and physical health outcomes post-concussion.

Mindfulness is the awareness of one's internal states and surroundings.<sup>46</sup> Research suggests higher mindfulness levels are associated with increased mental health,<sup>35</sup> physical health,<sup>36</sup> and subjective psychological well-being<sup>33</sup> – common impairments seen post-concussion, even in those with a concussion history. Additionally, higher mindfulness levels are associated with decreased

perceived stress.<sup>32–34</sup> Increased perceived stress; which is associated with increased depression,<sup>17</sup> anxiety,<sup>17</sup> and exhaustion<sup>17</sup> as well as decreased physical health,<sup>18</sup> life satisfaction,<sup>19</sup> and QOL;<sup>20</sup> may be heightened acutely post-concussion<sup>13</sup> and in those with a concussion history,<sup>26</sup> potentially predicting long-term post-concussion impairments.<sup>27</sup> Despite the connection between concussion and perceived stress, to our knowledge, limited studies have evaluated the impact of concussion rehabilitation interventions on perceived stress.

Mindfulness has been implemented into various therapeutic techniques such as mindfulness-based stress reduction (MBSR), mindfulness meditation, and yoga to improve mental and physical health disorders/symptoms including perceived stress.<sup>46</sup> In healthy populations, mindfulness-based interventions (specifically meditation and yoga) improve mindfulness and perceived stress.<sup>36–40</sup> Mindfulness-based techniques have been minimally used in TBI/concussion populations.<sup>244</sup> Specifically, majority of studies in the TBI and mindfulness space include participants with various severities of TBI (i.e., mild, moderate and/or severe) and utilize MSBR.<sup>139</sup> These studies suggest post-intervention improvements in QOL,<sup>42,43</sup> attention,<sup>44</sup> mental fatigue,<sup>44</sup> anxiety,<sup>44</sup> and depression.<sup>44</sup> Despite these findings, no concussion-specific mindfulness interventions have focused on the program's impact on concussion symptoms, a post-concussion impairment that may persist beyond typical recovery and impact return to life/school/sport, or mechanisms (i.e., perceived stress and mindfulness) that may explain the intervention's preliminary efficacy. Furthermore, mindfulness-based studies in concussion populations have focused on in-person, lengthy sessions presenting burden to participants. Recent mindfulness meditation-focused phone apps and online platforms have made programming more accessible to participants. However, to our knowledge, no online mindfulness interventions exist in concussionspecific populations. Additionally, previous research has utilized general mindfulness techniques

and practices, not ones designed specifically to improve post-concussion impairments. The LoveYourBrain Foundation's TBI-focused yoga and mindfulness meditations have been researched in individuals with all levels of TBI and found to improve resilience, QOL, emotional and behavioral dysregulation, cognition, positive affect, and well-being.<sup>135–137</sup> Work from these TBI yoga and meditation programs culminated in the creation of the LoveYourBrain Mindfulness Library - a free, online resource containing TBI-focused mindfulness exercises and meditations. This resource provides accessible mindfulness exercises/meditations focused on TBI-related symptoms and impairments – a focus that has not been utilized in the current concussion and mindfulness research.

Understanding the gaps in concussion and mindfulness research, this study determined the acceptability, feasibility, usability, and preliminary efficacy of an online, at-home, TBI-focused mindfulness intervention in young adults with a concussion history. We hypothesized participants would report high adherence (complete five days of the mindfulness exercises/meditations per week), and positive acceptability, feasibility, and intervention perceptions. Additionally, after completing the intervention, we hypothesized that participants would report decreased perceived stress, increased mindfulness, and decreased concussion symptoms compared to before the intervention.

# 6.2 Methods

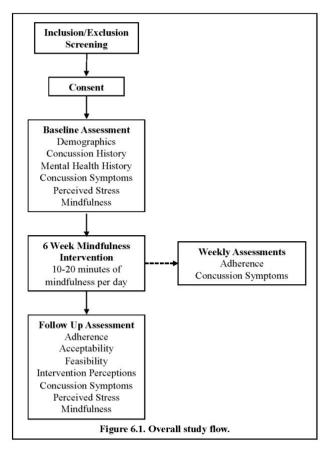
## 6.2.1 Study Design and Participants

This study was a pilot, single arm, mindfulness intervention study (NCT05399849) that included young adults (aged 18-30) with a concussion history (defined as experiencing a concussive injury within the past five years, but not within the past month). Participants were excluded for reporting a current mindfulness practice [defined as engaging in a mindfulness practice (meditation or yoga) at least once per week], any history of moderate and/or severe TBI, if they were currently under provider care for a concussion/TBI, and/or health risks (heart conditions, respiratory disorders, and/or neurological disorders) that put them at greater than minimal risk during the intervention. There was no exclusion based on self-report sex, race,

ethnicity, or mental health history. Institutional Review Board approval was obtained for the study and all participants completed informed consent.

## 6.2.2 Intervention Description

The overall study flow is outlined in Figure 6.1. After completing the informed consent process, participants completed a baseline assessment consistent of questionnaires for demographics, concussion history, mental health history, and the intervention outcomes of concussion symptoms mindfulness and perceived stress



symptoms, mindfulness, and perceived stress. Data were collected at a large state university between July and October 2022.

For the six-week intervention, participants were instructed to complete 10-20 minutes of mindfulness-focused exercises/meditations each day. Timing for the six week intervention was based on previous TBI mindfulness literature<sup>43,135,137</sup> and instructing 10-20 minutes of exercises/meditation per day was based on online/app-based mindfulness literature.<sup>37,289</sup> Mindfulness exercises were completed independently using the LoveYourBrain Foundation's

Meditation Library<sup>218</sup> - a free, online resource containing TBI-focused mindfulness-focused exercises/meditations. This library was created by the LoveYourBrain Foundation based on the researched backed yoga program and its participant feedback.<sup>135,136</sup> Mindfulness-based exercises/meditations to be completed were chosen by study personnel based on tools utilized in previous TBI mindfulness programs that are provided on the LoveYourBrain Meditation Library.<sup>42–44,218</sup> Specific mindfulness-based exercises/meditations included body scan, acceptance, awareness, and breathing techniques.<sup>44,218</sup> At intervention enrollment, participants were presented with a detailed manual providing them with beginner mindfulness tips and instructions as well as details on the purpose for the intervention. Throughout the six-week intervention, study personnel prompted participants via email at the beginning of each week with the specific exercises/meditations to be completed each day for that week. Participants were prompted via email at the end of each week to complete a questionnaire to assess adherence and track concussion symptoms (safety assessment).

Upon completion of the six-week trial, participants were prompted via email to complete a final assessment including questions regarding adherence, acceptability, feasibility, intervention perceptions, and the intervention outcomes of concussion symptoms, perceived stress, and mindfulness.

## 6.2.3 Measures

Participants self-reported demographic, concussion history, and mental health history information to describe the study sample. Demographic questions included age, sex, race, and ethnicity. Concussion history questions included number of concussions incurred and, for each concussion, how long ago the injury was and concussion mechanism (categorized binarily as sport-

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related vs. non-sport-related). Mental health history questions included mental health-related symptoms and diagnoses.

Throughout the intervention, participants were prompted to complete a weekly questionnaire to assess adherence. Subjects were asked which exercises/meditations they completed for that week and their enjoyment level for each completed exercise/meditation. The outcome for adherence was the number of mindfulness-based exercises/meditations completed per week.

Acceptability was assessed during the post-study assessment using the Acceptability of Intervention Measure (AIM). The AIM is a four-item validated measure assessing associations with an intervention.<sup>235</sup> It is assessed on a five-point scale from 1=completely disagree to 5=completely agree. A total score was computed by summing the responses for all four items (possible range=4-20, higher scores indicating more positive acceptance). The outcomes for acceptability were the mean, SD, and 95%CI of the total score and frequencies and percentages for each individual AIM item.

Feasibility was measured during the post-study assessment using the Feasibility of Intervention Measure (FIM), a four-item validated measure assessing intervention feasibility.<sup>235</sup> The FIM is assessed on a five-point scale from 1=completely disagree to 5=completely agree. A total score was computed by summing the responses for all four items (possible range=4-20, higher scores indicating more positive feasibility). The outcomes for feasibility were the mean, SD, and 95%CI of the total score and frequencies and percentages for each individual FIM item.

Intervention perceptions were measured during the post-study assessment. Participants were asked questions regarding facilitators and barriers to participation, potential changes to be made, usability of the LoveYourBrain Meditation Library, and overall if participants felt the

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exercises/meditations were helpful. Outcomes for intervention perceptions were frequencies and percentages of all scale items and summary of text using key words for all open-ended responses.

Concussion symptoms were measured at baseline and post-intervention using the Rivermead Post-Concussion Symptom Questionnaire (RPQ),<sup>189</sup> a validated measure<sup>192,193</sup> which asks participants to report the presence and severity (0-4) of 18 concussion-related symptoms compared with before their concussion. The RPQ has been frequently used in the study population.<sup>190,191</sup> Outcomes for the RPQ were total symptom severity (possible range=0-72) and total number of symptoms reported as worse than before the participant's concussion (indicated by rating a symptom as >1 on the severity scale, possible range=0-18). Higher scores indicate higher symptom severity and presence.

Perceived stress was measured at baseline and post-intervention using the Perceived Stress Scale, 10 question version (PSS-10), the most widely used psychological instrument for measuring perceived stress.<sup>180</sup> The PSS-10 is well validated and had been used in connection to mindfulness<sup>32–34,37,40</sup> and in brain injury populations.<sup>43</sup> The PSS-10 consists of 10 questions on a five-point scale (0=never to 4=very often) about how often a participant has felt or thought a certain way relative to their perceived stress in the past month. Final scores were obtained by reversing responses to the four positively stated items and then summing all 10 scale items (possible range=0-40, higher scores indicated higher perceived stress).<sup>181</sup>

Mindfulness was measured at baseline and post-intervention using the Five Facet Mindfulness Questionnaire (FFMQ), a widely used, valid survey to measure mindfulness.<sup>185</sup> Participants were asked 39 questions on a five-point scale (1=never/very rarely true to 5=very often/always true) related to general mindfulness tendencies in daily life. Questions focus on five facets of mindfulness including: 1) observing, noticing, and attending to sensations, perceptions,

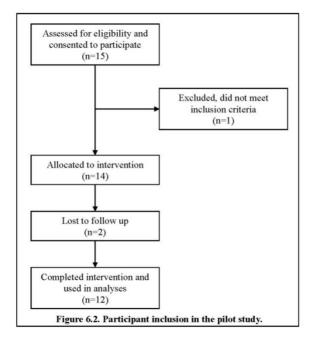
thoughts, and feelings; 2) describing/labeling one's experience with words; 3) acting with awareness; 4) non-judging; and 5) non-reactivity to inner experience. Each facet makes up a subscore of the FFMQ (observing, describing, awareness, and nonjudging sub-scores possible range=8-40; nonreactivity sub-score possible range=7-35; higher=more mindfulness). Final scores were obtained by reversing responses to the 19 reverse scored questions and then summing all 39 items (possible range=39-195, higher scores indicated greater mindfulness levels).<sup>186</sup>

#### 6.2.3 Statistical Analyses

Descriptive statistics were computed for all variables of interest. To describe the sample, means, SD, and 95% confidence intervals (95%CI) were computed for age, number of concussions incurred, and time since most recent concussion. Additionally, frequencies and percentages were computed for sex, race, ethnicity, number of concussions, most recent concussion mechanism, and mental health symptoms and diagnoses.

Descriptive statistics were used to determine intervention adherence, acceptability,

feasibility, and intervention perceptions. Specifically, means, SDs, and 95%CIs were computed for adherence (days per week completed), acceptability (AIM total score), feasibility (FIM total score), and intervention perception scale items. Frequencies and percentages were computed for the AIM and FIM items. Summary of text using key words was used to report open-ended intervention perception questions. To intervention's assess the



preliminary efficacy, paired sample t-tests were used to determine pre/post-intervention changes in concussion symptoms, perceived stress, and mindfulness, with p<0.05 identified as statistically significant.

# 6.3 Results

## 6.3.1 Study Sample and Demographics

A total of 15 participants were enrolled in the study with one upon further inclusion review not meeting study eligibility requirements. Two participants were lost to follow up (demographics and efficacy outcomes scores similar to study means). Overall, 12 participants completed the intervention and provided post-intervention adherence, acceptability, feasibility, and intervention perception data (Figure 6.2). Demographic data were reported on the 14 eligible participants who began the intervention (Table 6.1).

#### 6.3.2 Adherence

Each week, majority of participants completed five or more days per week of the mindfulness exercises/meditations (week 1=75.00%, week 2=66.67%, week 3=83.33%, week 4=83.33%, week 5=66.67%, week 6=66.67%). Mean, SD, and 95%CI for days/week of the mindfulness intervention completed are reported in Table 6.2. Post-hoc correlations did not suggest significant associations among adherence and pre/post-intervention changes in the preliminary efficacy outcomes (concussion symptoms, perceived stress, and mindfulness).

#### 6.3.3 Acceptability and Feasibility

The mean AIM total score was  $17.00\pm2.56$  (possible range=4-20, higher score=higher acceptability) and the mean FIM total score was  $17.42\pm1.83$  (possible rage=4-20, higher scores=higher feasibility). No participants disagreed or completely disagreed with any of the AIM

or FIM items and at least 80% agreed or strongly agreed with all items. AIM and FIM item frequencies are reported in Table 6.3.

# 6.3.4 Intervention Perceptions – Quantitative and Qualitative Data

The usability of the intervention was rated as a mean of  $8.50\pm1.17$  (possible range=0-10, higher score=more usable). When indicating which length of mindfulness exercise/meditation was best 58.33% reported 10 minutes, 33.33% 15 minutes, 0.00% 20 minutes, and 8.33% enjoyed all lengths. Quantitative intervention perceptions data are reported in Table 6.4.

Qualitative data were summarized using key words to further understand intervention perceptions and overall usability. When asked to describe the most challenging part about completing the intervention participants indicated challenges with finding time, remembering to do them, and difficulty focusing/staying still. Favorite parts about the LoveYourBrain mindfulness exercises/meditations focused on the LoveYourBrain mindfulness platform itself (body scan meditations, durations, and consistency with the pace/timing) as well as meditation-related feelings and results (setting aside time to thank myself and feeling more relaxed and feeling at peace, energized, and less stressed). When asked about their favorite parts of the study participants indicated the meditations were easy to follow, enjoyed having a weekly schedule provided, and enjoyed the destress/relaxing feeling and mind/body connection the meditations, different teachers/voices for various exercises/meditations, and not being able to complete two meditations in one day as some days were scheduled.

## 6.3.5 Preliminary Efficacy Outcomes

Pre/post-intervention descriptive statistics and the paired sample t-test results for the intervention's preliminary efficacy outcomes of concussion symptoms, perceived stress, and

mindfulness are reported in Table 6.5. There was a significant decrease in total concussion symptom severity after completing the mindfulness intervention  $(11.33\pm10.26)$  compared to before the intervention  $(24.50\pm17.18)$  [t(11)=3.03, p=0.01]. Additionally, there was a significant decrease in the total number of concussion symptoms reported as worse than before their concussion after completing the mindfulness intervention  $(2.67\pm3.91)$  compared to before the intervention  $(8.00\pm5.72)$  [t(11)=3.67, p=0.004]. Post-intervention, 83.33% (n=10) reported a lower concussion symptom severity and 75.00% (n=9) reported less concussion symptoms as worse than before injury compared to pre-intervention RPQ scores. No statistically significantly changes were observed for perceived stress or mindfulness; although, on average, perceived stress was lower and mindfulness higher following the mindfulness intervention.

	Mean±SD	95%CI
Age (Years)	20.46±3.62	18.27, 22.65
Number of Concussions	$2.93 \pm 1.44$	2.10, 3.76
Time Since Most Recent		
Concussion (Months)	17.21±18.28	6.66, 27.77
	Frequency	Percent
Sex		
Female	9	64.29
Male	5	35.71
Race		
White	9	64.29
Non-White	5	35.71
Ethnicity		
Non-Hispanic/Latino	13	92.86
Hispanic/Latino	1	7.14
Number of Concussions		
1	3	21.43
2	2	14.29
3	5	35.71
4	1	7.14
5+	3	21.43
Most Recent Concussion Mechanis	m	
Sport-Related	8	57.14
Non-Sport-Related	6	42.86
Mental Health-Related Diagnosis		
Yes	6	42.86
No	8	57.14
Experience Any Mental Health-Rel	lated Symptoms	
Yes	12	85.71
No	2	14.29
Mental Health Symptoms Worsen	After Concussion (n=12)	
Yes	6	50.00
No	6	50.00
Abbreviations: SD=standard devia	ation, 95%CI=95% confidence	ce interval.

-			25%	75%		
	Mean	SD	95%CI	Median	Quartile	Quartile
Days Per Week Completed						
Week 1	5.75	1.42	4.85, 6.65	6.00	4.50	7.00
Week 2	5.50	1.73	4.40, 6.60	6.00	4.00	7.00
Week 3	6.00	1.41	5.10, 6.90	7.00	5.00	7.00
Week 4	6.00	1.54	5.02, 6.98	7.00	5.50	7.00
Week 5	5.83	1.47	4.90, 6.77	7.00	4.00	7.00
Week 6	5.50	1.78	4.37, 6.63	6.50	3.50	7.00
Weekly Experience Rating						
Week 1	7.33	1.50	6.38, 8.28	8.00	6.00	8.50
Week 2	7.58	1.73	6.48, 8.68	7.50	6.50	9.00
Week 3	8.33	1.23	7.55, 9.12	8.50	7.50	9.00
Week 4	8.17	1.34	7.32, 9.02	8.00	7.00	9.50
Week 5	7.92	1.84	6.75, 9.08	8.50	6.00	9.50
Week 6	8.17	1.47	7.23, 9.10	8.00	7.00	9.50
Weekly Enjoyment Rating						
Week 1	7.08	1.88	5.89, 8.28	7.50	5.50	8.50
Week 2	7.33	1.83	6.17, 8.49	7.00	6.00	9.00
Week 3	7.67	1.87	6.48, 8.86	7.50	6.50	9.50
Week 4	7.50	1.51	6.54, 8.46	8.00	6.00	8.50
Week 5	8.00	1.54	7.02, 8.98	8.00	7.00	9.00
Week 6	8.17	1.40	7.27, 9.06	8.50	7.00	9.00
Weekly Effectiveness Rating						
Week 1	6.75	1.86	5.57, 7.93	7.00	5.50	8.00
Week 2	6.50	2.35	5.00, 8.00	7.50	4.00	8.00
Week 3	7.33	1.83	6.17, 8.49	8.00	5.50	9.00
Week 4	7.67	1.37	6.80, 8.54	7.50	6.50	9.00
Week 5	7.50	1.83	6.33, 8.67	7.50	6.00	9.00
Week 6	7.83	1.80	6.69, 8.98	8.00	6.00	9.50
Note: Days/week possible rar		weekly	experience, er	njoyment, an	d effectivenes	ss questions
possible range=0-10 (higher=	better).					

Feasibility of Interv	Completely Disagree (1)	Disagree (2)	Neither Agree nor Disagree (3)	Agree (4)	Completely Agree (5)
AIM					
The mindfulness					
intervention meets my approval.	0 (0.00)	0 (0.00)	1 (8.33)	8 (66.67)	3 (25.00)
The mindfulness					
intervention is	0 (0.00)	0 (0.00)	1 (8.33)	8 (66.67)	3 (25.00)
appealing to me.					
I like the					
mindfulness	0 (0.00)	0 (0.00)	1 (8.33)	3 (25.00)	8 (66.67)
intervention.					
I welcome the					
mindfulness	0 (0.00)	0 (0.00)	2 (16.67)	5 (41.67)	5 (41.67)
intervention.					
FIM					
The mindfulness	0 (0 00)	0 (0 00)	2(25,00)	4 (22.22)	5(41,67)
intervention seems	0 (0.00)	0 (0.00)	3 (25.00)	4 (33.33)	5 (41.67)
implementable.					
The mindfulness intervention seems	0 (0.00)	0 (0.00)	0 (0.00)	7 (58.33)	5 (41.67)
possible.	0 (0.00)	0 (0.00)	0 (0.00)	7 (30.33)	5 (41.07)
The mindfulness					
intervention seems	0 (0.00)	0 (0.00)	0 (0.00)	7 (58.33)	5 (41.67)
doable.	0 (0.00)	0 (0.00)	0 (0.00)	, (30.33)	5 (11.07)
The mindfulness					
intervention seems	0 (0.00)	0 (0.00)	0 (0.00)	7 (58.33)	5 (41.67)
easy to use.	- (	- (	- (	(2000)	- ( / )
Abbreviations: AIN	I=Acceptability	of Intervention	n Measure, FIM	=Feasibility o	of Intervention
Measure.	· · · · · · · · · · · · · · · · · · ·				

Table 6.3. Frequencies (percentages) of Acceptability of Intervention Measure (AIM) andFeasibility of Intervention Measure (FIM) items (n=12).

Table 6.4. Intervention percept	Table 6.4. Intervention perceptions after completing the mindfulness intervention (n=12).					
	Mean	SD	95%CI	Median	25% Quartile	75% Quartile
Felt that the mindfulness exercises/meditations were helpful <sup>a</sup>	1.75	0.62	1.36, 2.14	2.00	1.00	2.00
Felt that the mindfulness exercises/meditations were helpful for <i>mental health</i> <sup>a</sup>	1.58	0.51	1.26, 1.91	2.00	1.00	2.00
Felt that the mindfulness exercises/meditations were helpful for <i>mindfulness</i> <sup>a</sup>	1.50	0.80	0.99, 2.01	1.00	1.00	2.00
Felt that the mindfulness exercises/meditations were helpful for <i>stress</i> <sup>a</sup>	1.92	0.79	1.41, 2.42	2.00	1.00	2.50
Felt that the mindfulness exercises/meditations were helpful for <i>concussion</i> <i>symptoms</i> <sup>a</sup>	2.08	1.00	1.45, 2.72	2.00	1.00	3.00
Felt that the mindfulness exercises/meditations were helpful for <i>QOL</i> <sup>a</sup>	1.92	0.79	1.41, 2.42	2.00	1.00	2.50
Felt that the mindfulness exercises/meditations were helpful for <i>usable</i> <sup>b</sup>	8.50	1.17	7.76, 9.24	8.50	7.50	9.50
How likely are you to continue a mindfulness practice after completing this study? <sup>b</sup>	2.50	1.31	1.66, 3.34	2.00	1.50	3.50
Overall rating of the mindfulness exercises/meditations <sup>b</sup>	8.08	1.38	7.21, 8.96	8.00	7.00	9.50
<sup>a</sup> Range=1 (Strongly Agree) to 5 <sup>b</sup> Range=0-10 (higher=better). <b>Abbreviations:</b> SD=standard de		e ,	confidence i	nterval, QO	L=quality of	f life.

	Pre-Ir		re-Intervention Post-Intervention			T-Test	
	Cohen's d	Mean ±SD	95%CI	Mean ±SD	95%CI	T Value	P Value
Concussion Symptoms (	(RPQ)						
Total Symptom Severity	0.87	24.50 ±17.18	13.58, 35.42	11.33 ±10.26	4.81, 17.85	3.03	0.01*
Total Symptoms Worse than Before Injury	1.00	8.00 ±5.72	4.37, 11.63	2.67 ±3.91	0.18, 5.15	3.67	0.004*
Perceived Stress (PSS-1	0)						
Total	0.60	18.67 ±7.33	14.01, 23.32	14.92 ±6.23	10.96, 18.87	2.07	0.06
Mindfulness (FFMQ)							
Total	0.43	124.00 ±20.69	110.85, 137.15	132.92 ±16.89	122.19, 143.65	-1.48	0.17
Observing	0.42	22.79 ±3.47	20.78, 24.79	24.42 ±3.70	22.06, 26.77	-1.47	0.17
Describing	0.45	26.14 ±5.17	23.16, 29.13	28.33 ±4.77	25.30, 31.37	-1.57	0.14
Awareness	0.36	23.71 ±8.32	18.91, 28.52	27.50 ±5.00	24.32, 30.68	-1.26	0.23
Nonjudging	0.43	27.21 ±7.36	22.96, 31.46	29.67 ±8.05	24.55, 34.78	-1.49	0.16
Nonreactivity	0.09	21.79 ±4.41	19.24, 24.33	23.00 ±4.33	20.50, 25.75	-0.31	0.76

Table 6.5 Pre/nost-intervention descriptive statistics and t-test results for intervention

# \*p<0.05

Note: RPQ total symptom severity possible range=0-72 (higher=more total symptom severity), RPQ total symptoms worse than before injury possible range=0-18 (higher=more total symptoms worse than before injury), PSS-10 total possible range=0-40 (higher=more perceived stress), FFMQ total possible range=39-195 (higher=more mindfulness), FFMQ sub-scores of observing, describing, awareness, and nonjudging possible range=8-40 (higher=more mindfulness), FFM sub-score of nonreactivity possible range=7-35 (higher=more mindfulness). Abbreviations: SD=standard deviation, 95%CI=95% confidence interval, RPQ=Rivermead Post-Concussion Questionnaire, PSS-10=Perceived Stress Scale, FFMQ=Five Facet Mindfulness Questionnaire.

#### 6.4 Discussion

This study aimed to determine the acceptability, feasibility, usability, and preliminary efficacy of an online, at-home, TBI-focused mindfulness intervention in young adults with a concussion history. Our findings suggest positive adherence, acceptance, feasibility, intervention perceptions, and usability of the intervention. Most importantly, results suggest a significant decrease in concussion symptoms after completing the mindfulness intervention.

#### 6.4.1 Adherence

A priori hypotheses identified high adherence as completion of five days per week of the mindfulness exercises/meditations. Our results indicated each week the majority of participants completed five or more days per week of the mindfulness exercises/meditations (week 1: n=9, 75.50%; week 2: n=8, 66.67%; week 3: n=9, 75.50%; week 4: n=10, 83.33%; week 5: n=8, 66.67%; and week 6: n=8, 66.67%). Additionally, the mean number of days completed each week was also above five (range=5.50-6.00, i.e., high adherence for this study). We note a peak in adherence at weeks 3 and 4 – however, due to the small sample size of this pilot study that is only an additional one and two participants completing five or more days per week of the intervention respectively. Methods for this intervention instructed participants to complete meditation daily, with high adherence set at completing five days per week – methods which have been successfully implemented in other mindfulness interventions with healthy populations. In a study evaluating the use of app-based mediation in a healthy adult population, participants were instructed to complete 10-minutes of meditation daily for four weeks and adherence was set at completing 70% of the assigned intervention.<sup>289</sup> Adherence results indicated an average of 20 minutes of meditation per day and 103 minutes of meditation per week – with an adherence rate of 71%.<sup>289</sup> Another appbased meditation study in a healthy population instructed participants to complete at least three

minutes of meditation five days per week for the first four weeks and then, for weeks five to 12, participants continued to have app access and could meditate at their discretion.<sup>290</sup> The average days per week of meditating for weeks one to four was five, results similar to the current study, whereas the average days per week of meditating for weeks five to 12 was four.<sup>290</sup> Overall, the future expansion of this pilot study and other TBI mindfulness interventions could benefit from defining high adherence as 70-80% compliance to ensure feasibility without sacrificing efficacy.

Mindfulness intervention research specific to TBI/concussion populations has primarily focused on in-person and/or group class study designs - making it difficult to compare attendance/adherence to the current study's self-completed daily online intervention. Additionally, inconsistencies in intervention length also make studies difficult to compare. Specifically, a recent meta-analysis reported current TBI mindfulness intervention studies have a mean length of approximately 11 weeks with a range from a single session to 32 weeks.<sup>139</sup> Furthermore, none of the studies in this meta-analysis reported participant attendance/adherence (actual days of the intervention completed) as a primary outcome. Overall, only a few TBI/concussion mindfulness studies have reported some form of attendance at all. Specifically, when looking at LoveYourBrain's six-week in-person yoga, meditation, and psychoeducation programming, Donnelly et al.<sup>135</sup> reported that 82.00% of participants attended one or more weeks of the intervention. Additionally, LoveYourBrain's online version of the same intervention reported that 71.02% attended one or more of the live online classes.<sup>137</sup> With the inconsistencies in intervention durations and novelty of using online mindfulness interventions post-concussion future studies should emphasize reporting adherence to provide more data informing necessary intervention length to inform programming focused on improving injury outcomes.

# 6.4.2 Acceptability, Feasibility, and Intervention Perceptions

This study's acceptability data suggest the mindfulness intervention was well received by the study sample with the majority reporting they either agree or completely agree with the AIM measures for intervention approval, appeal, likeness, and welcomeness. Additionally, data suggest the mindfulness intervention is feasible with the majority reporting that they either agree or completely agree with the FIM measures asking if the intervention seems implementable, possible, doable, and easy to use. Qualitative data collected via the intervention perceptions questionnaire provide more insight into specific aspects of the intervention that drove the participant's high acceptability and feasibility responses. Specifically, when responding about study logistics, favorite parts included having a provided weekly schedule and consistency with the duration/pace of the exercises and meditations - results consistent with current mindfulness literature. Specifically, in a study investigating the impact of LoveYourBrain's six-week in-person yoga, mindfulness, and psychoeducation in individuals with TBI, qualitative data reported by participants and administrators identified the weekly routine/schedule as a primary factor for adherence and accountability.<sup>135,291</sup> Overall, providing a concise weekly schedule allows for maintaining a consistent pattern and supports literature identifying the importance of consistency when eliciting a behavior change (i.e., starting a mindfulness practice).<sup>292</sup>

Qualitative data describing participants most challenging parts of the study included difficulty finding time, remembering to complete the exercises/meditations, and focusing/staying still. At intervention enrollment all participants were presented with a detailed manual outlining the intervention's structure and purpose and identifying beginner mindfulness tips (i.e., designating a comfortable space with minimal distractions to practice in, picking a time of day to meditate that works well with your schedule, and education on mindfulness's purpose of

recognizing one's thoughts as a means to come back to the present moment).<sup>218</sup> Future studies expanding this pilot to a larger scale should include a more detailed pre-intervention meeting where study personnel can walk through the instruction manual - instructing participants to schedule a daily time to complete their exercises/meditations and providing more details on mindfulness's purpose. Additional data describing participants least favorite parts of the study included having different teachers/voices throughout the intervention and, on days when two exercises/meditations were assigned, not being able to complete both in one day. The LoveYourBrain Meditation Library has a limited number of 10-20-minute mindfulness exercises/meditations with the focus needed for this study and, in order to provide enough exercises/meditations for the six-week intervention, some days included two shorter meditations equaling 10-20 minutes. To improve adherence only one meditation should be assigned per day. Additionally, to provide more consistency with the intervention, minimal change in teachers should be used and/or specific teachers should be used for the same skills (i.e., have one person do all of the breathwork exercises, another body scan, etc.) -a suggestion which has been provided in broader yoga literature.<sup>293</sup>

# 6.4.3 Preliminary Efficacy Outcomes

Study findings highlight a significant post-intervention decrease in concussion symptom severity and number of concussion symptoms reported as worse than before injury. Furthermore, post-intervention, the vast majority of subjects reported lower concussion symptom severity (n=10, 83.33%) and less concussion symptoms as worse than before their injury (n=9, 75.00%). We do note that two participants reported a higher concussion symptom severity after completing the intervention; however, no participants reported higher concussion symptoms worse than before injury. These findings are important as they suggest that completing daily mindfulness may help

to mitigate concussion symptoms, results that can benefit those acutely post-concussion or individuals who experience long-term, persistent concussion symptoms. Most post-concussion mindfulness interventions have also included other severities of TBI (i.e., moderate and severe) within the study sample.<sup>139,245</sup> As such, concussion symptoms were not regularly included as an outcome. In TBI mindfulness studies that did include measures for concussion symptoms, some studies reported no significant pre/post-intervention change in concussion symptoms<sup>246,247</sup> and others suggested similar findings to the current study with significant improvements in concussion symptoms.<sup>139</sup> In a pilot MBSR study in individuals with persistent concussion symptoms, no significant pre/post changes in concussion symptoms were found. However, this study utilized MBSR and not TBI-focused mindfulness exercises/meditations as in the current study, a focus which may have further impacted concussion symptoms as a rehabilitation progression as other rehabilitation modalities typically do to indicate recovery/return to sport.<sup>131</sup>

The current study data also suggest perceived stress decreased, although not statistically significantly. This four-point decrease from pre- to post-intervention, however, may be clinically meaningful as PSS-10 scores were moderate levels of perceived stress pre-intervention and then trending toward low levels post-intervention.<sup>183</sup> Our small pilot study sample size may have impacted these outcomes and a larger sample may help to understand clinical meaningfulness and significance. Perceived stress has been minimally researched in concussion populations and not included as an outcome in TBI-based mindfulness intervention work despite research suggesting that perceived stress is heightened in individuals acutely post-concussion.<sup>13</sup> Perceived stress has been utilized as an outcome in healthy population mindfulness studies with results showing post-intervention decreases in perceived stress. Specifically, using a meditation app for twelve weeks

saw a significant decrease in perceived stress measured via the PSS-10.<sup>290</sup> In a study evaluating the use of app-based mediation in a healthy, college aged population, participants who completed daily meditation for eight weeks saw a significant decrease in perceived stress (measured via the PSS-10) compared to the control, education group.<sup>37</sup> Furthermore, these significant differences remained four weeks after study completion.<sup>37</sup> Similarly, in a study using an online meditation platform where healthy individuals were instructed to complete mindfulness breathing meditation 15 minutes per day for four weeks, the meditation group.<sup>294</sup>

Pre/post-intervention t-test results suggest no significant changes in mindfulness - total and sub-scale FFMQ measures. In previous longitudinal studies, the FFMQ has been used to track intervention-related mindfulness changes similar to the current study, but with mixed results. Again, referencing Huberty et al.,<sup>37</sup> healthy college aged participants who completed daily appbased meditation for eight weeks saw a significant increase in mindfulness (measured via the FFMQ 39 question version same as the current study) compared to the control, education group. These significant increases were also identified with the five FFMQ sub-scales/mindfulness constructs.<sup>37</sup> A shorter, validated 15-item version of the FFMQ (containing the same five subscale/mindfulness constructs) was created to minimize participant burden and has been widely used throughout the mindfulness intervention literature, suggesting similar outcomes.<sup>186,187</sup> Specifically, using a meditation app for twelve weeks showed significant improvements in FFMQ-15 total and sub-scores.<sup>290</sup> An additional study using the FFMQ-15 found that after completing a 4.5-month online mindfulness intervention, healthcare workers' results suggest mindfulness did not moderate intervention-related improvements in stress.<sup>245</sup> To note, the FFMQ measures trait mindfulness, a more permanent predisposition of daily life mindfulness, as opposed to state

mindfulness, a more temporary post-meditation mindful feeling.<sup>295</sup> With the current study incorporating shorter bouts of mindfulness (10-20 minutes per day), a timeframe longer than six weeks, such as the eight- or 12-week interventions seen in the healthy population app-based studies, may be needed to elicit trait mindfulness changes.

Theory behind the current study hypothesized that improving mindfulness would improve perceived stress resulting in decreased concussion symptoms. Despite this, results suggest postintervention concussion symptoms and perceived stress improvements absent from significant mindfulness changes. Understanding the concussion history sample, subjects may have engaged in the intervention with a focus on improving concussion symptoms. Additionally, mindfulness exercises/meditations chosen, specifically body scan and breathing techniques, may have elicited more focus on stress reduction versus mindfulness and the TBI-focus of the platform may have put more emphasis on concussion symptom improvement. Finally, the FFMQ asks questions regarding general, daily mindfulness. Questions may not have pertained to our concussion history sample of primarily college aged students and a concussion-specific mindfulness questionnaire may benefit future studies.

#### 6.4.4 Strengths, Limitations, and Future Research

This study has several strengths and limitations. The pilot nature of the study presented a small sample size with no comparison control group. Future research should expand the study design to a randomized control trial with a larger sample and comparison control group (i.e., education control group). Additionally, all measures used in this study were self-report, presenting the potential for response bias. Future studies should also include objective measure of adherence (i.e., tracking minutes of mindfulness completed) and physiologic measures for stress and mindfulness to deepen the validity of the study results. Finally, all measures for this study were

taken while the participants were actively completing the mindfulness intervention or immediately following. Future research should include a longitudinal timepoint to better understand the long-term impacts of this intervention. Despite these limitations, this study included many strengths. To our knowledge, this was the first online mindfulness intervention in a concussion history population that used TBI-focused mindfulness exercises/meditations. Additionally, this was the first concussion-focused mindfulness intervention study to include pre/post measures for concussion symptoms, a common measure of recovery/return to play, and potential intervention mechanisms (perceived stress and mindfulness). Future research should build upon the findings from this pilot study to tailor effective post-concussion mindfulness interventions and further understand mechanisms by which mindfulness interventions may impact concussion outcomes.

# 6.5 Conclusion

This study was a novel TBI-focused online mindfulness intervention in young adults with a concussion history. Findings from this study suggest positive adherence, acceptance, feasibility, intervention perceptions, and usability of the intervention. Additionally, results suggest a significant decrease in concussion symptoms after completing the mindfulness intervention. Future research is necessary to build upon these pilot findings to design concussion-focused mindfulness interventions focused on improving injury outcomes.

#### **CHAPTER 7: DISSERTATION SYNTHESIS**

This study's overall objective was to determine the association among perceived stress, mindfulness, and clinical and psychological concussion outcomes. Additionally, we aimed to determine the acceptability, feasibility, usability, and preliminary efficacy of an online mindfulness intervention in young adults with a concussion history. Results from this study will inform future comprehensive post-concussion interventions aimed to mitigate perceived stress and utilize mindfulness techniques to improve post-concussion clinical and psychologic deficits.

#### 7.1 Aims 1 and 2 Summary

- Aim 1. Estimate the associations among perceived stress, mindfulness, and clinical concussion outcomes (concussion symptoms, balance performance, ANS function, vestibular/ocular system function, and exertion tolerance) in young adults with a concussion history.
- Hypothesis: (1a) Participants with higher perceived stress will have worse clinical concussion outcomes indicated by higher concussion symptom burden, lower balance performance, higher ANS dysfunction, higher vestibular/ocular symptom provocation, and lower exertion tolerance when controlling for number of concussions, sex, and most recent concussion mechanism. (1b) Participants with higher mindfulness will have better clinical concussion outcomes indicated by lower concussion symptom burden, higher balance performance, lower ANS dysfunction, lower vestibular/ocular symptom provocation, and higher exertion

tolerance when controlling for number of concussions, sex, and most recent concussion mechanism. (1c) The association among perceived stress and clinical concussion deficits identified in (1a) will be moderated by mindfulness levels. Specifically, mindfulness will buffer the relationship between perceived stress and clinical concussion outcomes.

- Aim 2. Estimate the associations among perceived stress, mindfulness, and psychological concussion outcomes (neurocognitive performance, psychological distress, and QOL) in young adults with a concussion history.
- Hypothesis: (1a) Participants with higher perceived stress will have worse psychological concussion outcomes indicated by lower neurocognitive performance, higher psychological distress, and lower QOL when controlling for number of concussions, sex, and most recent concussion mechanism. (1b) Participants with higher mindfulness will have better psychological concussion outcomes indicated by higher neurocognitive performance, lower psychological distress, and higher QOL when controlling for number of concussions, sex, and most recent concussions, sex, and most recent concussion outcomes indicated by higher neurocognitive performance, lower psychological distress, and higher QOL when controlling for number of concussions, sex, and most recent concussion mechanism. (1c) The association among perceived stress and psychological concussion deficits identified in (1a) will be moderated by mindfulness levels. Specifically, mindfulness will buffer the relationship between perceived stress and clinical concussion outcomes.

To address Aims 1 and 2, a cross-sectional study was completed in which 80 young adults with a concussion history completed measures for demographics, concussion history, mental health history, current mindfulness practice, clinical concussion outcomes (concussion symptoms, balance performance, ANS function, vestibular/ocular system function, and exertion tolerance),

and psychological concussion outcomes (neurocognitive performance, psychological distress, and QOL). Data were analyzed via separate multivariable linear regression models for each clinical and psychological concussion outcome: 1) separate multivariable linear regression models were used to determine the association among perceived stress and each clinical and psychological concussion outcome; 2) separate multivariable linear regression models were used to determine the association among mindfulness and each clinical and psychological concussion outcome; and 3) an interaction term of perceived stress and mindfulness was included to test the potential moderation effect of mindfulness on the clinical and psychological concussion outcomes. All models controlled for number of concussions (1-5+), sex (male/female), and most recent concussion mechanism (sport/non-sport related).

Consistent with our hypotheses, results suggest higher perceived stress was significantly associated with higher concussion symptom severity, higher number of concussion symptoms reported as worse than before injury, higher psychological distress, and lower QOL (lower physical function, higher anxiety, higher depression, higher fatigue, lower social participation, higher pain interference, and higher pain intensity). No other significant associations among perceived stress and our clinical and psychological concussion outcomes were identified – results inconsistent with our hypotheses. Also consistent with our hypotheses, mindfulness models identified that higher mindfulness was significant associated with lower concussion symptom severity, lower number of concussion symptoms reported as worse than before injury, lower psychological distress, and higher QOL (higher physical function, lower anxiety, lower depression, lower fatigue, higher social participation, and lower pain intensity). However, contrary to our hypotheses, no other significant associations among mindfulness and our clinical and psychological concussion outcomes were identified as worse than before injury to our hypotheses, no other significant associations among mindfulness and our clinical and psychological concussion outcomes were identified. Inconsistent with our study hypotheses, there were not overall

statistically and clinically meaningful interaction effects observed between perceived stress and mindfulness for clinical or psychological-based concussion outcomes.

#### 7.2 Aim 3 Summary

- Aim 3.Determine the acceptability, feasibility, usability, and preliminary efficacy of an<br/>online mindfulness intervention in young adults with a concussion history.
- Hypothesis: Participants who participate in the mindfulness intervention will report high adherence (complete five days of the mindfulness/meditation exercises per week), positive acceptability, positive feasibility, and positive intervention perceptions. Additionally, after completing the intervention, participants will report decreased concussion symptoms, decreased perceived stress, and increased mindfulness compared to before the intervention.

To address Aim 3, a pilot, single arm mindfulness intervention study was completed in 15 young adults with a concussion history. Participants completed a baseline assessment consistent of questionnaires for demographics, concussion history, mental health history, and the intervention outcomes of concussion symptoms, mindfulness, and perceived stress. For the six-week intervention, participants were instructed to complete 10-20 minutes of mindfulness-focused exercises/meditations each day. Mindfulness exercises were completed independently using the LoveYourBrain Foundation's Meditation Library – a free, online resource containing TBI-focused mindfulness-focused exercises/meditations. Throughout the six-week intervention, participants completed weekly questionnaires to assess adherence and track concussion symptoms (safety assessment). Upon completion of the six-week trial, participants completed a final assessment including questions regarding adherence, acceptability, feasibility, intervention perceptions, and the intervention outcomes of concussion symptoms, perceived stress, and mindfulness. Descriptive

statistics were used to determine intervention adherence, acceptability, feasibility, and intervention perceptions. Paired sample t-tests were used to determine pre/post-intervention changes in concussion symptoms, perceived stress, and mindfulness.

A total of 15 participants were enrolled in the study with one upon further inclusion review not meeting study eligibility requirements. Two participants were lost to follow up; therefore, 12 participants completed the intervention. Adherence, acceptability, feasibility, and interventions perceptions results were consistent with the a priori study hypotheses. Specifically, adherence was identified as high with each week majority of participants completing five or more days per week of the mindfulness exercises/meditations. Acceptability and feasibility were also identified as high with 80% of participants reporting they agreed or strongly agreed with acceptability and feasibility questions. The usability of the intervention was rated as a mean of 8.50±1.17 (possible range=0-10, higher score=more usable). Consistent with our hypotheses, paired sample t-tests identified a significant decrease in total concussion symptom severity and total number of concussion symptoms reported as worse than before injury after completing the mindfulness intervention compared to before the intervention. Overall, post-intervention 83.33% (n=10) reported a lower concussion symptom severity and 75.00% (n=9) reported less concussion symptoms as worse than before injury compared to pre-intervention RPQ scores. No statistically significantly changes were observed for perceived stress or mindfulness – results contrary to the study hypotheses.

# 7.3 Scientific Lessons Learned and Dissertation Strengths

This study provided a novel understanding of the association among perceived stress, mindfulness, and comprehensive clinical and psychological concussion outcomes. Overall study results suggest perceived stress and mindfulness are most closely associated with concussion symptoms and QOL. Scientific lessons learned identify limitations and potential areas to improve upon in future research. Specifically, results may have been impacted by the perceived stress and/or mindfulness questionnaires used in this study. Although these are robust, validated, commonly used questionnaires, the questions themselves may not have properly targeted our study sample of young adults with a concussion history. Additionally, results from the Aim 3 intervention may have been influenced by the intervention duration and/or focus.

Despite these limitations, this dissertation also includes many strengths. To our knowledge, the Aims 1 and 2 study was the first to investigate the associations among perceived stress, mindfulness, and clinical and psychological concussion outcomes. Additionally, this study utilized a wide range of concussion assessments (questionnaires and physiologic), providing data on many aspects of concussion recovery. To our knowledge, the Aim 3 pilot intervention study was the first online mindfulness intervention in a concussion history population that used TBI-focused mindfulness exercises/meditations. Additionally, it was the first concussion-focused mindfulness intervention study to include pre/post measures for concussion symptoms, a common measure of recovery/return to play, and potential intervention mechanisms (perceived stress and mindfulness). High adherence and significant improvements in concussion symptoms provide evidence that this novel intervention provides evidence supporting: 1) an accessible, feasible online intervention option that does not sacrifice outcome improvement; and 2) TBI-focused exercises/meditations may help to improve concussion symptoms.

#### 7.4 Future Directions and Next Steps

Current study results provide a strong foundation for future research furthering the understanding of the impact of perceived stress and mindfulness post-concussion and how stress mitigation/mindfulness techniques may be used to improve injury outcomes. Future research should expand upon the Aims 1 and 2 cross-sectional study design to design a comprehensive,

longitudinal cohort study to better understand the impact of perceived stress and mindfulness at all stages of concussion recovery – findings which may help to mechanistically inform future concussion interventions. Additionally, although this dissertation's conceptual model focused on how perceived stress and mindfulness impact concussion outcomes, we recognize that additional psychological, social, and individualized factors may play a role in this model. Future research should investigate the impact of resilience and coping skills on these relationships. Finally, as previously discussed, results may have been influenced by the perceived stress and/or mindfulness questionnaires used. Future research investigating concussion and young adult specific measures of perceived stress and mindfulness could help to identify the impact of these variables post-concussion.

The Aim 3 pilot intervention provides robust data to build upon for future research. Specifically, future research should expand the study design to a randomized control trial with a larger sample and comparison control group. Additionally, intervention focus and length may have impacted the preliminary efficacy outcomes. Future studies should investigate the effectiveness of the TBI-focused mindfulness exercises/meditations versus more general mindfulness programming as well as the impact of different intervention lengths. Additional work investigating the impact of mindfulness in conjunction with other individualized, more physical activity-based rehabilitation protocols (aerobic exercise, yoga, etc.) could be interesting to research at various stages of concussion recovery. Finally, all measures used in the Aim 3 study were self-report, presenting the potential for response bias. Future studies should also include more objective measures for adherence and physiologic measures for stress and mindfulness to deepen the validity of the study results.

# 7.5 Dissertation Conclusions

Results from this dissertation suggest higher perceived stress was significantly associated with higher concussion symptoms, higher psychological distress, and lower QOL. Additionally, higher mindfulness was significantly associated with lower concussion symptoms, lower psychological distress, and lower QOL. Additionally, the pilot intervention results suggest positive adherence, acceptability, feasibility, and overall intervention perceptions as well as significantly decreased concussion symptoms post-intervention. Results provide a novel understanding of the association among perceived stress, mindfulness, and clinical and psychological concussion outcomes and the impact of an online mindfulness intervention in young adults with a concussion history. This study will inform future interventions aimed to improve concussion outcomes by mitigating stress and/or targeting mindfulness post-concussion.

Main Effects Independent Variable	Dependent Variable	Main Effects Outcomes	
	Concussion Symptoms	<ul> <li>Increased total concussion symptoms</li> <li>Increased total concussion symptom severity</li> </ul>	
	Balance Performance	<ul> <li>Increased BESS total errors</li> <li>Increased COM SD of acceleration</li> </ul>	
Increased Perceived Stress Decreased Mindfulness	ANS Function	<ul><li>Increased LF/HF</li><li>Increased average HR</li></ul>	
	Vestibular/Ocular Function	• Increased change in total symptom score (pre- vs. post-test) for each VOMS assessment	
	Exertion Tolerance	<ul> <li>Decreased number of steps</li> <li>Increased post-test RPE rating</li> </ul>	
Interaction Effects: Mindfuln Increased mindfulness will dec Dutcomes.	rease the effect of perceived s	tress on clinical concussion	
Abbreviations: BESS=Balanc ANS=autonomic nervous syste VOMS=Vestibular/Ocular Mot	m, LF/HF=low frequency/hig	h frequency, HR=heart rate	

# APPENDIX 1: AIMS 1 AND 2 EXPECTED MAIN AND INTERACTION EFFECTS

Main Effects Independent Variable	Dependent Variable	Main Effects Outcomes
	Neurocognitive Performance	• Decreased verbal memory, visual memory, psychomotor speed, cognitive flexibility, complex attention, processing speed, reaction time, executive functioning
Increased Perceived Stress Decreased Mindfulness	Psychological Distress	• Increased total score
	Quality of Life	<ul> <li>Decreased physical function, ability to participate in social roles</li> <li>Increased anxiety, depression, fatigue, sleep disturbances, pain interference, pain intensity</li> </ul>

#### **APPENDIX 2: INCLUSION/EXCLUSION SCREENER**

Thank you for your interest in our research study! We will ask you a few questions to see if you qualify for the study.

- 1. What is your first name?
- 2. What is your last name?
- 3. What is your email address? Example: <u>email@unc.edu</u>
- 4. May we contact you for future research studies?
  - 1 = Yes
  - 2 = No
- 5. Are you between 18 and 30 years old?
  - 1 = Yes
  - 0 = No
  - $\rightarrow$  Excluded if no, continue if yes.

<u>Definition of a concussion</u>: A change in brain function following a force to the head, which may be accompanied by temporary loss of consciousness and is identified in awake individuals with measures of neurologic and cognitive dysfunction. Common concussion symptoms include headache, feeling slowed down, difficulty concentrating or focusing, dizziness, balance problems/loss of balance, fatigue/loss of energy, feeling in a fog, irritability, drowsiness, nausea, memory loss, sensitivity to light/noise, and blurred vision.

<u>IMPORTANT</u>: A concussion can occur without being "knocked out" or unconscious; getting your "bell rung" or "clearing the cobwebs" is a concussion.

6. Given the definition above, have you ever had a concussion (related to sport or other activities)?

1 = Yes

0 = No

 $\rightarrow$  Excluded if no, continue if yes.

7. Approximately how long ago was your most recent concussion? Please answer in months

(12 months = 1 year).

 $\rightarrow$  *Excluded if* > 60 *months or* < 1 *month, continue if* 1 *to* 60 *months.* 

- 8. Do you have a history of any heart conditions?
  - 1 = Yes
  - 2 = No
  - $\rightarrow$  Excluded if yes, continue if no.
- 9. Do you have a history of any respiratory conditions?
  - 1 = Yes

2 = No

 $\rightarrow$  *Excluded if yes, continue if no.* 

- 10. Do you have a history of any neurological disorders?
  - 1 = Yes
  - 2 = No
  - $\rightarrow$  Excluded if yes, eligible if no.
- 11. Have you ever had a moderate or severe traumatic brain injury? <u>This does NOT include</u> <u>concussions.</u>

1 = Yes

0 = No

 $\rightarrow$  Excluded if yes, continue if no.

<u>Ineligible Response:</u> Unfortunately, you do not qualify for participation in this research study. Thank you for your interest!

<u>Eligible Response:</u> Congratulations! You have qualified for participation in this research study. The study team will reach out to schedule your study visit. Please click the next arrow to complete your survey. If you have any questions reach out to the study team at <u>chriscal@live.unc.edu</u>.

# **APPENDIX 3: DEMOGRAPHICS QUESTIONNAIRE**

# **General Demographics Questions**

1. Date and time of data collection (mm/dd/yyyy, hh:ss).

Given calendar to choose date and time.

2. What is your date of birth (mm/dd/yyyy)?

Given calendar to choose date.

3. Age

Hidden calculation from question 2.

- 4. What is your biological sex assigned at birth?
  - 1 = Male
  - 2 = Female
  - 3 = Other
  - 4 = Prefer not to answer
- 5. Do you consider yourself Hispanic/Latino or not Hispanic/Latino?

1 = Hispanic/Latino: A person of Cuban, Mexican, Puerto Rican, Southern or Central American, or other Spanish culture or origin, regardless of race. The term, "Spanish Origin," can be used in addition to, "Hispanic/Latino."

- 2 = not Hispanic/Latino
- 3 = Don't know/not sure
- 6. Which of the following five racial designations best describes you?

1 = American Indian or Alaska Native: A person having origins in any of the original peoples of North and Southern American (including Central America) and who maintains tribal affiliation or community attachment.

2 = Asian: A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent, including, for example, Cambodia, China,

India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam.

3 = Black or African American: A person having origins in any of the black racial groups of Africa. Terms such as, "Haitian," or, "Negro," can be used in addition to, "Black or African American."

4 = Native Hawaiian or Other Pacific Islander: A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.

5 = White: A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.

- 7. What is your highest education level?
  - 1 = Some high school
  - 2 = High school diploma
  - *3* = *Some college*
  - 4 = Trade/technical/vocational training
  - 5 = Associate degree
  - 6 = Bachelor's degree
  - 7 = Master's degree
  - 8 = *Professional or doctorate degree*
- 8. What is your marital status?
  - *1* = *Single, never married*
  - 2 = Married/domestic partnership
  - 3 = Widowed

4 = Divorced

- 5 = Separated
- 9. What is your employment status?
  - 1 = Employed for wages
  - 2 = Self-employed
  - *3* = *Out of work and currently looking*
  - 4 = Out of work but not currently looking
  - 5 = Homemaker
  - 6 = Student
  - 7 = Military
  - 8 = Retired
  - 9 = Unable to work
- 10. What level in school are you?

Question will display if the answer to question 9 is student.

- 1 = High school
- 2 = First year college
- 3 = Second year college
- *4* = *Third* year college
- 5 = Fourth/more year college
- 6 = Master's student
- 7 = Professional or doctorate degree student
- 11. What is your approximate height? Please answer in inches (in). Example: 5'6'' = 66.

Text entry.

12. What is your approximate weight? Please answer in pounds (lbs).

Text entry.

## **COVID-19 Information**

13. At any point during the COVID-19 pandemic have you tested positive for the virus?

1 = Yes

- 0 = No
- 14. How many times have you tested positive for COVID-19?

Question will display if the answer to question 13 is yes.

- 1 = 12 = 23 = 34 = 4
- 5 = 5 or more
- 15. When did you test positive for COVID-19 (mm/dd/yyyy)? If you have tested positive more than once, please indicate the date for the most recent time you tested positive.

*Question will display if the answer to question 13 is yes.* 

Given calendar to choose date.

16. How long did your COVID-19 symptoms last? Please indicate in days (1 week = 7 days).*Question will display if the answer to question 13 is yes* 

Text entry.

# **Sleep Information**

17. On an average night, approximately how many hours of sleep do you get?

1 = Less than 4

$$5 = 5$$
  
 $6 = 6$   
 $7 = 7$   
 $8 = 8$   
 $9 = 9$   
 $10 = 10 \text{ or more}$ 

18. How many hours of sleep did you get last night?

1 = Less than 4 5 = 5 6 = 6 7 = 7 8 = 8 9 = 9 10 = 10 or more

# **Caffeine Information**

19. On an average day, how much caffeine do you consume (1 cup = 8 ounces)?

0 = None 1 = 1 cup 2 = 2 cups 3 = 3 cups 4 = 4 cups 5 = 5 or more cups

20. How much caffeine have you consumed so far today (1 cup = 8 ounces)?

- 0 = None 1 = 1 cup 2 = 2 cups 3 = 3 cups 4 = 4 cups 5 = 5 or more cups
- 21. Please describe your caffeine intake today (i.e., how much and what types of caffeine have you consumed). Example: I have had one medium latte and one cup of green tea. *Text entry*.
- 22. How long ago did you consume caffeine? Please answer in hours (1 hour = 60 minutes).*Text entry.*

### **Alcohol Information**

- 23. On an average week, how much alcohol do you consume?
  - 0 = None 1 = 1 drink 2 = 2 drinks 3 = 3 drinks 4 = 4 drinks 5 = 5 or more drinks
- 24. In the past 24 hours, how much alcohol have you consumed?
  - 0 = None1 = 1 drink
  - 2 = 2 drinks

3 = 3 drinks
4 = 4 drinks
5 = 5 or more drinks
25. How much alcohol have you consumed today?
0 = None

- 1 = 1 drink 2 = 2 drinks 3 = 3 drinks 4 = 4 drinks 5 = 5 or more drinks
- 26. How long ago did you consume alcohol? Please answer in hours (1 hour = 60 minutes).

Text entry.

# **Current Sport Participation Information**

27. Do you currently participate in organized sport (i.e., professional, club, intramural, varsity

athletics)?

1 = Yes

- 0 = No
- 28. What level(s) of sport do you participate in? Choose all that apply.

Question will display if the answer to question 27 is yes.

1 = Professional/semiprofessional

- 2 = NCAA collegiate
- 3 = University club
- 4 = Recreational/intramural

- 5 = Club sport outside of university
- 6 = Other
- 29. Please specify the level of sport you participate in.

Question will display if other is chosen for question 28.

Text entry.

30. What sport(s) do you participate in? Choose all that apply.

Question will display if the answer to question 27 is yes.

- 1 = Baseball
- 2 = Basketball
- 3 = Bowling
- 4 = Cross country/track
- 5 = Diving
- 6 = Fencing
- 7 = *Field event*
- 8 = Field hockey
- 9 = Football
- 10 = Golf
- 11 = Gymnastics
- 12 = Ice hockey
- 13 = Lacrosse
- 14 = Rifle
- 15 = Rowing/crew
- 16 = Skiing

$$17 = Soccer$$

$$18 = Softball$$

$$19 = Swimming$$

$$20 = Tennis$$

$$21 = Volleyball$$

$$22 = Water polo$$

$$23 = Wrestling$$

$$24 = Other$$

31. Please specify the other sport you participate in.

Question will display if other is chosen for question 30. Text entry.

# **Previous Sport Participation Information (Past Five Years)**

32. In the past five years (not currently) did you participate in organized sport (i.e., professional, club, intramural, varsity athletics)?

1 = Yes

- 0 = No
- 33. How long ago did you participate in organized sport? Please answer in months (12 months
  - = 1 year).

Text entry.

34. What level(s) of sport did you participate in? Choose all that apply.

Question will display if the answer to question 32 is yes.

- 1 = Professional/semiprofessional
- 2 = NCAA collegiate

3 = University club

- 4 = Recreational/intramural
- 5 = Club sport outside of university
- 6 = Other
- 35. Please specify the level of sport you participated in.

Question will display if other is chosen for question 33. Text entry.

36. What sport(s) did you participate in? Choose all that apply.

Question will display if the answer to question 32 is yes.

- 1 = Baseball 2 = Basketball
- 3 = Bowling
- 4 = Cross country/track
- 5 = Diving
- 6 = Fencing
- 7 = *Field event*
- 8 = Field hockey
- 9 = Football
- 10 = Golf
- *11* = *Gymnastics*
- 12 = Ice hockey
- 13 = Lacrosse
- 14 = Rifle

- 15 = Rowing/crew
  16 = Skiing
  17 = Soccer
  18 = Softball
  19 = Swimming
  20 = Tennis
  21 = Volleyball
  22 = Water polo
  23 = Wrestling
  24 = Other
- 37. Please specify the other sport you participated in.

Question will display if other is chosen for question 35.

Text entry.

# **Physical Activity Information**

38. How many days per week do you do vigorous physical activity such as hiking, running,

heavy lifting, or bicycling fast?

- 0 = None
- 1 = 1 day per week
- 2 = 2 days per week
- 3 = 3 days per week
- 4 = 4 days per week
- 5 = 5 days per week
- 6 = 6 days per week

7 = 7 days per week

39. On one of those days, how much time do you spend doing vigorous physical activities?Please answer in minutes (60 minutes = 1 hour).

Text entry.

40. How many days per week do you do moderate physical activity such as brisk walking, carrying light loads, bicycling at a regular pace?

0 = None

- 1 = 1 day per week
- 2 = 2 days per week
- 3 = 3 days per week
- 4 = 4 days per week
- 5 = 5 days per week
- 6 = 6 days per week
- 7 = 7 days per week
- 41. On one of those days, how much time do you spend doing moderate physical activities?

Please answer in minutes (60 minutes = 1 hour).

Text entry.

#### **Menstrual Cycle Information**

42. Have you ever menstruated?

1 = Yes

0 = No

43. When did your last menstrual period begin?

Question will display if the answer to question 41 is yes.

Given calendar to choose date.

44. What phase of your menstrual cycle are you currently in?

Question will display if the answer to question 41 is yes.

*l* = *Menstrual phase (I currently have my period)* 

- 2 = Follicular phase (my period was 1-6 days ago)
- 3 = Ovulation phase (my period was 7-11 days ago)
- 4 = Luteal phase (my period was 12-23 days ago)

0 = I don't know

#### **APPENDIX 4: CONCUSSION HISTORY QUESTIONNAIRE**

The next set of questions are about your concussion history.

<u>Definition of a concussion</u>: A change in brain function following a force to the head, which may be accompanied by temporary loss of consciousness and is identified in awake individuals with measures of neurologic and cognitive dysfunction. Common concussion symptoms include headache, feeling slowed down, difficulty concentrating or focusing, dizziness, balance problems/loss of balance, fatigue/loss of energy, feeling in a fog, irritability, drowsiness, nausea, memory loss, sensitivity to light/noise, and blurred vision.<sup>2</sup>

<u>IMPORTANT</u>: A concussion can occur without being "knocked out" or unconscious; getting your "bell rung" or "clearing the cobwebs" is a concussion.

- 1. Given the definition above, have you ever had a concussion (related to sport or other activities)?
  - 1 = Yes
  - 0 = No

Participants will be excluded from participation if they answer no to question 1. The following questions will display if question 1 is answered yes.

- 2. How many concussions have you had?
  - 1 = 1 2 = 2 3 = 3 4 = 4 5 = 5 or more

- 3. How many of these concussions did you report/disclose to a medical professional (physician, athletic trainer, etc.) or someone in authority (coach, teacher, etc.) at the time of injury?
  - 0 = None 1 = 1 2 = 2 3 = 3 4 = 4 5 = 5 or more

## **First Concussion Information**

Approximately how long ago was your first concussion? Please answer in months (12 months = 1 year).

Question will display if the answer to question 2 is 1-5.

Text entry.

5. Approximately how long did it take for your symptoms to subside after your first concussion? Please answer in months (12 months = 1 year).

Question will display if the answer to question 2 is 1-5.

Text entry.

6. How did your first concussion occur?

Question will display if the answer to question 2 is 1-5.

- *l* = *Sport related (during a sporting event)*
- 2 = Motor vehicle accident
- *3* = *Military related*

*4* = *Fall* (*in a non-sporting event*)

5 = Direct hit to the head (in a non-sporting event)

6 = Other

7. Please specify how your first concussion occurred.

Question will display if other is chosen for question 6.

Text entry.

## **Second Concussion Information**

Approximately how long ago was your second concussion? Please answer in months (12 months = 1 year).

*Question will display if the answer to question 2 is 2-5. Text entry.* 

9. Approximately how long did it take for your symptoms to subside after your second concussion? Please answer in months (12 months = 1 year).

*Question will display if the answer to question 2 is 2-5.* 

*Text entry.* 

10. How did your second concussion occur?

*Question will display if the answer to question 2 is 2-5.* 

- *l* = *Sport related (during a sporting event)*
- 2 = Motor vehicle accident
- *3* = *Military related*
- *4* = *Fall* (*in a non-sporting event*)
- 5 = Direct hit to the head (in a non-sporting event)

6 = Other

11. Please specify how your second concussion occurred.

Question will display if other is chosen for question 10.

Text entry.

### **Third Concussion Information**

12. Approximately how long ago was your third concussion? Please answer in months (12 months = 1 year).

Question will display if the answer to question 2 is 3-5.

*Text entry.* 

13. Approximately how long did it take for your symptoms to subside after your third concussion? Please answer in months (12 months = 1 year).

*Question will display if the answer to question 2 is 3-5.* 

*Text entry.* 

14. How did your third concussion occur?

*Question will display if the answer to question 2 is 3-5.* 

- *l* = *Sport related (during a sporting event)*
- 2 = Motor vehicle accident
- *3* = *Military related*
- *4* = *Fall* (*in a non-sporting event*)
- 5 = Direct hit to the head (in a non-sporting event)
- 6 = Other
- 15. Please specify how your third concussion occurred.

Question will display if other is chosen for question 14.

*Text entry.* 

#### **Fourth Concussion Information**

16. Approximately how long ago was your fourth concussion? Please answer in months (12 months = 1 year).

Question will display if the answer to question 2 is 4 or 5.

Text entry.

17. Approximately how long did it take for your symptoms to subside after your fourth concussion? Please answer in months (12 months = 1 year).

*Question will display if the answer to question 2 is 4 or 5.* 

Text entry.

18. How did your fourth concussion occur?

*Question will display if the answer to question 2 is 4 or 5.* 

*l* = *Sport related* (*during a sporting event*)

- 2 = *Motor vehicle accident*
- *3* = *Military related*
- *4* = *Fall* (*in a non-sporting event*)
- 5 = Direct hit to the head (in a non-sporting event)
- 6 = Other
- 19. Please specify how your fourth concussion occurred.

*Question will display if other is chosen for question 18.* 

*Text entry.* 

## **Fifth Concussion Information**

20. Approximately how long ago was your fifth concussion? Please answer in months (12 months = 1 year).

Question will display if the answer to question 2 is 5.

*Text entry.* 

21. Approximately how long did it take for your symptoms to subside after your fifth concussion? Please answer in months (12 months = 1 year).

Question will display if the answer to question 2 is 5.

*Text entry.* 

22. How did your fifth concussion occur?

Question will display if the answer to question 2 is 5.

*l* = *Sport related (during a sporting event)* 

- 2 = Motor vehicle accident
- *3* = *Military related*
- 4 = Fall (in a non-sporting event)
- *5* = *Direct hit to the head (in a non-sporting event)*
- 6 = Other
- 23. Please specify how your fifth concussion occurred.

Question will display if other is chosen for question 22.

Text entry.

### **APPENDIX 5: MENTAL HEALTH HISTORY QUESTIONNAIRE**

The next set of questions are about your mental health history.

 Have you experienced symptoms related to one/more of these mental health disorders? Choose all that apply.

0 = None

1 = Anxiety

- 2 = Attention-deficit hyperactivity disorder (ADHD)/Attention-deficit disorder (ADD)
- *3* = *Autism spectrum disorder*
- 4 = Bipolar disorder
- 5 = Communication disorder (i.e., language disorder, speed sound disorder, childhood onset fluency disorder, and/or social communication disorder)
- 6 = Depression
- 7 = Eating disorder
- 8 = Obsessive-compulsive disorder
- 9 = Panic disorder
- *10* = *Personality disorder*
- 11 = Post-traumatic stress disorder (PTSD)
- 12 = Schizophrenia
- 13 = Other
- 2. Please specify the other mental health symptoms you have experienced.

Question will display if other is chosen for question 1.

Text entry.

- 3. Have you ever been diagnosed with one/more of these mental health disorders? Choose all that apply.
  - 0 = None
  - 1 = Anxiety
  - 2 = Attention-deficit hyperactivity disorder (ADHD)/Attention-deficit disorder (ADD)
  - *3* = *Autism spectrum disorder*
  - 4 = Bipolar disorder
  - 5 = Communication disorder (i.e., language disorder, speed sound disorder, childhood onset fluency disorder, and/or social communication disorder)
  - 6 = Depression
  - 7 = Eating disorder
  - 8 = Obsessive-compulsive disorder
  - 9 = Panic disorder
  - *10* = *Personality disorder*
  - 11 = Post-traumatic stress disorder (PTSD)
  - 12 = Schizophrenia
  - 13 = Other
- 4. Please specify the other mental health disorders you have been diagnosed with.

Question will display if other is chosen for question 3.

Text entry.

### **Mental Health Symptom Information**

5. Do you still experience symptoms of the indicated disorders?

Question will display if the answer to questions 1 and/or 3 is not none.

1 = Yes

- 0 = No
- 6. How long did/have you been experiencing symptoms of the indicates disorders? Please answer in months (12 months = 1 year).

Question will display if the answer to questions 1 and/or 3 is yes.

Text entry.

7. Did your mental health symptoms worsen after your concussion?

*Question will display if the answer to questions 1 and/or 3 is not none.* 

1 = Yes

0 = No

8. Which mental health symptoms worsened after your concussion? Choose all that apply. *Question will display if the answer to question 7 is yes.* 

1 = Anxiety

2 = Attention-deficit hyperactivity disorder (ADHD)/Attention-deficit disorder (ADD)

- *3* = *Autism spectrum disorder*
- 4 = Bipolar disorder

5 = Communication disorder (i.e., language disorder, speed sound disorder, childhood onset fluency disorder, and/or social communication disorder)

6 = Depression

- 7 = *Eating disorder*
- 8 = Obsessive-compulsive disorder
- 9 = Panic disorder
- *10* = *Personality disorder*

11 = Post-traumatic stress disorder (PTSD)

*12* = *Schizophrenia* 

13 = Other

9. Please specify the other mental health symptoms that worsened after your concussion. *Question will display if other is chosen for question 8.* 

Text entry.

## **Mental Health Treatment Information**

10. Did/do you receive treatment (therapeutic, pharmaceutical, etc.) from a mental health professional for the indicated disorder?

Question will display if the answer to questions 1 and/or 3 is not none.

1 = Yes

0 = No

11. Who provides/provided your mental health treatment(s)? Choose all that apply.

Question will display if the answer to question 9 is yes.

- 1 = Therapist
- 2 = Counselor
- 3 = Psychiatrist (medical doctor)
- 4 = Sports psychologist (therapist/counselor with specific sports training)
- 5 = Other
- 12. Please specify your other provider(s) for your mental health treatment(s).*Question will display if the answer to question 10 is other.Text entry.*
- 13. What type(s) of treatment(s) did/do you receive? Choose all that apply.

Question will display if the answer to question 9 is yes.

- *l* = *Cognitive behavioral therapy (CBT)*
- 2 = Dialectical behavioral therapy (DBT)
- *3* = *Mindfulness-based cognitive therapy*
- *4* = *Motivational interviewing*
- 5 = Positive psychology
- 6 = *Psychodynamic therapy*
- 7 = Medication(s)
- 8 = Unknown
- 9 = Other
- 14. Please specify your other mental health treatment(s).

*Question will display if the answer to question 12 is other.* 

Text entry.

15. Are you still receiving these mental health treatments?

Question will display if the answer to question 9 is yes.

- 1 = Yes
- 0 = No
- 16. How long did/have you been receiving treatment(s)? Please answer in months (12 months

= 1 year).

*Question will display if the answer to question 9 is yes.* 

17. How helpful did/do you find your mental health treatment(s)?

Question will display if the answer to question 9 is yes.

1 = Not useful at all

- 2 = Slightly useful
- 3 = Moderately useful
- 4 = Very useful
- 5 = Extremely useful

## **APPENDIX 6: CURRENT MINDFULNESS PRACTICE QUESTIONNAIRE**

1. Do you have a current mindfulness (i.e., yoga or meditation) practice?

$$1 = Yes$$

0 = No

### **Meditation Practice Information**

2. Do you practice meditation as a part of your mindfulness practice?

Question will display if the answer to question 1 is yes.

1 = Yes

0 = No

3. What type of meditation practices do you engage in? Choose all that apply.

Question will display if the answer to question 2 is yes.

- 1 = Visualization
- 2 = Breathing
- 3 = Body scan
- 4 = Transcendental
- 5 = Focused attention
- 6 = Loving kindness
- 7 = *Resting awareness*
- 8 = Reflection
- 9 = Noting
- *10* = *Skillful compassion*
- 11 = Walking/moving mindfulness

12 = Sleep

- 13 = Mantra 14 = Zen 15 = Vipassana 16 = Chakra 17 = Qigong 18 = Sound bath 19 = Other
- 4. Please describe the other type(s) of meditation practices you engage in.

Question will display if the answer to question 3 is other.

Text entry.

5. Do you engage in guided or unguided meditation?

Question will display if the answer to question 2 is yes.

- 1 = Guided
- 2 = Unguided
- 3 = I use both in my practice
- 6. How many days/week do you meditate?

Question will display if the answer to question 2 is yes.

- 0 = Less than one day per week
- 1 = 1 day per week
- 2 = 2 days per week
- 3 = 3 days per week
- 4 = 4 days per week
- 5 = 5 days per week

6 = 6 days per week

7 = 7 days per week

On average, how long is each meditation session? Please answer in minutes (60 minutes = 1 hour).

Question will display if the answer to question 2 is yes.

Text entry.

8. How do you access your meditation practice? Choose all that apply.

Question will display if the answer to question 2 is yes.

- *l* = *Phone application/online (i.e., Headspace, Calm)*
- $2 = In \ a \ class$
- 3 = Self-practice
- 4 = Other
- 9. Please specify the other way(s) you access your meditation practice.

*Question will display if the answer to question 8 is other.* 

Text entry.

### **Yoga Practice Information**

10. Do you practice yoga as a part of your mindfulness practice?

Question will display if the answer to question 1 is yes.

1 = Yes

0 = No

11. What type(s) of yoga do you engage in? Choose all that apply.

Question will display if the answer to question 10 is yes.

1 = Vinyasa

- 2 = Hatha
  3 = Iyengar
  4 = Kundalini
  5 = Ashtanga
  6 = Bikram
  7 = Yin
  8 = Restorative
  9 = Pre/post-natal
  10 = Anusara
  11 = Jivamuki
  12 = Other
- 12. Please describe the other type(s) of yoga you engage in.

Question will display if other is chosen for question 11.

*Text entry.* 

13. How many days per week do you practice yoga?

Question will display if the answer to question 10 is yes.

- 0 = Less than one day per week
- 1 = 1 day per week
- 2 = 2 days per week
- 3 = 3 days per week
- 4 = 4 days per week
- 5 = 5 days per week
- 6 = 6 days per week

7 = 7 days per week

14. On average, how long is each yoga session? Please answer in minutes (60 minutes = 1 hour).

Question will display if the answer to question 10 is yes.

15. How do you access your yoga practice? Choose all that apply.

Question will display if the answer to question 10 is yes.

- *1* = *Phone application/online*
- 2 = In-person class
- *3* = *Self-practice*
- 4 = Other
- 16. Please specify the other way(s) you access yoga.

Question will display if the answer to question 15 is other.

*Text entry.* 

#### **APPENDIX 7: PERCEIVED STRESS SCALE (PSS)**<sup>180</sup>

The Perceived Stress Scale (PSS) is a classic stress assessment instrument. The tool, while originally developed in 1983, remains a popular choice for helping us understand how different situations affect our feelings and our perceived stress. The questions in this scale ask about your feelings and thoughts during the last month. In each case, you will be asked to indicate how often you felt or thought a certain way. Although some of the questions are similar, there are differences between them, and you should treat each one as a separate question. The best approach is to answer fairly quickly. That is, don't try to count up the number of times you felt a particular way; rather indicate the alternative that seems like a reasonable estimate.

<u>Response Scale:</u> 0 = Never, 1 = Almost never, 2 = Sometimes, 3 = Fairly often, 4 = Very often

- 1. In the last month, how often have you been upset because of something that happened unexpectedly?
- 2. In the last month, how often have you felt that you were unable to control the important things in your life?
- 3. In the last month, how often have you felt nervous and stressed?
- 4. In the last month, how often have you felt confident about your ability to handle your personal problems?
- 5. In the last month, how often have you felt that things were going your way?
- 6. In the last month, how often have you found that you could not cope with all the things that you had to?
- 7. In the last month, how often have you been able to control irritations in your life?
- 8. In the last month, how often have you felt that you were on top of things?

- 9. In the last month, how often have you been angered because of things that happened that were outside of your control?
- 10. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?

#### Scoring

- 1. Reverse scores for questions 4, 5, 7, and 8. On these four questions, change to scores to the following: 0 = 4, 1 = 3, 2 = 2, 3 = 1, 4 = 0.
- 2. Add up scores for each item to get a total.
- 3. Individual scores on the PSS can range from 0 to 40 with higher scores indicating higher perceived stress.
  - a. Scores ranging from 0 to 13 would be considered low stress.
  - b. Scores ranging from 14 to 26 would be considered moderate stress.
  - c. Scores ranging from 27 to 40 would be considered high perceived stress.

The PSS is interesting and important because your perception of what is happening in your life is most important. Consider the idea that two individuals could have the exact same events and experiences in their lives for the past month. Depending on their perception, total score could put one of those individuals in the low stress category and the total score could put the second person in the high stress category. *Disclaimer: The scores on the following self-assessment do not reflect any particular diagnosis or course of treatment. They are meant as a tool to help assess your level of stress. If you have any further concerns about your current well-being, you may contact EAP and talk confidentially to one of our specialists.* 

#### APPENDIX 8: FIVE FACET MINDFULNESS QUESTIONNAIRE (FFMQ)<sup>187</sup>

<u>Response Scale:</u> 1 = Never or very rarely true, 2 = Rarely true, 3 = Sometimes true, 4 = Often true,

5 = Very often or always true

- 1. When I'm walking, I deliberately notice the sensations of by body moving.
- 2. I'm good at finding words to describe my feelings.
- 3. I criticize myself for having irrational or inappropriate emotions.
- 4. I perceive my feelings and emotions without having to react to them.
- 5. When I do things, my mind wanders off and I'm easily distracted.
- 6. When I take a shower or bath, I stay alert to the sensations of water on my body.
- 7. I can easily put my beliefs, opinions, and expectations into words.
- I don't pay attention to what I'm doing because I'm daydreaming, worrying, or otherwise distracted.
- 9. I watch my feelings without getting lost in them.
- 10. I tell myself I shouldn't be feeling the way I'm feeling.
- 11. I notice how foods and drinks affect my thoughts, bodily sensations, and emotions.
- 12. It's hard for me to find the words to describe what I'm thinking.
- 13. I am easily distracted.
- 14. I believe some of my thoughts are abnormal or bad and I shouldn't think that way.
- 15. I pay attention to sensations, such as the wind in my hair or the sun on my face.
- 16. I have trouble thinking of the right words to express how I feel about things.
- 17. I make judgments about whether my thoughts are good and bad.
- 18. I find it difficult to stay focused on what's happening in the present.

- 19. When I have distressing thoughts or images I "step back" and am aware of the thought or image without getting taken over by it.
- 20. I pay attention to sounds, such as clocks ticking, birds chirping, or cars passing.
- 21. In difficult situations, I can pause without immediately reacting.
- 22. When I have a sensation in my body, it's difficult for me to describe it because I can't find the right words.
- 23. It seems I am "running on automatic" without much awareness of what I'm doing.
- 24. When I have distressing thoughts or images, I feel calm soon after.
- 25. I tell myself I shouldn't be thinking the way I'm thinking.
- 26. I notice the smells and aromas of things.
- 27. Even when I'm feeling terribly upset, I can find a way to put into words.
- 28. I rush through activities without being really attentive to them.
- 29. When I have distressing thoughts or images, I am able to just to notice them without reacting.
- 30. I think some of my emotions are bad or inappropriate and I shouldn't feel them.
- 31. I notice visual elements in art or nature, such as colors, shapes, textures, or patterns of light and shadow.
- 32. My natural tendency is to put my experiences into words.
- 33. When I have distressing thoughts or images, I just notice them and let them go.
- 34. I do jobs or tasks automatically without being aware of what I'm doing.
- 35. When I have distressing thoughts or images, I judge myself as good or bad depending on what the thought or image is about.
- 36. I pay attention to how my emotions affect my thoughts and behavior.

- 37. I can usually describe how I feel at the moment in considerable detail.
- 38. I find myself doing things without paying attention.
- 39. I disapprove of myself when I have irrational ideas.

### Scoring

<u>Note:</u> R = reverse scored item

- <u>Observing:</u> 1 + 6 + 11 + 15 + 20 + 26 + 31 + 36
- <u>Describing:</u> 2 + 7 + 12R + 16R + 22R + 27 + 32 + 37
- Acting with Awareness: 5R + 8R + 13R + 18R + 23R + 28R + 34R + 38R
- <u>Nonjudging:</u> 3R + 10R + 14R + 17R + 25R + 30R + 35R + 39R
- <u>Nonreactivity:</u> 4 + 9 + 19 + 21 + 24 + 29 + 33
- <u>Total FFMQ:</u> add subscale scores

<u>Note:</u> Some researchers divide the total in each category by the number of items in that category to get an average category score. The total FFMQ can be divided by 39 to get an average item score.

## APPENDIX 9: RIVERMEAD POST-CONCUSSION SYMPTOMS QUESTIONNAIRE (RPQ)<sup>189</sup>

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 indicate the number closest to your answer.

<u>Response Scale:</u> 0 = Not experienced at all, 1 = No more of a problem now than before the accident,

2 = A mild problem now, 3 = A moderate problem now, 4 = A severe problem now

Prompt: Compared with before your brain injury, do you now (i.e., over the last 24 hours) suffer

from:

- 1. Headaches.
- 2. Feelings of dizziness.
- 3. Nausea and/or vomiting.
- 4. Noise sensitivity or easily upset by loud noise.
- 5. Sleep disturbance.
- 6. Fatigue, tiring more easily.
- 7. Being irritable, easily angered.
- 8. Feeling depressed or tearful.
- 9. Feeling frustrated or impatient.
- 10. Forgetfulness, poor memory.
- 11. Poor concentration.
- 12. Taking longer to think.
- 13. Blurred vision.
- 14. Light sensitivity or easily upset or irritated by bright light.

- 15. Double vision.
- 16. Restlessness.
- 17. Reduced tolerance to stress or emotional excitement.
- 18. Fear of permanent symptoms/brain damage.

# Scoring

- <u>RPQ Total Score (Symptom Severity):</u> sum of all answers
- <u>Number of Symptoms Worse than Before Injury:</u> study personnel indicate how many symptoms were scored as a 2, 3, or 4

#### APPENDIX 10: BALANCE ERROR SCORING SYSTEM (BESS)<sup>296</sup>

#### Instructions

Note: Study personnel instructions are in *italics* and examiner scripts are in **bold**.

For the BESS test you will perform three different stances on both the ground and a foam pad. I will describe and show you the stances as the assessment goes along. Please take off your shoes and roll up your pant legs above your ankle (if applicable). Throughout each stance I will record errors, or the number of times you move out of place. Errors include taking your hands off your hips, opening your eyes, taking a step, lifting your toes or your heels. If you move out of the testing stance, open your eyes, regain your balance, get back into the testing position as quickly as possible, and close your eyes again.

<u>Firm Double Leg Stance:</u> We will start by having you stand on the ground with your feet side by side (touching), your hands on your hips, and your eyes closed. *Study personnel demonstrates stance and gets participant into position.* Ready, go. *Study personnel starts watch and counts errors.* After 20 seconds: Stop.

Firm Single Leg Stance: What is your dominant leg/what leg would you kick a soccer ball with? *Record leg.* Next, we will have you stand on the ground balancing on your non-dominant foot (*insert right or left*). Your hip should be flexed to approximately 30 degrees and knee flexed to approximately 45 degrees. Keep your hands on your hips and eyes closed. *Study personnel demonstrates stance and gets participant into position.* Ready, go. *Study personnel starts watch and counts errors. After 20 seconds:* Stop.

<u>Firm Tandem Stance:</u> Next, we will have you stand on the ground heel to toe with your nondominant foot (insert right or left) in the back with your heel of the dominant foot touching the toe of your non-dominant foot. Keep your hands on your hips and eyes closed. *Study personnel*  demonstrates stance and gets participant into position. Ready, go. Study personnel starts watch and counts errors. After 20 seconds: Stop.

Now we are going to do those three stances again but on the foam pad.

Foam Double Leg Stance: Stand on the foam surface with your feet side by side (touching), your hands on your hips, and your eyes closed. Study personnel demonstrates stance and gets participant into position. Ready, go. Study personnel starts watch and counts errors. After 20 seconds: Stop.

<u>Single leg stance</u>: Next, we will have you stand on the foam surface balancing on your nondominant foot (*insert right or left*). Your hip should be flexed to approximately 30 degrees and knee flexed to approximately 45 degrees. Keep your hands on your hips and eyes closed. *Study personnel demonstrates stance and gets participant into position.* Ready, go. *Study personnel starts watch and counts errors. After 20 seconds:* Stop.

Foam Tandem Stance: Last, we will have you stand on the foam surface heel to toe with your non-dominant foot (insert right or left) in the back with your heel of the dominant foot touching the toe of your non-dominant foot. Keep your hands on your hips and eyes closed. *Study personnel demonstrates stance and gets participant into position*. Ready, go. *Study personnel starts watch and counts errors*. *After 20 seconds:* Stop.

## Scoring

Record the number of errors on the provided scorecard. Errors include hands lifting off of the iliac crest, opening eyes, step/stumble/fall, moving hip into >30 degrees of abduction, lifting the forefoot or feel, and/or remaining out of the test position for >5 seconds. Record which foot was tested (i.e., the participant's non-dominant foot).

Scorecard (Errors)	Firm Surface	Foam Surface
<b>Double Leg Stance</b>		
(Feet Together)		
Single Leg Stance		
(Non-Dominant Foot)		
Tandem Stance		
(Non-Dominant Foot in		
Back)		
Total Scores		
BESS Total		

#### **APPENDIX 11: CENTER OF MASS**

#### Instructions

Note: Study personnel instructions are in *italics* and examiner scripts are in **bold**.

Before starting the assessment, place the Delsys IMU on the Polar strap. Place the strap on the participant's trunk (same placement as the HRV assessment).

To measure your center of mass you will stand as still as possible with both of your feet together. We will complete two, one-minute trials.

<u>Eyes Open:</u> The first trial you will keep your eyes open. Stand as still as possible with both of your feet together. Focus your gaze on something in the distance that is not moving. The oneminute timer is starting now.

Begin one-minute timer. When the timer is complete: You are done, you can relax.

**Eyes Closed:** The second trial you will close your eyes. Stand as still as possible with both of your feet together. Close your eyes. The one-minute timer is starting now.

Begin one-minute timer. When the timer is complete: You are done, you can relax.

#### Scoring

- Eyes open trial standard deviation of acceleration anterior/posterior and medial/lateral planes
- Eyes closed trial standard deviation of acceleration anterior/posterior and medial/lateral planes

#### APPENDIX 12: HEART RATE VARIABILITY (HRV)<sup>58,199</sup>

#### Instructions

Note: Study personnel instructions are in *italics* and examiner scripts are in **bold**.

#### Set Up

- 1. Set up chair with no wheels in a quiet room with minimal distractors.
- 2. Place HR monitor on. Have the participant tie the strap around their chest, just below the chest muscles.
- 3. Turn on the Kubios HRV app. Ensure it is signed into the study email, check connection with HR monitor, and click the (+) at the bottom of the screen.

#### Procedure

<u>Seated One:</u> I am now going to test your heart rate. The first part of this test will include three six-minute sections. We will first start by measuring your heart rate while seated. Please sit evenly on this chair with both feet planted firmly on the ground and your arms relaxed at your sides. Please try to sit as still as possible, don't talk, and think about something calming. Feel free to (instruct on distractor) while we are taking the measurement. Do you have any questions?

#### I am starting the measurement now.

Study personnel start HRV measurement. Use the "Open HRV Reading" option, set the time limitation to 05:59, turn off default breathing practice, position "Sitting." Click "Take Test" to begin reading. Record start time.

With two minutes left say: There are two minutes left.With one minute left say: There is one minute left.Record stop time.

<u>Standing:</u> I am now going to test your heart rate while standing. Please stand with your feet planted firmly on the ground and your arms relaxed at your sides. Please try to stay as still as possible, don't talk, and think about something calming. Feel free to (instruct on distractor) while we are taking the measurement. Do you have any questions?

#### I am starting the measurement now.

Study personnel start HRV measurement. Use the "Open HRV Reading" option, set the time limitation to 05:59 turn off default breathing practice, position "Standing." Click "Take Test" to begin reading. Record start time.

With two minutes left say: There are two minutes left.

With one minute left say: There is one minute left.

Record stop time.

<u>Seated Two:</u> I am now going to test your heart rate again while seated. Please sit down again. Please sit evenly on this chair with both feet planted firmly on the ground and your arms relaxed at your sides. Please try to sit as still as possible, don't talk, and think about something calming. Feel free to (instruct on distractor) while we are taking the measurement. Do you have any questions?

#### I am starting the measurement now.

Study personnel start HRV measurement. Use the "Open HRV Reading" option, set the time limitation to 05:59, turn off default breathing practice, position "Sitting." Click "Take Test" to begin reading. Record start time.

With two minutes left say: There are two minutes left.

With one minute left say: There is one minute left.

Record stop time.

#### **Processing HRV Data**

After all seated/standing positions view data and export.

- To export: home > profile (top right) > export data.
- The exported data is sent to the study email. This will export all files at once, double check file name (time stamp) are the correct ones for your current participant. Open the exported data that was emailed to the study email as a zip file and save to the study computer/study drive. Within the study folder, create a folder with the subject ID and save all documents there. Save the file name as: SUBJECTID\_PROTOCOL\_DATE. Protocol options are SEATED1, STANDING, SEATED2.
- Open the file in Kubios. Save Kubios results as a PDF and txt file.

#### **HRV Outcomes**

Record all HRV outcomes in RedCap. Total power is found in the PDF file, all other outcomes should be recorded straight from Kubois. Include as many decimal places as possible.

#### Seated Trial 1

- 1. Seated Trial 1 Start Time (hh:mm)
- 2. Seated Trial 1 End Time (hh:mm)
- 3. Seated Trial 1 Comments
- 4. Seated Trial 1 Average Heart Rate (1/min)
- 5. Seated Trial 1 Average Heart Rate Standard Deviation (1/min)
- 6. Seated Trial 1 Average RR Interval (ms)
- 7. Seated Trial 1 Average RR Interval Standard Deviation (ms)
- 8. Seated Trial 1 HF Power (ms<sup>2</sup>)
- 9. Seated Trial 1 HF Power (norm n.u.)

- 10. Seated Trial 1 LF Power (ms<sup>2</sup>)
- 11. Seated Trial 1 LF Power (norm n.u.)
- 12. Seated Trial 1 LF/HF Ratio
- 13. Seated Trial 1 Total Power (ms<sup>2</sup>)
- 14. Seated Trial 1 Sample Entropy

#### Standing Trial

- 15. Standing Trial Start Time (hh:mm)
- 16. Standing Trial End Time (hh:mm)
- 17. Standing Trial Comments
- 18. Standing Trial Average Heart Rate (1/min)
- 19. Standing Trial Average Heart Rate Standard Deviation (1/min)
- 20. Standing Trial Average RR Interval (ms)
- 21. Standing Trial Average RR Interval Standard Deviation (ms)
- 22. Standing Trial HF Power (ms<sup>2</sup>)
- 23. Standing Trial HF Power (norm n.u.)
- 24. Standing Trial LF Power (ms<sup>2</sup>)
- 25. Standing Trial LF Power (norm n.u.)
- 26. Standing Trial LF/HF Ratio
- 27. Standing Trial Total Power (ms<sup>2</sup>)
- 28. Standing Trial Sample Entropy

#### Seated Trial 2

- 29. Seated Trial 2 Start Time (hh:mm)
- 30. Seated Trial 2 End Time (hh:mm)

- 31. Seated Trial 2 Comments
- 32. Seated Trial 2 Average Heart Rate (1/min)
- 33. Seated Trial 2 Average Heart Rate Standard Deviation (1/min)
- 34. Seated Trial 2 Average RR Interval (ms)
- 35. Seated Trial 2 Average RR Interval Standard Deviation (ms)
- 36. Seated Trial 2 HF Power (ms<sup>2</sup>)
- 37. Seated Trial 2 HF Power (norm n.u.)
- 38. Seated Trial 2 LF Power (ms<sup>2</sup>)
- 39. Seated Trial 2 LF Power (norm n.u.)
- 40. Seated Trial 2 LF/HF Ratio
- 41. Seated Trial 2 Total Power (ms<sup>2</sup>)
- 42. Seated Trial 2 Sample Entropy

#### APPENDIX 13: VESTIBULAR OCULAR MOTOR SCREENING (VOMS)<sup>195</sup>

<u>Note:</u> Scripted material to be said by study personnel to participants is in **bold.** Instructions for study personnel are in *italics*.

I am now going to test your vestibular/ocular-motor functioning. This screening will consist of 7 tests. I will demonstrate each along the way. After each test I will ask you about some concussion symptoms.

First, before we start this exam, what is your [headache, dizziness, nausea and fogginess] on a scale from 0-10, 0 being none and 10 being the worse it has ever been.

Throughout script repeat this question for each symptom.

Record headache, dizziness, nausea and fogginess on 0-10 scale prior to beginning screening.

1. Smooth Pursuits

Next, we will do a test called smooth pursuits. While keeping your head still, follow my finger with your eyes.

- Both patient and examiner are seated.
- Hold a fingertip at a distance of 3 feet from the patient.
- Move the target smoothly in the horizontal direction 1.5 ft. to the right and 1.5 ft. to the left of midline.
- Do two repetitions (one repetition = when the target moves back and forth to the starting position).
  - The target should be moved at a rate of 2 seconds to go fully from left to right and 2 seconds to go fully from right to left.

After completion: What is your [headache, dizziness, nausea and fogginess] on a scale from

#### 0-10, 0 being none and 10 being the worse it has ever been?

#### 2. Horizontal Saccades

Next, we are going to do a test called horizontal saccades. Move your eyes as quickly as possible from one finger to the next, back and forth 10 times (back and forth is one repetition).

- Hold two fingers horizontally at a distance of 3 ft. from the patient, and 1.5 ft. to the right and 1.5 ft. to the left of midline.
- Complete 10 repetitions (one repetition = eyes move back and forth to the starting position)
  After completion: What is your (headache, dizziness, nausea and fogginess) on a scale from
  0-10, 0 being none and 10 being the worse it has ever been.
  - 3. Vertical Saccades

Next, we are going to do a test called vertical saccades. Move your eyes as quickly as possible from one finger to the next, back and forth 10 times (back and forth is one repetition).

- Hold two fingers vertically at a distance of 3 ft. from the patient, and 1.5 ft. to the right and 1.5 ft. to the left of midline.
- Complete 10 repetitions (one repetition = eyes move back and forth to the starting position)
  After completion: What is your (headache, dizziness, nausea and fogginess) on a scale from
  0-10, 0 being none and 10 being the worse it has ever been.
  - 4. Near Point Convergence

Now we are going to do a test called convergence. Stay focused on the target as you slowly move it closer toward your nose. Stop moving the target when you see two distinct images, hold the target in place and let me know when you see two distinct images. I will then measure the distance between your nose and the target. We will do this three times.

• *Repeated a total of 3 times with measures recorded each time.* 

• Abnormal is a near point of convergence  $\geq 6$  cm from the tip of the nose.

After completion: What is your (headache, dizziness, nausea and fogginess) on a scale from 0-10, 0 being none and 10 being the worse it has ever been.

5. Horizontal VOR Test

Now we are going to do the horizontal VOR test. Move your head side to side while focusing on this target. Do your best to maintain the pace of this metronome. Do this 10 times (back and forth is one).

- *Turn on metronome (180 beats/minute)*
- Complete 10 repetition (one repetition = when the head moves back and forth to the starting position)

After completion: What is your (headache, dizziness, nausea and fogginess) on a scale from 0-10, 0 being none and 10 being the worse it has ever been.

6. Vertical VOR Test

Now we are going to do the vertical VOR test. Move your head up and down while focusing on this target. Do your best to maintain the pace of this metronome. Do this 10 times (back and forth is one).

- *Turn on metronome (180 beats/minute)*
- Complete 10 repetition (one repetition = when the head moves back and forth to the starting position)

After completion: What is your (headache, dizziness, nausea and fogginess) on a scale from 0-10, 0 being none and 10 being the worse it has ever been.

#### 7. Visual Motion Sensitivity (VMS) Test

Finally, we are going to complete the visual motion sensitivity test. For this test hold your arm outstretched and focus on your thumb. While maintaining focus on your thumb, rotate your head, eyes, and trunk together back and forth to the pace of this metronome. You will go back and forth five times.

- Stand next to and slightly behind the patient, so that the patient is guarded but the movement can be performed freely.
- Turn on metronome (50 beats/min).
- Complete five repetitions (one repetition = when the trunk rotates back and forth to the starting position)

After completion: What is your (headache, dizziness, nausea and fogginess) on a scale from 0-10, 0 being none and 10 being the worse it has ever been.

## Scoring

All results are recording on the following:

	Not Tested	Headache 0-10	Dizziness 0-10	Nausea 0-10	Fogginess 0-10	Comments
Baseline Symptoms	N/A					
Smooth Pursuits						
Saccades Horizontal						
Saccades Vertical						
Convergence (Near Point)						Measure 1: Measure 2: Measure 3:
VOR Horizontal						
VOR Vertical						
Visual Motion Sensitivity Test						

• <u>Total symptom scores</u> were computed for each assessment by summing the ratings for the four symptoms

• <u>Change in symptom scores</u> were computed for each assessment by subtracting the

assessment's total symptom score from the baseline total symptom score

#### **APPENDIX 14: EXERTION TOLERANCE STEP TEST**

#### Instructions

<u>Note:</u> Scripted material to be said by study personnel to participants is in **bold.** Instructions for study personnel are in *italics*.

Before beginning the step test, affix the pedometer to the participant's left shoe.

For two minutes, please complete as many steps as possible making sure both feet are flat on the step and on the ground. *Study personnel demonstrate*. We will start by doing 30 seconds of rest, standing still with your arms relaxed by your side.

Begin timer. After 30 seconds say: Begin stepping and complete as many as you can in 2 minutes.

Study personnel count the number of steps. One step = both feet move to the top of the step and then back on the floor.

*After 2 minutes of stepping say:* **Please stop and rest standing for 30 seconds.** *Record rest period of 30 seconds (total time = 3 minutes).* 

#### Scoring

- <u>Total steps (counted)</u>: record the total number of steps that were counted by study personnel. One step = both feet move to the top of the step and then back on the floor.
- <u>Total steps (pedometer)</u>: record the total number of steps indicated on the pedometer
  - Note: this number will need to be divided by four to indicate the final total number of steps for the step test
- <u>Rate of Perceived Exertion (RPE)</u>: After completing the step test, ask the participant to rate their perceived exertion on the following scale:
  - $\circ$  0 = Nothing at all
  - $\circ$  0.5 = Very, very slight (just noticeable)
  - $\circ$  1 = Very slight
  - $\circ$  2 = Slight
  - $\circ$  3 = Moderate
  - $\circ$  4 = Somewhat severe
  - $\circ$  5 = Severe
  - o 6
  - $\circ$  7 = Very severe
  - o 8
  - $\circ$  9 = Very, very severe (almost maximal)
  - $\circ$  10 = Maximal

## APPENDIX 15: CNS VITAL SIGNS<sup>208</sup>

After the participant completes CNS Vital Signs on the study computer, save the scores in the study folder and record the following scores in RedCap:

- Verbal memory
- Visual memory
- Psychomotor speed
- Cognitive flexibility
- Complex attention
- Processing speed
- Reaction time
- Executive functioning

#### APPENDIX 16: BRIEF SYMPTOM INVENTORY (BSI-18)<sup>212</sup>

Below is a list of problems people sometimes have. Read each one carefully and mark the number that best describes how much that problem has distressed or bothered you during the past seven days including today. Do not skip any items.

<u>Response Scale:</u> 0 = Not at all, 1 = A little bit, 2 = Moderately, 3 = Quite a bit, 4 = Extremely<u>Prompt:</u> How much were you distressed by:

- 1. Faintness or dizziness
- 2. Feeling no interest in things
- 3. Nervousness or shakiness inside
- 4. Pains in the heart or chest
- 5. Feeling lonely
- 6. Feeling tense or keyed up
- 7. Nausea or upset stomach
- 8. Feeling blue
- 9. Suddenly scared for no reason
- 10. Trouble getting your breath
- 11. Feeling of worthlessness
- 12. Spells of terror or panic
- 13. Numbness or tingling in parts of your body
- 14. Feeling of hopelessness about the future
- 15. Feeling so restless you could not sit still
- 16. Feeling weak in parts of your body
- 17. Thoughts of ending your life

18. Feeling fearful

#### Scoring

Global Severity Index (Total): Sum of all questions.

<u>Note:</u> The BSI-18 asks sensitive information. Question 17 refers to harming oneself, i.e., "Thoughts of ending your life." After each participant completes the BSI-18, the PI, Christine Callahan, will review the response to Question 17. If a participant responds to Question 17 with moderately (2), quite a bit (3) or extremely (4), the PI will talk to the participant to determine risk. If it is determined there is not a risk, the participant will be provided with resources and may be allowed to leave the testing session. If it is determined there is a risk, the participant must be referred to a health care professional for additional care and the. PI's mentor, Johna Register-Mihalik, will be notified. If imminent danger is apparent, the PI will call 911.

#### APPENDIX 17: PATIENT-REPORTED OUTCOMES MEASUREMENT (PROMIS-

#### 29<sup>®</sup>)<sup>297</sup>

#### **Physical Function**

<u>Response Scale:</u> 5 = Without any difficulty, 4 = With little difficulty, 3 = With some difficulty, 2

= With much difficulty, 1 = Unable to do

- 1. Are you able to do chores such as vacuuming or yard work?
- 2. Are you able to go up and down stairs at a normal pace?
- 3. Are you able to go for a walk of at least 15 minutes?
- 4. Are you able to run errands and shop?

#### Anxiety

<u>Response Scale:</u> 1 = Never, 2 = Rarely, 3 = Sometimes, 4 = Often, 5 = Always

Prompt: In the past seven days...

- 5. I felt fearful.
- 6. I found it hard to focus on anything other than my anxiety.
- 7. My worries overwhelmed me.
- 8. I felt uneasy.

#### Depression

<u>Response Scale:</u> 1 = Never, 2 = Rarely, 3 = Sometimes, 4 = Often, 5 = Always

Prompt: In the past seven days...

- 9. I felt worthless.
- 10. I felt helpless.
- 11. I felt depressed.
- 12. I felt hopeless.

#### Fatigue

<u>Response Scale:</u> 1 = Not at all, 2 = A little bit, 3 = Somewhat, 4 = Quite a bit, 5 = Very much<u>Prompt:</u> In the past seven days...

- 13. I felt fatigued.
- 14. I have trouble starting things because I am tired.
- 15. How run-down do you feel on average?
- 16. How fatigued were you on average?

#### **Sleep Disturbance**

<u>Response Scale:</u> 5 = Very poor, 4 = Poor, 3 = Fair, 2 = Good, 1 = Very good

Prompt: In the past seven days...

17. My sleep quality was...

<u>Response Scale:</u> 5 = Not at all, 4 = A little bit, 3 = Somewhat, 2 = Quite a bit, 1 = Very much

Prompt: In the past seven days...

- 18. My sleep was refreshing.
- 19. I had a problem with my sleep.
- 20. I had difficulty falling asleep.

#### Ability to Participate in Social Roles and Activities

<u>Response Scale:</u> 5 = Never, 4 = Rarely, 3 = Sometimes, 2 = Usually, 1 = Always

- 21. I have trouble doing all of my regular leisure activities with others.
- 22. I have trouble doing all of the family activities I want to do.
- 23. I have trouble doing all of my usual work (including work at home).
- 24. I have trouble doing all of the activities with friends that I want to do.

#### **Pain Interference**

<u>Response Scale:</u> 1 = Not at all, 2 = A little bit, 3 = Somewhat, 4 = Quite a bit, 5 = Very much<u>Prompt:</u> In the past seven days...

- 25. How much did pain interfere with your day-to-day activities?
- 26. How much did pain interfere with work around the home?
- 27. How much did pain interfere with your ability to participate in social activities?
- 28. How much did pain interfere with your household chores?

#### **Pain Intensity**

<u>Response Scale:</u> 0 = No pain to 10 = Worst imaginable pain

Prompt: In the past seven days...

29. How would you rate your pain on average?

## APPENDIX 18: PATIENT-REPORTED OUTCOMES MEASUREMENT (PROMIS-29®)

### SCORING<sup>261</sup>

### **Physical Function**

- 1. Sum responses of all physical function questions for the raw score.
- Convert to t-score (higher t-score indicates more physical functioning i.e., good) using the following:

Raw Summed Score	t-score	Standard Error
4	22.5	4.0
5	26.6	2.8
6	28.9	2.5
7	30.5	2.4
8	31.9	2.3
9	33.2	2.3
10	34.4	2.3
11	35.6	2.3
12	36.7	2.3
13	37.9	2.3
14	39.2	2.4
15	40.5	2.4
16	41.9	2.5
17	43.5	2.6
18	45.5	2.8
19	48.3	3.3
20	57.0	6.6

# Anxiety

- 1. Sum responses of all anxiety questions for the raw score.
- 2. Convert to t-score (higher t-score indicates more anxiety i.e., bad) using the following:

Raw Summed Score	t-score	Standard Error
4	40.3	6.1
5	48.0	3.6
6	51.2	3.1
7	53.7	2.8
8	55.8	2.7
9	57.7	2.6
10	59.5	2.6
11	61.4	2.6
12	63.4	2.6
13	65.3	2.7
14	67.3	2.7
15	69.3	2.7
16	71.2	2.7
17	73.3	2.7
18	75.4	2.7
19	77.9	2.9
20	81.6	3.7

# Depression

- 1. Sum responses of all depression questions for the raw score.
- 2. Convert to t-score (higher t-score indicates more depression i.e., bad) using the following:

Raw Summed Score	t-score	Standard Error
4	41.0	6.2
5	49.0	3.2
6	51.8	2.7
7	53.9	2.4
8	55.7	2.3
9	57.3	2.3
10	58.9	2.3
11	60.5	2.3
12	62.2	2.3
13	63.9	2.3
14	65.7	2.3
15	67.5	2.3
16	69.4	2.3
17	71.2	2.4
18	73.3	2.4
19	75.7	2.6
20	79.4	3.6

# Fatigue

- 1. Sum responses of all fatigue questions for the raw score.
- 2. Convert to t-score (higher t-score indicates more fatigue -i.e., bad) using the following:

Raw Summed Score	t-score	Standard Error
4	33.7	4.9
5	39.7	3.1
6	43.1	2.7
7	46.0	2.6
8	48.6	2.5
9	51.0	2.5
10	53.1	2.4
11	55.1	2.4
12	57.0	2.3
13	58.8	2.3
14	60.7	2.3
15	62.7	2.4
16	64.6	2.4
17	66.7	2.4
18	69.0	2.5
19	71.6	2.7
20	75.8	3.9

# **Sleep Disturbance**

- 1. Sum responses of all sleep disturbance questions for the raw score.
- Convert to t-score (higher t-score indicates more sleep disturbance i.e., bad) using the following:

Raw Summed Score	t-score	Standard Error
4	32.0	5.2
5	37.5	4.0
6	41.1	3.7
7	43.8	3.5
8	46.2	3.5
9	48.4	3.4
10	50.5	3.4
11	52.4	3.4
12	54.3	3.4
13	56.1	3.4
14	57.9	3.3
15	59.8	3.3
16	61.7	3.3
17	63.8	3.4
18	66.0	3.4
19	68.8	3.7
20	73.3	4.6

## Ability to Participate in Social Roles and Activities

- 1. Sum responses of all ability to participate in social roles and activities questions for the raw score.
- Convert to t-score (higher t-score indicates more ability to participate in social roles and activities – i.e., good) using the following:

Raw Summed Score	t-score	Standard Error
4	27.5	4.1
5	31.8	2.5
6	34.0	2.3
7	35.7	2.2
8	37.3	2.1
9	38.8	2.2
10	40.5	2.3
11	42.3	2.3
12	44.2	2.3
13	46.2	2.3
14	48.1	2.2
15	50.0	2.2
16	51.9	2.2
17	53.7	2.3
18	55.8	2.3
19	58.3	2.7
20	64.2	5.1

## Pain Interference

- 1. Sum responses of all pain interference questions for the raw score.
- 2. Convert to t-score (higher t-score indicates more pain interference i.e., bad) using the following:

Raw Summed Score	t-score	Standard Error
4	41.6	6.1
5	49.6	2.5
6	52.0	2.0
7	53.9	1.9
8	55.6	1.9
9	57.1	1.9
10	58.5	1.8
11	59.9	1.8
12	61.2	1.8
13	62.5	1.8
14	63.8	1.8
15	65.2	1.8
16	66.6	1.8
17	68.0	1.8
18	69.7	1.9
19	71.6	2.1
20	75.6	3.7

### **Pain Intensity**

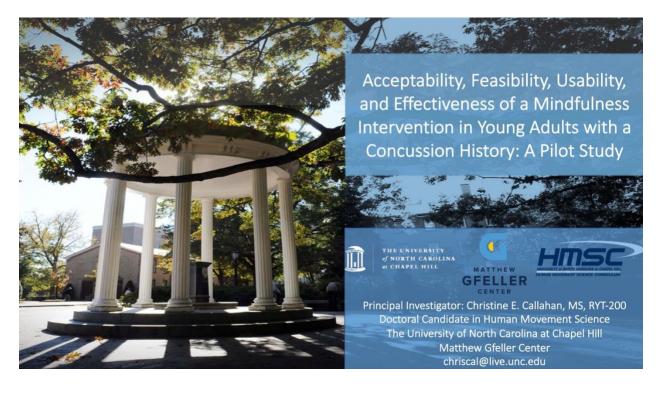
There is no t-score for pain intensity. The score indicated on the single question is the final score, with higher scores indicating more pain (i.e., bad).

	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Week 1	• Body scan meditation (11:15)	<ul> <li>CALM meditation (6:05)</li> <li>Easy inner space meditation (9:20)</li> </ul>	<ul> <li>A calm place meditation (8:23)</li> <li>Breath, not breath meditation (5:00)</li> </ul>	Breathing clarity meditation (10:00)	<ul> <li>Balance meditation (10:20)</li> <li>Awareness meditation (5:07)</li> </ul>	Rotation of consciousne ss (12:07)	<ul> <li>Mindfulness of breath meditation (10:19)</li> <li>Sweet and short meditation (4:44)</li> </ul>
Week 2	<ul> <li>Acceptance meditation (10:06)</li> <li>Sound and touch meditation (9:51)</li> </ul>	<ul> <li>Awareness, gratitude, and empowerme nt meditation (6:47)</li> <li>Tonglen meditation (11:21)</li> </ul>	<ul> <li>Seasons of breath meditation (8:15)</li> <li>Progressive relaxation (6:59)</li> </ul>	<ul> <li>Three anchors to steady the mind (9:25)</li> <li>Cycle of breath meditation (5:23)</li> </ul>	<ul> <li>Finding freedom meditation (11:52)</li> <li>STOP meditation (2:42)</li> </ul>	<ul> <li>Spatial awareness meditation (6:37)</li> <li>Stillness and ease meditation (6:20)</li> </ul>	• Yoga nidra: find relaxation through the body (17:08)
Week 3	<ul> <li>Exploring our senses (12:07)</li> <li>Breath calming meditation (5:02)</li> </ul>	<ul> <li>Acceptance and joy (10:08)</li> <li>I am enough meditation (8:34)</li> </ul>	• Breathe, relax, feel, watch, allow meditation (14:33)	<ul> <li>Challenges meditation (11:53)</li> <li>Breathing into the unknown meditation (7:14)</li> </ul>	<ul> <li>Multidimen sional meditation (12:04)</li> <li>Stillness and ease meditation (6:20)</li> </ul>	<ul> <li>Unlock your potential meditation (9:49)</li> <li>Move into ease meditation (8:31)</li> </ul>	• Body scan yoga nidra meditation (16:09)
Week 4	• Body scan meditation (11:15)	• CALM meditation (6:05)	• A calm place meditation (8:23)	Breathing clarity meditation (10:00)	Balance meditation (10:20)	Rotation of consciousne ss (12:07)	• Mindfulness of breath meditation (10:19)

### APPENDIX 19: AIM 3 MINDFULNESS-BASED EXERCISES AND MEDITATIONS

		• Easy inner space meditation (9:20)	• Breath, not breath meditation (5:00)		• Awareness meditation (5:07)		• Sweet and short meditation (4:44)
Week 5	<ul> <li>Acceptance meditation (10:06)</li> <li>Sound and touch meditation (9:51)</li> </ul>	<ul> <li>Awareness, gratitude, and empowerme nt meditation (6:47)</li> <li>Tonglen meditation (11:21)</li> </ul>	<ul> <li>Seasons of breath meditation (8:15)</li> <li>Progressive relaxation (6:59)</li> </ul>	<ul> <li>Three anchors to steady the mind (9:25)</li> <li>Cycle of breath meditation (5:23)</li> </ul>	<ul> <li>Finding freedom meditation (11:52)</li> <li>STOP meditation (2:42)</li> </ul>	<ul> <li>Spatial awareness meditation (6:37)</li> <li>Stillness and ease meditation (6:20)</li> </ul>	• Yoga nidra: find relaxation through the body (17:08)
Week 6	<ul> <li>Exploring our senses (12:07)</li> <li>Breath calming meditation (5:02)</li> </ul>	<ul> <li>Acceptance and joy (10:08)</li> <li>I am enough meditation (8:34)</li> </ul>	• Breathe, relax, feel, watch, allow meditation (14:33)	<ul> <li>Challenges meditation (11:53)</li> <li>Breathing into the unknown meditation (7:14)</li> </ul>	<ul> <li>Multidimen sional meditation (12:04)</li> <li>Stillness and ease meditation (6:20)</li> </ul>	<ul> <li>Unlock your potential meditation (9:49)</li> <li>Move into ease meditation (8:31)</li> </ul>	• Body scan yoga nidra meditation (16:09)

### **APPENDIX 20: AIM 3 INTERVENTION MANUAL**



# Welcome!

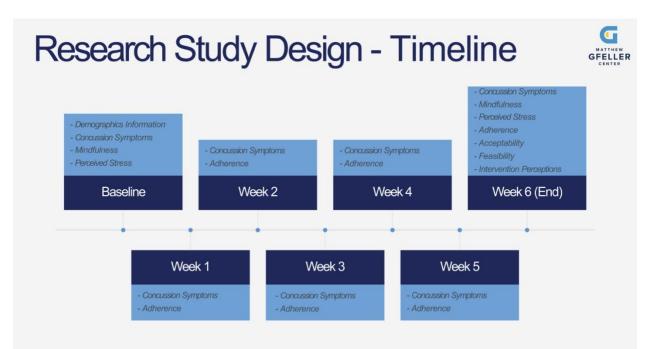
Welcome to the research study Acceptability, Feasibility, Usability, and Effectiveness of a Mindfulness Intervention in Young Adults with a Concussion History: A Pilot Study! Thank you for participating in this research study. This manual is designed to outline the overall research study, detail why mindfulness may be impactful after a concussion, describe what is expected of you as a participant, and provide tips on how to best practice the mindfulness-based exercises and meditations throughout the intervention.



# **Research Study Design**



- The <u>purpose of this study</u> is to understand the acceptability, feasibility, usability, and effectiveness of a novel, home-based mindfulness intervention in young adults with a concussion history
- Timeline: 6 weeks
- You will complete <u>10-20 minutes</u> of mindfulness-focused exercises and meditations <u>each day</u> using the LoveYourBrain Meditation Library
- Throughout the intervention you will complete <u>weekly assessments</u> for concussion symptoms and adherence
- After six weeks, at the end of the intervention, you will complete a <u>final</u> <u>follow-up assessment</u> measuring concussion symptoms, mindfulness, perceived stress, adherence, acceptability, feasibility, and intervention perceptions



# 228

# What is mindfulness?



Mindfulness is a technique focusing on attention (bringing your awareness and experiences to focus on the present moment) and acceptance (observing any feelings or sensations without judgment and letting them go without reaction).

https://dictionary.apa.org/mindfulness

# Why mindfulness?



# Research using mindfulness-based interventions have shown:



Donofry 2020, Atanes 2015, Lu 2019, Zollars 2019, Huberty 2019, Economides 2018, Marshall 2020, Lemay 2019, Nien 2020, Mohammed 2018, Azulay 2013, Bedard 2003, Johansson 2012

# What is expected of you?





Complete the daily assigned mindfulnessbased exercises/meditations. This will take 10-20 minutes and some days is broken up into two exercises/meditations. Emails will be sent on Mondays with links to that week's assigned exercises/mediations.

Complete the weekly assessments. These will take 5-15 minutes. Emails and texts will be sent on Sundays with the link to the weekly assessment.

/	-	_	
	-		
	-		
	-		

# Mindfulness Tips



- <u>Be comfortable</u>. Feel free to be seated or laying down and use pillows or any other props to help you feel at ease and relaxed.
- <u>Minimize noise or distractions.</u> Find somewhere quiet and less prone to interruption. Turn the mindfulness exercise on your device and then darken the screen or face it away from you. But, if you hear a car honk or a phone buzz, notice it and let it go. That is a part of your practice!
- <u>Practice whenever feels right for you.</u> Pick a time in the day that works with your schedule.
- <u>Recognize that thoughts will still dance around your mind, and that is</u> <u>normal</u>. Meditation is a practice of coming back to your present experience without judgment. If you notice your mind has wandered, just return to your meditation with openness.
- <u>Have fun with it!</u> Meditation is, at its roots, a way to explore what it feels like to be you. Use this as an opportunity to explore yourself and just be!

https://loveyourbrain.com/meditation-library

# Questions?





Throughout the research study please reach out to Christine Callahan at <u>chriscal@live.unc.edu</u> with any questions or concerns.

This research study is IRB#22-0732 at the University of North Carolina at Chapel Hill. The IRB can be contacted via email at <u>irb\_subjects@unc.edu</u> or via phone at 919-966-3113.

### **APPENDIX 21: ADHERENCE QUESTIONNAIRE**

- 1. In the past week, how many days of mindfulness-based exercises/meditations did you complete?
  - 0 = 0 1 = 1 2 = 2 3 = 3 4 = 4 5 = 5 6 = 67 = 7

### **Overall Ratings**

2. On a scale from 0-10 rate your overall experience with the mindfulness-based exercise and meditations. Higher ratings = better experience.

*9* = *9* 

10 = 10

*11* = *I* did not complete any of the exercises/meditations.

3. On a scale from 0-10 rate your overall enjoyment with the mindfulness-based exercise and meditations. Higher ratings = more enjoyment.

*11* = *I* did not complete any of the exercises/meditations.

On a scale from 0-10 rate the mindfulness-based exercises/meditations effectiveness.
 Higher ratings = more effectiveness.

*I1* = *I* did not complete any of the exercises/meditations.

#### **Completed Exercises/Meditations**

- 5. In the past week, which exercise(s)/meditation(s) did you complete? Choose all that apply.
  - *1* = [*Name of first exercise/meditation*]
  - 2 = [Name of second exercise/meditation]
  - *3* = [*Name of third exercise/meditation*]
  - *4* = [*Name of fourth exercise/meditation*]
  - 5 = [Name of fifth exercise/meditation]
  - 6 = [Name of sixth exercise/meditation]
  - 7 = [Name of seventh exercise/meditation]
  - ... etc.

The following will display for each exercise/meditation chosen for question 5.

- 6. On a scale from 0-10 rate your experience with the [insert exercise/meditation name].Higher ratings = better experience.
  - 0 = 0
  - 1 = 1

#### Not Finished Exercises/Meditations

- In the past week, did you start but not finish any of the following exercise(s)/meditation(s)?
   Choose all that apply.
  - *l* = [*Name of first exercise/meditation*]
  - 2 = [Name of second exercise/meditation]
  - *3* = [*Name of third exercise/meditation*]
  - 4 = [Name of fourth exercise/meditation]
  - 5 = [Name of fifth exercise/meditation]
  - 6 = [Name of sixth exercise/meditation]
  - 7 = [Name of seventh exercise/meditation]
  - ... etc.

The following will display for each exercise/meditation chosen for question 7.

8. Why did you not finish [insert exercise/meditation name]?

Text entry

# APPENDIX 22: ACCEPTABILITY OF INTERVENTION MEASURE (AIM)<sup>235</sup>

<u>Response Scale:</u> 1 = Completely disagree, 2 = Disagree, 3 = Neither agree nor disagree, 4 = Agree,

## 5 =Completely agree

Scoring Instructions: No items need to be reversed coded. Sum each item for a total score.

- 1. The mindfulness intervention meets my approval.
- 2. The mindfulness intervention is appealing to me.
- 3. I like the mindfulness intervention.
- 4. I welcome the mindfulness intervention.

# APPENDIX 23: FEASIBILITY OF INTERVENTION MEASURE (FIM)<sup>235</sup>

<u>Response Scale:</u> 1 = Completely disagree, 2 = Disagree, 3 = Neither agree nor disagree, 4 = Agree,

## 5 =Completely agree

Scoring Instructions: No items need to be reversed coded. Sum each item for a total score.

- 1. The mindfulness intervention seems implementable.
- 2. The mindfulness intervention seems possible.
- 3. The mindfulness intervention seems doable.
- 4. The mindfulness intervention seems easy to use.

#### **APPENDIX 24: INTERVENTION PERCEPTIONS QUESTIONNAIRE**

1. On a scale from 0-10 what was your overall rating of the mindfulness-based exercises and

meditations? Higher scores = more satisfaction.

- 0 = 0 1 = 1 2 = 2 3 = 3 4 = 4 5 = 5 6 = 6 7 = 7 8 = 8 9 = 910 = 10
- 2. Which total length of exercises/meditations on a day was best for you?
  - 1 = 10 minutes
  - 2 = 15 minutes
  - 3 = 20 minutes
  - 4 = I enjoyed all lengths
- 3. Please describe the most challenging part about completing the exercises/meditations.

Text entry

4. What was your favorite part about the LoveYourBrain exercises/meditations?

Text entry

- 5. Overall, I felt that the LoveYourBrain mindfulness-based exercises and meditations were helpful.
  - *1* = *Strongly agree*
  - 2 = Agree
  - 3 = Neutral
  - 4 = Disagree
  - 5 = Strongly disagree
- Overall, I felt that the LoveYourBrain mindfulness-based exercises and meditations were helpful for my mental health.
  - 1 = Strongly agree
  - 2 = Agree
  - 3 = Neutral
  - 4 = Disagree
  - 5 = Strongly disagree
- 7. Overall, I felt that the LoveYourBrain mindfulness-based exercises and meditations were helpful for my mindfulness.
  - *1* = *Strongly agree*
  - 2 = Agree
  - 3 = Neutral
  - 4 = Disagree
  - 5 = Strongly disagree
- 8. Overall, I felt that the LoveYourBrain mindfulness-based exercises and meditations were helpful for my stress.

- *1* = *Strongly agree*
- 2 = Agree
- 3 = Neutral
- 4 = Disagree
- 5 = Strongly disagree
- 9. Overall, I felt that the LoveYourBrain mindfulness-based exercises and meditations were helpful for my concussion symptoms.
  - *1* = *Strongly agree*
  - 2 = Agree
  - 3 = Neutral
  - 4 = Disagree
  - 5 = Strongly disagree
  - 0 = Not applicable
- 10. Overall, I felt that the LoveYourBrain mindfulness-based exercises and meditations were helpful for my quality of life.
  - *1* = *Strongly agree*
  - 2 = Agree
  - 3 = Neutral
  - 4 = Disagree
  - 5 = Strongly disagree
  - 0 = Not applicable
- 11. On a scale from 0-10 how usable were the LoveYourBrain mindfulness-based exercises and meditations? Higher scores = more usability.

12. How likely are you to continue a mindfulness practice after completing this study?

- 1 = Extremely likely2 = Very likely
- 3 = Moderately likely
- 4 = Slightly likely
- 5 = Not at all likely
- 13. Did the effects of the mindfulness-based exercises and meditations impact your life outside of the exercises themselves?
  - 1 = Yes0 = No
- 14. Please describe how they impacted you.

Question will display if the answer to question 12 is yes.

Text entry.

15. Describe your favorite part about this study,

Text entry

16. Describe your least favorite part about this study,

Text entry

1 and 2 study sam	Mean	SD	95%CI	Min	Max	Median	1Q	3Q
General Demograp	hics							
Age (Years)	21.39	2.59	20.78, 22.00	18.00	30.00	21.00	20.00	22.00
Height (Inches)	66.72	3.91	65.85, 67.59	58.00	76.00	66.00	64.00	69.00
Weight (Pounds)	150.80	31.71	143.44, 157.86	92.00	325.00	145.00	130.0 0	165.00
Concussion History	ý							
Concussion Number	2.50	1.50	2.17, 2.83	1.00	5.00	2.00	1.00	3.50
Time Since Most Recent Concussion (Months)	24.18	17.75	20.23, 28.13	1.00	58.00	24.00	7.50	37.00
COVID-19 History	<sub>7</sub> a							
COVID-19 Number	1.20	0.41	1.09, 1.32	1.00	2.00	1.00	1.00	1.00
COVID-19 Symptoms (Days)	8.59	13.07	4.84, 12.35	0	90.00	5.00	4.00	7.00
Time Since COVID-19 (Days)	199.73	202.20	141.02, 258.44	10.00	868.00	135.00	90.00	202.00
Sleep								
Average Hours of Sleep	7.01	0.85	6.82, 7.20	5.00	9.00	7.00	7.00	8.00
Hours Slept Last Night	6.86	1.44	6.54, 7.18	1.00	9.00	7.00	6.00	8.00
Caffeine Consumption	tion							
Average Cups of Caffeine Per Day	1.14	1.09	0.90, 1.38	0	5.00	1.00	0	2.00
Cups of Caffeine Consumed Today	0.61	0.74	0.44, 0.77	0	3.00	0	0	1.00

# APPENDIX 25: AIMS 1 AND 2 SUPPLEMENTARY TABLES

Average Drinks Consumed Per Day	1.49	1.51	1.15, 1.82	0	5.00	1.00	0	3.00
Drinks Consumed in the Past 24 Hours	0.30	0.82	0.12, 0.48	0	5.00	0	0	0
Physical Activity								
Days/Week of Vigorous Physical Activity	3.14	1.78	2.74, 3.53	0	7.00	3.00	2.00	4.00
Time/Day in Vigorous Physical Activity (Minutes)	69.86	45.37	59.20, 80.52	0	200.00	60.00	30.00	90.00
Days/Week of Moderate Physical Activity	4.59	2.00	4.15, 5.04	0	7.00	5.00	3.00	7.00
Time/Day in Moderate Physical Activity (Minutes)	53.51	31.61	46.39, 60.64	1.00	200.00	60.00	30.00	60.00
Menstrual Cycle <sup>b</sup>								
Time Since Last Menstrual Cycle (Days)	41.63	117.47	8.59, 74.66	0	767.00	13.00	8.00	21.00
<sup>a</sup> COVID-19 inform diagnosis (n=49).	ation self	-reported f	for those w	ho indic	cated yes a	t receiving	g a COVI	D-19
diagnosis (n=49). <sup>b</sup> Menstrual cycle in cycle (n=62).		-				-	-	

	Frequency	Percent
Number of Concussions		
1	29	36.25
2	17	21.25
3	14	17.50
4	5	6.25
5+	15	18.75
Mechanism of Most Recent Concus	ssion	
Sport-Related	41	51.25
Non-Sport-Related	39	48.75
Sex		
Female	62	77.50
Male	18	22.50
Ethnicity <sup>a</sup>		
Non-Hispanic/Latino	74	93.67
Hispanic/Latino	5	6.33
Race		
White	62	77.50
Non-White	18	22.50
Highest Education Level		
High School Diploma	5	6.25
Some College	42	52.50
Associate Degree	3	3.75
Bachelor's Degree	23	28.75
Master's Degree	6	7.50
Professional/Doctoral		
Degree	1	1.25
Marital Status		
Single, Never Married	77	96.25
Married/Domestic		
Partnership	3	3.75
Employment		
Employed for Wages	21	26.25
Out of Work and Currently		
Looking	2	2.50
Student	57	71.25
School Level <sup>b</sup>	<u> </u>	
First Year College	2	3.51
Second Year College	9	15.79
Third Year College	16	28.07
Fourth+ Year College	15	26.32
Master's Student	6	10.53
Professional/Doctoral	-	
Degree Student	9	15.79

COVID-19 History		
Yes	49	61.25
No	31	38.75
<sup>a</sup> Self-report ethnicity data missing	g n=1.	
<sup>b</sup> Self-report school level only repo	orted for those who identified	as a student (n=57).

<b>▲</b>	<u>a history for the Aims 1 an</u> Frequency	Percent
Experience Any Mental Health-Rela	- · ·	
Yes	65	81.25
No	15	18.75
Mental Health-Related Symptoms R	eported <sup>a</sup>	
Anxiety	59	90.77
ADD/ADHD	20	30.77
Autism	0	0.00
Bipolar	3	4.62
Communication Disorder	0	0.00
Depression	40	61.54
Eating Disorder	15	23.08
OCD	10	15.38
Panic Disorder	4	6.15
Personality Disorder	2	3.08
PTSD	14	21.54
Schizophrenia	0	0.00
Other	2	3.08
Iental Health-Related Diagnosis		
Yes	33	41.25
No	47	58.75
Aental Health Diagnoses Reported <sup>b</sup>		
Anxiety	28	84.85
ADD/ADHD	10	30.30
Autism	0	0.00
Bipolar	2	6.06
Communication Disorder	0	0.00
Depression	18	54.55
Eating Disorder	4	12.12
OCD	3	9.09
Panic Disorder	1	3.03
Personality Disorder	1	3.03
PTSD	5	15.15
Schizophrenia	0	0.00
Other	2	6.06
Iental Health Symptoms Worsen A	fter Concussion	
Yes	43	67.19
No	21	32.81
pecific Mental Health Symptoms W	Vorsen After Concussion	
Anxiety	31	72.09
ADD/ADHD	8	18.60
Autism	0	0.00
Bipolar	2	4.65
Communication Disorder	0	0.00
Depression	25	58.14

Eating Disorder	2	4.65
OCD	2	4.65
Panic Disorder	2	4.65
Personality Disorder	2	4.65
PTSD	2	4.65
Schizophrenia	0	0.00
Other	1	2.33
Receive Mental Health Treatment		
Yes	36	55.38
No	29	44.62
Mental Health Treatment Providers <sup>c</sup>		
Therapist	27	75.00
Counselor	5	13.89
Psychiatrist	21	58.33
Sports Psychologist	3	8.33
Other	3	8.33
Mental Health Treatment Types <sup>c</sup>		
Cognitive Behavioral Therapy	19	52.78
Dialectical Behavioral Therapy	3	8.33
Mindfulness-Based Cognitive Therapy	8	22.22
Motivational Interviewing	2	5.56
Positive Psychology	0	0.00
<i>Medication(s)</i>	24	66.67
Unknown	4	11.11
Other	3	8.33

<sup>a</sup>Mental health-related symptoms only asked to those who responded yes to experiencing mental health-related symptoms (n=65). Question was a choose all that apply.

<sup>b</sup>Mental health-related diagnoses only asked to those who responded yes to experiencing a mental health-related diagnosis (n=33). Question was a choose all that apply.

<sup>c</sup>Mental health treatment providers and types were only asked to those who responded yes to receiving mental health treatment (n=36). Question was a choose all that apply.

 Table A.7. Breakdown of participants with a current mindfulness practice (yes/no) and practice type (meditation/yoga) for the Aims 1 and 2 study sample.

	n	Frequency	Percentage
Current Mindfulness Pract	ice		
Yes	80	24	30.00
No	80	56	70.00
Meditation Practice			
Yes	24	12	50.00
No	24	12	50.00
Yoga Practice			
Yes	24	18	75.00
No	24	6	25.00

# Table A.8. Breakdown of the yoga current mindfulness practice information for the Aims 1 and 2 study sample (n=24).

1 and 2 study sample (n=24).		
	Mean±SD	95%CI
Yoga Length (Minutes)	40.28±20.76	29.96, 50.60
Days/Week of Yoga	2.06±1.89	1.11, 3.00
	Frequency	Percentage
Types of Yoga Practices <sup>a</sup>		
Vinyasa	11	61.11
Hatha	7	38.89
Iyengar	0	0.00
Kundalini	0	0.00
Ashtanga	0	0.00
Bikram	1	5.56
Yin	2	11.11
Restorative	0	0.00
Pre/Post-Natal	0	0.00
Anusvara	0	0.00
Jivamukti	0	0.00
Other	0	0.00
Yoga Access		
Phone App/Online	9	50.00
Class	8	44.44
Self-Practice	4	22.22
Other	0	0.00
<sup>a</sup> Choose all that apply.		

the Aims 1 and 2 study sample (n=24).						
	Mean±SD	95%CI				
Meditation Length (Minutes)	$15.42 \pm 10.10$	9.00, 21.84				
Days/Week of Meditation	3.92±2.61	2.26, 5.57				
	Frequency	Percentage				
Types of Meditation Practices <sup>a</sup>		<u> </u>				
Visualization	3	25.00				
Breathing	6	50.00				
Body Scan	2	16.67				
Transcendental	0	0.00				
Focused Attention	5	41.67				
Loving Kindness	3	25.00				
Resting Awareness	3	25.00				
Reflection	1	8.33				
Noting	1	8.33				
Skillful Compassion	0	0.00				
Walking/Moving Mindfulness	1	8.33				
Sleep	5	41.67				
Mantra	0	0.00				
Zen	1	8.33				
Vipassana	0	0.00				
Chakra	0	0.00				
Qigong	0	0.00				
Sound Bath	0	0.00				
Other	2	16.67				
Meditation Delivery						
Guided	6	50.00				
Unguided	3	25.00				
Both	3	25.00				
Meditation Access						
Phone App/Online	8	66.67				
Class	1	8.33				
Self-Practice	5	41.67				
Other	0	0.00				
<sup>a</sup> Choose all that apply.						

Table A.9. Breakdown of the meditation current mindfulness practice information forthe Aims 1 and 2 study sample (n=24).

covariates [number of c	oncussions, s	-			
_mechanism(sport/non-s	port)]. Perceived Stress (PSS-10) Total	Mindfulness (FFMQ) Total	Number of Concussions	Sex	Most Recent Concussion Mechanism
Concussion Symptoms (I	RPQ)				
Total Symptom Severity	0.51*a	-0.42*a	0.05 <sup>a</sup>	0.30* <sup>b</sup>	0.06 <sup>b</sup>
Total Symptoms Worse than Before Injury	0.50*a	-0.38*a	-0.03 <sup>a</sup>	0.29* <sup>b</sup>	0.08 <sup>b</sup>
Balance Performance (BI	(225				
Total Errors	0.12 <sup>a</sup>	-0.08 <sup>a</sup>	0.05 <sup>a</sup>	0.02 <sup>b</sup>	0.21 <sup>b</sup>
Balance Performance (CO		-0.08	0.05	0.02*	0.21
	<i>J</i> <b>IVI</b> <i>)</i>				
Eyes Open Trial Anterior/Posterior					
Plane SD of	0.05 <sup>b</sup>	-0.14 <sup>b</sup>	0.12 <sup>b</sup>	0.11 <sup>b</sup>	0.06 <sup>b</sup>
Acceleration <sup>c</sup>	0.05	-0.14	$0.12^{\circ}$	0.11	0.00
Medial/Lateral Plane					
SD of Acceleration <sup>c</sup>	$0.07^{b}$	-0.09 <sup>b</sup>	$0.04^{*b}$	0.19 <sup>b</sup>	-0.07 <sup>b</sup>
Eyes Closed Trial					
Anterior/Posterior					
Plane SD of	$0.08^{b}$	-0.16 <sup>b</sup>	$0.24^{*b}$	-0.04 <sup>b</sup>	0.04 <sup>b</sup>
Acceleration <sup>c</sup>	0.00	0.10	0.24	0.04	0.04
Medial/Lateral Plane					
SD of Acceleration <sup>c</sup>	$0.12^{b}$	-0.17 <sup>b</sup>	$0.08^{b}$	0.11 <sup>b</sup>	-0.01 <sup>b</sup>
ANS Function (HRV)					
Seated 1 HR <sup>d</sup>	0.19 <sup>a</sup>	-0.11ª	0.05 <sup>a</sup>	0.21 <sup>b</sup>	0.07 <sup>b</sup>
Seated 1 LF/HF Ratio	-0.03 <sup>b</sup>	0.02 <sup>b</sup>	-0.03 <sup>b</sup>	-0.13 <sup>b</sup>	-0.17 <sup>b</sup>
Standing HR <sup>d</sup>	0.11ª	-0.03 <sup>a</sup>	-0.01ª	0.11 <sup>b</sup>	0.09 <sup>b</sup>
Standing LF/HF Ratio	-0.07 <sup>b</sup>	0.01 <sup>b</sup>	0.01 <sup>b</sup>	-0.31* <sup>b</sup>	-0.11 <sup>b</sup>
Seated 2 HR <sup>d</sup>	0.22ª	-0.14 <sup>a</sup>	0.01 <sup>a</sup>	0.21 <sup>b</sup>	0.05 <sup>b</sup>
Seated 2 LF/HF Ratio	-0.04 <sup>b</sup>	-0.08 <sup>b</sup>	-0.08 <sup>b</sup>	-0.19 <sup>b</sup>	-0.16 <sup>b</sup>
Vestibular/Ocular Function				~/	
Smooth Pursuits	-0.10 <sup>b</sup>	0.17 <sup>b</sup>	0.26 <sup>b</sup>	-0.04 <sup>b</sup>	$0.06^{b}$
Horizontal Saccades	0.04 <sup>b</sup>	0.10 <sup>b</sup>	0.25*b	0.07 <sup>b</sup>	0.14 <sup>b</sup>
Vertical Saccades	0.06 <sup>b</sup>	0.01 <sup>b</sup>	0.17 <sup>b</sup>	0.14 <sup>b</sup>	0.18 <sup>b</sup>
Near Point	0.08 <sup>b</sup>	0.15 <sup>b</sup>	0.29* <sup>b</sup>	0.09 <sup>b</sup>	0.19 <sup>b</sup>
Convergence					
Horizontal VOR	0.07 <sup>b</sup>	0.15 <sup>b</sup>	0.32*b	-0.01 <sup>b</sup>	0.14 <sup>b</sup>
Vertical VOR	0.14 <sup>b</sup>	0.16 <sup>b</sup>	0.30* <sup>b</sup>	-0.02 <sup>b</sup>	0.17 <sup>b</sup>
VMS	0.16 <sup>b</sup>	0.17 <sup>b</sup>	0.24* <sup>b</sup>	0.07 <sup>b</sup>	0.08 <sup>b</sup>
Exertion Tolerance (Step		0.000		o col	o col
Number of Steps	-0.01 <sup>a</sup>	-0.02 <sup>a</sup>	-0.13 <sup>a</sup>	0.13 <sup>b</sup>	-0.08 <sup>b</sup>
RPE	-0.11 <sup>a</sup>	0.03 <sup>a</sup>	0.08 <sup>a</sup>	0.19 <sup>b</sup>	0.14 <sup>b</sup>

Table A.10. Correlations between clinical concussion outcomes and multivariable regression model independent variables (perceived stress and mindfulness) and covariates [number of concussions, sex (male/female), and most recent concussion mechanism(sport/non-sport)].

## \*p-value <0.05

<sup>a</sup>Pearson correlation used, Pearson R reported.

<sup>b</sup>Spearman correlations were used with non-normally distributed outcomes (all COM outcomes, HRV ratio outcomes, and all VOMS outcomes) and categorical covariates [sex (male/female) and most recent concussion mechanism (sport/non-sport)],  $\rho$  reported. <sup>c</sup>Units= cm/s<sup>2</sup>.

### <sup>d</sup>Units=beats/minute.

**Abbreviations:** PSS-10=Perceived Stress Scale, FFMQ=Five Facet Mindfulness Questionnaire, RPQ=Rivermead Post-Concussion Questionnaire, BESS=Balance Error Scoring System, COM=center of mass, ANS=autonomic nervous system, HRV=heart rate variability, HR=heart rate, LF/HF=low frequency/high frequency, VOMS=Vestibular/Ocular Motor Screening, VOR=vestibular/ocular reflex, VMS=visual motion sensitivity, RPE=rate of perceived exertion.

Table A.11. Correlations between heart rate variability outcomes and demographic         variables that may influence the outcomes.					
	Hours Slept Night Before Testing	Cups of Caffeine Consumed Day of Testing	Alcoholic Drinks Consumed in 24 Hours Before Testing	COVID-19 History	
Seated 1 HR	-0.15 <sup>a</sup>	-0.16 <sup>a</sup>	0.03ª	0.11 <sup>b</sup>	
Seated 1 LF/HF Ratio	-0.16 <sup>b</sup>	-0.01 <sup>b</sup>	0.08 <sup>b</sup>	0.07 <sup>b</sup>	
Standing HR	-0.15 <sup>a</sup>	-0.15 <sup>a</sup>	0.07 <sup>a</sup>	0.19 <sup>b</sup>	
Standing LF/HF Ratio	-0.03 <sup>b</sup>	-0.02 <sup>b</sup>	0.37* <sup>b</sup>	-0.04 <sup>b</sup>	
Seated 2 HR	-0.12 <sup>a</sup>	-0.16 <sup>a</sup>	$0.08^{a}$	0.09 <sup>b</sup>	
Seated 2 LF/HF Ratio	-0.05 <sup>b</sup>	-0.05 <sup>b</sup>	0.14 <sup>b</sup>	0.05 <sup>b</sup>	

\*p-value<0.05.

<sup>a</sup>Pearson correlation used, Pearson R reported.

<sup>b</sup>Spearman correlations were used with non-normally distributed outcomes (HRV ratio outcomes), ρ reported.

**Abbreviations:** LF/HF=low frequency/high frequency.

[number of concussion	, .	emale), and mo	st recent concu	ission	
<u>mechanism(sport/non-</u>	sport)]. Perceived Stress (PSS-10) Total	Mindfulness (FFMQ) Total	Number of Concussions	Sex	Most Recent Concussion Mechanism
Neurocognitive Perform		ital Signs) <sup>c</sup>			Mechanishi
Verbal Memory	-0.21ª	0.14 <sup>a</sup>	-0.10 <sup>a</sup>	-0.08 <sup>b</sup>	0.01 <sup>b</sup>
Visual Memory	0.10 <sup>a</sup>	0.02ª	-0.03 <sup>a</sup>	-0.21 <sup>b</sup>	-0.07 <sup>b</sup>
Psychomotor Speed	-0.21 <sup>a</sup>	0.19 <sup>a</sup>	0.05 <sup>a</sup>	-0.22 <sup>b</sup>	-0.03 <sup>b</sup>
Cognitive Flexibility	-0.09 <sup>a</sup>	0.13 <sup>a</sup>	0.10 <sup>a</sup>	-0.20 <sup>b</sup>	-0.04 <sup>b</sup>
Complex Attention	-0.06 <sup>a</sup>	0.09 <sup>a</sup>	0.13 <sup>a</sup>	-0.15 <sup>b</sup>	$0.08^{b}$
Processing Speed	-0.17 <sup>a</sup>	0.11 <sup>a</sup>	0.09 <sup>a</sup>	-0.03 <sup>b</sup>	-0.02 <sup>b</sup>
Reaction Time	-0.11 <sup>a</sup>	0.19 <sup>a</sup>	-0.02 <sup>a</sup>	-0.13 <sup>b</sup>	-0.21 <sup>b</sup>
Executive Function	-0.08 <sup>a</sup>	0.14 <sup>a</sup>	0.10 <sup>a</sup>	-0.16 <sup>b</sup>	-0.07 <sup>b</sup>
Psychiatric Distress (BS	SI-18)				
Total	0.63*a	-0.49*a	0.20 <sup>a</sup>	0.26 <sup>b</sup>	0.04 <sup>b</sup>
QOL (PROMIS-29)					
Physical Function <sup>d</sup>	-0.36* <sup>b</sup>	0.31* <sup>b</sup>	-0.20 <sup>b</sup>	-0.19 <sup>b</sup>	-0.04 <sup>b</sup>
Anxiety <sup><math>d</math></sup>	0.72* <sup>a</sup>	-0.62*a	0.19 <sup>a</sup>	0.23* <sup>b</sup>	0.01 <sup>b</sup>
<i>Depression</i> <sup>d</sup>	0.65* <sup>b</sup>	-0.54*b	$0.07^{b}$	0.23* <sup>b</sup>	0.05 <sup>b</sup>
$Fatigue^d$	0.53*a	-0.37*a	$0.06^{a}$	0.25* <sup>b</sup>	0.11 <sup>b</sup>
Sleep Disturbance <sup>d</sup>	-0.07 <sup>a</sup>	-0.01ª	-0.10 <sup>a</sup>	-0.10 <sup>b</sup>	-0.10 <sup>b</sup>
Social Participation <sup>d</sup>	-0.60* <sup>b</sup>	0.54* <sup>b</sup>	-0.01 <sup>b</sup>	-0.16 <sup>b</sup>	-0.20 <sup>b</sup>
Pain Interference <sup>d</sup>	0.36* <sup>b</sup>	-0.24* <sup>b</sup>	0.14 <sup>b</sup>	0.14 <sup>b</sup>	0.19 <sup>b</sup>
Pain Intensity	0.33* <sup>b</sup>	-0.23*b	0.12 <sup>b</sup>	0.16 <sup>b</sup>	0.14 <sup>b</sup>

Table A.12. Correlations between psychological concussion outcomes and multivariable regression model independent variables (perceived stress and mindfulness) and covariates [number of concussions, sex (male/female), and most recent concussion mechanism(mert/nen sport)]

\*p-value < 0.05

<sup>a</sup>Pearson correlation used, Pearson R reported.

<sup>b</sup>Spearman correlations were used with non-normally distributed outcomes (QOL physical function, depression, social participation, pain interference, and pain intensity scales) and categorical covariates [sex (male/female) and most recent concussion mechanism (sport/non-sport)], ρ reported.

<sup>c</sup>CNS Vital signs results are standard scores normalized by age to a mean of 100 and SD of 15. <sup>d</sup>PROMIS-29 scales reported as t-scores.

**Abbreviations:** SD=standard deviation, 95%CI=95% confidence interval, PSS-10=Perceived Stress Scale, FFMQ=Five Facet Mindfulness Questionnaire, BSI=Brief Symptom Inventory, QOL=quality of life, PROMIS=Patient Reported Outcomes Measurement Information System.

		Model		Parameter Estimates					
	F Value	p Value	Adjusted R <sup>2</sup>	β	Standardize dβ	Standardize d 95%CI	p Value		
Concussion Symptoms (	RPQ)				•				
<b>Total Symptom Severity</b>	7								
Perceived Stress				0.83	0.45	0.25, 0.64	<.0001*		
Concussion Number	9.42	< 0.001*	0.30	1.57	0.19	-0.01, 0.38	0.05		
Sex	9.42	<0.001*	0.50	5.71	0.19	0.01, 0.38	0.05		
Concussion Mechanism				-0.46	-0.02	-0.21, 0.17	0.85		
<b>Total Symptoms Worse</b>	Than Before I	njury							
Perceived Stress				0.31	0.43	0.24, 0.63	<.0001*		
Concussion Number	8.94	< 0.001*	0.20	0.63	0.20	0.01, 0.39	0.05		
Sex	8.94	<0.001**	0.29	2.14	0.19	-0.01, 0.38	0.06		
Concussion Mechanism				0.15	0.02	-0.18, 0.21	0.87		
Balance Performance (B	BESS)								
Total Errors									
Perceived Stress				0.05	0.10	-0.13, 0.32	0.41		
Concussion Number	1.34	0.26	0.02	0.11	0.04	-0.18, 0.27	0.70		
Sex	1.54	0.20	0.02	-0.38	-0.04	-0.27, 0.18	0.71		
Concussion Mechanism				1.75	0.23	0.01, 0.45	0.05		
Balance Performance (C	COM)								
Eyes Open Trial Anterio	or/Posterior Pla	ane SD of Acc	eleration						
Perceived Stress				0.01	0.02	-0.22, 0.26	0.85		
Concussion Number	0.62	0.64	0.02	0.44	0.17	-0.06, 0.40	0.14		
Sex	0.63	0.64	-0.02	-0.22	-0.02	-0.26, 0.21	0.84		
Concussion Mechanism				-0.21	-0.03	-0.26, 0.21	0.81		
Eyes Open Trial Medial	/Lateral Plane	SD of Acceler	ation						
Perceived Stress				0.01	0.01	-0.23, 0.23	0.99		
Concussion Number	1 74	0.15	0.04	1.02	0.18	-0.04, 0.41	0.11		
Sex	1.74	0.15	0.04	4.53	0.22	-0.01, 0.46	0.05		
Concussion Mechanism				-0.38	-0.02	-0.25, 0.20	0.84		
Eyes Closed Trial Anter	ior/Posterior P	lane SD of Ac	celeration						
Perceived Stress				0.02	0.04	-0.19, 0.27	0.73		
Concussion Number	1.67	0.17	0.03	0.51	0.25	0.02, 0.47	0.03		

				0.00	0.12	0.11.0.05	0.01
Sex .				0.89	0.12	-0.11, 0.35	0.31
Concussion Mechanism	<b></b>			0.05	0.01	-0.22, 0.24	0.94
Eyes Closed Trial Medial	Lateral Plan	e SD of Acceler	ation				
Perceived Stress				0.05	0.04	-0.18, 0.27	0.69
Concussion Number	2.67	0.04*	0.08	1.35	0.27	0.04, 0.48	0.02
Sex	2.07	0.01	0.00	3.83	0.21	-0.02, 0.43	0.07
Concussion Mechanism				0.20	0.01	-0.21, 0.24	0.91
ANS Function (HRV)							
Seated 1 HR							
Perceived Stress				0.28	0.16	-0.07, 0.38	0.18
Concussion Number	1.37	0.25	0.02	0.13	0.02	-0.21, 0.24	0.88
Sex	1.37	0.23	0.02	4.58	0.16	-0.07, 0.39	0.16
Concussion Mechanism				1.61	0.07	-0.16, 0.29	0.55
Seated 1 LF/HF Ratio							
Perceived Stress				0.05	0.15	-0.09, 0.38	0.21
Concussion Number	0.48	0.75	-0.03	-0.09	-0.06	-0.29, 0.17	0.63
Sex	0.48	0.75	-0.05	-0.40	-0.07	-0.30, 0.16	0.54
Concussion Mechanism				-0.16	-0.03	-0.26, 0.20	0.77
Standing HR							
Perceived Stress				0.16	0.09	-0.15, 0.32	0.47
Concussion Number	0.64	0.64	-0.02	-0.24	-0.03	-0.26, 0.20	0.81
Sex	0.04	0.04	-0.02	2.77	0.09	-0.14, 0.32	0.44
Concussion Mechanism				2.69	0.10	-0.12, 0.33	0.36
Standing LF/HF Ratio							
Perceived Stress				-0.01	-0.01	-0.24, 0.22	0.94
Concussion Number	0.62	0.65	-0.02	0.09	0.02	-0.21, 0.25	0.86
Sex	0.02	0.05	-0.02	-2.77	-0.18	-0.41, 0.52	0.13
Concussion Mechanism				0.05	0.004	-0.23, 0.23	0.97
Seated 2 HR							
Perceived Stress			0.04	0.34	0.19	-0.04, 0.42	0.10
Concussion Number	1 74	0.15		0.91	-0.04	-0.26, 0.19	0.74
Sex	1.74	0.15		5.41	0.19	-0.04, 0.41	0.10
Concussion Mechanism				0.96	0.04	-0.18, 0.26	0.72
Seated 2 LF/HF Ratio						,	
Perceived Stress	0.44	0.50	0.02	0.03	0.10	-0.14, 0.33	0.42
Concussion Number	0.44	0.78	-0.03	-0.11	-0.09	-0.33, 0.14	0.42
				0.11	0.07	0.00, 0.11	0.12

						0.46
			-0.20	-0.05	-0.28, 0.18	0.63
on (VOMS)						
					· ·	0.66
1 80	0.12	0.04			,	0.02
1.09	0.12	0.04	-0.35	-0.14	-0.36, 0.08	0.21
			-0.09	-0.04	-0.26, 0.18	0.71
			0.0002	0.0006	-0.23, 0.23	0.99
1.40	0.22	0.02	0.35	0.26	0.03, 0.48	0.03
1.40	0.22	0.02	-0.26	-0.05	-0.28, 0.17	0.63
			0.34	0.08	-0.14, 0.31	0.46
			0.01	0.05	-0.19, 0.28	0.69
0.70	0.54	0.01	0.23	0.17	-0.06, 0.40	0.15
0.79	0.54	-0.01	0.01	0.002	-0.23, 0.23	0.98
			0.36	0.09	-0.14, 0.32	0.45
			0.01	0.01	-0.21, 0.24	0.89
2.29	0.07	0.00	0.55	0.30	0.08, 0.52	0.01
2.28	0.07	0.06	0.02	0.003	-0.22, 0.22	0.98
			0.82	0.15	-0.07, 0.37	0.18
			0.01	0.03	-0.19, 0.25	0.81
2.72	0.04*	0.00	0.79	0.32	0.11, 0.54	0.004
2.13	0.04*	0.08	-0.52	-0.06	-0.28, 0.16	0.59
			1.08	0.15	-0.07, 0.37	0.17
			0.06	0.10	-0.12, 0.32	0.36
2.00	0.02*		0.73	0.30	0.08, 0.51	0.01
2.90	0.03*		-0.49	-0.06	-0.27, 0.16	0.62
			1.27	0.17	,	0.12
					,	
<b>a</b> o <i>i</i>	0.10	0.07	0.03	0.05	-0.17, 0.28	0.65
2.04	0.10	0.05	0.68	0.24	0.01, 0.46	0.04
	m (VOMS) 1.89 1.46 0.79 2.28 2.73 2.90 2.04	1.89 $0.12$ $1.46$ $0.22$ $0.79$ $0.54$ $2.28$ $0.07$ $2.73$ $0.04*$ $2.90$ $0.03*$	1.89 $0.12$ $0.04$ $1.46$ $0.22$ $0.02$ $0.79$ $0.54$ $-0.01$ $2.28$ $0.07$ $0.06$ $2.73$ $0.04*$ $0.08$ $2.90$ $0.03*$	$1.89$ $0.12$ $0.04$ $\begin{array}{c} 0.01\\ 0.18\\ -0.35\\ -0.09\end{array}$ $1.46$ $0.22$ $0.02$ $\begin{array}{c} 0.0002\\ 0.35\\ -0.26\\ 0.34\end{array}$ $0.79$ $0.54$ $-0.01$ $\begin{array}{c} 0.01\\ 0.23\\ 0.01\\ 0.36\end{array}$ $2.28$ $0.07$ $0.06$ $\begin{array}{c} 0.01\\ 0.23\\ 0.01\\ 0.36\end{array}$ $2.73$ $0.04*$ $0.08$ $\begin{array}{c} 0.01\\ 0.79\\ -0.52\\ 1.08\end{array}$ $2.90$ $0.03*$ $\begin{array}{c} 0.06\\ 0.73\\ -0.49\\ 1.27\end{array}$	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	$\begin{array}{c c c c c c c c c c c c c c c c c c c $

Sex				0.42	0.04	-0.18, 0.26	0.72
Concussion Mechanism				1.56	0.18	-0.04, 0.40	0.11
<b>Exertion Tolerance (Step</b>	Test)						
Number of Steps							
Perceived Stress				0.01	0.003	-0.23, 0.23	0.98
Concussion Number	1.01	0.41	0.001	-1.00	-0.14	-0.37, 0.08	0.21
Sex	1.01	0.41	0.001	3.95	0.16	-0.07, 0.39	0.17
Concussion Mechanism				-2.45	-0.12	-0.34, 0.11	0.31
RPE							
Perceived Stress				-0.05	-0.19	-0.41, 0.03	0.09
Concussion Number	<b>2</b> (1	0.04*	0.09	0.12	0.11	-0.11, 0.33	0.32
Sex	2.61	0.04*	0.08	0.90	0.23	0.01, 0.45	0.04
Concussion Mechanism				0.64	0.20	-0.02, 0.41	0.08
*p<0.05							
•							

**Abbreviations:** PSS-10=Perceived Stress Scale, 95%CI=95% confidence interval, RPQ=Rivermead Post-Concussion Questionnaire, BESS=Balance Error Scoring System, COM=center of mass, ANS=autonomic nervous system, HRV=heart rate variability, HR=heart rate, LF/HF=low frequency/high frequency, VOMS=Vestibular/Ocular Motor Screening, VOR=vestibular/ocular reflex, VMS=visual motion sensitivity, RPE=rate of perceived exertion.

		Model		Parameter Estimates				
	F Value	p Value	Adjusted R <sup>2</sup>	β	Standardize dβ	Standardize d 95%CI	p Value	
Concussion Symptoms (	(RPQ)							
<b>Total Symptom Severity</b>	y							
Mindfulness				-0.25	-0.38	-0.58, -0.18	0.0003*	
Concussion Number	7.49	< 0.001*	0.25	2.08	0.25	0.06, 0.45	0.01	
Sex	7.49	<0.001	0.25	6.07	0.21	0.01, 0.40	0.04	
Concussion Mechanism				-0.68	-0.03	-0.22, 0.17	0.78	
<b>Total Symptoms Worse</b>	Than Before I	njury						
Mindfulness				-0.08	-0.34	-0.54, -0.13	0.001*	
Concussion Number	6.44	< 0.001*	0.22	0.83	0.26	0.06, 0.46	0.01	
Sex	0.44	<0.001*	0.22	2.33	0.20	0.01, 0.40	0.05	
Concussion Mechanism				0.11	0.01	-0.19, 0.21	0.91	
Balance Performance (I	BESS)							
Total Errors								
Mindfulness				-0.01	-0.05	-0.28, 0.18	0.66	
Concussion Number	1.21	0.31	0.01	0.15	0.06	-0.17, 0.28	0.61	
Sex	1.21	0.51	0.01	-0.32	-0.04	-0.26, 0.19	0.76	
Concussion Mechanism				1.76	0.23	0.01, 0.46	0.05	
Balance Performance (	COM)							
Eyes Open Trial Anteri	or/Posterior P	ane SD of Ac	celeration					
Mindfulness				-0.03	-0.13	-0.36, 0.10	0.27	
Concussion Number	0.93	0.45	-0.003	0.44	0.17	-0.05, 0.40	0.13	
Sex	0.93	0.45	-0.003	-0.37	-0.04	-0.28, 0.19	0.73	
Concussion Mechanism				-0.32	-0.04	-0.27, 0.19	0.71	
Eyes Open Trial Media	l/Lateral Plane	SD of Accele	ration					
Mindfulness				-0.04	-0.10	-0.32, 0.13	0.41	
Concussion Number	1.02	0.11	0.05	1.00	0.18	-0.04, 0.40	0.11	
Sex	1.93	0.11	0.05	4.25	0.21	-0.02, 0.44	0.07	
Concussion Mechanism				-0.59	-0.04	-0.26, 0.19	0.76	
Eyes Closed Trial Anter	rior/Posterior	Plane SD of A	cceleration					
Mindfulness	2.00	0.10	0.05	-0.02	-0.13	-0.36, 0.09	0.25	
Concussion Number	2.00	0.10	0.05	0.51	0.25	0.03, 0.46	0.03	

				0.70	0.10	0.12.0.22	0.27
Sex				0.78	0.10	-0.13, 0.33	0.37
Concussion Mechanism				-0.03	-0.01	-0.23, 0.22	0.97
Eyes Closed Trial Media	I/Lateral Pla	ne SD of Accel	eration	0.04	0.11	0.00.011	0.00
Mindfulness				-0.04	-0.11	-0.33, 0.11	0.32
Concussion Number	2.90	0.03*	0.09	1.37	0.27	0.05, 0.48	0.02
Sex	2.20	0.05	0.07	3.62	0.19	-0.03, 0.42	0.08
Concussion Mechanism				0.06	0.01	-0.21, 0.22	0.97
ANS Function (HRV)							
Seated 1 HR							
Mindfulness				-0.05	-0.07	-0.30, 0.16	0.53
Concussion Number	1.00	0.41	-0.0002	0.32	0.04	-0.19, 0.26	0.72
Sex	1.00	0.41	-0.0002	4.94	0.17	-0.06, 0.40	0.14
Concussion Mechanism				1.73	0.07	-0.16, 0.30	0.53
Seated 1 LF/HF Ratio							
Mindfulness				-0.02	-0.13	-0.37, 0.10	0.25
Concussion Number	0.41	0.80	-0.03	-0.06	-0.02	-0.26, 0.19	0.75
Sex	0.41	0.80	-0.03	-0.38	-0.07	-0.30, 0.16	0.56
Concussion Mechanism				-0.18	-0.04	-0.27, 0.19	0.74
Standing HR							
Mindfulness				0.00002	0.00002	-0.23, 0.23	0.99
Concussion Number	0.50	0.74	0.02	-0.12	-0.01	-0.24, 0.21	0.90
Sex	0.50	0.74	-0.03	3.15	0.10	-0.13, 0.33	0.38
Concussion Mechanism				2.90	0.11	-0.12, 0.34	0.33
Standing LF/HF Ratio							
Mindfulness				0.02	0.06	-0.17, 0.29	0.60
Concussion Number	0.00	0.60	0.00	0.09	0.02	-0.21, 0.25	0.86
Sex	0.69	0.60	-0.02	-2.66	-0.17	-0.40, 0.06	0.14
Concussion Mechanism				0.14	0.01	-0.22, 0.24	0.92
Seated 2 HR							
Mindfulness			0.01	-0.07	-0.10	-0.33, 0.12	0.40
Concussion Number	1.04	0.00		-0.07	-0.01	-0.23, 0.21	0.94
Sex	1.24	0.30		5.77	0.20	-0.03, 0.43	0.08
Concussion Mechanism				1.06	0.04	-0.18, 0.27	0.70
Seated 2 LF/HF Ratio							
Mindfulness				-0.004	-0.05	-0.28, 0.19	0.70
Concussion Number	0.32	0.87	-0.04	-0.10	-0.08	-0.31, 0.15	0.49

Sex				-0.34	-0.08	-0.31, 0.15	0.50
Concussion Mechanism				-0.19	-0.05	-0.28, 0.18	0.66
Vestibular/Ocular Functi	on (VOMS)						
Smooth Pursuits							
Mindfulness				-0.007	-0.12	-0.34, 0.10	0.29
Concussion Number	2.15	0.08	0.05	0.19	0.27	0.05, 0.48	0.02
Sex	2.15	0.08	0.05	-0.38	-0.15	-0.37, 0.07	0.18
Concussion Mechanism				-0.11	-0.05	-0.27, 0.17	0.64
Horizontal Saccades							
Mindfulness				-0.01	-0.08	-0.30, 0.15	0.51
Concussion Number	1.58	0.19	0.03	0.35	0.26	0.03, 0.48	0.02
Sex	1.38	0.19	0.05	-0.31	-0.06	-0.29, 0.16	0.57
Concussion Mechanism				0.30	0.07	-0.15, 0.30	0.52
Vertical Saccades							
Mindfulness				-0.01	-0.09	-0.32, 0.14	0.45
Concussion Number	0.90	0.47	-0.01	0.24	0.17	-0.05, 0.40	0.13
Sex	0.90	0.47	-0.01	-0.01	-0.003	-0.23, 0.23	0.98
Concussion Mechanism				0.33	0.08	-0.15, 0.31	0.49
Near Point Convergence							
Mindfulness				-0.01	-0.04	-0.26, 0.18	0.72
Concussion Number	2.31	0.07	0.06	0.55	0.30	0.08, 0.52	0.01
Sex	2.31	0.07	0.00	-0.0007	-0.0001	-0.22, 0.22	0.99
Concussion Mechanism				0.80	0.14	-0.08, 0.36	0.19
Horizontal VOR							
Mindfulness				-0.02	-0.10	-0.32, 0.12	0.35
Concussion Number	2.96	0.02*	0.09	0.79	0.33	0.11, 0.54	0.003
Sex	2.90	0.02	0.09	-0.61	-0.07	-0.29, 0.15	0.52
Concussion Mechanism				1.00	0.14	-0.08, 0.36	0.21
Vertical VOR							
Mindfulness				-0.03	-0.15	-0.37, 0.07	0.17
Concussion Number	3.22	0.02*	(	0.76	0.31	0.09, 0.52	0.01
Sex	3.22	0.02	ι.	-0.54	-0.06	-0.28, 0.15	0.57
Concussion Mechanism				1.19	0.16	-0.05, 0.38	0.14
VMS							
Mindfulness	2.11	0.09	0.05	-0.02	-0.08	-0.30, 0.15	0.50
Concussion Number	2.11	0.09	0.05	0.70	0.24	0.02, 0.46	0.03

Sex				0.39	0.04	-0.18, 0.26	0.74
Concussion Mechanism				1.51	0.17	-0.05, 0.40	0.12
Exertion Tolerance (Step	Test)						
Number of Steps	,						
Mindfulness				-0.01	-0.02	-0.25, 0.21	0.84
Concussion Number	1.02	0.40	0.001	-1.01	-0.14	-0.37, 0.08	0.21
Sex	1.02	0.40	0.001	3.88	0.16	-0.07, 0.38	0.18
Concussion Mechanism				-2.50	-0.12	-0.35, 0.11	0.30
RPE							
Mindfulness				0.01	0.10	-0.13, 0.32	0.39
Concussion Number	2.01	0.10	0.05	0.09	0.08	-0.14, 0.30	0.46
Sex	2.01	0.10	0.05	0.84	0.22	-0.01, 0.44	0.06
Concussion Mechanism				0.62	0.19	-0.03, 0.41	0.09
*p<0.05							
<b>Abbreviations:</b> FFMQ=Fi	ive Facet Min	dfulness Questi	onnaire, 95%CI	=95% confiden	ce interval, RF	Q=Rivermead Pos	st-
Conquestion Questionnaire	DESS-Dolor	a Error Coorir	a System CON	I_aantar of mag	ANS-outon	-	om

Concussion Questionnaire, BESS=Balance Error Scoring System, COM=center of mass, ANS=autonomic nervous system, HRV=heart rate variability, HR=heart rate, LF/HF=low frequency/high frequency, VOMS=Vestibular/Ocular Motor Screening, VOR=vestibular/ocular reflex, VMS=visual motion sensitivity, RPE=rate of perceived exertion.

		Model			Parameter	· Estimates	
	F Value	p Value	Adjusted R <sup>2</sup>	β	Standardiz ed β	Standardiz ed 95%CI	p Value
<b>Concussion Symptoms</b>	s (RPQ)						
<b>Total Symptom Sever</b>	ity						
Interaction				0.002	0.09	-0.78, 0.97	0.83
Perceived Stress				0.43	0.23	-0.95, 1.41	0.69
Mindfulness				-0.12	-0.18	-0.75, 0.39	0.53
Concussion Number	6.33	< 0.001*	0.29	1.68	0.20	0.01, 0.40	0.04
Sex				5.59	0.19	-0.01, 0.38	0.05
Concussion Mechanism				-0.70	-0.03	-0.22, 0.16	0.77
Total Symptoms Wors	se Than Befor	e Injury					
Interaction				0.0004	0.05	-0.84, 0.94	0.91
Perceived Stress				0.23	0.33	-0.87, 1.52	0.59
Mindfulness				-0.02	-0.09	-0.66, 0.49	0.77
Concussion Number	5.85	< 0.001*	0.27	0.65	0.20	0.01, 0.40	0.04
Sex				1.13	0.18	-0.01, 0.38	0.06
Concussion Mechanism				0.11	0.01	-0.18, 0.21	0.91
<b>Balance Performance</b>	(BESS)						
Total Errors							
Interaction				0.009	1.38	0.39, 2.37	0.01*
Perceived Stress				-0.96	-1.68	-3.02, -0.35	0.01
Mindfulness				-0.15	-0.74	-1.38, -0.10	0.02
Concussion Number	2.26	0.05	0.09	0.18	0.07	-0.15, 0.29	0.53
Sex				-0.37	-0.04	-0.26, 0.18	0.71
Concussion				1.63	0.21	-0.01, 0.43	0.05
Mechanism	(0010)			1.00	··= 1		
Balance Performance							
Eyes Open Trial Ante Interaction	rior/Posterior 1.03	0.41	Acceleration 0.002	0.01	0.66	-0.38, 1.73	0.21
Interaction	1.05	0.41	0.002	0.01	0.00	-0.50, 1.75	0.21

Perceived Stress				-0.59	-1.03	-2.49, 0.39	0.15
Mindfulness				-0.12	-0.63	-1.32, 0.07	0.08
<b>Concussion Number</b>				0.53	0.21	-0.02, 0.44	0.08
Sex				-0.42	-0.05	-0.28, 0.19	0.70
Concussion				-0.31	-0.04	-0.27, 0.19	0.73
Mechanism				-0.51	-0.04		0.75
<b>Eyes Open Trial Medi</b>	al/Lateral Pla	ne SD of Acco	eleration				
Interaction				0.01	0.39	-0.64, 1.43	0.45
Perceived Stress				-0.84	-0.66	-2.09, 0.74	0.35
Mindfulness				-0.19	-0.43	-1.11, 0.25	0.22
Concussion Number	1.50	0.19	0.04	1.16	0.21	-0.02, 0.43	0.07
Sex				4.19	0.21	-0.02, 0.44	0.08
Concussion				0.54	0.02	-0.26, 0.20	0.70
Mechanism				-0.54	-0.03		0.78
Eyes Closed Trial Ante	erior/Posterio	or Plane SD of	Acceleration				
Interaction				0.01	0.67	-0.36, 1.70	0.20
Perceived Stress				-0.47	-1.00	-2.41, 0.39	0.16
Mindfulness				-0.10	-0.61	-1.28, 0.07	0.08
Concussion Number	1.71	0.13	0.05	0.58	0.28	0.05, 0.50	0.02
Sex				0.74	0.10	-0.13, 0.33	0.39
Concussion				-0.02	-0.01	-0.23, 0.22	0.98
Mechanism				-0.02	-0.01		0.98
Eyes Closed Trial Med	lial/Lateral P	lane SD of Ac	celeration				
Interaction				0.01	0.60	-0.41, 1.61	0.24
Perceived Stress				-1.01	-0.87	-2.26, 0.50	0.21
Mindfulness				-0.21	-0.52	-1.18, 0.15	0.13
Concussion Number	2.20	0.05	0.09	1.49	0.29	0.07, 0.51	0.01
Sex				3.53	0.19	-0.03, 0.42	0.09
Concussion				0.05	0.01	-0.22, 0.22	0.98
Mechanism				0100	0.01		0170
ANS Function (HRV)							
Seated 1 HR				0.000	0.10		0.51
Interaction				-0.003	-0.19	-1.23, 0.85	0.71
Perceived Stress	0.96	0.46	-0.003	0.83	0.47	-0.93, 1.87	0.51
Mindfulness				0.12	0.19	-0.48, 0.86	0.58

Concussion Number				0.04	0.01	-0.23, 0.24	0.96
Sex				4.66	0.16	-0.01, 0.39	0.16
Concussion				1.80	0.08	-0.15, 0.30	0.51
Mechanism				1.00	0.00		0.31
Seated 1 LF/HF Ratio							
Interaction				-0.003	-0.78	-1.83, 0.27	0.14
Perceived Stress				0.40	1.13	-0.29, 2.54	0.12
Mindfulness				0.05	0.38	-0.30, 1.06	0.27
<b>Concussion Number</b>	0.71	0.64	-0.02	-0.11	-0.07	-0.30, 0.17	0.57
Sex				-0.41	-0.07	-0.30, 0.16	0.53
Concussion				-0.13	-0.03	-0.26, 0.20	0.81
Mechanism				-0.15	-0.05		0.81
Standing HR							
Interaction				-0.002	-0.09	-1.14, 0.97	0.87
Perceived Stress				0.56	0.29	-1.13, 1.72	0.68
Mindfulness				0.12	0.18	-0.51, 0.86	0.61
Concussion Number	0.52	0.79	-0.04	-0.35	-0.04	-0.28, 0.19	0.73
Sex				2.90	0.09	-0.14, 0.33	0.42
Concussion				2.93	0.11	-0.12, 0.35	0.33
Mechanism				2.95	0.11		0.33
Standing LF/HF Ratio							
Interaction				0.002	0.20	-0.85, 1.26	0.70
Perceived Stress				-0.19	-0.19	-1.62, 1.23	0.79
Mindfulness				-0.0007	-0.002	-0.69, 0.68	0.99
Concussion Number	0.51	0.80	-0.04	0.06	0.01	-0.22, 0.25	0.90
Sex				-2.71	-0.17	-0.41, 0.06	0.14
Concussion				0.11	0.01	-0.22, 0.24	0.94
Mechanism				0.11	0.01		0.94
Seated 2 HR							
Interaction				-0.001	-0.06	-1.09, 0.97	0.91
Perceived Stress				0.57	0.31	-1.07, 1.70	0.65
Mindfulness	1.16	0.34	0.01	0.06	0.10	-0.57, 0.77	0.77
Concussion Number				-0.35	-0.04	-0.27, 0.19	0.71
Sex				5.47	0.19	-0.04, 0.42	0.10

Concussion				1.08	0.04	-0.18, 0.27	0.69
Mechanism				1.08	0.04		0.09
Seated 2 LF/HF Ratio							
Interaction				-0.0006	-0.22	-1.28, 0.85	0.69
Perceived Stress				0.11	0.41	-1.02, 1.85	0.57
Mindfulness				0.02	0.17	-0.52, 0.86	0.63
Concussion Number	0.33	0.92	-0.05	-0.12	-0.10	-0.34, 0.13	0.39
Sex				-0.37	-0.09	-0.32, 0.15	0.47
Concussion				-0.18	-0.05	-0.28, 0.19	0.68
Mechanism				-0.18	-0.05		0.08
Vestibular/Ocular Fun	ction (VOMS	5)					
<b>Smooth Pursuits</b>							
Interaction				-0.0004	-0.24	-1.26, 0.78	0.64
Perceived Stress				0.04	0.24	-1.14, 1.61	0.73
Mindfulness				-0.002	-0.04	-0.70, 0.62	0.91
Concussion Number	1.47	0.20	0.03	0.19	0.27	0.04, 0.50	0.02
Sex				-0.37	-0.15	-0.37, 0.08	0.20
Concussion				-0.11	-0.05	-0.27, 0.17	0.66
Mechanism				-0.11	-0.03		0.00
<b>Horizontal Saccades</b>							
Interaction				-0.001	-0.34	-1.14, 0.69	0.51
Perceived Stress				0.10	0.33	-1.05, 1.72	0.63
Mindfulness				0.004	0.04	-0.63, 0.70	0.91
Concussion Number	1.19	0.32	0.01	0.36	0.27	0.03, 0.49	0.02
Sex				-0.29	-0.06	-0.29, 0.17	0.60
Concussion				0.31	0.08	-0.15, 0.30	0.50
Mechanism				0.31	0.08		0.30
Vertical Saccades							
Interaction				-0.001	-0.36	-1.40, 0.69	0.50
Perceived Stress				0.13	0.43	-0.99, 1.84	0.55
Mindfulness				0.01	0.09	-0.60, 0.77	0.80
Concussion Number	0.67	0.67	-0.03	0.23	0.17	-0.06, 0.40	0.15
Sex				-0.01	-0.001	-0.23, 0.23	0.99
Concussion Mechanism				0.35	0.08	-0.15, 0.32	0.47

Near Point Convergen	ce						
Interaction				-0.001	-0.24	-1.25, 0.78	0.64
Perceived Stress				0.12	0.28	-1.09, 1.65	0.68
Mindfulness				0.01	0.07	-0.58, 0.73	0.82
Concussion Number	1.55	0.18	0.04	0.55	0.30	0.07, 0.52	0.01
Sex				0.01	0.001	-0.22, 0.23	0.99
Concussion				0.81	0.15	-0.08, 0.37	0.19
Mechanism				0.01	0.15		0.19
Horizontal VOR							
Interaction				-0.0006	-0.10	-1.10, 0.89	0.83
Perceived Stress				0.02	0.04	-1.31, 1.39	0.96
Mindfulness				-0.02	-0.11	-0.76, 0.53	0.73
Concussion Number	2.00	0.08	0.07	0.82	0.34	0.12, 0.56	0.004
Sex				-0.57	-0.07	-0.29, 0.16	0.56
Concussion				1.01	0.14	-0.08, 0.36	0.21
Mechanism				1.01	0.14		0.21
Vertical VOR							
Interaction				-0.002	-0.27	-1.26, 0.73	0.59
Perceived Stress				0.18	0.33	-1.01, 1.67	0.62
Mindfulness				-0.003	-0.01	-0.66, 0.63	0.96
Concussion Number	2.15	0.06	0.08	0.75	0.30	0.08, 0.53	0.01
Sex				-0.53	-0.06	-0.28, 0.16	0.58
Concussion				1.21	0.16	-0.05, 0.38	0.14
Mechanism				1.21	0.10		0.14
VMS							
Interaction				-0.001	-0.21	-1.23, 0.81	0.68
Perceived Stress				0.17	0.27	-1.11, 1.64	0.70
Mindfulness				0.008	0.04	-0.63, 0.70	0.91
Concussion Number	1.40	0.23	0.03	0.69	0.24	0.01, 0.47	0.04
Sex				0.39	0.04	-0.19, 0.26	0.74
Concussion				1.53	0.18	-0.05, 0.40	0.12
Mechanism				1.33	0.10		0.12
Exertion Tolerance (St	tep Test)						
Number of Steps		_	_		_		_
Interaction	1.05	0.40	0.003		-0.76	-1.79, 0.28	0.15

Perceived Stress				1.50	0.97	-0.43, 2.36	0.17
Mindfulness				0.21	0.39	-0.29, 1.06	0.26
Concussion Number				-1.09	-0.16	-0.39, 0.08	0.18
Sex				3.91	0.16	-0.07, 0.39	0.18
Concussion				-2.30	-0.11	-0.34, 0.12	0.34
Mechanism							
RPE							
Interaction				-0.001	-0.42	-1.43, 0.58	0.40
Perceived Stress				0.01	0.30	-1.05, 1.66	0.66
Mindfulness				0.01	0.16	-0.50, 0.81	0.64
<b>Concussion Number</b>	1.88	0.10	0.06	0.12	0.11	-0.11, 0.33	0.33
Sex				0.89	0.23	0.01, 0.45	0.04
Concussion Mechanism				0.64	0.20	-0.02, 0.42	0.08

\*p<0.05

**Abbreviations:** PSS=Perceived Stress Scale, FFMQ=Five Facet Mindfulness Questionnaire, 95%CI=95% confidence interval, RPQ=Rivermead Post-Concussion Questionnaire, BESS=Balance Error Scoring System, COM=center of mass, ANS=autonomic nervous system, HRV=heart rate variability, HR=heart rate, LF/HF=low frequency/high frequency, VOMS=Vestibular/Ocular Motor Screening, VOR=vestibular/ocular reflex, VMS=visual motion sensitivity, RPE=rate of perceived exertion.

	ission outcomes. Model			Parameter Estimates				
	F Value	p Value	Adjusted R <sup>2</sup>	β	Standardize dβ	Standardize d 95%CI	p Value	
Neurocognitive Perform	ance (CNS Vi	tal Signs)						
Verbal Memory								
Perceived Stress				-0.43	-0.20	-0.43, 0.03	0.09	
Concussion Number	0.97	0.69	-0.02	-0.57	-0.06	-0.29, 0.17	0.61	
Sex	0.97			-0.89	-0.03	-0.25, 0.20	0.82	
Concussion Mechanism				0.50	0.02	-0.21, 0.24	0.88	
Visual Memory								
Perceived Stress				0.32	0.15	-0.08, 0.38	0.20	
Concussion Number	1.64	0.17	0.03	-0.44	-0.05	-0.27, 0.18	0.69	
Sex	1.04			-8.93	-0.26	-0.49, -0.04	0.02	
Concussion Mechanism				-0.86	-0.03	-0.25, 0.19	0.79	
Psychomotor Speed								
Perceived Stress				-0.37	-0.20	-0.42, 0.03	0.09	
Concussion Number	1.69	0.16	0.03	0.81	0.10	-0.13, 0.32	0.40	
Sex	1.09			-5.54	-0.18	-0.41, 0.04	0.11	
Concussion Mechanism				0.31	0.01	-0.21, 0.24	0.91	
Cognitive Flexibility								
Perceived Stress	0.81	0.52	-0.01	-0.22	-0.09	-0.32, 0.15	0.47	
Concussion Number				1.54	0.13	-0.11, 0.36	0.28	
Sex				-6.22	-0.15	-0.38, 0.09	0.21	
Concussion Mechanism				-0.38	-0.01	-0.24, 0.22	0.93	
Complex Attention								
Perceived Stress				-0.21	-0.09	-0.32, 0.15	0.46	
Concussion Number	1.10	0.36	0.01	1.84	0.17	-0.08, 0.41	0.18	
Sex				-4.88	-0.13	-0.36, 0.11	0.29	
Concussion Mechanism				5.06	0.16	-0.08, 0.39	0.19	
Processing Speed								
Perceived Stress				-0.39	-0.20	-0.43, 0.04	0.10	
Concussion Number	0.88	0.48	-0.01	1.10	0.12	-0.11, 0.35	0.29	
Sex				1.62	0.05	-0.18, 0.28	0.66	
Concussion Mechanism				0.41	0.02	-0.21, 0.24	0.90	

Reaction Time							
Perceived Stress				-0.17	-0.08	-0.31, 0.15	0.48
Concussion Number	1.34		0.01	-0.02	-0.01	-0.23, 0.23	0.98
Sex		0.26		-1.56	-0.05	-0.28, 0.18	0.67
<b>Concussion Mechanism</b>				-6.20	-0.23	-0.46, -0.01	0.05
<b>Executive Function</b>						,	
Perceived Stress				-0.19	-0.07	-0.31, 0.16	0.51
Concussion Number	0.50	0.69	0.02	1.36	0.12	-0.11, 0.35	0.31
Sex	0.58	0.68	-0.02	-4.10	-0.10	-0.33, 0.13	0.39
Concussion Mechanism				-0.93	-0.03	-0.26, 0.20	0.81
<b>Psychological Distress (B</b>	SI-18)						
BSI-18 Total	· · · · · · · · · · · · · · · · · · ·						
Perceived Stress				0.83	0.59	0.41, 0.77	< 0.001*
Concussion Number	14.07	-0.001*	0.40	0.62	0.10	-0.08, 0.27	0.28
Sex	14.07	<0.001*	0.40	3.08	0.14	-0.04, 0.31	0.13
Concussion Mechanism				0.50	0.03	-0.15, 0.20	0.76
QOL (PROMIS-29)							
Physical Function							
Perceived Stress				-0.18	-0.30	-0.51, -0.08	0.01*
Concussion Number	3.60	0.01*	0.12	-0.44	-0.16	-0.37, 0.05	0.14
Sex	5.00	0.01*	0.12	-1.28	-0.13	-0.34, 0.09	0.23
Concussion Mechanism				0.07	0.01	-0.20, 0.22	0.94
Anxiety							
Perceived Stress				0.98	0.71	0.55, 0.87	< 0.001*
Concussion Number	22.68	<0.001*	0.52	0.40	0.06	-0.09, 0.22	0.41
Sex				2.30	0.10	-0.05, 0.26	0.20
Concussion Mechanism				-1.67	-0.09	-0.25, 0.07	0.26
Depression							
Perceived Stress				0.90	0.64	0.46, 0.82	< 0.001*
Concussion Number	15.14	<0.001*	0.42	-0.15	-0.02	-0.20, 0.15	0.79
Sex				3.05	0.14	-0.04, 0.31	0.13
Concussion Mechanism				-0.42	-0.02	-0.20, 0.15	0.80
Fatigue							
Perceived Stress				0.66	0.51	0.31, 0.70	< 0.001*
Concussion Number	8.14	< 0.001*	0.27	-0.20	-0.03	-0.23, 0.16	0.73
Sex				3.15	0.15	-0.04, 0.35	0.12

Concussion Mechanism				-0.45	-0.03	-0.22, 0.17	0.79
Sleep Disturbance							
Perceived Stress				-0.02	-0.04	-0.27, 0.20	0.76
Concussion Number	0.56	0.70	-0.02	-0.21	-0.10	-0.33, 0.13	0.41
Sex	0.30	0.70	-0.02	-0.45	-0.06	-0.29, 0.17	0.62
Concussion Mechanism				-0.70	-0.11	-0.33, 0.12	0.36
Social Participation							
Perceived Stress				-0.70	-0.60	-0.79, -0.42	< 0.001*
Concussion Number	12.37	< 0.001*	0.37	0.13	0.02	-0.16, 0.21	0.79
Sex	12.57	<0.001	<0.001 0.37	-0.40	-0.02	-0.20, 0.16	0.82
Concussion Mechanism				-1.97	-0.13	-0.31, 0.05	0.17
Pain Interference							
Perceived Stress				0.34	0.32	0.11, 0.54	0.01*
Concussion Number	4.04	0.01*	0.13	0.61	0.13	-0.08, 0.34	0.23
Sex	4.04	0.01	0.15	1.33	0.08	-0.13, 0.29	0.47
Concussion Mechanism				1.92	0.13	-0.08, 0.35	0.21
Pain Intensity							
Perceived Stress				0.09	0.32	0.11, 0.54	0.01*
Concussion Number	3.85	0.01*	0.13	0.12	0.10	-0.11, 0.31	0.35
Sex	5.85	0.01*	0.15	0.56	0.13	-0.09, 0.34	0.25
Concussion Mechanism				0.33	0.09	-0.12, 0.30	0.40
*p value<0.05							
Abbreviations: PSS=Perce	eived Stress S	Scale, BSI=Brief	Symptom Inve	ntory, PROMIS	=Patient Repo	orted Outcomes M	easurement
Information System.				-			

		Model			Parameter	• Estimates	
-	F Value	p Value	Adjusted R <sup>2</sup>	β	Standardize dβ	Standardize d 95%CI	p Value
Neurocognitive Performa	ance (CNS Vita	al Signs)			•		
Verbal Memory							
Mindfulness				0.10	0.14	-0.10, 0.37	0.25
Concussion Number	0.57	0.69	-0.02	-0.84	-0.09	-0.31, 0.14	0.45
Sex	0.37	0.69	-0.02	-1.23	-0.04	-0.27, 0.19	0.76
Concussion Mechanism				0.48	0.02	-0.21, 0.25	0.89
Visual Memory							
Mindfulness				-0.01	-0.02	-0.24, 0.21	0.89
Concussion Number	1 10	0.22	0.01	-0.21	-0.02	-0.25, 0.20	0.85
Sex	1.19	0.32		-8.27	-0.24	-0.47, -0.01	0.04
Concussion Mechanism				-0.51	-0.02	-0.24, 0.21	0.88
Psychomotor Speed							
Mindfulness				0.11	0.17	-0.06, 0.40	0.14
Concussion Number	1.40	0.21	0.01	0.95	0.07	-0.15, 0.29	0.55
Sex	1.49	0.21	0.21	-5.67	-0.19	-0.41, 0.04	0.10
Concussion Mechanism				0.47	0.02	-0.21, 0.24	0.87
Cognitive Flexibility							
Mindfulness				0.10	0.11	-0.12, 0.34	0.34
Concussion Number	0.02	0.46	0.01	1.38	0.12	-0.11, 0.35	0.32
Sex	0.92	0.46	-0.01	-6.02	-0.14	-0.37, 0.09	0.23
Concussion Mechanism				-0.13	-0.01	-0.24, 0.23	0.98
Complex Attention							
Mindfulness				0.08	0.09	-0.14, 0.33	0.44
Concussion Number	1.10	0.26	0.01	1.68	0.15	-0.09, 0.40	0.20
Sex	1.12	0.36	0.01	-4.86	-0.13	-0.36, 0.11	0.30
Concussion Mechanism				5.11	0.16	-0.08, 0.40	0.19
Processing Speed							
Mindfulness				0.09	0.12	-0.11, 0.36	0.30
Concussion Number	0.45	0.70	0.02	0.84	0.09	-0.13, 0.32	0.42
Sex	0.45	0.78	-0.03	1.26	0.04	-0.19, 0.27	0.74
Concussion Mechanism				0.35	0.01	-0.22, 0.24	0.91

Reaction Time							
Mindfulness				0.11	0.15	-0.08, 0.38	0.19
Concussion Number		o 4 <b>-</b>	0.02	-0.12	-0.01	-0.24, 0.21	0.91
Sex	1.67	0.17	0.03	-1.25	-0.04	-0.26, 0.19	0.73
Concussion Mechanism				-5.83	-0.22	-0.44, 0.01	0.06
<b>Executive Function</b>						,	
Mindfulness				0.11	0.13	-0.10, 0.36	0.27
Concussion Number	0.70	0.54	0.01	1.25	0.11	-0.12, 0.34	0.34
Sex	0.79	0.54	-0.01	-3.80	-0.09	-0.32, 0.14	0.42
<b>Concussion Mechanism</b>				-0.64	-0.02	-0.25, 0.21	0.87
<b>Psychological Distress (BS</b>	SI-18)						
BSI-18 Total							
Mindfulness				-0.23	-0.46	-0.65, -0.26	< 0.001*
Concussion Number	0.07	.0.001*	0.04	1.14	0.18	-0.01, 0.37	0.07
Sex	8.06	<0.001*	0.26	2.22	0.16	-0.04, 0.35	0.11
Concussion Mechanism				1.85	0.02	-0.17, 0.22	0.83
QOL (PROMIS-29)							
Physical Function							
Mindfulness				0.06	0.26	0.05, 0.48	0.02*
Concussion Number	3.18	0.02*	0.10	-0.55	-0.20	-0.41, 0.01	0.07
Sex	3.18	0.02*	0.10	-1.34	-0.14	-0.35, 0.08	0.22
Concussion Mechanism				0.13	0.02	-0.20, 0.23	0.88
Anxiety							
Mindfulness				-0.30	-0.61	-0.79, 0.43	< 0.001*
Concussion Number	14.43	< 0.001*	0.40	1.01	0.16	-0.01, 0.34	0.07
Sex	14.45	<0.001	0.40	2.70	0.12	-0.05, 0.30	0.17
Concussion Mechanism				-1.95	-0.10	-0.28, 0.07	0.24
Depression							
Mindfulness				-0.25	-0.51	-0.71, 0.32	< 0.001*
Concussion Number	8.70	< 0.001	0.28	0.41	0.07	-0.13, 0.26	0.50
Sex	0.70	<0.001	0.28	3.53	0.16	-0.04, 0.35	0.11
Concussion Mechanism				-0.58	-0.03	-0.22, 0.16	0.75
Fatigue							
Mindfulness				-0.16	-0.35	-0.56, -0.13	0.001*
Concussion Number	3.87	0.01*	0.13	0.22	0.04	-0.17, 0.25	0.71
Sex				3.68	0.18	-0.03, 0.39	0.10

Concussion Mechanism				-0.42	-0.02	-0.24, 0.19	0.82
Sleep Disturbance							
Mindfulness				-0.01	-0.04	-0.27, 0.19	0.72
Concussion Number	0.56	0.69	-0.02	-0.23	-0.10	-0.33, 0.12	0.37
Sex	0.50	0.09	-0.02	-0.54	-0.07	-0.30, 0.16	0.56
Concussion Mechanism				-0.76	-0.11	-0.34, 0.12	0.32
Social Participation							
Mindfulness				0.21	0.53	0.33, 0.72	< 0.001*
Concussion Number	8.87	< 0.001*	0.29	-0.30	-0.06	-0.25, 0.13	0.55
Sex	0.07	<0.001		-0.67	-0.04	-0.23, 0.16	0.71
Concussion Mechanism			-1.76	-0.11	-0.31, 0.08	0.25	
Pain Interference							
Mindfulness				-0.08	-0.22	-0.44, 0.01	0.05
Concussion Number	2.69	0.04*	0.08	0.83	0.18	-0.04, 0.39	0.11
Sex	2.09	0.04	0.08	1.60	0.09	-0.13, 0.31	0.40
Concussion Mechanism				1.92	0.13	-0.09, 0.35	0.23
Pain Intensity							
Mindfulness				-0.02	-0.23	-0.45, -0.01	0.04*
Concussion Number	2.67	0.04*	0.08	0.18	0.15	-0.07, 0.36	0.18
Sex	2.07	0.04	0.08	0.62	0.14	-0.08, 0.36	0.21
Concussion Mechanism				0.33	0.09	-0.13, 0.31	0.42
*p value<0.05							
Abbreviations: FFMQ=Fiv	ve Facet Mind	dfulness Question	naire, BSI=Brie	ef Symptom Inve	entory, PROM	IS=Patient Report	ed Outcomes
Measurement Information S	System.					_	

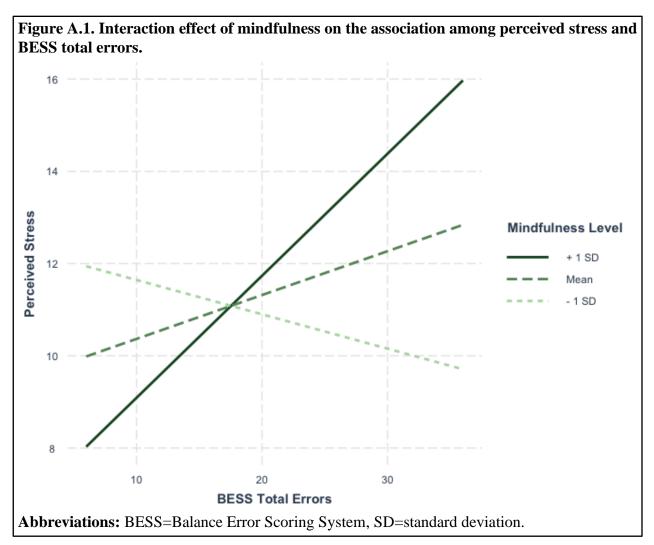
Table A.18. Separate multivariable linear regression models determining the moderation effect of mindfulness on perceived
stress by estimating the association among the interaction of perceived stress (PSS-10 total) and mindfulness (FFMQ total)
with psychological concussion outcomes.

		Model		Parameter Estimates					
-	F Value	p Value	Adjusted R <sup>2</sup>	β	Standardize dβ	Standardize d 95%CI	p Value		
Neurocognitive Performa	ance (CNS Vit	al Signs)			•				
Verbal Memory									
Interaction				-0.01	-0.10	-1.15, 0.95	0.85		
Perceived Stress				-0.17	-0.08	-1.50, 1.34	0.91		
Mindfulness	0.64	0.70	-0.03	0.03	0.04	-0.64, 0.72	0.90		
Concussion Number	0.04	0.70	-0.03	-0.58	-0.06	-0.29, 0.17	0.61		
Sex				-0.91	-0.03	-0.26, 0.21	0.82		
Concussion Mechanism				0.51	0.02	-0.21, 0.25	0.88		
Visual Memory									
Interaction			0.05	-0.02	-0.72	-1.73, 0.29	0.16		
Perceived Stress				2.62	1.23	-0.13, 2.59	0.08		
Mindfulness	1 (0	0.14		0.45	0.60	-0.06, 1.25	0.07		
Concussion Number	1.68	0.14		-0.74	-0.08	-0.30, 0.15	0.50		
Sex				-8.72	-0.25	-0.48, -0.03	0.03		
Concussion Mechanism				-0.23	-0.01	-0.23, 0.21	0.94		
Psychomotor Speed									
Interaction				-0.01	-0.51	-1.54, 0.52	0.33		
Perceived Stress				0.96	0.51	-0.88, 1.89	0.47		
Mindfulness	1.20	0.27	0.02	0.23	0.34	-0.32, 1.01	0.31		
Concussion Number	1.30	0.27	0.02	0.68	0.08	-0.15, 0.31	0.49		
Sex				-5.50	-0.18	-0.41, 0.05	0.12		
Concussion Mechanism				0.55	0.02	-0.21, 0.25	0.85		
Cognitive Flexibility									
Interaction				-0.01	-0.33	-1.40, 0.74	0.54		
Perceived Stress				1.12	0.43	-1.01, 1.85	0.56		
Mindfulness	0.66	0.60	0.02	0.27	0.30	-0.39, 0.98	0.40		
Concussion Number	0.66	0.68	-0.03	1.34	0.11	-0.13, 0.35	0.35		
Sex				-6.08	-0.14	-0.38, 0.09	0.23		
Concussion Mechanism				-0.01	-0.0004	-0.24, 0.24	0.99		
Complex Attention									

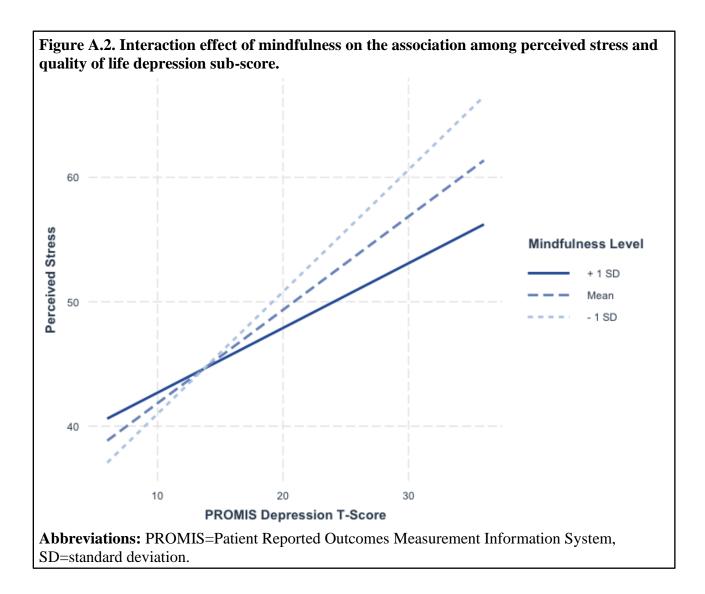
Interaction				0.00	0.00	1 72 0 11	0.00
				-0.02	-0.68	-1.73, 0.41	0.22
Perceived Stress				1.97	0.84	-0.62, 2.25	0.26
Mindfulness	1.00	0.43	0.0004	0.36	0.43	-0.27, 1.12	0.22
Concussion Number				1.70	0.15	-0.09, 0.41	0.22
Sex				-5.11	-0.13	-0.37, 0.11	0.27
Concussion Mechanism				5.42	0.17	-0.07, 0.41	0.17
Processing Speed							
Interaction				-0.01	-0.49	-1.54, 0.56	0.35
Perceived Stress				0.84	0.42	-0.99, 1.83	0.55
Mindfulness	0.73	0.63	-0.02	0.17	0.24	-0.44, 0.92	0.48
Concussion Number	0.75	0.05	-0.02	1.03	0.11	-0.12, 0.35	0.33
Sex				1.58	0.05	-0.18, 0.28	0.67
Concussion Mechanism				0.51	0.02	-0.21, 0.25	0.87
Reaction Time							
Interaction				-0.00004	-0.002	-1.33, 1.47	0.99
Perceived Stress				0.14	0.07	-1.33, 1.47	0.92
Mindfulness	1.11	0.36	0.01	0.14	0.20	-0.47, 0.87	0.56
Concussion Number	1.11	0.30		-0.21	-0.02	-0.26, 0.21	0.84
Sex				-1.33	-0.04	-0.27, 0.19	0.72
Concussion Mechanism				-5.80	-0.21	-0.44, 0.02	0.07
Executive Function							
Interaction				-0.01	-0.32	-1.38, 0.74	0.55
Perceived Stress				1.15	0.46	-0.97, 1.88	0.53
Mindfulness	0.50	074	0.02	0.30	0.34	-0.35, 1.02	0.33
Concussion Number	0.58	0.74	-0.03	1.12	0.10	-0.14, 0.34	0.41
Sex				-3.88	-0.10	-0.34, 0.14	0.42
Concussion Mechanism				-0.48	-0.01	-0.25, 0.22	0.90
<b>Psychological Distress (BSI-</b>	18)					,	
BSI-18 Total	,						
Interaction				-0.01	-0.39	-1.20, 0.41	0.34
Perceived Stress				1.48	1.05	-0.04, 2.13	0.06
Mindfulness	0.40	00011	0.00	0.07	0.15	-0.37, 0.68	0.57
Concussion Number	9.49	<.0001*	0.39	0.60	0.10	-0.08, 0.28	0.29
Sex				3.03	0.13	-0.04, 0.31	0.14
Concussion Mechanism				0.51	0.03	-0.15, 0.21	0.76
QOL (PROMIS-29)				0.01	0.02	0.10, 0.21	0.70

Physical Function				0.0003	0.05	-0.93, 1.03	0.92
Perceived Stress				-0.17	-0.28	-0.93, 1.03	0.92 0.67
Mindfulness				0.02	0.08	-0.56, 0.72	0.80
Concussion Number	2.43	0.03*	0.10	-0.47	-0.17	-0.39, 0.05	0.80
Sex				-1.24	-0.17	-0.39, 0.03	0.13
Sex Concussion Mechanism				0.12	-0.13	-0.20, 0.23	0.23
Anxiety				0.12	0.01	-0.20, 0.23	0.09
Interaction				0.005	0.30	-0.40, 1.01	0.39
Perceived Stress				0.005	0.30	-0.40, 1.01	0.39
Mindfulness				-0.19	-0.39	-0.85, 0.07	0.70
Concussion Number	16.36	< 0.001*	0.54	0.56	-0.39		0.09 0.26
Concussion Number Sex				2.15	0.09	-0.07, 0.25 -0.06, 0.25	0.26 0.22
Sex Concussion Mechanism				-2.01	-0.11	· ·	0.22 0.17
				-2.01	-0.11	-0.26, 0.05	0.17
<b>Depression</b> Interaction				-0.01	-0.78	-1.55, -0.01	0.05
Perceived Stress				-0.01 2.21	-0.78 1.57	0.52, 2.62	0.05
	11.31						
Mindfulness		< 0.001*	0.44	0.16	0.32	-0.18, 0.82	0.21 0.74
Concussion Number				-0.18	-0.03	-0.20, 0.14	
Sex · · · · ·				2.96	0.13	-0.04, 0.30	0.13
Concussion Mechanism				-0.37	-0.02	-0.19, 0.15	0.82
Fatigue				0.000	0.10	1 05 0 50	0.70
Interaction				-0.002	-0.18	-1.07, 0.72	0.70
Perceived Stress				0.99	0.77	-0.44, 1.99	0.21
Mindfulness	5.34	< 0.001*	0.25	0.06	0.14	-0.44, 0.73	0.63
Concussion Number				-0.24	-0.04	-0.24, 0.16	0.68
Sex				3.17	0.15	-0.04, 0.35	0.13
Concussion Mechanism				-0.37	-0.02	-0.22, 0.18	0.83
Sleep Disturbance				0.001	0.00	0.70 1.00	0.60
Interaction				0.001	0.28	-0.78, 1.33	0.60
Perceived Stress				-0.25	-0.50	-1.93, 0.92	0.49
Mindfulness	0.53	0.79	-0.04	-0.05	-0.30	-0.98, 0.39	0.39
Concussion Number	0.00	0.17	0.01	-0.17	-0.08	-0.31, 0.16	0.51
Sex				-0.49	-0.06	-0.29, 0.17	0.60
Concussion Mechanism				-0.78	-0.12	-0.35, 0.11	0.31

Interaction				-0.002	-0.22	-1.04, 0.60	0.60
Perceived Stress				-0.20	-0.22	-1.28, 0.94	0.00
Mindfulness				0.13	0.32	-0.21, 0.86	0.70
Concussion Number	8.73	< 0.001*	0.37	0.01	0.003	-0.18, 0.19	0.23
						· ·	0.98
Sex				-0.28	-0.02	-0.20, 0.17	
Concussion Mechanism				-1.72	-0.11	-0.29, 0.07	0.23
Pain Interference							
Interaction				-0.003	-0.23	-1.21, 0.75	0.64
Perceived Stress			0.11	0.68	0.64	-0.68, 1.96	0.34
Mindfulness	0.77	0.00*		0.06	0.15	-0.48, 0.79	0.63
Concussion Number	2.67	0.02*		0.58	0.12	-0.10, 0.34	0.27
Sex				1.34	0.08	-0.14, 0.29	0.47
Concussion Mechanism				1.99	0.14	-0.08, 0.36	0.20
Pain Intensity							
Interaction				-0.0003	-0.10	-1.08, 0.88	0.84
Perceived Stress				0.12	0.45	-0.88, 1.77	0.50
Mindfulness	0.51	0.02*	0.10	0.005	0.05	-0.58, 0.69	0.87
Concussion Number	2.51	0.03*	0.10	0.12	0.10	-0.12, 0.32	0.37
Sex				0.56	0.13	-0.09, 0.34	0.25
Concussion Mechanism				0.34	0.09	-0.13, 0.31	0.40
*p value<0.05						,	
Abbreviations: PSS=Perce	eived Stress S	cale. FFMO=Fiv	e Facet Mindf	ulness Ouestionn	aire, BSI=Bri	ief Symptom Inven	torv.
PROMIS=Patient Reported				-			
i iconino-i anoni icopolice		icustitement mitor	mation byster	11.			



**APPENDIX 26: AIMS 1 AND 2 MODERATION GRAPHS** 



3 study sample (n=	Mean	SD	95%CI	Min	Max	Median	1Q	3Q
General Demograph	hics							
Age (Years)	20.46	3.62	18.27, 22.65	10.00	25.00	21.00	20.00	22.00
Height (Inches)	68.71	3.87	66.48, 70.95	62.00	74.00	68.50	66.00	73.00
Weight (Pounds)	170.43	49.35	141.93, 198.92	128.0 0	325.00	157.50	140.0 0	180.00
Concussion History	/							
Concussion Number	2.93	1.44	2.10, 3.76	1.00	5.00	3.00	2.00	4.00
Time Since Most Recent Concussion (Months)	17.21	18.28	6.66, 27.77	1.00	54.00	7.50	5.00	36.00
COVID-19 History COVID-19 Number	1.25	0.46	0.86, 1.64	1.00	2.00	1.00	1.00	1.50
COVID-19 Symptoms (Days)	6.38	4.07	2.97, 9.78	2.00	15.00	5.00	4.00	8.00
Time Since COVID-19 (Days)	262.88	184.28	108.81, 416.94	148.0 0	715.00	208.50	190.5 0	221.00
Sleep								
Average Hours of Sleep	6.57	0.94	6.03, 7.11	5.00	8.00	7.00	6.00	7.00
Caffeine Consumpt	tion							
Average Cups of Caffeine Per Day	1.00	1.04	0.40, 1.60	0.00	3.00	1.00	0.00	2.00
Alcohol Consumpti	ion							
Average Drinks Consumed Per Day	1.00	1.04	0.40, 1.60	0.00	3.00	1.00	0.00	2.00
Physical Activity Days/Week of Vigorous Physical Activity	2.50	1.83	1.44, 3.56	0.00	5.00	3.00	0.00	4.00

## **APPENDIX 27: AIM 3 SUPPLEMENTARY TABLES**

Time/Day in Vigorous Physical Activity (Minutes)	69.23	44.98	39.01, 99.45	0.00	150.00	65.00	45.00	90.00
Days/Week of Moderate Physical Activity	4.36	1.78	3.33, 5.39	2.00	7.00	5.00	2.00	6.00
Time/Day in Moderate Physical Activity (Minutes)	61.93	40.66	38.45, 85.40	2.00	150.00	52.50	40.00	60.00
Menstrual Cycle <sup>b</sup>								
Time Since Last Menstrual Cycle (Days)	52.50	39.88	19.16, 85.84	15.00	104.00	38.50	17.00	95.00
<sup>a</sup> COVID-19 inform	ation self-	-reported	for those w	who indic	ated yes at	t receiving	g a COVI	D-19
diagnosis (n=8). <sup>b</sup> Menstrual cycle in cycle (n=9).	formation	self-repo	orted for the	ose who	indicated y	yes at hav	ing a men	strual

Frequency Percent
3 21.43
2 14.29
5 35.71
1 7.14
3 21.43
8 57.14
6 42.86
9 64.29
5 35.71
13 92.86
1 7.14
9 64.29
5 35.71
1 7.14
6 42.86
2 14.29
3 21.43
2 14.29
1 7.14
13 92.86
1 7.14
4 28.57
10 71.43
10 /1.75
1 10.00
5 50.00
3 30.00
1 10.00
8 42.86
8 6 or those who

Table A.21. Complete mental health h	istory for the Aim 3 Frequency	study sample (n=14). Percent
Experience Any Mental Health-Related		
Yes	12	85.71
No	2	14.29
Mental Health-Related Symptoms Report		
Anxiety	59	90.77
ADD/ADHD	20	30.77
Autism	0	0.00
Bipolar	3	4.62
Communication Disorder	0	0.00
Depression	40	61.54
Eating Disorder	15	23.08
OCD	10	15.38
Panic Disorder	4	6.15
Personality Disorder	2	3.08
PTSD	14	21.54
Schizophrenia	0	0.00
Other	2	3.08
Mental Health-Related Diagnosis		
Yes	6	42.86
No	8	57.14
Mental Health Diagnoses Reported <sup>b</sup>		
Anxiety	4	66.67
ADD/ADHD	1	16.67
Depression	3	50.00
Eating Disorder	2	33.33
PTSD	1	16.67
Mental Health Symptoms Worsen After	Concussion <sup>c</sup>	
Yes	6	50.00
No	6	50.00
Specific Mental Health Symptoms Wors	en After Concussion	
Anxiety	2	33.33
ADD/ADHD	1	16.67
Depression	4	66.67
Eating Disorder	1	16.67
OCD	1	16.67
Other	1	16.67
Receive Mental Health Treatment <sup>e</sup>		
Yes	6	50.00
No	6	50.00
Mental Health Treatment Providers <sup>f</sup>		
Therapist	3	50.00
Counselor	1	16.67
Psychiatrist	4	66.67
Sports Psychologist	1	16.67

Other	1	16.67
Mental Health Treatment Types <sup>f</sup>		
Cognitive Behavioral	2	33.33
Therapy	_	
Mindfulness-Based Cognitive	1	16.67
Therapy	-	10107
Positive Psychology	1	16.67
Medication(s)	3	50.00
Unknown	1	16.67
Other	1	16.67

<sup>a</sup>Mental health-related symptoms only asked to those who responded yes to experiencing mental health-related symptoms (n=12). Question was a choose all that apply.

<sup>b</sup>Mental health-related diagnoses only asked to those who responded yes to experiencing a mental health-related diagnosis (n=6). Question was a choose all that apply.

<sup>c</sup>Worsening symptoms post-concussion only asked to those who indicated they had experienced mental health-related symptoms (n=12).

<sup>d</sup>Specific mental health symptoms worsening post-concussion only asked to those who responded yes to having worsening symptoms post-concussion (n=6). Question was a choose all that apply.

<sup>e</sup>Mental health treatment (yes/no) question only asked to those who indicated they had experienced mental health-related symptoms (n=12).

<sup>f</sup>Mental health treatment providers and types were only asked to those who responded yes to receiving mental health treatment (n=6). Question was a choose all that apply.

Table A22. Co (n=12).	omprehens	sive descr	riptive data	on the m	indfulnes	ss intervent	tion outco	omes
Timepoint	Mean	SD	95%CI	Min	Max	Median	1Q	3Q
<b>RPQ</b> Concuss	sion Sympt	tom Seve	rity					
Baseline	24.50	17.18	13.58, 35.42	2.00	57.00	27.50	9.50	34.00
Week 1	20.75	15.50	10.90, 30.60	4.00	54.00	20.00	6.00	29.50
Week 2	17.00	12.29	9.19, 24.81	0.00	47.00	16.50	8.50	22.50
Week 3	14.33	11.58	6.78, 21.69	0.00	42.00	14.50	5.00	20.00
Week 4	14.50	11.31	7.31, 21.69	4.00	46.00	10.50	7.50	18.00
Week 5	14.50	10.31	7.95, 21.05	1.00	40.00	13.00	7.50	18.50
Follow Up (Week 6)	11.33	10.26	4.81, 17.85	1.00	38.00	8.00	5.00	15.50
<b>RPQ</b> Concuss	sion Sympt	toms Wo	rse Than B	efore Inju	ıry			
Baseline	8.00	5.72	4.37, 11.63	0.00	18.00	8.50	3.50	12.00
Week 1	6.33	6.07	2.48, 10.19	0.00	18.00	5.50	1.00	10.50
Week 2	5.08	5.07	1.86, 8.31	0.00	17.00	3.50	1.50	8.00
Week 3	3.33	4.19	0.67, 5.99	0.00	13.00	2.00	0.00	5.00
Week 4	3.58	4.70	0.60, 6.57	0.00	16.00	2.00	1.00	4.50
Week 5	3.67	4.23	0.98, 6.35	0.00	14.00	2.00	1.00	5.00
Follow Up (Week 6)	2.67	3.91	0.18, 5.15	0.00	14.00	1.50	0.00	3.00
Perceived Str	ess (PSS-1	0) Total						
Baseline	18.67	7.33	14.01, 23.32	8.00	31.00	19.50	13.00	24.50
Follow Up (Week 6)	14.92	6.23	10.96, 18.87	9.00	29.00	13.50	10.00	17.50
FFMQ Mindf	ulness Tot	al						
Baseline	124.00	20.69	110.85, 137.15	91.00	157.00	119.50	112.50	139.00
Follow Up (Week 6)	132.92	16.89	122.19, 143.65	108.00	155.00	130.00	119.50	150.50

Table A22 Comprehensive descriptive data on the mindfulness intervention outcomes

**Possible scale ranges:** RPQ total concussion symptom severity=0-72 (higher=more total concussion symptom severity), RPQ total concussion symptoms worse than before injury=0-18 (higher=more symptoms worse than before injury), PSS-10 total=0-40 (higher=more perceived stress), FFMQ total=39-195 (higher=more mindfulness).

**Abbreviations:** SD=standard deviation, 95%CI=95% confidence interval, RPQ=Rivermead Post-Concussion Questionnaire, PSS-10=Perceived Stress Scale, FFMQ=Five Facet Mindfulness Questionnaire.

Table A.23. Comprehensive week 1 adherence and rating data (n=12).									
	Range	Mean	SD	95%CI	Min	Max	Median	1Q	3Q
Week 1 Days Completed	0-7	5.75	1.42	4.85, 6.65	3.00	7.00	6.00	4.50	7.00
Rate Your <u>Experience</u> with the Week 1 Exercises/Meditations	0-10	7.33	1.50	6.38, 8.28	5.00	9.00	8.00	6.00	8.50
Rate Your <u>Enjoyment</u> with the Week 1 Exercises/Meditations	0-10	7.08	1.88	5.89, 8.28	4.00	10.00	7.50	5.50	8.50
Rate the <u>Effectiveness</u> of the Week 1 Exercises/Meditations	0-10	6.75	1.86	5.57, 7.93	4.00	10.00	7.00	5.50	8.00

Table A.24. Specific mindfulness e	xercises/meditations completed	during week 1 (n=12).
Mindfulness Exercise/Meditation	Number Who Completed n (%)	Rating 0-10 <i>Mean±SD</i>
None	0 (0.00%)	N/A
Body Scan Mediation Monday	9 (75.00%)	7.00±2.45
CALM Meditation Tuesday	11 (91.67%)	7.45±1.51
Easy Inner Space Meditation Tuesday	10 (83.33%)	6.70±1.57
A Calm Place Meditation Wednesday	11 (91.67%)	7.18±1.54
Breath, Not Breath Meditation Wednesday	12 (100.00%)	6.50±2.24
Breathing Clarity Meditation Thursday	10 (83.33%)	6.60±1.71
Balance Meditation Friday	11 (91.67%)	6.45±2.11
Awareness Meditation Friday	10 (83.33%)	7.60±1.84
Rotation of Consciousness Saturday	8 (66.67%)	6.50±1.60
Mindfulness of Breath Meditation Sunday	8 (66.67%)	7.38±1.60
Short and Sweet Meditation Sunday	7 (58.33%)	7.14±2.03

Table A.25. Comprehensive week 2 adherence and rating data (n=12).									
	Range	Mean	SD	95%CI	Min	Max	Median	1Q	3Q
Week 2 Days Completed	0-7	5.50	1.73	4.40, 6.60	2.00	7.00	6.00	4.00	7.00
Rate Your <u>Experience</u> with the Week 2 Exercises/Meditations	0-10	7.58	1.73	6.48, 8.68	5.00	10.00	7.50	6.50	9.00
Rate Your <u>Enjoyment</u> with the Week 2 Exercises/Meditations	0-10	7.33	1.83	6.17, 8.49	5.00	10.00	7.00	6.00	9.00
Rate the <u>Effectiveness</u> of the Week 2 Exercises/Meditations	0-10	6.50	2.35	5.00, 8.00	3.00	10.00	7.50	4.00	8.00

Mindfulness Exercise/Meditation	Number Who Completed	Rating 0-10
Mindruiness Exercise/Meditation	n (%)	Mean±SD
None	0 (0.00%)	N/A
Acceptance Meditation Monday	11 (91.67)	7.27±2.65
Sound and Touch Meditation Monday	9 (75.00)	7.00±2.74
Awareness, Gratitude, Empowerment <i>Tuesday</i>	11 (91.67)	7.82±1.83
Tonglen Meditation Tuesday	11 (91.67)	7.09±1.81
Seasons of Breath Meditation Wednesday	9 (75.00)	7.44±2.51
Progressive Relaxation Exercise Wednesday	11 (91.67)	8.00±1.95
Three Anchors to Steady the Mind Thursday	8 (66.67)	8.00±1.69
Cycle of Breath Meditation Thursday	11 (91.67)	7.27±2.37
Finding Freedom Meditation <i>Friday</i>	7 (58.33)	7.57±1.81
STOP Meditation Friday	7 (58.33)	7.00±1.53
Special Awareness Meditation Saturday	6 (50.00)	7.67±2.07
Stillness and Ease Meditation Saturday	6 (50.00)	6.50±2.43
Relaxation Through the Body Sunday	8 (66.67)	8.13±1.46

Table A.27. Comprehensive week 3 adherence and rating data (n=12).									
	Range	Mean	SD	95%CI	Min	Max	Median	1Q	3Q
Week 3 Days Completed	0-7	6.00	1.41	5.10, 6.90	3.00	7.00	7.00	5.00	7.00
Rate Your <u>Experience</u> with the Week 3 Exercises/Meditations	0-10	8.33	1.23	7.55, 9.12	6.00	10.00	8.50	7.50	9.00
Rate Your <u>Enjoyment</u> with the Week 3 Exercises/Meditations	0-10	7.67	1.87	6.48, 8.86	4.00	10.00	7.50	6.50	9.50
Rate the <u>Effectiveness</u> of the Week 3 Exercises/Meditations	0-10	7.33	1.83	6.17, 8.49	5.00	10.00	8.00	5.50	9.00

Table A.28. Specific mindfulness ex	xercises/meditations completed	during week 3 (n=12).
Mindfulness Exercise/Meditation	Number Who Completed	Rating 0-10
	n (%)	Mean±SD
None	0 (0.00%)	N/A
Exploring Our Senses Meditation Monday	10 (83.33)	7.10±2.13
Breath Calming Meditation Monday	12 (100.00)	6.83±2.17
Acceptance and Joy Meditation <i>Tuesday</i>	9 (75.00)	8.67±1.12
I am Enough Meditation <i>Tuesday</i>	10 (83.33)	8.20±1.40
Breath, Relax, Feel, Watch, Allow Wednesday	10 (83.33)	7.40±1.26
Challenges Meditation Thursday	9 (75.00)	7.11±1.62
Breathing into the Unknown Thursday	10 (83.33)	7.44±1.67
Multidimensional Meditation Friday	7 (58.33)	7.00±1.63
Stillness and Ease Meditation Friday	9 (75.00)	7.89±1.36
Unlock your Potential Meditation Saturday	11 (91.67)	7.63±1.75
Move into Ease Meditation Saturday	10 (83.33)	7.40±2.01
Body Scan Meditation Sunday	10 (83.33)	7.30±1.64

Table A.29. Comprehensive week 4 adherence and rating data (n=12).									
	Range	Mean	SD	95%CI	Min	Max	Median	1Q	3Q
Week 4 Days Completed	0-7	6.00	1.54	5.02, 6.98	3.00	7.00	7.00	5.50	7.00
Rate Your <u>Experience</u> with the Week 4 Exercises/Meditations	0-10	8.17	1.34	7.32, 9.02	6.00	10.00	8.00	7.00	9.50
Rate Your <u>Enjoyment</u> with the Week 4 Exercises/Meditations	0-10	7.50	1.51	6.54, 8.46	5.00	10.00	8.00	6.00	8.50
Rate the <u>Effectiveness</u> of the Week 4 Exercises/Meditations	0-10	7.67	1.37	6.80, 8.54	6.00	10.00	7.50	6.50	9.00

Table A.30. Specific mindfulness en	xercises/meditations completed	during week 4 (n=12).
Mindfulness Exercise/Meditation	Number Who Completed n (%)	Rating 0-10 <i>Mean±</i> SD
None	0 (0.00%)	N/A
Body Scan Mediation Monday	10 (83.33)	7.79±1.34
CALM Meditation Tuesday	11 (91.67)	7.73±1.42
Easy Inner Space Meditation <i>Tuesday</i>	11 (91.67)	7.50±1.72
A Calm Place Meditation Wednesday	11 (91.67)	7.64±1.36
Breath, Not Breath Meditation Wednesday	8 (66.67)	7.13±2.23
Breathing Clarity Meditation Thursday	10 (83.33%)	7.40±1.84
Balance Meditation Friday	9 (75.00)	7.67±1.58
Awareness Meditation Friday	8 (66.67)	7.75±1.49
Rotation of Consciousness Saturday	9 (75.00)	7.33±1.73
Mindfulness of Breath Meditation Sunday	8 (66.67)	6.88±1.81
Short and Sweet Meditation Sunday	9 (75.00)	8.00±2.06

Table A.31. Comprehensive week 5 adherence and rating data (n=12).									
	Range	Mean	SD	95%CI	Min	Max	Median	1Q	3Q
Week 5 Days Completed	0-7	5.83	1.47	4.90, 6.77	4.00	7.00	7.00	4.00	7.00
Rate Your <u>Experience</u> with the Week 5 Exercises/Meditations	0-10	7.92	1.84	6.75, 9.08	5.00	10.00	8.50	6.00	9.50
Rate Your <u>Enjoyment</u> with the Week 5 Exercises/Meditations	0-10	8.00	1.54	7.02, 8.98	5.00	10.00	8.00	7.00	9.00
Rate the <u>Effectiveness</u> of the Week 5 Exercises/Meditations	0-10	7.50	1.83	6.33, 8.67	4.00	10.00	7.50	6.00	9.00

Mindfulness Exercise/Meditation	Number Who Completed n (%)	uring week 5 (n=12) Rating 0-10 <i>Mean±</i> SD		
None	0 (0.00%)	N/A		
Acceptance Meditation Monday	11 (91.67)	8.18±1.60		
Sound and Touch Meditation Monday	11 (91.67)	7.55±1.44		
Awareness, Gratitude, Empowerment <i>Tuesday</i>	11 (91.67)	8.40±1.58		
Tonglen Meditation Tuesday	9 (75.00)	8.22±1.31		
Seasons of Breath Meditation Wednesday	10 (83.33)	7.00±1.70		
Progressive Relaxation Exercise Wednesday	10 (83.33)	6.70±2.50		
Three Anchors to Steady the Mind <i>Thursday</i>	10 (83.33)	7.50±1.58		
Cycle of Breath Meditation Thursday	12 (100.00)	7.00±2.26		
Finding Freedom Meditation <i>Friday</i>	7 (58.33)	7.29±2.36		
STOP Meditation Friday	7 (58.33)	7.86±1.46		
Special Awareness Meditation Saturday	7 (58.33)	8.14±1.68		
Stillness and Ease Meditation Saturday	8 (66.67)	7.00±1.85		
Relaxation Through the Body Sunday	9 (75.00)	7.11±1.69		

Table A.33. Comprehensive week 6 adherence and rating data (n=12).									
	Range	Mean	SD	95%CI	Min	Max	Median	1Q	3Q
Week 6 Days Completed	0-7	5.50	1.78	4.37, 6.63	3.00	7.00	6.50	3.50	7.00
Rate Your <u>Experience</u> with the Week 6 Exercises/Meditations	0-10	8.17	1.47	7.23, 9.10	6.00	10.00	8.00	7.00	9.50
Rate Your <u>Enjoyment</u> with the Week 6 Exercises/Meditations	0-10	8.17	1.40	7.27, 9.06	6.00	10.00	8.50	7.00	9.00
Rate the <u>Effectiveness</u> of the Week 6 Exercises/Meditations	0-10	7.83	1.80	6.69, 8.98	5.00	10.00	8.00	6.00	9.50

Table A.34. Specific mindfulness exercises/meditations completed during week 6 (n=12).					
Mindfulness Exercise/Meditation	Number Who Completed	Rating 0-10			
	n (%)	Mean±SD			
None	0 (0.00%)	N/A			
Exploring Our Senses Meditation Monday	10 (83.33)	7.70±1.34			
Breath Calming Meditation Monday	10 (83.330	7.00±2.00			
Acceptance and Joy Meditation <i>Tuesday</i>	9 (75.00)	8.22±1.56			
I am Enough Meditation Tuesday	9 (75.00)	8.11±1.76			
Breath, Relax, Feel, Watch, Allow Wednesday	10 (83.33)	7.50±1.72			
Challenges Meditation Thursday	9 (75.00)	8.33±1.32			
Breathing into the Unknown Thursday	8 (66.67)	7.13±2.23			
Multidimensional Meditation Friday	9 (75.00)	7.44±1.42			
Stillness and Ease Meditation Friday	8 (66.67)	7.50±1.31			
Unlock your Potential Meditation Saturday	9 (75.00)	7.56±1.74			
Move into Ease Meditation Saturday	7 (58.33)	8.00±1.63			
Body Scan Meditation Sunday	8 (66.67)	7.63±1.60			

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