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IDENTIFICATION OF CHRONIC POSTURAL STABILITY IMPAIRMENTS  
ASSOCIATED WITH HISTORY OF CONCUSSION

by

Nicholas G. Reilly  
B.S. August 2016, Pennsylvania State University  
M.S. May 2017, University of Delaware

A Dissertation Submitted to the Faculty of  
Old Dominion University in Partial Fulfillment of the  
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Approved by:

Eric Schussler (Director)

Steven Morrison (Member)

Anastasia Raymer (Member)

Daniel Russell (Member)

## ABSTRACT

### IDENTIFICATION OF CHRONIC POSTURAL STABILITY IMPAIRMENTS ASSOCIATED WITH HISTORY OF CONCUSSION

Nicholas G. Reilly  
Old Dominion University, 2021  
Director: Dr. Eric Schussler

Concussion is the most common form of traumatic brain injury (TBI). However, there is a disproportionate level of understanding between the acute and chronic impairments associated with traumatic brain injury. Specifically, problems maintaining balance during standing and walking are cardinal signs of acute concussion, but the temporal extent to which postural control deficits remain following the initial injury are not well defined or understood. The purpose of the projects composing this dissertation was to examine the long-term effects of a prior history of concussion on static (i.e. standing) and dynamic (i.e. gait) postural control. To address this, healthy adults aged 18-45 reporting a prior history of concussion(s) as well as age-matched controls with no documented concussion history were recruited to participate. Static postural control was assessed using a force plate system to track each participant's center-of-pressure during standing. Spatiotemporal parameters as well as head stability during gait were assessed using a pressure-sensitive walkway and accelerometers placed at the head, neck, and lower trunk, respectively. The findings of these projects indicate that concussion has detrimental effects on both static and dynamic postural stability years after the initial injury and clinical determination of recovery. Specifically, individuals with a prior history of concussion demonstrated greater postural sway displacement and reduced sway regularity under dual-task conditions compared to the control group. In addition, previously concussed individuals demonstrated less variability in their gait cadence and step length, which suggests a reduction in the complexity of the neural networks

contributing to postural control. Lastly, individuals with a history of concussion demonstrated greater triaxial accelerations at the head during gait, indicating a reduced ability to attenuate gait-related oscillations and stabilize the head. Collectively, these findings indicate that concussion is associated with impaired postural control that persists for years after the initial injury and well beyond the point where clinical testing protocols can identify deficits in maintaining balance. Future efforts should be directed toward incorporating more sophisticated measures and analyses of postural stability in concussion screenings to improve clinicians' abilities to identify the scope in which concussion negatively impacts the function of the central nervous system.

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This thesis is dedicated to the notion that victory is built upon what we learn from failure.

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To Mom and Dad,

Against all the odds and through all the pain, I made it to the top of the mountain. However, my objective is not complete, and I am not even close. I will work for the rest of my life to prove the faith you had in me and the support you provided me was worth the hardships that we not only faced as a family, but you both personally undertook as the parents of an irrationally competitive kid that spent more time in the emergency room than with a smile on his face.

I remember being tested for The Gifted Program in the third grade. I remember the pressure that came with being told what those tests deemed I could achieve.

They were correct.

Your son is a doctor.

For everything that I previously, currently and will ever have.

Thank you.

Your sacrifices will not be forgotten or go unrecognized.

This I swear.

I love you both so much.

To the members of my committee, I extend my sincerest gratitude for their consistent support throughout my studies at Old Dominion University. Despite my ever-present stoicism and inclination to avoid asking for help, your mentorships have shaped me into a researcher that is better equipped to leave my mark in the scientific community.

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It was all worth it.

It was all for science.

## NOMENCLATURE

<i>AP</i>	Anteroposterior
<i>ApEn</i>	Approximate entropy
<i>BESS</i>	Balance Error Scoring System
<i>CN</i>	Cranial nerve
<i>CoM</i>	Center-of-mass
<i>CoP</i>	Center-of-pressure
<i>CT</i>	Computerized tomography
<i>CTSIB</i>	Clinical Test of Sensory Interpretation on Balance
<i>GCS</i>	Glasgow Coma Scale
<i>LQYBT</i>	Lower Quarter Y-Balance Test
<i>mBESS</i>	Modified Balance Error Scoring System
<i>ML</i>	Mediolateral
<i>MSE</i>	Multiscale entropy
<i>MRI</i>	Magnetic resonance imaging
<i>mTBI</i>	Mild traumatic brain injury
<i>PCSS</i>	Post-Concussion Symptom Scale
<i>SampEn</i>	Sample entropy
<i>SEBT</i>	Star Excursion Balance Test
<i>SOT</i>	Sensory Organization Test
<i>TBI</i>	Traumatic brain injury
<i>YBT</i>	Y-Balance Test

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## CHAPTER 1

### INTRODUCTION AND RESEARCH AIMS

#### **1.1 Theoretical Formulations**

Despite all efforts to navigate the world safely and efficiently, it is logistically impossible to eliminate the risk of injury from both competitive sports as well as activities of daily life. Therefore, proper and thorough understanding of the consequences and changes that result from injury can better inform clinicians how to identify and manage treatments and for injured individuals themselves how to prevent further complications of injury. While we can and have made great strides in identifying and treating the deficits associated with common injuries such as ankle sprains and bone fractures [1,2], not all frequently occurring injuries, such as concussion, are as well understood. The long-term complications and deficits that result from injury are often not considered once a clinical determination of recovery allows an injured individual to return to regular levels of activity, leaving a gap in the literature in the form of a lack of an objective determination of the duration of a full recovery. There is perhaps no injury that combines troublingly high incidence rates and lack of detailed knowledge of the nature of the injury more prominently than concussion.

Concussion is the most common type of mild traumatic brain injury (mTBI) in the United States with conservative estimates reporting an average of 2.5 million cases occurring annually [3]. From a diagnostic perspective, concussion can manifest in a wide spectrum of symptoms that can be cognitive, neuropsychological and/or somatic in nature [4,5]. However, not all potential symptoms are equally apparent or straightforward to identify and assess. Physiological deficits and



impairments of postural stability can require specialized training and expensive equipment to properly screen for and detect. These obstacles limit the availability of these testing protocols in most clinical sites, which has led most practitioners to rely on self-reports of cognitive symptoms from patients themselves and largely ineffective screening tools. Additionally, the combination of improper education to identify symptoms associated with concussion and the notion that reporting symptoms will result in termination of athletic participation results in both a woeful rate of underreporting of concussion incidences as well as premature returns to full levels of activity in identified cases of concussion [6,7].

Despite the objective evidence that concussion can result in symptoms that are cognitive, biomechanical, and physiological in nature, screening and management for concussion is disproportionately reliant on self-reports of neurocognitive symptoms. Furthermore, balance assessments commonly utilized in screenings for concussion such as the Balance Error Scoring System (BESS), Y-Balance test (YBT), and Romberg test raise questions about how accurately they can detect postural stability impairments beyond the acute phases of concussion, raising concerns over the sensitivities of these protocols [8,9]. Proper maintenance of balance requires the integration of multiple neural tracts and structures that are not directly and/or precisely examined during clinical screening protocols for concussion [10]. As a result, deficits in maintaining balance stemming from a concussion can go undetected and untreated. Consequently, these outcomes result in concussed individuals being declared fully recovered prematurely and thereby placing them at a higher risk for secondary, more severe injuries, which can be devastating and even fatal under rare circumstances [11,12].

In addition, the long-term consequences of sustaining one or multiple concussions is not as well understood as the impairments seen in the acute stages following the initial injury.

Concussion presents a troubling premise for optimal rehabilitation due to the unique physiological properties of the brain. Specifically, tissue within the central nervous system does not have the same capabilities to repair damage and regenerate seen in other types of tissue including the peripheral nervous system [13]. Rather than regenerate damaged tissue, repair of axons within the central nervous system consists of generating scar tissue at the site of damaged axons, resulting in a stable, yet sub-optimally functioning neural tract [14,15]. As a result, damage to the central nervous system often does not fully resolve to allow a return to pre-injury levels of functioning. Long-term deficits in physiological function across multiple areas of the brain associated with concussion would suggest that areas of cortex and subcortical structures associated with postural stability (i.e. primary motor cortex, cerebellum, vestibular nuclei) would also be affected by traumatic impacts [16,17]. It stands to reason that the deficits in postural stability associated with the acute stages of concussion would persist for years as the damaged tissue fails to function as it did prior to sustaining trauma. However, the potential detrimental effects of concussion on static and dynamic postural stability are not well understood beyond the scope of several months after the initial injury compared to the effects on cognition related to concussion history that can begin to appear decades later in life.

## **1.2 Purpose**

The overall purpose of this project was to better understand the potentially chronic impairments associated with prior concussion history. The goals of this study were to assess the static and dynamic postural stability of currently healthy individuals that have previously sustained one or multiple concussions and assess how they compare to those that have never sustained a concussion. Postural stability deficits are often not considered in the determination of medical

clearance from concussion unless the deficits are gross in nature. Furthering the understanding of how concussion can affect the ways in which we navigate the world on a daily basis can help prevent premature returns to full activity, decrease risks of further injury following concussion, and improve our understanding of the neurological damage that is done on the level of the neural networks themselves.

### **1.3 Aims and Hypotheses**

The aims and hypotheses of the three experiments that composed this project are broken down as follows:

#### *Experiment 1*

The aim of this study was to determine the effect of concussion history on static postural stability as measured by center-of-pressure (CoP) parameters under single and dual-task conditions.

It was hypothesized that:

- 1) Individuals with a history of concussion will demonstrate greater deficits in postural sway parameters indicated by increased sway displacement, velocity and regularity compared to those with no prior history of concussion.
- 2) Individuals with a history of concussion will exhibit greater dual-task cost during standing compared to individuals that have never sustained a concussion.

#### *Experiment 2*

The aim of this study was to determine the effect of concussion history on dynamic stability and variability during preferred and tandem gait.

It was hypothesized that:

- 1) Individuals with a history of concussion will demonstrate gait patterns with greater emphasis on maintenance of stability marked by reduced velocities and wider strides compared to those with no prior history of concussion.
- 2) Individuals with a history of concussion will demonstrate a less variable (i.e. decreased coefficients of variation) gait pattern during preferred and tandem gait compared to those with no prior history of concussion.

### *Experiment 3*

The aim of this study was to determine the effect of concussion history on stabilization of gait-related oscillatory movements at the head.

It was hypothesized that:

- 1) Individuals with a history of concussion will display increased gait-related accelerations at the head compared to those with no prior history of concussion.
- 2) Individuals with a history of concussion will display decreased attenuation of gait-related accelerations at the neck and trunk compared to those with no prior history of concussion.

## CHAPTER 2

### LITERATURE REVIEW

Concussion is a unique type of neurological injury in the sense that it can manifest in a wide spectrum of symptoms unlike any other type of injury matching its incidence rate on an epidemiological scale. As a result, the detrimental effects of concussion have garnered a growing amount of mainstream attention in part due to the direct associations with contact sports and common traumatic events such as motor vehicle accidents, falls, and combat-related events within the military. However, the chronic implications of a prior history of concussion are not as well defined as the challenges faced during the acute stages of injury. This chapter will address how the scientific literature presents the current state of the scope of understanding surrounding the detrimental effects of concussion from neurological, physiological, epidemiological, and biomechanical contexts. In depth, this review will focus on how impairments of postural stability during standing and gait following concussion are currently understood, assessed, and identified. Finally, this review will examine the current state of the literature regarding the chronic deficits resulting from concussion; namely how impairments associated with concussion can persist beyond the determinations of recovery made by currently utilized protocols and standards of treatment only to be made apparent when drawing comparisons to those that have no prior history of concussion, therefore highlighting the need to objectively identify resonating deficits stemming from concussion. This review ultimately aims to highlight the current gaps in the literature regarding the effects of concussion on postural stability that are to be addressed in Chapters 3, 4 and 5 of this dissertation.

## 2.1 Neural Foundations of Postural Stability

The central nervous system consists of a complex combination of sensory receptors, signal transmission networks, information processing sites and specialized cells designed to help maintain a homeostatic environment that all work in seamless tandem to produce the movements and behaviors that serve as the baseline for proper and healthy functioning. Such functions include the subconscious regulation of sensory feedback information to maintain upright posture as well as volitional activation of neural structures and pathways to execute movements of various complexity including gait and sudden corrections to maintain stability when faced with external perturbations to mechanical equilibrium. The ever present nature of the biological necessity of these functions is evident in the physical properties (i.e. fortification provided by skull and spinal column) and physiological measures (i.e. reflexive priorities to protect the head) taken to preserve optimal functioning of the brain and central nervous system as a whole. As such, trauma to the structures and networks of central nervous system can have systemic consequences on a multitude of regulatory and performative functions that can range drastically in severity based on the extent of and location of the sustained damage.

Postural control is an innate motor function in humans. Proper maintenance of balance is a crucial aspect of healthy functioning that humans utilize to safely navigate the everchanging external environments in which we are exposed. Balance is defined as the dynamics of retaining posture to avoid falling under the force of gravity [18]. Specifically, balance is achieved by keeping the body's center-of-mass (CoM) within the base of support created by the limb or limbs on the ground regardless of the position or surface [19,20]. During upright standing, postural stability will remain intact as long as the body has the musculoskeletal capacity to adapt to any encountered

perturbations and return to a more stable position [21]. In the healthy population, maintenance of both static and dynamic postural stability does not require a large amount of conscious effort and can be regulated through subconscious reflexive actions of the central nervous system to interpret and act in accordance to perceived sensory feedback information. Specifically, maintenance of balance is achieved by utilizing feedback from three sensory sources: (1) visual information, (2) somatosensory information (i.e. touch, proprioception), and (3) vestibular information [22]. Clinical balance assessments will typically increase the difficulty of a balance task by manipulating the type and/or amount of information being processed by these three sensory feedback systems [23]. Of the three, it has been previously noted that vestibular feedback is the most consistent source of sensory feedback used to maintain upright posture because of the body's constant exposure to the force of gravity [24,25]. As a result, a healthy individual's vestibular nuclei and feedback system are able to contribute a sufficient amount of feedback required to maintain upright posture when there is less or altered feedback from the visual (i.e. eyes closed) and/or somatosensory (i.e. unsteady floor surface) systems.

While superficially seeming simple, maintenance of balance and upright postural stability requires the integration of multiple neural networks and structures within the brain and spinal cord to function in tandem seamlessly in order to maintain balance under a variety of circumstances [10]. This parallel organizational structure not only allows neurons and larger structures to serve more than one purpose, but allows for at least partial compensation should any specific area of the brain be damaged or compromised in order to attempt to retain full function and maintenance of postural stability [26]. This capability of neuroplasticity within the postural control system is made apparent in cases of trauma (i.e. concussion, stroke), intoxication (i.e. ethanol metabolism) and neurological disease (i.e. Parkinson's disease, cerebral palsy) in which most cases result in an

impaired, but not completely lost ability to maintain balance. As such, assessments of standing balance provide useful insight concerning the function of the central nervous system and can potentially contribute information to pinpoint the anatomical location of damage in cases of observable dysfunction. However, the compensatory functions made possible by the parallel organizational structure within the postural control system can strengthen the system's capabilities to achieve its goals of maintaining mechanical equilibrium of the body, making pathological signs of damage and/or degeneration of tissue more difficult to objectively identify. In cases of concussion, compensatory measures can be taken to alleviate a certain amount of stress placed on the postural control system during quiet standing including widening the feet to create a larger base of support and using visual anchoring techniques to create a reliable point of reference. This contributes to the complexity of the diagnostic process for concussion, and thus requires carefully designed testing protocols to account for said compensatory measures during quiet standing and avoid false negative testing outcomes.

Gait presents a more complex challenge for the postural control system as the dynamic nature of locomotion results in constant fluctuations in the relative area of the body's base of support. Like standing balance, gait requires the integration of multiple structures within the brain in order to create efferent motor output in conjunction with afferent sensory feedback signals [27]. As a result, gait is often incorporated in clinical settings as a metric with which to assess for the presence of neurological injury or decline. In contrast to standing balance, there have been previously documented findings using animal models suggesting the involvement of the limbic system in control of gait [28,29]. The established functions of the limbic system (i.e. emotional regulation, motivation, reward) indicate that gait is regulated through self-motivated means and shaped by behavioral contexts utilizing cognitive interpretation. Collectively, it has been shown



that gait incorporates a greater amount of neural resources compared to upright standing and thus the threshold of damage at which impairments of postural stability would manifest is lower during gait than for upright standing. In the context of concussion, gait presents a useful metric to determine the presence of damage to the postural control system that can potentially reveal impairments that are not observable during quiet standing. However, the technology and analytical techniques required to assess the specific kinematic qualities of gait in which postural instability can be identified has not been widely applied in clinical screenings for concussion.

### *2.1.1 Central nervous system overview*

Within the central nervous system exists a hierarchal organization of structures that interact with one another to integrate afferent feedback from sensory receptors and generate efferent signals to position the body in a way that result in proper maintenance of postural stability. Involved structures, from most to least complex, include the cerebrum, the cerebellum, the basal ganglia, the brainstem, and the spinal cord. The hierarchy is organized in an identical order in the contexts of both static and dynamic stability. As a result, damage to any one of these structures and/or the axonal tracts that interconnect them can result in an impaired ability to maintain postural control either temporarily or permanently depending on the severity of the sustained trauma. The location of the sustained damage within the hierarchy can also provide prognostic value by determining what alterations in neurological function can be expected to manifest as a result of the said damage as well as what strategies can be implemented for therapeutic and compensatory approaches to restoring overall function.

At the top of the hierarchy is the cerebrum. Also referred to as the cerebral cortex, the cerebrum is the most rostral portion of the brain and represents the largest portion by area. The

cerebrum is organized into five distinct divisions: the frontal lobes, the parietal lobes, the temporal lobes, the occipital lobes, and the insula. The cerebrum is responsible for a wide variety of functions including but not limited to planning and decision making, somatosensory signal interpretation, emotional regulation, visual and auditory information processing, memory recall, language functions, higher order thought processes, and attention span [30]. In the context of maintaining postural stability, the cerebrum is home to multiple areas that are directly involved with keeping humans upright, the most influential of which is the precentral gyrus, also known as primary motor cortex or M1. Animal models have consistently shown that M1 is essential for voluntary, non-reflexive movements regardless if the movement is cyclical or discrete in nature [31–34]. In line with these prior findings, M1 plays a significant role in activation of the distal musculature of the lower limbs needed to facilitate gait as well as maintenance of proper muscle tone of the axial musculature required to overcome the force of gravity and maintain upright posture. Aiding in the facilitation of voluntary movement are the premotor and supplementary motor areas located directly adjacent to M1. The premotor and supplementary motor areas work in conjunction when learning complex, new movements and are heavily involved in preparatory anticipations of learned movements including those experienced during standing and gait [35,36]. M1 uses output from these two areas of cortex to optimize appropriate motor output to execute movements to complete the task at hand.

M1 serves as the origin site for two of the most important neural tracts for maintenance of balance: the medial and lateral corticospinal tracts. The lateral corticospinal tract innervates the lower motor neurons in the spinal cord that in turn innervate motor units to activate and control skeletal muscle fibers. This tract ultimately allows for complex, discrete and controlled use of the limbs and is responsible for voluntary movement, including assuming new postures without

collapsing [37]. In contrast, the medial corticospinal tract innervates the thoracic spinal cord and allows for control of axial musculature for the neck and trunk. Damage to the medial corticospinal tract results in the loss of one's ability to maintain proper posture [38]. The corticospinal tracts work together to maintain balance whether the body is stationary or in motion, allowing healthy individuals to navigate the environment without constant attention being paid to postural control. In addition, M1 also has direct connections to multiple subcortical areas within the brain to both provide feedback for initiating movements as well as receive feedback in order to correct movements.

Damage to the cerebrum is most commonly the result of traumatic events including, but not limited to, concussion and stroke that can range considerably in severity. If damage is sustained or should neural tissue be killed, the return of full function of the tissue is limited because unlike axons in the periphery, central nervous system neurons and axons do not have the extensive capacity for repair seen elsewhere in the body. Specifically, central nervous system tissue does not regenerate upon being damaged but rather forms scar tissue over the site of the damage which leads to impeded electrical transmission between neurons and larger neural structures [39]. In addition, neurogenesis is limited to a select few sites within the brain once developmental maturity is reached, making the likelihood of replacing damaged or lost tissue unfeasible for a large proportion of the central nervous system [40,41]. The catastrophic consequences of damaging central nervous system tissue and structures are evident in the design of the structures that inherently protect them. The spinal cord is heavily fortified within the vertebral column and the brain is guarded by the skull, which contains several of the hardest, most resilient bones in the body, as well as the shock-absorbing properties of cerebrospinal fluid (CSF). Despite these biological protections, humans are readily capable to being subjected to high-energy, traumatic

impacts (i.e. motor vehicle accidents, collisions in sport, blast exposure) that can result in permanent alterations or loss of neurological function.

Sitting caudal to the cerebrum is the cerebellum (Latin for ‘little brain’). The cerebellum is the densest portion of the brain, containing half of all of the brain’s neurons despite accounting for approximately ten percent of the brain’s total mass [42]. The primary function of the cerebellum is the facilitation of smooth, coordinated movements in real time. To do this, the cerebellum has input and output connections with multiple areas of the brain that contribute to motor control including the brainstem, basal ganglia, M1 and primary somatosensory cortex (S1). The combination of sensorimotor information being processed within the cerebellum allows for subtle corrections in trajectory during movement to adjust for alterations or obstacles in the environment [43,44]. Damage to the cerebellum results in ataxia, a motor disorder defined by uncoordinated, imprecise movements despite cognitive efforts to the contrary [45]. Cerebellar dysfunction is commonly induced transiently through alcohol consumption but is also seen in various genetic conditions (i.e. spinocerebellar ataxia), the result of a stroke, or severe blunt trauma.

The cerebellum serves as a critical junction point for multiple ascending and descending neural tracts. The cortico-ponto-cerebellar circuit is composed of the pontocerebellar and corticopontine tracts to form a direct neural pathway linking the cerebellum, the brainstem and M1. Within this circuit, the cerebellum receives motor output from M1 and sensory feedback ascending from the spinal cord relayed by the brainstem in order to provide a real-time, ongoing movement error correction system. In addition, it has been demonstrated that the cerebellum has a remarkable capacity for plasticity, wherein more frequently performed actions reinforce the pathway to become more fine-tuned to these frequent actions to establish a sense of “motor memory” [46]. In addition, the central structure of the cerebellum, the vermis, has output

connections to the brainstem that ultimately contribute to the ventromedial spinal tracts that innervate the axial musculature that contribute to upright posture and balance regulation. Another crucial portion of the cerebellum is the fastigial nucleus. One of the four deep cerebellar nuclei, the fastigial nucleus receives sensory feedback information from the occipital lobes (vision), the vestibular nuclei (vestibular) and the spinocerebellar tract (somatosensory). This feedback is utilized to facilitate smooth motor output to ultimately contribute to proper motor coordination including maintenance of static and dynamic postural stability.

The basal ganglia are a group of nuclei located throughout the subcortical areas of the brain. The basal ganglia are composed of five primary nuclei: the caudate, the putamen, the globus pallidus, the substantia nigra and the subthalamic nucleus. Collectively, the primary function of the basal ganglia is to gate and automatize movement, essentially initiating and terminating movements when appropriate by assessing inputs from the cerebral cortex to predict and anticipate future movements [47]. The basal ganglia work directly with the motor cortex, the cerebellum and sensory processing centers including those for visual and vestibular information in order to gauge the most appropriate motor function given the task at hand and the cognitive input from higher order cortical centers [48–51]. When working synchronously, the basal ganglia serve as critical components of the motor control system that allow for fluid, coordinated movement that is not completely reliant on cognizant interpretations of intrinsic and extrinsic sensory feedback information to properly maneuver through the external environment.

The five nuclei of the basal ganglia serve distinct roles within the circuits of the motor control system to initiate or terminate selective movements. The caudate and the putamen collectively form a structure referred to as the striatum. The striatum serves as the primary input structure for the basal ganglia to receive signals for action from M1. From here, the basal ganglia

form two distinct networks: the direct and indirect pathways. The direct pathway serves as the primary excitatory pathway for initiating movements. In the direct pathway, upon being stimulated by cortical cells via dopamine receptors (D1 receptors), the striatum sends inhibitory impulses to the internal segment of the globus pallidus, which in turn stops sending inhibitory impulses to the ventral nucleus of the thalamus, allowing the thalamus to initiate the desired movement [52,53]. The indirect pathway serves as the primary inhibitory pathway of the basal ganglia, where upon being stimulated by cortical cells on a different type of dopamine receptor (D2 receptors), the striatum sends excitatory signals to the external segment of the globus pallidus, which in turn inhibits the internal segment of the globus pallidus as well as the subthalamic nucleus. The inhibition of these structures leads to inhibition of the thalamus, which is desirable when attempting to suppress unwanted or inappropriate motor functions [54–56]. The emphasis for a seamless automatization process is crucial for proper static and dynamic postural ability because of the frequent exposure to external perturbations against stable upright posture.

The importance of the basal ganglia towards maintenance of postural stability is most clearly exemplified by observing the results of degeneration of its component nuclei. One of the most common neurodegenerative diseases in the United States, Parkinson's disease is characterized by degeneration and atrophy of the dopaminergic cells within the substantia nigra [57–59]. The loss of available dopamine results in motor dysfunction and markers for decreased postural stability including increased sway displacement, bilateral motor asymmetries, and episodic freezing of gait [60–62]. In addition, Parkinson's disease is commonly associated with bradykinesia, a slowing of the initiation of voluntary movement. This slowing of movement signifies that impairment of the basal ganglia is also associated with a decreased capability to correct for perturbations placed upon the body, making an individual with basal ganglia

dysfunction more susceptible to a systemic failure of the postural control system. Parkinsonian patients also walk with a more variable gait pattern, indicating a reduction in the control of their locomotor system [63,64]. In contrast, another form of neurodegeneration at the site of the basal ganglia, specifically the striatum, manifests as a condition known as Huntington's disease. Whereas Parkinson's disease is characterized by slowed, impaired motor initiation, Huntington's disease is identified by a lack of motor inhibition exemplified by uncontrollable, sporadic movements throughout the body (i.e. chorea) and slow, writhing movements of the limbs, face, and trunk (i.e. athetosis) [65,66]. The degeneration of inhibitory structures within the basal ganglia circuitry seen in cases of Huntington's disease ultimately results in excessive and involuntary motor outputs from M1. The excessive, unpredictable movements throughout the body predictably makes maintaining upright postural stability during standing and gait markedly more difficult as the disease progresses. In both conditions, the motor control deficits seen with basal ganglia degeneration indicate that postural control requires intact neural connections between structures throughout the brain as well as a well-maintained homeostatic balance of neurotransmitters [67–69].

Located inferior to the cerebellum, the brainstem is the most primitive and caudal portion of the brain. The brainstem is divided into three distinct functional sections: (1) the midbrain, (2) the pons, and (3) the medulla. In addition to serving as a significant synaptic site within multiple sensory and motor tracts within the postural control system, the brainstem is responsible for the regulation of multiple vital functions including ventilation, cardiovascular regulation, and maintenance of consciousness. The contributions of the brainstem toward maintaining such vital aspects of biological function inherently mean that damage to the brainstem not only results in gross reductions in postural stability but can also be physiologically catastrophic if not outright

fatal. Despite the drastic outcomes associated with brainstem trauma, mild instances of injury are unsettlingly common in cases of concussion, exhibited in the forms of transient loss of consciousness and autonomic dysregulation of cardiac rhythmic activity [70,71]. In particular, loss of consciousness was long considered to be a defining characteristic of traumatic brain injury, with the duration until consciousness was regained serving as a metric for defining the severity of the injury.

The divisions of the brainstem each have unique roles that coordinate with other structures and tracts within the motor control system. For instance, the midbrain is the site of the substantia nigra, one of the key nuclei composing the basal ganglia. The pons, specifically a structure within it known as the reticular formation, has a direct connection with the fastigial nucleus of the cerebellum where it has a direct association with activation and maintenance of muscle tone [72,73]. The medulla plays a unique role within the motor control system as the site of pyramidal decussation of the descending corticospinal tracts (i.e. voluntary muscle activation) before reaching the spinal cord and the ascending dorsal-column medial lemniscal tract (i.e. tactile sensation and proprioception) before arriving at the reticular formation within the pons. Despite the clinical significance in recognizing the crossover of these neural tracts, the exact developmental purpose of the crossover from a biological perspective is currently inconclusive.

The brainstem also plays a crucial role for maintenance of postural stability by serving as the origin site for multiple neural tracts including the vestibulospinal and reticulospinal tracts [73–75]. The medial and lateral vestibulospinal tracts relay information from the vestibular nuclei to innervate musculature that stabilizes the head and neck, respectively. Stabilization of the head is crucial for maintenance of stability during standing and walking. Dysfunction and conflicting sensory feedback from the visual and vestibular fields can be brought on from damage to the



vestibulospinal tracts and manifest as persistent dizziness and an inability to properly converge the two fields of vision acquired from each independent eye (i.e. diplopia). The vestibulospinal tracts are also the source of the righting reflex, which creates an impulse to correct posture and assume an upright position when external perturbations change the orientation of the body [76]. Conversely, the medial (pontine) and lateral (medullary) reticulospinal tracts innervate and modulate the flexor and extensor musculature of the proximal limbs. The reticulospinal tracts also work in conjunction with the brainstem, cerebellum and vestibular nuclei in order to coordinate the modulation of muscle tone during movements including gait [77,78]. The reticular formation serves as a critical junction point along the reticulospinal tracts that coordinate multiple sources of sensorimotor information that is processed at multiple sites in order to produce functional maintenance of postural stability under both static and dynamic conditions. Much like its role in regulating the cardiovascular and respiratory systems, the contributions of the brainstem toward postural control are fundamental for the subconscious aspects of proper functioning.

The final major neural structure along the path of motor output is the spinal cord. The integral nature of the spinal cord for voluntary movement in addition to balance is exemplified by the design of the spine itself, which heavily fortifies the spinal cord, a structure that is no wider than a common coin. The spinal cord is a bundle of axons that serves as the central nervous system's 'interstate highway', serving as a route for descending motor output to reach the tissues of the periphery and the ascending sensory information to reach the appropriate processing centers within the brain. In addition to the aforementioned corticospinal tracts, dorsal column medial lemniscal tracts, additional tracts that are crucial for proper maintenance of postural stability utilizing the spinal cord to relay information between to and from the brain include the tectospinal tract (i.e. coordination of head and eye movements), the reticulospinal tracts (i.e. upper limb

musculature and autonomic reflexive activation) and the vestibulospinal tracts (i.e. spatial orientation and head stabilization). Collectively, the parallel facilitation provided by the various tracts of the spinal cord serve as a direct connection between the brain and the multitude of systems of the body that allows human beings to navigate the external environment appropriately.

The spinal cord does have a few functions that are independent of cognitive implementation from the brain. The spinal cord houses ganglia that regulate the reciprocal inhibition and stretch reflexes of the skeletal musculature; both of which are crucial for maintenance of upright posture. In addition, the spinal cord plays a critical role during gait by processing sensory feedback during the stance phases of the gait cycle so that cognitive input is not required for all aspects of maintaining postural control during gait [79]. Despite these capabilities, the spinal cord does not independently possess the neural resources and circuitry to maintain standing posture and produce gait without access to the motor output from the brain. Hence, lesions of the spinal cord result in a colossal loss of function at the level of and inferior to the site of the lesion. However, the established motor pathways and “motor memory” established in the brain are not lost in the case of a spinal cord lesion. The technology to allow spinal cord lesion patients to perform gait is not widely available, but the early results indicate that modern advances in technology are beginning to move toward a paradigm shift in which neurological injury is a challenge to be overcome rather than a sudden permanent change in an individual’s quality of life.

Static and dynamic postural stability are sustained by utilizing an intricate system within the central nervous system that streamlines an abundant amount of feedback in real time to efficiently output smooth and coordinated motor efferent signals to complete a wide variety of tasks, feats and movements to navigate the external environments we face on a daily basis [27,80]. The large, complex neural network that contributes to maintaining postural control allows for a

certain degree of compensation should any link in the circuitry become compromised or be rendered completely unusable. This level of intricacy within the system allows humans to not only perform incredible feats of athleticism without losing balance, but also overcome injury or disease that would have dismantled quality of life decades ago. The summarization of functions of the various structures and neural tracts utilized in the maintenance of postural control provides a foundation of knowledge of how neurological disease and/or injury impacts the system and the mechanisms for how symptoms associated with these pathologies can manifest and require be compensated for elsewhere within the circuitry.

### *2.1.2 Variability and regularity*

Human beings are imperfect by their nature. As such, two defining characteristics seen in human movement are the concepts of variability and regularity observed during standing and walking. The concept of motor variability has been described as the amount of change in the performance of a movement across multiple repetitions [81]. This concept is easily observable when manually writing out a signature multiple times, which results in no two tracings being perfectly replicated. Conversely, regularity has been defined as the repeatability and predictability of a pattern throughout a movement [82]. Regularity can be instilled into a movement pattern with the application of a metronome in comparison to a freely performed movement. Both variability and regularity have been thoroughly assessed in the literature to gain further insight into the fundamentals of static and dynamic postural stability and the changes that occur upon incurring damage to the postural control system via injury and/or disease.

The physiological concepts of movement variability have been analyzed for decades from numerous different perspectives, much of which stems from the work of Nikolai Bernstein.

Bernstein claimed that repeated movements were not based on a neurologically driven repetitive pattern, but that each repetitive movement was an individual, successive task [83]. Based on this concept, it was believed that variability of movements was indicative of error or inaccuracies during repetition of a specified movement. In this context, greater amounts of variability were interpreted as a more unstable system that is unable to repeat a movement with efficacious precision, and thus, those who demonstrated less movement variability were interpreted as more stable [84]. Over time, more variables were introduced to expanding models in order to attempt to explain the multi-faceted nature of movement variability such as the idea of selective utilization of a subset of movement patterns amidst an excess of neural resources required to complete a given task to account for variations in movement (i.e. uncontrolled manifold hypothesis) [85] and the consideration of how movement and behavioral contexts are affected by factors within the external environment (i.e. Dynamical Systems Theory). As the theories and models evolved, understanding of motor control progressed by identifying how the capacity for variability contributed to the capacity for motor adaptations and limited volitional movement under a variety of circumstances.

Collectively, these differing perspectives have been applied to a wide spectrum of motor tasks that overall concluded that repetition and experience plays a significant role in the variability expressed during movement in the healthy population; namely that repetition helps establish successful movement patterns within a scope of potential options made possible by the amount of variability within the movement, effectively reducing overall variability as the movement is repeated successfully more frequently. [86–90]. Based on these principles, an individual's movement patterns would become considerably less variable, or more constrained, as the movement is repeated and practiced. By this logic, the best performers would be able to replicate their movement patterns to a consistent, nearly perfect degree. While the findings based on these

theories have been widely applied across the generic, healthy population with a fair amount of consistency, an interesting phenomenon arises when assessing the movement patterns of elite performers. Elite performers are able to outperform novices despite displaying greater variability within their movements while remaining able to successfully accomplish a task, effectively demonstrating that greater demonstrations of variability are not necessarily markers of performance or stability. Understanding the population in question is inherently critical to interpreting the patterns of motor variability they display. This is particularly important in the context of concussion, as the injury rates for concussion are consistently among the highest of all reported injuries in multiple skill ranges spanning youth (i.e. novices) to collegiate and professional athletes (i.e. experts) [91]. Future studies examining healthy, elite level performers can potentially utilize crossover tasks to see the effect a moderation on the expert skill has on variability.

Variability of linear gait parameters has been utilized in clinical settings as a metric for assessing neurological function in populations including Parkinson's disease and multiple sclerosis patients. Within these populations, increases in variability of stride characteristics and gait velocity are commonly demonstrated in correlation with the progression of the disease [92,93]. Additionally, similar increases in stride length variability have been observed in healthy older adults [94,95]. While neurological disease amplifies the deficits in dynamic stability during gait, older adults can present with a certain degree of neurological decline associated with the biological aging process. The similarities in alterations in gait variability between healthy older adults and neuropathological patients are indicative that neurological decline, whether pathological in nature or not, are associated with motor control changes that ultimately reduce dynamic postural stability. These findings are further supported by the findings indicating that these same populations are at

a higher risk of sustaining a fall [96–98]. Together, these findings indicate that impaired neurological function results in an increase in movement variability in the context of gait, which ultimately places individuals in a more unstable movement pattern that raises the likelihood of the postural control system to accommodate an external perturbation resulting in a fall.

Despite its nature as a neurological injury, variability of movement parameters has not been widely utilized in diagnostic screening protocols for concussion. Gait assessments for concussion are typically not heavily instrumented, instead relying on subjective assessments of performance and/or time to complete a task [99]. Under current standards of treatment, gait assessments are graded on a pass-or-fail standard in which failure of the assessment is determined by failing to meet a benchmark time or by gross deficiency in one's ability to maintain balance. This creates a tradeoff in which expedience and accessibility of the protocol are prioritized over sensitivity and specificity of the results. Variability of spatiotemporal gait parameters (i.e. stride length, cadence, percent time in double-limb support) can provide insight to assess neurological function during gait; a valuable input when managing the treatment of a traumatic brain injury such as concussion. Gait variability offers a potentially useful metric for creating a more comprehensive picture of the duration and extent to which the damage to the central nervous system sustained following a concussion truly manifests that currently remains undetermined.

While variability studies have not focused on motor patterns to date, the effects of acute concussion on variability within the autonomic nervous system have been previously examined. Regulation of heart rate is the result of the scaling contributions of the sympathetic (i.e. excitatory) and parasympathetic (i.e. inhibitory) nervous systems. Therefore, measurements of heart rate variability can provide insight to the functioning of the autonomic nervous system, wherein delays in reflexes in response to stimuli and/or uncoupling of the contributions of the two branches of the

autonomic nervous system are indicators of neural dysfunction. Previous studies have indicated that concussion results in significant uncoupling of the branches of the autonomic nervous system, resulting in reductions in heart rate variability and inappropriate heart rate responses at rest and during exercise [100,101]. Acutely concussed athletes also demonstrate delayed autonomic reflex activations indicative of alterations in neural function. Studies assessing the human dive reflex, a normally immediate autonomic activation of the trigeminal (CN V) and vagus (CN X) nerves that lowers heart rate and increases blood pressure in response to cold temperature exposure on the face [102], have shown that this response is attenuated, but not absent, in recently concussed athletes, further indicating that concussion results in a disruption of the functioning and reduction in complexity between the two branches of the autonomic nervous system [103,104]. In addition, these deficits have been shown to remain after a concussed athlete has been clinically deemed to have recovered and capable to return to full participation in competition [105]. These findings indicate that concussion can result in alterations in autonomic function and changes in the regulation of consistency in signal output. Because of the wide variety of symptoms associated with concussion including balance impairments, the presence of changes in physiological variability associated with concussion suggest that changes in motor control would be present as well.

For assessments of standing posture, nonlinear measures of regularity have proven to be useful in the determination of impairments of postural stability. In particular, entropy has been utilized in postural stability assessments as a measure of regularity of postural sway as determined by center-of pressure (CoP) tracings during standing. Entropy is a measure of chaos within a signal. Physiologically, entropy values are interpreted to represent the amount of regularity within a signal in the time domain [106]. The use of entropy in physiological studies started with the application

of approximate entropy (ApEn). Over time, sample entropy (SampEn) has grown favor over ApEn because SampEn eliminates the presence of self-selection bias during calculation, one of the biggest limitations in using ApEn for analyses. Recently, multiscale entropy (MSE) has been implemented in assessments of CoP tracings in order to evaluate SampEn values on multiple time scales, creating a more comprehensive analytical scale that has shown to be more sensitive than SampEn values on any singular timescale [107]. Regardless of the specific type, entropy values are unitless and measured on a scale from 0 to 2, with lower values representing a more regular, predictable pattern (i.e. a sine wave) and higher values being indicative of a more irregular, chaotic pattern (i.e. white noise) [108].

Entropy measures of postural sway parameters have been shown to be an effective metric to quantify reductions in static postural stability in multiple neuropathological populations. From a motor control perspective, regular (i.e. lower entropy values) are interpreted to be indicative of a less stable system, as damage to neural tissue results in a reduced capacity for the complex oscillatory networks within the brain to produce and maintain upright posture under a wider variety of movement patterns. In cases of concussion, injured individuals have been shown to demonstrate decreased entropy values of their postural sway displacement for weeks after a return-to-play decision has been made [109,110]. Acutely concussed individuals have also been shown to demonstrate more regular sway patterns under both single and dual-task conditions. These findings are troubling because they signify that neurological deficits stemming from a concussion remain and go undetected by current screening protocols for concussion [111]. Similar alterations in CoP entropy values have been determined in Parkinsonian patients. Specifically, patients with Parkinson's disease demonstrate more regular postural sway patterns compared to healthy older adults [112,113]. The similarities in reductions in sway regularity seen in both neurodegenerative



disease (i.e. Parkinson's) and traumatic brain injury (i.e. concussion) supports the notion that damage to neural tissue results in a reduction in the capacity of the motor control circuitry within the brain to maintain upright posture, and thus manifests as a more protective postural control mechanism. Future efforts should be made to incorporate entropy measures in clinical settings, as ApEn, SampEn and MSE have all been shown to reveal deficits in postural stability that cannot be ascertained by looking at linear parameters of postural sway patterns alone.

### *2.1.3 Strategies for stabilization*

Within healthy individuals, both automatized and volitional mechanisms are implemented to retain postural stability when the mechanical equilibrium of the body is challenged. The implementation of voluntary movements to correct changes in posture is limited by musculoskeletal health and physiological reaction time as determined by the speeds of neural conduction and cognitive integration and processing. However, the autonomic reflexes based within the spinal cord can coordinate skeletal muscle activations that provide faster motor output to correct posture as well as anticipatory reflexes when movements are foreseen to occur [114]. Despite the lack of cortical input for the activation of these reflexes, humans are able to utilize the spinal reflexes under a variety of positions and variations of circumstances to maintain their base of support [115]. The combination of utilizing spinal reflexes and voluntary alterations in posture to maintain equilibrium allows humans the ability to navigate the external environment and correct perturbations to their posture and return the center-of-mass (CoM) within their base of support before sustaining a fall or injury. As such, neurological disease and/or injury can produce a direct effect on the body's capability to maintain postural stability on both an autonomous and volitional level depending on the site and extent of the neurological tissue damage.

The presence of autonomic postural control reflexes is evidenced by the fact that the center-of-pressure (CoP) created during standing is not stationary, ultimately creating sway displacement. Despite this constant fluctuation in the location of the CoP during standing, neurologically healthy individuals do not need to exhaust cognitive resources to properly maintain upright postural stability under most circumstances. In addition, movement of the trunk and upper extremities causes the body's CoM to be in a state of flux that must be accounted for by the postural control system [116]. These subtle changes in equilibrium are corrected by the autonomic postural control reflexes as they occur by activating muscle groups that antagonize each other, such as the quadriceps and hamstrings [117]. In addition, the musculature of the trunk and hips contribute to postural stability during standing and movement, demonstrating that maintenance of postural control of the body requires contributions from the entire body [19]. Such contrasting activity of the musculature allows for a proper equilibrium of activity between the large muscle groups that allows for consistent and purposeful action in maintaining postural stability both during quiet standing and during locomotion.

Efforts to optimize postural control have also been shown to utilize sensory feedback information to prepare for displacements of the body's CoM that may result from an anticipated perturbation. Specifically, postural control reflexes incorporate somatosensory feedback (i.e. proprioception) to determine how the skeletal muscles respond to fluctuations in postural sway. Prior research utilizing electromyography (EMG) have assessed the role of muscle contractions in the lower limbs and how these muscles activate in relation to postural sway [118]. Paradoxically, muscle fibers were shown to contract when the individuals were swaying in a direction that would lengthen the muscle fibers and lengthen in the opposite direction [119,120]. These contractions also occurred in short bursts rather than a single activation to correct for displacements in CoM,

indicating an ability to scale appropriately sized responses to correct the location of the body's CoM based on how greatly it has been displaced. In addition, these muscle activations are initiated reflexively by circuits housed within the spinal cord and thus do not require volitional cortical input. As a result, these autonomic responses occur faster than a typical stimulus-based reaction time (approximately 120-150 milliseconds) and allow for quick corrections when faced with external perturbations to the body's equilibrium. These findings indicate that to maintain proper muscle tone and upright posture, muscle fiber activation is anticipatory in nature and driven by available sensory feedback information [121,122]. This notion is supported by corresponding decreases in postural stability seen in conditions in which somatosensory feedback information is reduced such as peripheral neuropathy [123]. In the context of concussion, these findings collectively indicate that the postural stability deficits observed following concussion could be the manifestation of altered sensory feedback integration within the central nervous system, resulting in impaired functioning of both volitional and autonomic corrections to changes in equilibrium during upright standing.

When autonomic responses cannot overcome a disruption of equilibrium, systemic adjustments must be made to implement strategies for maintaining stability and correcting perturbations. In these cases, the structures of the brain including the cerebral cortex, cerebellum, and basal ganglia are interconnected thoroughly to respond accordingly to various types of sensory feedback indicating a need to initiate motor output in order to restore mechanical equilibrium. These adjustments can be either precautionary or reactionary in nature. Depending on the level of functioning of a given individual's postural control system based on prior sustained injury or identified pathology, the proportional distribution toward either strategy may vary in nature to optimize postural stability under a variety of circumstances. The overall goal of any postural

control strategy is to keep the body's CoM within the base of support created by the posture being assumed. This can be achieved in two manners: (1) increasing the area comprising one's base of support, or (2) changing one's posture to manipulate the location of the body's CoM. For example, these strategies can respectively be implemented by (1) widening one's stance during upright standing and step width during gait, and (2) abducting the shoulder's ninety degrees from anatomical position to maintain stability during tandem gait. However, not all strategies are feasible without sacrifice. For example, stiffening the musculature of the lower limbs can reduce overall postural sway displacement at the cost of increasing sway velocity [124,125]. In cases of acute concussion, compensatory strategies for maintaining postural stability appear to be precautionary in nature, as evidenced by alterations in gait initiation and widening of the base of support during quiet standing as well as gait [126,127]. However, the objective duration to which these altered postural control strategies remain following a concussion is currently inconclusive.

A key component of maintaining postural stability is the prioritization to stabilize the head during movement. The vestibular nuclei work in conjunction with feedback from the optic nerves to facilitate the vestibulo-ocular reflex (VOR), which stabilizes the visual field by coordinating eye movements in relation to movements of the head [128]. It has been previously established that healthy aging as well as neurological disease are associated with increased movement of the head during gait as well as an increase in falls risk. Within both of these populations, it is believed that the oscillations produced during gait are not attenuated while ascending the kinetic chain from the feet to the head, resulting in head movements of greater magnitude and a decrease in dynamic stability as the postural control system fails to accommodate these excessive movements [129–131]. As a compensatory mechanism, populations that demonstrate decreased stability at the level of the head adjust their gait pattern (i.e. reduced velocity) to mitigate these deficits in postural

control and maximize stability at the head [132,133]. Interestingly, the potential association between alterations in gait patterns and stabilization of the head have not been explored in the contexts of concussion or prior history of concussion. As the most common form of traumatic brain injury, concussion represents a neurological pathology that has recently seen a growing amount of connections to long-term consequences stemming from a prior history of injury [134,135]. Analysis of the stability of the head during gait could potentially provide greater context as to how damage sustained from a concussion affects the postural control system.

## **2.2 Pathophysiology of Concussion**

The brain is a staggeringly complex and metabolically expensive organ. As such, damage incurred via traumatic impact or disease can fundamentally alter the brain's ability to execute its plethora of functions and roles to maintain homeostasis and allow the body to navigate and thrive in the external environment. Thorough understanding of the pathophysiology of a disease and/or injury is crucial for efficacious treatment. For decades, the specific physiological nature of the damage sustained following a concussion was poorly understood and therefore not considered during clinical evaluations. Recently, the cultural narrative that concussion is an injury that athletes should be able to "power through" or "walk off" has been gradually dissipated in light of the ongoing findings that concussion can result in neurological impairments not only acutely, but far beyond the point of the initial traumatic incident [136,137]. However, because cases of concussion do not consistently present with outwardly apparent signs of physiological impairment, concussion is still primarily treated based on identified symptoms rather than the underlying pathophysiology of the traumatic injury itself.

These long-term changes in neurological function can be attributed to the unique physiology of the central nervous system and specifically how trauma sustained during a concussion can result in persistent changes in brain function on both cellular and systemic levels. The pathophysiology of concussion is further complicated due to the numerous complex networks and structures within the brain that are directly responsible for proper implementation and maintenance of cognitive, somatic and autonomic functioning. Taken in context, these obstacles have contributed to understanding the physiological changes stemming from concussion being the greatest source of difficulty in management of concussion.

### *2.2.1 Mechanisms of injury*

Despite heavy fortification provided by the skull and shock-dispersing capabilities of the surrounding cerebrospinal fluid (CSF), the brain is vulnerable to injury when the head is subjected to a traumatic event. There are several characteristics of head trauma that contribute to the severity of damage to brain tissue and the likelihood of sustaining a concussion. These variables include location of impact, force of impact, type of impact (blunt impact, shockwave, etc.), and resulting head accelerations. The brain's unique physical properties ultimately allow its tissue to react differently depending on the type of trauma it undergoes based on the type of acceleration or pressure to which it is subjected. As such, the brain is able to withstand certain types and amounts of physical stress more readily compared to others.

While the idea of a specific injury threshold for concussion is debated, there is a general consensus that there is a limit to how much acceleration, be it linear or rotational in nature, the brain can withstand before tissue damage occurs [138,139]. Traditionally, studies examining brain trauma utilized animal models to study the effects of linear acceleration on the brain, as this was

thought to be the driving factor behind whether the impact would or would not result in a concussion. These studies identified how brain tissue is able to change its properties based on the forces applied to it [140,141]. In most cases, the brain is able to withstand the changes in intracranial pressure brought on by increases in linear acceleration. Brain tissue does not easily deform under slow and transient increases in pressure, which is beneficial when trauma manifests from purely linear acceleration of the brain as this would minimize any risk of damage or injury to tissue [142]. It has also been noted that the threshold for cellular damage to neurons and astrocytes brought on by linear acceleration is much higher than the amounts of linear acceleration experienced in head impacts that resulted in diagnosed concussions [143]. In fact, spikes in linear acceleration have been shown to be more effective predictors for skull fractures rather than concussion, which has led to helmet manufacturers using linear acceleration as their grading metric for safety [144–146]. Despite this, multiple studies have attempted to calculate an injury threshold based on linear acceleration of the head during impact to predict whether or not a concussion has occurred [139,147–150]. Though the numbers vary between models such as the Wayne State Tolerance Curve (WSTC), these studies have resulted in functions to estimate the likelihood of sustaining a concussion based on linear accelerations with proposed injury thresholds for concussion defined from approximately 80 to 110 Gs [151–154].

While the brain can withstand linear accelerations relatively well, it is much more vulnerable to the effects of rotational acceleration. Brain tissue has a considerably low shear modulus, meaning the tissue is particularly vulnerable to shear stress brought on by large amounts of rotational acceleration [155,156]. Mechanical strain induced by high amounts of rotational acceleration (approximately 5500 rad/s/s or greater) [147,157] results in greater amount of tissue deformation and axonal damage than that brought on by purely linear acceleration. This degree of

damage impairs axonal function and communication between neurons which can manifest in numerous symptoms that are commonly associated with concussion [158,159]. The location of the head impact also seems to be a crucial component of the severity of the resulting damage. The brainstem and thalamus are the most vulnerable structures to shear stress [139]. Incidentally, these two structures are also severely affected by trauma in the coronal plane and from the top of the head down [160]. Prior research has shown that coronal plane rotational acceleration leads to the greatest amount of diffuse axonal injury as well as the greatest amount of damage to the deep structures of the brain including the diencephalon and brainstem [143,155,161]. These factors indicate that rotational, not linear, acceleration is the driving force behind concussion and traumatic brain injury. While a combination of increases in rotational and linear acceleration put an individual at the greatest risk of sustaining a concussion, research has shown that if the greater the amount of rotational acceleration and resulting shear stress, the less that linear acceleration and corresponding changes in intracranial pressure contribute to sustaining damage severe enough to be identified as a concussion [148].

Blast injuries like those commonly seen in military combat environments produce a unique mechanism of injury to the brain. Because the brain is composed primarily of water, brain tissue is particularly vulnerable to shockwaves produced by an explosive blast. Unlike pressure gradients created by blunt traumas and linear accelerations, injuries from a blast result in much more widespread intracranial pressure increases rather than at a focal point based on the site of a blunt impact [162]. Currently, long-term effects of traumatic brain injury stemming from blast exposure are not as well understood as injuries resulting from blunt trauma. However, there are significant associations between repeated blast exposure and symptoms associated with concussion, such as emotional dysregulation, balance impairments and chronic headaches [163–165]. These symptoms



are respectively indicative of damage to the structures of the limbic system, the vestibular system, the sensorimotor networks, and widespread inflammation throughout the cerebral cortex. Troublingly, the relation between blast exposure and concussion are not typically addressed in military settings, as soldiers returning home that were exposed to more blasts reported more symptoms associated with concussion and poorer neuropsychological function despite not being diagnosed with a concussion, possibly because of the absence of documented blunt head trauma [166,167]. More recently, however, blast exposure has been shown to be associated with a decrease of apolipoprotein E4, a protein that is essential for maintaining integrity of white matter, which could potentially help explain the symptomatology that appears to be associated with excessive and repeated blast exposure [168]. Future endeavors should direct more attention and resources toward identifying the incidence and effects of blast trauma in populations that are regularly subjected to exposure to shockwaves.

### 2.2.2 *Metabolic dysfunction*

At rest, the brain is predominantly the most metabolically active organ of the body. Despite accounting for approximately two percent of the body's total mass, the brain receives approximately fourteen percent of the body's resting cardiac output and accounts for twenty percent of total body oxygen consumption [169,170]. While a high resting metabolic rate is crucial to allow the brain to properly allocate resources towards completing its numerous functions, it can be particularly problematic in cases of traumatic injury. As with all injuries to somatic tissue, the damage to brain tissue sustained during a traumatic impact results in a re-distribution of metabolic resources to initiate and facilitate the repair of damaged cells and tissue and advance the recovery process at the site of the injury. In cases of concussion, the sequence of metabolic changes that

occur following a traumatic brain injury has been termed the “neurometabolic cascade” [171]. The neurometabolic cascade is triggered immediately upon sustaining trauma to the brain as neural activity is disrupted by gradually increasing imbalances of ionic concentration gradients created as damaged tissue fails to properly regulate ionic flow across its membranes. To address the sudden changes in equilibrium following concussion, an influx of metabolic resources that serve as a means to address the damage that triggered the response flood the site of injury to restore ionic equilibrium, but also presents an internal environment that leaves the brain vulnerable to further, more severe damage in the form of excitotoxicity if the response is unexpectedly disrupted or exacerbated [172,173].

A troubling contributing factor in assessing physiological changes associated with concussion is the lack of large-scale damage that can be located or even detected with sophisticated neuroimaging techniques [174,175]. Instead, immediately upon sustaining a traumatic impact, damage to neural microstructural tissue impairs the brain’s ability to maintain a homeostatic ionic environment. Traumatic damage causes perforations in the lipid membranes of neural cells that ordinarily only allow ions to pass in or out of the cells via specialized protein pumps embedded within the cell membranes. By allowing concentration gradients to allow ionic flow between the intracellular and extracellular regions without proper regulation from the protein channels, a resulting influx of sodium and efflux of potassium quickly creates a problematic environment for proper neural activity to take place. Additionally, an influx of calcium ions into the mitochondria can potentially disrupt cellular respiration and thus obstruct cellular energy production. To counter this drastic and compounding change in the ionic environment, the cellular ionic pumps drastically increase their rate of activity in an attempt to remove excess calcium and sodium ions from the intracellular environment and bring extracellular potassium ions back into the cell [176]. However,

depending on the extent of the sustained damage, this strategy is often insufficient to restore homeostasis. The cellular ionic pumps are dependent on adenosine triphosphate (ATP) to optimally function. Therefore, to work at a rate in which ATP is utilized faster than it is replenished quickly placed the cells in an anaerobic state, leading to the build-up of extracellular metabolites including lactic acid and adenosine [177–179] as well as a reduction of extracellular glucose as the depletion of ATP requires the utilization of anaerobic metabolism in order to produce viable forms of energy [180]. Predictably, this strategy for homeostatic restoration is not sustainable for long periods of time, and is thus followed by a period of cerebral hypometabolism due to the lack of available metabolic resources in combination with remaining structural damage that has yet to be completely resolved.

The state of cerebral hypometabolism following a traumatic brain injury can persist up to ten days following the initial impact [181,182]. This window is believed to be of crucial importance during the recovery process as it is the stage of the neurometabolic cascade in which the brain is as its most vulnerable to secondary and more severe injury. Experimental impacts conducted on animal models have indicated that secondary concussive impacts during the period of hypometabolism in which less extracellular glucose is available had cumulative effects upon the initial injury that could potentially exacerbate damage within the ionic environment as well as the surrounding cytoskeleton and axonal networks [183,184]. However, when similar concussive impacts were applied after resolution of the ionic environment, the two impacts displayed the characteristics of two independent injuries, suggesting a restored ability to properly attenuate metabolic resources in response to injury [185]. These findings indicate the presence of a time-sensitive window within the neurometabolic cascade during which the brain is hypersensitive to a secondary traumatic injury that results in a severe, potentially catastrophic metabolic crisis.

In humans, the vulnerability of the hypometabolic window following a concussion has been most frequently observed in cases in which athletes have been administered a premature clearance to return to activity. Clinical assessments of cognitive function and balance have been shown to lack sensitivity to detect the presence of symptoms and predispose concussed individuals, particularly those that have sustained multiple prior concussions and are thus familiar with testing protocols, to receive an inaccurate declaration of full recovery [9,186]. An athlete sustaining a secondary concussive impact in the midst of the hypometabolic window is at an increased risk of developing “second-impact syndrome”, a life-threatening condition in which the brain loses its ability to properly regulate intracranial cerebrospinal fluid (CSF) and cerebral blood pressures, leading to dangerous, fast-onset encephalopathy, reduction in cerebral blood flow, and dangerous rises in acidosis [187,188]. While cases of second-impact syndrome are clinically rare, the incidence rate is currently inconclusive because of continued debate over the nature and definition of the condition. However, most confirmed cases are fatal in nature with death occurring within minutes of the secondary impact. Because metabolic function is rarely taken into account when making return-to-play decisions for concussion, the hypometabolic window and lingering danger of a secondary impact causing a catastrophic physiological collapse are often overlooked, particularly when cognitive and somatic symptoms commonly associated with concussion (headache, dizziness, nausea, balance impairment, etc.) are absent during screening. Until metabolic testing becomes a facet of concussion treatment and management, the return-to-play decision will need to rely on safety recommendations and increasing patient knowledge of concussion symptomology in order to maximize safety and avoid further injury when determining whether a concussion has been fully resolved.

As the ionic environment gradually returns concentrations of sodium, potassium and calcium ions to proper levels and glial cells contribute to repairing damaged axons and cytoskeletal structures, the cerebral internal environment recovers, and the metabolic rate returns to resting levels. Fortunately, most cases of concussion are mild in nature and appear to resolve without permanent neurophysiological dysfunction. However, studies have shown that trauma inducing severe metabolic dysfunction can have malignant effects decades following the initial trauma. Neural tissue that is not repaired beyond the resolution of the hypometabolic window is prone to protein degradation and in extreme cases, apoptosis [189]. Traumatic brain injury has been associated with chronic metabolic dysfunction and resulting cell death that has been linked to multiple neuropathological conditions including Parkinson's disease, Alzheimer's disease and amyotrophic lateral sclerosis (ALS) [190–193]. Recently, the link between repetitive head trauma and the development of chronic traumatic encephalopathy (CTE) has received a growing amount of mainstream attention in part to its association with a disproportionate number of cases identified in former contact-sport athletes [135,136,194]. While no causal link between concussion history and CTE has been definitively established, increases in widespread awareness and long-term concerns over neurological well-being have sparked long overdue discussions about the potential consequences of concussion beyond the resolution of subjectively observable symptoms.

Further research is required to identify physiological factors of traumatic brain injury that may contribute to neurodegeneration years and decades following the initial trauma. In addition, it remains to be determined how long-term cerebral metabolic dysfunction can impact the postural control system over time regarding both a potentially reduced ability to regulate postural stability and/or the possible development of neurodegenerative disease. Reductions in cortical activity levels have been identified using electroencephalography (EEG) and transcranial magnetic

stimulation (TMS) to persist after the clinical resolution of balance impairments following concussion, indicating that voluntary activation and control of movement can potentially be affected by reduced cerebral metabolic rates long after the initial injury has been sustained and possibly deemed to be recovered by medical professionals [16,195]. However, because metabolic dysfunction on the cellular level is difficult to identify by current clinical screening methods, addressing the potential dangers and consequences of failing to take protective actions following a concussion to address metabolic dysfunction remains a challenge for both those that sustain and treat injury.

### 2.2.3 *Symptom manifestation*

The complex nature of the brain's connectivity allows it to perform a vast amount of physiological functions and regulate multiple systems in the body's periphery. As a result, concussion can result in a wide spectrum of symptoms manifesting in many unique combinations depending on the location, type, and severity of undertaken trauma. Clinically, this presents a challenge as concussion can present with a medley of symptoms that can be neurocognitive, biomechanical and/or physiological in nature with no standardized pattern of symptoms to fit the presentation of every sustained injury [4]. Therefore, symptom management of concussion must be treated carefully on a case-to-case basis to specifically address the combination of symptoms that present with each individual injury. Unfortunately, because some potential symptoms are more difficult to identify and objectively assess than others, the standard assessments used to screen for concussion places disproportionate emphasis on symptoms that can be identified quickly and accurately with a reasonable degree of certainty rather than those that can pose a risk for persistent, more severe impairment. Failure to account for all possible symptoms that can arise following

concussion can result in false negative diagnostic screenings and/or premature declarations of medical clearance, both of which predispose an injured individual to a secondary concussion or more severe neurological trauma.

The majority of symptoms identified in cases of concussion are cognitive and/or neuropsychological in nature and are among those that present the most frequently in cases of concussion. As such, multiple screening guidelines have been developed to identify symptoms associated with concussion including the Sport Concussion Assessment Tool (SCAT-5) and the Concussion Recognition Tool (version 5) [196–198]. These screening tools are advantageous because they can be administered quickly following a suspected injury and can determine the presence of concussion symptoms without the need for specialized equipment. In addition, these screening tools explicitly look to identify symptoms that not only arise immediately following a traumatic impact, but also those that can persist for hours and days following the injury in order to grade recovery progress. For example, headache is among the most common symptoms that present with concussion and is a hallmark symptom of post-concussion syndrome (PCS) [199,200]. Paradoxically, there are no nociceptors within cerebral tissue itself, and thus direct damage to brain tissue does not elicit pain. Headache following a traumatic brain injury is thought to be brought on by widespread inflammation that irritates and thus stimulates the nociceptors within the meninges and major cerebral veins and arteries [201]. Because inflammation of cerebral tissue cannot be accurately located without medical imaging techniques, headache does not often provide context as to where the specific damage is located and therefore what symptoms can be expected to coincide. However, several symptoms of concussion can provide health care professionals with insight towards what part of the brain has sustained the most significant damage following a traumatic impact.

Many of the symptoms associated with concussion can be attributed to damage or dysfunction within the divisions of the cerebrum. As the most superficial segment of the brain and the largest portion by both mass and surface area, the cerebrum is often the most prominent portion of the brain to withstand the force of a traumatic impact. The frontal lobes regulate executive function, language production (i.e. Broca's area) and voluntary movement via the primary, premotor, and supplementary motor areas [202–206]. Thus, dysfunction of the frontal lobes can manifest as deficits in maintaining concentration, attention deficits, emotional expression, rational decision making, and movement planning. The parietal lobes play significant roles in somatosensory perception, voluntary actions involving tool use, and spatial coordination within the external environment [207–210]. As such, concussive trauma to the parietal lobes can result in impaired sensorimotor integration, postural instability, and in severe cases, difficulties using tools and an inability to recognize objects in space (i.e. agnosia) and faces of friends and relatives (i.e. prosopagnosia). The temporal lobes contain the primary auditory cortex as well as centers for memory consolidation and language comprehension (i.e. Wernicke's area) [211–213]. Damage to the temporal lobes associated with concussion can result in tinnitus, heightened sensitivity to noise, and short-term memory loss. Of note, head impacts at the site of the temporal bones generating large amounts of rotational acceleration have been indicated to present the worst prognosis in cases of concussion [155]. Lastly, the occipital lobes are primarily responsible for generating vision created by signals relayed from the optic nerves [214–216]. Damage to the occipital lobes following concussion can produce blurred vision, diplopia, alterations to near point of convergence, and in severe cases, developments contributing to agnosia. The vast array of symptoms following concussion associated with damage to the cerebrum can be difficult to comprehensively assess. However, identification of the presence of such symptoms can provide



important context about the severity of the sustained damage, what constitutes the most appropriate course of treatment, and the projected outcome of the aforementioned treatment [217,218].

Postural instability arising from concussion can also be indicative of damage to or dysfunction of brain structures outside of the cerebrum. Widespread white matter damage throughout the brain can result in impaired communication between the structures of the postural control system, most notably involving the thalamus. The thalamus is often referred to as the “switchboard” of the brain; an integral structure that directs neural communications to and from numerous sensorimotor areas and networks throughout the brain. Injury to the microstructures that interconnect with the thalamus following concussion have been shown to correlate positively with the presence of post-concussion symptoms for several months following the initial trauma [219,220]. Functional impairment of the thalamus can interfere with proper communication of multiple neural tracts that contribute to proper maintenance of postural control including the lateral corticospinal tracts (voluntary control of distal musculature), dorsal column medial lemniscal tract (proprioceptive feedback), and the cerebellothalamic tract (motor adaptation and long-term potentiation). In addition, damage to the cerebellum can also cause immediate dysfunction of postural control. Depending on the specific site of the lesion or inflammation, cerebellar damage can result in truncal or appendicular ataxia, conditions characterized by a loss of proper motor coordination of the axial and limb musculature, respectively [221,222]. Previous studies assessing the long-term implications of concussion history have found that concussion is not associated with chronic structural damage to the cerebellum, but rather an increased rate of functional abnormalities [223,224]. These previous findings indicate that postural instability associated with concussion can potentially be exacerbated by dysfunction of the white matter networks and

interconnections associated with the thalamus and cerebellum that persists long after clinical resolution of the injury.

The most severe cases of traumatic brain injury involve trauma to the brainstem. Compression and trauma to the brainstem can result in swelling, herniation, coma, and irreversible damage as the result of a hemorrhagic stroke if the trauma does not initially result in death [225,226]. Despite the potentially drastic consequences, brainstem trauma is unsettlingly common in cases of severe concussion. The most common symptom of a brainstem injury associated with concussion is an immediate but transient loss of consciousness and concurrent loss of skeletal muscle tone and upright postural stability [71,227]. However, concussion resulting in loss of consciousness can be accompanied by involuntary extension of the upper limbs referred to as the “fencing response”, named in reference to its resemblance to the asymmetric tonic neck reflex, also referred to as the “fencing reflex”, commonly displayed by infants [228,229]. The fencing response is believed to be the result of the mechanical force of a traumatic head impact triggering activation of the lateral vestibular nucleus of the brainstem; a structure that works in conjunction with the cerebellum to conduct a significant role in initiating reflexive corrections during sudden perturbations of upright postural stability including extending the arms to brace for a potential loss of balance [230,231]. Although the fencing response typically wanes after only a few seconds as the upper limb extensor muscles gradually relax, identification of this sign of brainstem trauma in cases of concussion is a valuable and crucial clinical metric for determining the severity of the injury and proper course of treatment, as it has been reported that over half of all cases of concussion presenting with loss of consciousness also present with a fencing response [228]. More severe cases of brainstem injury can result in the injured individual involuntarily assuming one of

two clinically distinct, rigid postures while unconscious classified as (1) decorticate posturing and (2) decerebrate posturing.

Decorticate posturing is the result of trauma to the midbrain that results in disinhibition of the red nucleus, resulting in involuntary activation of the flexor muscles of the upper extremities as output from the rubrospinal and medullary reticulospinal tracts overcome the extensor responses from the vestibulospinal tracts and pontine reticulospinal tract [232]. However, trauma to the brainstem also disrupts the function of the lateral corticospinal tract, allowing the vestibulospinal and pontine reticulospinal tracts to activate the extensor muscles of the lower limbs. As a result, decorticate posturing presents with the arms and wrists flexed over the chest and the legs extended and rotated toward the midline of the body [232,233]. Conversely, decerebrate posturing arises as a result of brainstem damage to the rubrospinal tract inferior to the red nucleus and throughout the reticular formation [234]. This combination leads to disinhibited excitation of the vestibulospinal and pontine reticulospinal tracts as well as a lack of reflexive responses to external stimuli (i.e. those intended to elicit pain to test for alertness). As a result, decerebrate posturing presents with an unconscious individual demonstrating rigid cervical extension, clenched teeth, arms and elbows profoundly extended and legs extended with internal rotation [235,236]. An individual exhibiting either decorticate or decerebrate posturing scores a maximum of a three on the Glasgow Coma Scale and is thus considered to be undergoing a medical emergency requiring immediate intervention to restore proper brain function [237]. Prognoses for both decorticate and decerebrate posturing are poor because the trauma in these cases is sited near the autonomic nervous system's regulatory centers within the brainstem, which vastly increases the risks of sudden onsets of cardiac arrest and/or respiratory failure.

## 2.3 Epidemiology of Concussion

Over the past several decades, significant advances have been made in increasing the emphasis on implementation of rules and safety protocols in athletics as well as in the development of technology designed to protect against and reduce the risk of sustaining concussions. Despite these improvements, incidence rates of concussion have consistently remained high within athletic populations in the United States [238]. Recently, concussion has gained more mainstream attention within populations ranging from youth athletes to professionals as the long-term detrimental effects of concussion are beginning to become more apparent [135,239]. Efforts to curtail the incidence rate of concussion are made difficult by a combination of factors including heavy reliance on subjective self-reports of symptoms, a lack of objective diagnostic testing and imaging techniques, predisposition to premature returns to activity increasing risk of secondary injury, and a culture that prioritizes mental toughness and perseverance over accepting medical treatment in the face of injury.

### 2.3.1 Injury rates

Concussion is an injury that is commonly associated with sports that include physical collisions (i.e. rugby, American football, ice hockey) and elements of combat (i.e. boxing, mixed martial arts, ice hockey). However, athletes are not a comprehensive representation for the overall population that experiences traumatic brain injury in the United States. According to the Center for Disease Control (CDC), across the general United States population, falls account for nearly half of all emergency room visits attributed to traumatic brain injury, followed by motor vehicle accidents accounting for approximately twenty percent [240]. In contrast, for physically active, young (i.e. 18-30 years old) individuals, head impacts during sports rank as the second most

common cause of concussion trailing only motor vehicle accidents [241]. The majority of reported sport-related concussions occur in individuals aged nineteen and under and in sports that incorporate the potential for violent bodily collisions such as American football and ice hockey [242,243]. Athletes competing in these sports are often the subject of discussion when concussion rates and injury risks are brought into the limelight. While rule changes and equipment upgrades have improved safety during gameplay for athletes [244,245], the incidence rate of not only concussion during sport remains troublingly high, but risks of secondary injuries and development of pathologies later in life have recently been gaining more attention as potential consequences of concussion that have long been overlooked [246,247].

Concussion is consistently among the most commonly seen injuries in competitive sports, trailing only lateral ankle sprains in reported frequency [248]. However, it is difficult to accurately calculate the incidence rate of concussion as not all cases are reported to medical professionals and diagnostic screening criteria are more heavily reliant on subjective symptom reporting rather than objective evidence of neural tissue damage to identify cases, making concealment of symptoms an ill-advised, yet feasible option for injured, irrationally driven athletes [249]. As a result, reports of the number of cases of concussion occurring annually in the United States have varied significantly in both number of cases and terminology. Reported estimates range considerably from 1.6 to 3.8 million annual cases of concussion occurring an estimated rate of 3.89 to 9.21 sport-related concussions per 10,000 athlete-exposures (participation in a game or structured practice) depending on the sport and environment in question, with greater numbers of injuries being reported during competitive game environments compared to more controlled, structured practices [242,250–252]. Despite fluctuations in estimates of the number of cases, there is a general consensus that the number of identified cases of concussion has been steadily increasing for years

[253]. In addition, athletes that have a prior history of concussion have been shown to be more likely to sustain a subsequent or multiple additional traumatic brain injuries at rates ranging from fifty to three hundred percent compared to those that have never sustained a concussion [254,255]. This association between concussion history and increased risk of sustaining a concussion creates a cumulative pattern of damage that has been theorized to stem from aggressive playing styles mandated by the sport of choice [256] and/or decreases in cortical activity levels resulting from premature returns to activity leaving athletes vulnerable when responding to stimuli within a dynamic environment [16,257]. The reported number of cases is even more striking when considering that it has been noted that underreporting rates of concussion in sports have been documented as high as forty percent [258]. Combined in context, the data suggest that number of sustained concussions in sports is not only remaining high despite institutional and technological adaptations, but the incidence rate likely remains higher than epidemiological studies can accurately detect and report.

Active military personnel represent another population that is regularly at a high risk of sustaining a concussion or another, more severe form of traumatic brain injury. Over three hundred thousand cases of traumatic brain injury have been reported by United States military personnel since the turn of the twenty-first century [259]. While the U.S. military classifies traumatic brain injury to include both closed (i.e. concussion) and open (i.e. penetrative) head trauma, cases of closed head trauma consistently and easily outnumber the latter [260]. Recent studies examining soldiers that faced combat in Iraq and Afghanistan since the dawn of the twenty-first century revealed that detonations and subsequent explosions caused by improvised explosive devices (IEDs) were the most common cause of injury in combat [261,262]. Mild traumatic brain injury, or concussion, is a common injury following exposure to a nearby explosion or blast trauma and

was the most common reported injury from American soldiers serving in Iraq and Afghanistan, outnumbering shrapnel wounds and tympanic membrane (i.e. eardrum) ruptures [261]. Furthermore, mild traumatic brain injury resulting from an explosion has been shown to have impacted a sizable proportion of the military, with estimates as high as twenty percent of veterans returning from combat having sustained at least one blast-induced traumatic brain injury [263]. The shockwaves created by an explosion have a distinct detrimental effect on brain tissue unlike what is sustained during blunt trauma such as a head impact commonly seen in contact sports, making management of the injury challenging to clinicians that typically specialize in treating sport-related concussion [168]. In addition, blast trauma is associated with increases in vestibular dysfunction and additional symptoms associated with post-traumatic stress disorder (i.e. insomnia, emotional regulation) [163,264–266]. Post-traumatic stress disorder stemming from one or multiple mild traumatic brain injuries presents a persistent problem that thousands of men and women that have served in combat must contend with years after sustaining their most recent injury and long after their service has come to an end.

The combination of the semi-unpredictable nature of competitive sports, the violent nature of combat, and the wide disparity between the numbers of actual and reported cases of concussion have sparked an initiative to attempt to identify qualities within individuals that could potentially predispose them to concussion. Sex has been repeatedly assessed as a potential predisposing risk factor for concussion and predictor for severity of post-concussion outcomes. There have been conflicting findings based on how sex potentially influences concussion risk and incidence. Prior reports have stated that male and female athletes playing the same sport experience concussions at similar rates [267]. However, multiple prior studies have identified higher incidence rates of concussion among female athletes compared to males when looking across a variety of sports

[238,268,269]. In addition, injured female athletes repeatedly reported a greater number of concussion symptoms to clinicians and experienced longer recovery times compared to their concussed male counterparts [270–272]. A similar trend was found in studies assessing traumatic brain injury rates of female soldiers, which stated that women were more likely to report long-term symptoms consistent with post-concussion syndrome (PCS) and post-traumatic stress disorder (PTSD) compared to men [273]. Studies examining the effect of sex differences on outcomes in traumatic brain injury in the military are currently limited, but the findings currently unearthed are worthy of further and more thorough examination. Together, the findings based on athlete and military populations suggest a disparity between males and females regarding predisposition to sustaining and outcomes of recovery from concussion.

It is worth noting that the researchers conducting these studies did not specifically name sex as an objective precursor to concussion risk. Specifically, an association was identified which stated that females were more likely to disclose a state of injury and symptoms to medical personnel compared to males, who are generally more likely to conceal symptoms and perform through injury [274,275]. Symptom reporting rates between sexes do not align well with the incidence rates of concussion when broken down by sport, as sports involving predominantly male athletes such as American football are consistently among the most prevalent regarding incidences of injuries including concussion [252,276]. In military populations, previous studies have found that while women were more likely to report symptoms compared to men, the epidemiological rate of post-traumatic stress disorder is higher in men that have sustained a traumatic brain injury during military service compared to the general population, suggesting that male combat veterans are less likely to address symptomatic developments to medical personnel [277,278]. This distinction is critical in understanding the role of sex in concussion diagnostics, as women are



reportedly sustaining concussions and symptoms more frequently out of a sense of transparency and a potential reporting bias rather than a physiological predisposition to injury compared to their male counterparts [279]. Future evaluations of the intrinsic and environmental factors surrounding and embedded within the cultures of athletics and military service could potentially provide more insight into the causal nature of the discrepancies between concussion reporting and incidence rates between men and women.

Further complicating the management of concussion is a recently revealed association between concussion and lower-body orthopedic injuries including lateral ankle sprains and anterior cruciate ligament (ACL) tears. Multiple previous studies have identified impairments of dynamic postural stability during gait following concussion [280,281]. These findings suggest that concussed individuals are also potentially less stable while performing more complex and ballistic movements such as those commonly performed during athletics. Insufficient postural control can result in kinematic patterns that increase the risk of orthopedic injury during movement, particularly at the knee and ankle joints created by excessive rotational accelerations and torques resulting in severe structural damage to the supporting ligaments and tendons. Exploratory efforts have identified an increased incidence rate of lower-body orthopedic injuries in the weeks and months following a concussion [282]. Recently concussed athletes have been shown to be approximately two to three times as likely to sustain a lower-limb orthopedic injury compared to their uninjured counterparts up to twelve months following the initial injury, despite being clinically deemed safe to return to normal levels of activity [283–285]. Because post-concussion screenings often do not closely examine neural mechanisms of motor control, the deficits and/or alterations in functioning that contribute to this increased injury risk are frequently undetected and overlooked. Additionally, the link between musculoskeletal injury and concussion appears to be

chronic in nature, as history of concussion has previously been positively correlated with prevalence of musculoskeletal injury across the lifespan of former athletes [286]. Despite the numerous reports signifying an increased risk of orthopedic injury following concussion, no study to date has identified a causal basis for this relationship. Future efforts should be directed toward identifying the neurological foundations of this increased injury risk following concussion and how to objectively identify said risk before the occurrence of a catastrophic injury.

The combination of the subjective nature of the current screening techniques for concussion, relative ease of symptom concealment in mild cases, and the sheer number of cases occurring among a wide variety of populations makes concussion a uniquely difficult injury to accurately document for epidemiological purposes. While the potential for inaccurate reporting rates for concussion is troubling, the notion that reports could be underestimating the actual number of annual cases on a scale of millions is alarming and warrants increased attention and efforts to correct the methods currently used to detect cases of concussion. Furthermore, the normalization of underreporting rates of concussion increases the likelihood that individuals who do sustain one or more concussions will experience chronic impairments of neurological function without properly addressing the underlying injury or even recognizing the state of impairment.

### *2.3.2 Obstacles to reporting*

Proper treatment of concussion is a complex, multi-faceted endeavor that requires a comprehensive understanding of the neurophysiological basis of the injury itself, the combinations of symptoms that can potentially arise from a traumatic brain injury, and sensitive testing equipment and/or protocols that can accurately detect the presence of symptoms for the purposes of diagnostics and determination of recovery. Unfortunately, there are multiple factors contributing

toward a discrepancy between the total number of sustained concussions and the number of cases reported to medical professionals in the United States. Both intrinsic and extrinsic in nature, these factors can result in false negative diagnoses, mismanagement during the rehabilitation process leading to premature decisions to administer medical clearance, and an increased risk of subsequent and potentially more severe traumatic brain injury.

Even though concussion can present with somatic symptoms clearly indicative of dysfunction (i.e. nausea, balance impairment), neurocognitive symptoms can be difficult to detect without disclosure from the injured individual and thus can be concealed if minor in nature [287,288]. As a result, injured individuals themselves must be able to identify the presence of symptoms, recognize that their health has been compromised, and come forward to medical professionals in cases of concussion where symptoms are not outwardly apparent. Recently, efforts have been made to increase education among athletes and other high-risk populations about concussion symptoms in an attempt to increase disclosure rates from injured individuals [289]. Topics have included how concussions can occur, prevention strategies, what symptoms can be associated with a concussion, how to identify the presence of symptoms, and the proper course of action should a sustained concussion be suspected by a teammate or oneself including alerting supervisors and/or medical personnel [290].

The development of concussion education programs has revealed numerous noticeable trends among athletes. First, it was made apparent that many athletic programs lacked formal concussion education programs, with up to one third of athletes reporting having never received education about concussion protocols and treatment [291]. Second, concussion education programs implemented over the course of the last decade have revealed that while many athletes have a fundamental knowledge of what causes a concussion, a large proportion were unfamiliar

with the symptoms of concussion, treatment protocols and return-to-play procedures implemented by their sports' governing bodies [292,293]. Third, athletes that had previously experienced a concussion and thus had first-hand experience in the treatment process were shown to be less likely to report symptoms to a medical professional [294]. In context, athletes that are unaware of the causes and symptoms associated with a concussion are less likely to identify an injury and thus are less likely to consult medical personnel for treatment. Despite the revealed shortcomings, improving education concerning concussion among the populations most likely to sustain one is likely to increase reporting rates, a sign of increased identification of cases rather than one suggesting more injuries are occurring. However, improvements are still needed as there is no standardized, uniform concussion curriculum and the proportion of athletes that have yet to receive formal education about concussion risks and symptoms remains troublingly high [295,296].

A well-recognized but often unspoken aspect integral to the nature of competitive sports is the idea of resilience in the face of injury. Competition is a strong driving force in the world of sports, where anything short of maximum effort can be the difference between a victory and a loss. Therefore, a great amount of pressure is placed on athletes, particularly those at elite levels of competition, to persevere through obstacles including injury to achieve the overarching goal of securing a victory [297]. The pressure from coaches and teammates to perform through or even attempt to ignore injury is notoriously ingrained into the culture of sports that incorporate violence, aggression, and mental fortitude with the acquisition of respect (i.e. American football, ice hockey, combat sports). In these sports, this culture dynamic plays a particularly large role when athletes sustain a concussion and can feasibly conceal symptoms well enough to continue to participate in sport. Collegiate football players were shown to be approximately two times less likely to disclose a concussion to an athletic trainer compared to any other type of injury [298]. Similarly,

approximately one-third of collegiate ice hockey players reported experiencing at least one head impact that resulted in concussion-like symptoms, with over eighty percent of these potentially concussed athletes electing to continue to play rather than seek medical attention [299]. Competitive fighters were also prone to downplaying the severity of head trauma, with approximately one in five fighters actively encouraging hiding symptoms from medical personnel to continue to perform [300]. Interestingly, in addition to athletes feeling pressure to perform, over half of observed clinicians reported being pressured by injured athletes and/or coaches themselves to prematurely administer medical clearance to a concussed athlete [301]. Competition creates both intrinsic and extrinsic obstacles for concussed athletes that need, but may not receive, medical attention following a sustained injury. From the perspectives of both athletes and clinicians, the combination of internalized expectations and feelings of pressure with the inherent risks of injury in sports creates a complex culture in which success and the benefits of a team may be prioritized over personal well-being and self-preservation [275,297].

Theoretical frameworks have been utilized in attempts to better understand the mindsets that contribute to underreporting of concussion. Notably, the tenets of the Theory of Planned Behavior have been aptly applied to sport culture, where the perceived beliefs of others, the perceived benefits of taking part in an action and the perceived amount of control of a given situation contribute toward one's likelihood of taking part in a behavior [302]. In the context of reporting concussion symptoms, the perceptions of control and the beliefs of others can play significant roles in one's decision to play through injury, as athletes that are more heavily depended upon by their team and coaches may be more inclined to play through concussion symptoms if they believe they are able to do so [6]. In contrast, Protection Motivation Theory has been implemented to assess how the negative aspects of taking part in a given behavior, such as the

severity of the events and the potential to worsen the status of the current situation, influence one's chances of partaking in said behavior [303]. Under Protection Motivation Theory, athletes that prioritize avoiding worsening their health, being a liability to their team while playing injured, or sustaining a more severe injury and missing playing time, would be inclined to avoid choosing to continue playing and to seek medical care instead [304]. The significant underreporting rates and observed willingness of athletes across multiple sports to play through concussion symptoms without seeking treatment indicates that there is a widespread notion that the benefits of participation outweigh the potential consequences of playing through injury in the culture of athletics. This distinction is likely to provide a long-term problem for clinicians and a consistent source of underreporting of concussion symptoms as competition serves as a driving force to perform and persist no matter the obstacle, even if that obstacle will cost the individual their short-term and/or long-term health and well-being.

## **2.4 Balance Testing and Concussion**

Balance impairment is a cardinal sign of a concussion and serves as one of the most common objective indications of injury [305]. Because achieving and maintaining balance requires multiple input and integration centers spanning the entire brain, damage to any of these structures and/or portion of the axonal networks interconnecting the cortex and subcortical structures can result in balance impairments [10]. Specifically, if cortical tissue and axons undergo a significant amount of shear stress brought on by high amounts of rotational acceleration (approximately 6000 rad/s/s or greater), entire neural networks can be compromised and proper systemic function will be impaired [142,148]. For healthy individuals, balance requires input and integration from the visual, vestibular, and somatosensory (i.e. proprioception) receptors and respective integration

centers within cortex [306]. Concussion can result in a variety of symptoms indicative of damage to sensory processing centers and receptors including impairments of visual information (i.e. diplopia) and vestibular information (i.e. dizziness). Consequently, if either the sensory receptors or the areas of cortex that are responsible for sensorimotor feedback information processing are damaged as the result of head trauma, balance impairment is likely to follow suit. However, because damage to these areas cannot be accurately detected using medical imaging technology, balance assessments have been designed to stress the various components of the postural control system in such a way that overall functional impairments (i.e. maintaining upright posture) will be made evident upon testing.

Testing protocols designed to examine static balance and postural stability following a suspected concussion commonly test an individual's ability to retain their body's center-of-mass within their base of support while assuming a stationary posture. Balance testing batteries for concussion also commonly include assessments of postural stability incorporating dynamic balance that challenge an individual to control their center-of-mass as their body is moving and/or changing positions. Clinical assessments of static and dynamic postural stability have been designed to place individuals in various postures and under various combinations of sensory feedback withholding to determine if they can effectively maintain their balance under conditions of varying difficulties. In laboratory settings, instrumented assessments of balance utilizing specialized equipment (i.e. force plates, accelerometers, virtual reality software) are able to detect and monitor an individual's center-of-pressure during stance to track metrics of postural stability including postural sway displacement, sway velocity and sway pattern regularity (i.e. approximate and sample entropy). These protocols of varying methodology and sophistication have been designed to examine different aspects of balance and postural stability under a multitude of testing

environments. Each assessment has contributed to the comprehensive goal of objectively identifying the detrimental effects of concussion by either revealing novel facets of impairment following injury and/or serving as the foundation for testing protocols of greater sensitivity and effectiveness upon which to be built.

#### *2.4.1 Clinical balance screening*

Balance assessments provide a somewhat objective means to diagnose a concussion and are commonly instituted in athletic populations on the sideline in cases of suspected injury. Multiple assessments have been developed and widely utilized to serve as cost-effective and efficient methods to detect balance impairments stemming from a concussion, including the Romberg test [307], the Y-Balance test [308], the Balance Error Scoring System (BESS) [8,309], and the Clinical Test of Sensory Interaction on Balance (CTSIB) [310]. The incorporation of balance testing for concussion management demonstrated that the resolution of cognitive (i.e. confusion, problems with memory recall) and somatic (i.e. nausea, dizziness) symptoms does not automatically confirm a complete recovery from injury. Balance testing using these protocols have contributed to the widespread notion that the majority of concussions are resolved within three to seven days post-injury [311]. While significant advances have been made in the physiological basis of the postural control system and the methods utilized to examine variables contributing to maintenance of balance, elements of the aforementioned testing protocols have remained as fundamentals pieces of the management plan for concussion [312].

Moritz Heinrich Romberg developed the namesake Romberg test in the mid-nineteenth century to detect balance impairments by altering a subject's visual feedback (i.e. closing eyes). By limiting sensory feedback from the visual system, maintenance of balance becomes more



reliant on input from the vestibular and somatosensory feedback systems, and thus any present impaired functioning of the latter two systems will become evident [313]. The original protocol for Romberg's test had the subject stand with their feet together and place their arms at their sides or crossed over their chest. The subject is then instructed to close his/her eyes as the administering clinician monitors how long the subject can maintain balance. The clinician can make the test more challenging by administering minor perturbations (i.e. slight touch/push) during the test. A failed test and therefore positive "Romberg sign" is defined as a subject losing balance during the trial, which can be subjectively interpreted as shifting the feet mid-trial, gross increases in involuntary postural sway or sustaining a complete loss of balance and/or fall. Of note, a positive Romberg sign using the original protocol is interpreted as an impairment of the dorsal column tracts of the spinal cord (i.e. tabes dorsalis) and/or the higher-order somatosensory integration centers of the cerebrum rather than dysfunction of the vestibular nuclei or cerebellum [314,315].

Since its inception, the Romberg test has been applied to several different populations with varying metrics for effectiveness. The subjective nature of the Romberg test severely limits the reliability and validity of its results. In neurologically healthy individuals, researchers have observed a measurable learning effect when performing the Romberg test repeatedly, resulting in poor test-retest reliability [316,317]. In comparison, patients with Parkinson's disease consistently demonstrated greater postural sway path length of their standing center-of-pressure, but unexpectedly demonstrated greater stability with their eyes closed, indicating that Parkinsonian patients do not utilize vision as a means for postural control to the same magnitude as healthy individuals [318]. To increase the difficulty of the protocol, variations of Romberg's original protocol have since been developed and implemented including the Sharpened Romberg Test. The Sharpened Romberg Test expands on the original test by having the patient place their feet in three

different positions rather than only one during testing. These positions include (1) feet together, (2) semi-tandem, and (3) tandem. The addition of multiple foot positions was notably effective in detecting balance deficits in neuropathological populations including Parkinson's disease, with test-retest reliability measures above 0.80 [319]. In addition, the Romberg test has been implemented using different floor surfaces (firm vs. foam) to increase the challenge of the protocol. The use of different floor surfaces has reportedly been able to detect vestibular impairment with sensitivity and specificity measures of up to sixty-one and fifty-eight percent, respectively [320]. These metrics support Romberg's original interpretation of results in which the Romberg's test should not be utilized as a diagnostic protocol for vestibular impairment. However, conclusions about the efficacy of the Romberg test to accurately detect a concussion cannot currently be stated. To date, there are no documented data pertaining to the validity of the Romberg test in the context of concussion. Instead, balance assessments for concussion have since evolved based on the fundamentals of the Romberg test to assess more intricate measures of postural stability.

The Y-Balance test (YBT) is a commonly utilized clinical protocol for assessing dynamic balance. The Y-Balance test has multiple variations and can be implemented to assess stability and control for both the upper and/or lower extremities. In the context of concussion, the lower-quarter Y-Balance test (LQYBT) is derived from the Star Excursion Balance Test (SEBT) and serves as a fundamental assessment tool for screening protocols. Unlike the Romberg test or BESS, the Y-Balance test assesses an individual's ability to maintain upright postural stability as the body is in motion rather than stationary. The LQYBT has a participant stand on one leg while reaching for maximum distance with the other leg in three directions: (1) anterior, (2) posterior-medial, and (3) posterior-lateral. The participant then switches the support leg and reaches with the other in each of the three same directions. The maximum distance of three reaches in each direction for each leg

is taken as a result. A composite score for each leg is calculated by taking the sum of the three directional reach distances and dividing the result by three times the length of the reaching leg. Each individual's composite score is used as a reference point to predict the risk of lower body injury to each leg compared to the sample population. Based on this scoring system, the LQYBT is a useful protocol for assessing how potential asymmetries between the lower limbs can contribute to balance impairments [321].

Dynamic balance assessments including the LQYBT have been used as tools to predict the risk of a future injury taking place rather than a diagnostic tool for a previously sustained injury. Athletes registering maximum reach distances below their population mean in each direction were nearly twice as likely to sustain a lower-limb injury and those demonstrating a disparity between limbs in the posterior-medial direction of or greater than four centimeters were nearly four times more likely to sustain an injury [322]. However, recent developments have indicated that the LQYBT lacks proper sensitivity to reliably detect an increased risk of sustaining a non-contact lower limb injury independent of additional screening techniques [323,324]. It has been noted that the pre-determined cut-off points for composite scores on the LQYBT are not generalizable across different sports, age groups and to the general population, and thus making predictions of lower-limb injury risk referencing these cut-off points is fundamentally inaccurate [325]. In addition, the sensitivity and specificity values of the standard LQYBT for detecting cases of concussion are currently inconclusive. A previous study has indicated that prior history of concussion had no significant effects on performance of the LQYBT, but reinforced the notion that further developments are needed for increasing the sensitivity of assessments of dynamic balance associated with concussion [326]. Despite this, there remains an increased risk of lower-limb orthopedic injury and concussion [284,285], although changes in dynamic balance as determined

by the SEBT and/or LQYBT have not been identified as a contributing factor. Dynamic balance assessments for concussion have since been conducted in laboratory settings using the framework and protocol of the LQYBT, but with the addition of technological instrumentation in an attempt to improve reliability measurements.

The BESS was developed at the University of North Carolina at Chapel Hill based on interpretations of the foundations of the Romberg test. The protocol for the BESS has participants assume three postures (double-leg, non-dominant leg, tandem stance) without shoes for twenty seconds with their eyes closed on two different types of flooring (firm ground and foam pad) for a total of six conditions. Participants are instructed to assume each posture with their hands on their iliac crests for the duration of the trials. Examiners watch the participants throughout each trial to look for errors during testing. Errors include (1) opening eyes, (2) removing hands from iliac crests, (3) stumble or fall, (4) abduction or flexion of hip past thirty degrees, (5) lifting heel or forefoot off ground, and (6) failure to assume proper testing position for greater than five seconds. Each error is considered a deduction from a total possible score of ten per trial, thirty per floor surface condition, and sixty for the entire protocol. The BESS quickly gained popularity as a cost-effective, expedient and easy-to-administer assessment for concussion in the athletic population [9,327,328].

Despite its popularity, research examining the results of the BESS has exposed several shortcomings. First, while the BESS has demonstrated high specificity values in concussed athletes on the day of injury [328], sensitivity measures have varied tremendously, with reported values falling below 0.5 up to seven days after the initial injury [329]. These low sensitivity measures indicate that the BESS is best used as a screening tool immediately following a suspected concussion and not to determine if recovery has taken place over a longitudinal scope. In addition, the strong reliance on rater interpretation of errors during the protocol provides poor interrater

reliability for the BESS [312]. In addition, multiple variables have been shown to have an impact on BESS performance including environmental distractions [330,331], muscle fatigue [332], ankle instability [333] and a marked learning effect [334,335], raising concerns over the true cause of any seen deficits in balance observed by examiners. Lastly, age has been shown to be an influential factor for BESS performance. Adolescents and adults are consistently shown to score better than children, which could be reflective of overall improved motor control associated with biological maturity rather than children exhibiting balance impairments associated with injury [336,337]. However, the precise cause of this association has not been clearly identified. If age can produce changes in the results of a test designed to detect the ill effects of a concussion, the same standards and scoring system cannot be universally applied to the general population. A modified version of the BESS (mBESS) has since been developed, in which the protocol remains mostly unchanged with the exception that the test is performed exclusively on a firm surface, not foam. Since its introduction to the clinical field, the mBESS has been incorporated into the Sport Concussion Assessment Tool (SCAT-5) as a standard component of the concussion screening battery and gold standard of clinical balance testing for athletes [338]. Specificity measures with the mBESS showed significant improvements over the original test, rising from 60 percent to 71.4 percent [339]. However, this number still fails to meet adequate standards for both specificity and sensitivity, raising further questions about the utility of the test itself.

The Clinical Test of Sensory Interaction on Balance (CTSIB) was developed based on the foundations of the Sensory Integration Test (SOT), but with a more concise, clinician-friendly approach [310]. As its name suggests, the CTSIB assesses the interactions of multiple sensory feedback systems and how hindering and/or eliminating one or multiple sources of sensory input influences an individual's ability to maintain standing balance. The CTSIB consists of six total

conditions performed three time each for thirty seconds per trial. The CTSIB assesses standing balance by manipulating somatosensory and visual feedback by changing the floor surface (firm vs. foam) and type of available visual feedback (eyes open vs. eyes closed vs. wearable dome producing perception conflict between visual and vestibular feedback). The resulting six conditions consist of the following combinations: (1) firm surface, eyes open, (2) firm surface, eyes closed, (3) firm surface, visual conflict dome, (4) foam surface, eyes open, (5) foam surface, eyes closed, and (6) foam surface, visual conflict dome [23]. Based on these combinations, clinicians can detect postural control deficiencies based on which conditions results in a loss of balance. Of note, conditions three through six target specific sensory feedback systems that confirm an inability to adapt to reductions in sensory input and utilize all sources of input with equal efficiency to maintain balance. The CTSIB can help clinicians determine whether balance impairments are exacerbated by changes in vision (conditions two, three, five and six), vestibular impairment (conditions three and six) and/or somatosensory feedback (conditions four, five and six). A modified version of the CTSIB (CTSIB-M) has also been developed that leaves the protocol largely unchanged with the exception of the removal of conditions utilizing the visual conflict dome, effectively leaving conditions one, two, four and five to be conducted as defined in the original protocol. In addition, another variation of the CTSIB has been developed for the pediatric population (P-CTSIB), in which the original protocol is again mostly unchanged with the exception of the addition of heel-to-toe tandem stance to be added alongside having the patients keep their feet together, producing twelve total testing conditions with six per foot stance condition [340].

Like the Romberg test and LQYBT, validity and reliability measures for the CTSIB in the context of concussion are currently limited. As a less advanced, modified version of the SOT, the

CTSIB is generally seen to be more accessible to be administered in clinical settings, but a less accurate means to detect deficits in postural stability compared to its predecessor. While research has demonstrated that the CTSIB is an effective tool to distinguish sensory feedback integration deficits that contribute to postural instability, there have only been a limited number of validation studies to identify balance impairments in specific patient demographics. In particular, previous research examining older adults found that the CTSIB is a reliable tool to detect balance impairments with an interclass correlation coefficient exceeding 0.9 [341]. However, additional analyses revealed that results indicative of balance impairment from the CTSIB do not reliably predict an increased risks of falls in the elderly population, raising questions about the clinical applications of the protocol [342]. While the CTSIB shows merit in separating the sensory feedback systems to better examine the causal roots of postural instability, applications in clinical testing environments for concussion are limited. Normative values for CTSIB-M scores derived from collegiate athletes showed a discrepancy based on sex, namely that female athletes outperformed their male counterparts in each individual condition as well as overall composite score at baseline testing [343]. However, there have been no studies to date assessing the validity or test-retest reliability of the CTSIB regarding concussion patients. Because sensitivity measures cannot be generalized between clinical populations, the efficacy of the CTSIB for detecting the presence and/or determining the resolution of balance impairments attributable to concussion has yet to be determined.

While these tests have been examined and have been considered reliable enough to detect balance impairments in the field [9], they each present with limitations in their protocols and scoring systems. Without sophisticated measuring techniques, clinical balance assessments are influenced by subjective scoring systems, which leaves the possibilities of declaring a false

positive or missing a true positive unfortunately and worryingly present. Clinical balance testing protocols have traditionally prioritized expedience and applicability over sensitivity and specificity of results. These protocols have proven to be useful clinical tools to distinguish balance impairments associated with neurological disease but are less effective at detecting milder forms of balance impairments such as those observed with concussion. In addition, while several clinical balance testing protocols (i.e. Romberg's test, CTSIB) have shown promise in detecting reductions in sensory feedback adaption, there is limited evidence to support the notion that these protocols are independently sensitive enough to produce reliable and valid results to consistently detect cases of concussion and/or determine the resolution of a concussion within a week post-injury [312,344]. These shortcomings leave the objective duration of the presence of balance deficits associated with concussion uncertain from a clinical perspective. Future efforts should be directed toward developing and validating a clinician-friendly balance testing procedure that can accurately and objectively detect the presence of impairments indicative of concussion on both immediate (i.e. diagnostic) and longitudinal (i.e. recovery) scales.

#### 2.4.2 *Instrumented balance testing*

The advent of technology in conjunction with increased awareness of the shortcomings of clinical balance assessments has provided researchers with novel opportunities to assess postural stability in relation to concussion. Studies assessing the complexities of postural stability following concussion have developed protocols utilizing numerous pieces of sophisticated equipment including force plates, accelerometers, inertial measurement units (IMUs), and other sophisticated pieces of equipment to elicit specific variables that are unattainable when solely using clinical balance testing protocols. Protocols have included data collections specifically designed to elicit



certain variables under unique conditions as well as standardized testing assessments including the Sensory Organization Test (SOT) [345] and the Concussion Balance Test (COBALT) [346]. These protocols have allowed researchers to assess the central nervous system and the foundations of postural control to draw conclusions about changes in balance that cannot be easily discerned by what is observable solely by the naked eye. Furthermore, studies utilizing these advanced pieces of equipment have the advantage of producing results based on data-driven calculations rather than subjective assessments of performance, a facet of balance testing that researchers assessing concussion have hoped increases the sensitivity and validity of their testing measures.

For decades, force plates have served as staples of laboratories specializing in assessing human biomechanics. In the context of assessing balance, force plates allow researchers to continuously track an individual's standing center-of-pressure (CoP) within the base of support created by the limb(s) contacting the plate. Based on tracking the location of the individual's CoP in the anteroposterior and mediolateral planes, researchers are able to derive parameters that provide context for postural control including CoP sway displacement, path length, velocity, and elliptical area representative of ninety-five percent confidence intervals. Increases in the averages of these linear variables are generally interpreted as indicators for poorer postural control during quiet standing [347,348]. More recently, nonlinear parameters of CoP tracings have provided insight toward the complexity of postural stability. Calculations of CoP approximate (ApEn), sample (SampEn), and multiscale entropy (MSE) have been used as measurements of regularity of postural sway patterns; a representation of the complexity of neural oscillator networks within the central nervous system [106,108,349]. In addition, analyses in the frequency domain have also been used to assess postural control based on the characteristics of sway oscillations. Specifically, Fast Fourier transforms and higher-resolution wavelet transforms can identify parameters within

the frequency spectrum of a CoP tracing, which provides information about the oscillatory networks of the postural control system as well as how different oscillations originating from various parts of the body can potentially contribute to the overall sway patterns of a CoP tracing during quiet standing [350,351]. In addition to the variety of acquirable variables, force plates can be transported relatively easily to allow access to a wider range of patient populations compared to other sophisticated pieces of technology that cannot be relocated outside of a laboratory setting.

While there is currently no consensus on a standardized protocol outlining the optimal method to assess standing postural stability, CoP analyses have proven to be effective at eliciting objective differences in postural control between healthy individuals and populations with neurological injury (i.e. concussion) and/or disease (i.e. Parkinson's disease). Concussed individuals display greater deficits in standing postural stability evidenced by increases in linear CoP parameters including anteroposterior and mediolateral sway displacements, velocity, and path length [327,348,352]. In addition, these impairments can be experimentally exacerbated by manipulating sensory feedback availability (closing eyes, standing on compliant surface, etc.) [347] and/or dividing attentional resources with the use of a concurrent cognitive task [353,354]. The presence of postural instability associated with concussion is notably evident when assessing nonlinear parameters of CoP tracings. Prior studies analyzing regularity (i.e. entropy) of postural sway have indicated that concussion results in a decrease in CoP regularity that is present for several weeks and months after the initial injury [355–358]. Prolonged reductions in regularity of postural sway in conjunction with increases of linear sway parameters indicate that concussion can have lasting effects on the function of the brain structures contributing to postural control and/or the complexity of the networks that interconnect them. By identifying these alterations in stability, CoP analyses can help widen the scope of knowledge of how concussion affects the functionality

of the brain's postural control system and how the complex networks and structures work to adapt and compensate when trauma is sustained.

Multiple studies have reported that postural control deficits observed within CoP parameters persist beyond resolution of balance impairments determined by clinical testing protocols such as the BESS [109,335,359]. In addition, prior studies show that individuals with a history of multiple prior concussions demonstrate greater standing CoP displacement and velocity compared to individuals with no concussion history as well as those that have experienced only one prior concussion, suggesting that there is a cumulative detrimental effect of concussion on the postural control system and longer times to recovery following each successive injury [254,360]. However, there is currently no consensus regarding the duration in which alterations in CoP parameters remain present following concussion, as studies that have assessed "long-term" differences in postural control do not explore beyond the scope of several months and up to one or two years post-injury. The prospect of permanent damage following a concussion is typically only considered in cases that also present with severe or life-threatening symptoms such as skull fracture, prolonged unconsciousness, or internal hemorrhage. Because CoP tracings are not often considered in screenings of balance for concussion, indicators of reduced postural control (increased CoP displacement, reduced CoP regularity, etc.) can be present yet swiftly overlooked. For individuals with a history of concussion, the prolonged alterations in CoP parameters indicative of reductions in postural control following injury suggest that there is a manifestation of damage to neural tissue and/or white matter stemming from one or multiple traumatic head impacts that may persist for years after the traumatic event without ever recovering to pre-injury levels of functioning despite a determination of clinical and medical recovery.

Accelerometers and inertial measurement units have been used to assess human kinematics during a wide variety of movements from sprinting to standing postural sway. The two sensors are similar in function. Accelerometers measure the rate of change in velocity (i.e. acceleration) in the three planes of motion. In contrast, IMUs combine the function of accelerometers with that of a gyroscope, which measures angular velocity about a given axis, giving IMUs up to six degrees of freedom compared to the maximum of three provided solely by an accelerometer. IMUs can also contain a magnetometer to measure the fluctuations in the Earth's magnetic field during movement oriented about the magnetic North Pole, creating a sensor with up to nine degrees of freedom. When oriented and calibrated properly, affixing these sensors to the body provides a reference for the changes in position, velocity and/or acceleration of the body and/or its segments during movement. Wearable sensors including accelerometers and IMUs that are capable of detecting triaxial motion placed at the level of the lumbar spine (L4-L5) have been validated as proxies for the body's center-of-mass during movement [361,362]. By having a trackable representation of the body's center-of-mass throughout an assessment, researchers can better interpret the strategies being undertaken by an individual to keep their center-of-mass within the area of their base of support. In addition, these sensors are typically small, wireless, and relatively simple to implement and affix to a test subject, lending to their appeal for applications in biomechanics research.

The incorporation of accelerometers and IMUs into existing protocols has provided a useful perspective when assessing standing postural stability, as clinical balance testing protocols fail to account for the indication that movements of the body's center-of-mass can have on performance or neural function. Studies assessing the CTSIB in conjunction with IMUs have shown promise by being able to distinguish between subtypes of Parkinsonian patients based on falls risk, significantly improving the testing accuracy of the non-instrumented protocol within the

same population [363,364]. When examining the effects of concussed individuals, IMUs have been implemented in assessments of dynamic postural stability during movement rather than solely standing postural control. Instrumented versions of the LQYBT assessing concussed athletes revealed that alterations in dynamic postural stability persist beyond the point of return to pre-injury levels of testing as measured by changes in sample entropy and jerk (i.e. rate of change in acceleration) [308,365]. Improvements in discerning the longevity of presence of the balance deficits associated with different types of neurological injury and disease have supported the notion to include IMUs and/or other means to track the body's center-of-mass when moving forward in research assessing the maintenance of postural control.

As understanding of pathophysiology grew and novel methodologies were developed, the goal of developing a standardized, reliable assessment for detecting postural stability deficits following concussion has become a challenge for clinicians and researchers alike. Among the most well-recognized standardized laboratory tests for standing postural stability is the Sensory Organization Test. The Sensory Organization Test uses a postural tracking system developed by NeuroCom International (Clackamas, OR). Like its clinician-friendly counterpart (i.e. CTSIB), the SOT challenges the postural control system by systematically manipulating the body's sources of visual and somatosensory feedback information. However, the SOT expands on the protocol with the incorporation of an apparatus including a force platform to track the patient's standing center-of-pressure and the use of postural sway referencing instead of a visual conflict headpiece. Sway referencing refers to the consistency of movement between the patient's surroundings in the testing area in relation to their visual feedback as they sway. As the patient's surroundings move in reference to their postural sway, conflict arises between the visual and vestibular systems as the visual feedback is unable to accurately discern movement of the body in relation to the external

environment. The patient's actions and strategies in response allow researchers to assess how patients are able to ignore counter-intuitive or conflicting information to prioritize maintaining balance throughout the trial [99,329]. The outline of the six conditions of the SOT is instructed as follows: (1) firm surface, eyes open, (2) firm surface, eyes closed, (3) firm surface, sway-referenced vision, (4) foam surface, eyes open, (5) foam surface, eyes closed, and (6) foam surface, sway referenced vision. Each condition is performed three times for a duration of twenty seconds per trial.

Following completion of the SOT protocol, fourteen scores are utilized to calculate one composite score to grade the patient's balance. The fourteen individual scores are based on the equilibrium score measures derived from the average amount of postural sway recorded in reference to the center of the base of support on the force platform at the commencement of the trial. From there, the averages of the scores of conditions 1 and 2 are taken with the individual scores of each of the three trials from conditions 3, 4, 5 and 6 to produce a weighted average to represent the overall composite score with higher scoring representing overall greater performance [99]. The combinations included within the conditions of the SOT allow researchers to identify potential sources of impairments in sensory feedback integration by assessing the scores of certain conditions in comparison to condition 1 (eyes open, firm surface) serving as a baseline, with lower scores being indicative of poorer integration of the given tested sensory feedback source. Three calculated ratios representing the vestibular system (condition 5 / condition 1), the visual system (condition 4 / condition 1), and the somatosensory system (condition 2 / condition 1) help elicit specific sources of postural control deficits in a tested individual or population and thus direct more appropriate treatments and rehabilitative methods moving forward.

Despite its cost of implementation and lack of widespread clinical accessibility, the SOT has shown considerable merit for applications in several clinical populations. The various task difficulties associated with the six different conditions of the SOT have been noted to result in increases in sway displacement and reduced sway regularity as the conditions become more challenging across multiple populations [366,367]. As a result, normative scores have been established based on different age groups in the general, healthy population, with a negative correlation having been identified between age and overall composite score on the SOT [368]. Tests conducted on healthy individuals have also garnered moderate test-retest reliability measures, indicating that the SOT is an applicable protocol for detecting different sensory feedback impairments contributing to postural instability [367,369]. In addition, the SOT has demonstrated promise in discerning the severity of neurodegenerative disease. The SOT has been shown to be an excellent screening tool for patients with multiple sclerosis (MS), with interclass correlation coefficients for reliability of approximately 0.9 based on the stage of progression of the disease [370]. Similar trends were found in patients with Parkinson's disease, who demonstrated no significant differences in all six SOT conditions in comparison to healthy controls when scoring below a twenty on the Unified Parkinson's Disease Rating Scale (UPDRS), but significantly worse than controls when scoring above a twenty on the UPDRS, signaling worsening postural stability with the progression of the disease [371,372]. Multiple studies have also reported the efficacy of the SOT in identifying patients with vestibular dysfunction with varying reports of sensitivity measures ranging from forty to eighty-five percent [373,374]. Collectively, these results demonstrate moderate effectiveness of the SOT for determining postural stability impairments but raise a concern for wariness when drawing conclusions about clinical populations should the results of the SOT be the sole measures of implemented balance testing.

Because balance impairments presenting with concussion are typically milder in severity compared to advanced neurodegenerative disease, ascertaining accurate and reliable detections of the presence of postural instability using the SOT has proven to be challenging. Postural stability testing using the SOT has been able to identify deficits stemming from concussion that defied long-held, clinically backed beliefs that balance impairments following a concussive impact are resolved within a week of the initial trauma, but rather remain present for weeks and even months post-injury [375,376]. However, prior studies have determined sensitivity and specificity values for detecting concussion with the SOT of approximately fifty-eight and eighty percent, respectively [377,378]. These observed reports of suboptimal reliability indicate that additional testing measures are necessary to create a more comprehensive assessment of postural stability in cases of concussion. In addition, multiple studies have observed a marked learning effect when participants undergo the SOT multiple times, fueling speculation about the accuracy of initial testing measures as a reflection of postural stability and the effectiveness of using the SOT to detect concussion in individuals that have experienced multiple previous injuries and thus may be preemptively familiar with and unequivocally prepared for the testing protocol [345,379]. While prior findings have helped to expand the scope in which concussion symptoms can be detected, the modest sensitivity measures and potential for sandbagging in accordance with repeated testing raises concern for the SOT to be used as the sole protocol for identifying the presence of postural instability following concussion. Therefore, identification of chronic presence of postural stability impairments associated with concussion using the SOT becomes less plausible as time passes and the individual becomes more familiar and comfortable with the testing protocol, leaving the objective duration to which postural instability remains following concussion ambiguous and undetermined.



Building on the fundamentals of sensory feedback adaptation presented with the SOT, the Concussion Balance Test (COBALT) was developed by Bertec (Columbus, OH) to provide a challenging and more sensitive balance assessment for athletes suspected of having sustained a concussion. Like the SOT, the COBALT tests an individual's standing postural stability on a force plate to measure postural sway parameters via CoP tracing while manipulating the type of available sensory feedback information. Specifically, the COBALT incorporates two types of floor surfaces (i.e. firm and compliant) to manipulate somatosensory feedback with four distinct conditions performed twice on each surface for twenty seconds per trial, amassing a total of eight conditions and sixteen total trials. The four testing conditions are as follows: (1) eyes open, (2) eyes closed, (3) eyes closed with volitional head movements spanning approximately sixty degrees of rotation set to a metronome (120 beats per minute), and (4) eyes open with visual focus affixed on a target placed directly in front of the participant during concurrent volitional head movements spanning approximately sixty degrees of rotation set to a metronome (forty beats per minute). Conditions 5, 6, 7 and 8 repeat the same four procedures on the compliant surface [346]. Conditions 3, 4, 7 and 8 expand on the CTSIB and SOT by directly assessing the effect of head movement in conjunction with standing postural stability. The medial vestibulospinal tract controls the axial musculature that work with the vestibular nuclei to move the head while maintaining proper spatial orientation [380]. The COBALT provides insight as to which sensory integration systems are providing reliable feedback by challenging this facet of the vestibular system with and without anchoring from a reference point provided by the visual system and the vestibulo-ocular reflex. In addition, the methods of the COBALT translate more effectively to real-life situations compared to the SOT as movement of the head during standing and gait is commonly performed to increase and/or maintain awareness of one's surroundings to optimize stability and avoid hazards whereas the

postural sway referencing implemented in the SOT is an experimental manipulation that is unlikely to be encountered during activities of daily living.

Unlike the SOT, the COBALT was specifically designed to assess and identify sources of balance impairment following cases of concussion. To date, the COBALT lacks verified test-retest reliability measures due in part to its present status as a novel protocol. Despite this, the COBALT addresses aspects of sensorimotor integration contributing directly to standing postural stability (i.e. head movement and vestibular reflex function) that have largely been unexplored in both clinical and laboratory-based protocols for concussion screening. Of the three sources of sensory input contributing to maintenance of balance, vestibular feedback is the most challenging to manipulate experimentally due to the ever-present effects of gravity [25]. The incorporation of more pointed examinations of the vestibular system in conjunction with assessments of CoP during standing has the potential to identify a physiological basis for postural control deficits and strategies used for compensation. In addition, these approaches can expand the understanding of the pathophysiology of concussion as well as a causal mechanism for persistent symptomatology that can remain well beyond the resolution of other symptoms associated with traumatic brain injury.

Despite the advances in uncovering the pathophysiological bases of deficits in balance resulting from concussion by targeting sensory feedback and integration systems within the brain, some cortical parameters contributing to postural stability are often overlooked in the field of concussion management. Interestingly, both clinical and instrumented protocols assessing balance in suspected cases of concussion often do not incorporate a cognitive element within the assessment. Cognitive impairment is among the most recognizable symptoms of concussion and is often the hallmark of a positive diagnostic screening [381,382]. However, assessments for

cognitive impairments are not traditionally done concurrently with balance testing. While maintenance of upright posture is a mostly subconscious process in the healthy populations, proper allocation of attention becomes crucial when balance is perturbed either by external forces and/or neural dysfunction resulting from trauma such as a concussion [383,384]. Prior laboratory assessments have identified deficits in standing postural stability that are exacerbated by the inclusion of a concurrent cognitive task in the acute phases of concussion [385–387]. These findings collectively indicate that individuals with a prior history of concussion require a greater proportion of their neural resources to direct their attention toward stabilizing upright posture and that concurrent increases in cognitive demand via a secondary task will redirect said resources away from maintaining balance, resulting in decreases in postural stability. In addition, studies examining the neuroelectric activity of the frontal lobes in individuals with a prior history of concussion have revealed long-term impairments of cortical activation in relation to cognitive performance including delayed recognition of errors and deficits in attention allocation and working memory [388–390]. These observations of chronic changes in neural activation patterns suggest that concussion is associated with persisting reductions of cortical function of the cerebrum, which could also potentially include areas contributing to maintenance of postural control (i.e. Brodmann’s areas 4 and 6). To date, however, evidence is limited in determining the temporal extent to which long-term consequences of concussion affect an individual’s ability to maintain postural control with simultaneous increases in cognitive demand during static standing.

Instrumented laboratory assessments of postural stability have shown great promise in being able not only to detect impairments of standing balance associated with neurological pathologies including concussion, but also to provide greater insight into the specific sensory integration deficits and potential physiological bases of impairment seen following injury. In

addition, the inclusion of both linear and nonlinear analyses of CoP tracings has revealed that the duration of postural stability impairment following concussion extends beyond the scope previously determined by sideline and clinical balance testing, raising concerns about premature declarations of recovery as well as questions about the objective extent to which postural stability deficits associated with concussion can remain following injury. However, there is currently limited evidence supporting the sensitivity, reliability, and validity of standardized protocols including the SOT and COBALT regarding the identification of concussion in both acute and chronic timeframes. As a result, current methodology for assessing standing postural stability following concussion serves as a ‘piece of the puzzle’; one component of a group of testing protocols that compose a comprehensive, holistic evaluation of the effects and symptoms that manifest in cases of concussion. Moving forward, research building upon the rationales and findings of instrumented postural stability assessments by assessing the complexities of sensorimotor input, integration, and output can potentially uncover objective evidence of injury following a traumatic impact that can be identified in both acute stages for diagnostic purposes and chronic stages to determine the prospect of recovery.

## **2.5 Gait Assessments and Concussion**

Gait presents a commonly performed but kinematically complex movement pattern that provides useful perspectives into the function of the nervous system as multiple sensorimotor integration and motor output structures must work seamlessly and continuously in tandem to perform smooth, stable locomotion [80]. The increased metabolic demands of moving the entire body through space can also reveal the functional capabilities of the cardiovascular and pulmonary systems. As such, testing protocols incorporating gait are often included as a core component of

functional assessments and therapeutic interventions in various clinical populations, including those with a limited ability for ambulation [391–394]. These protocols can vary considerably in terms of ease of administration, required equipment, and acquired variables and measures used for analyses. However, diagnostic tests that use gait-based protocols are typically designed to identify exercise intensity thresholds and modulate progression in patients with chronic health conditions such as congestive heart failure, muscular atrophy or frailty, or chronic obstructive pulmonary disease (COPD) [393,395,396]. In comparison, individuals presenting with concussion are more commonly younger, more physically conditioned, and thus are able to complete these protocols without being sufficiently challenged in order to ascertain clinically meaningful results.

Although balance impairment is a widely recognized symptom of concussion, standard assessments typically focus on standing static and dynamic balance to identify deficits indicative of concussion. Postural control deficits during gait are often not readily considered when screening suspected cases of concussion unless the impairments are egregious and are apparent with minimal or no external perturbation. However, this leaves the screening process prone to false negatives as concussed individuals have been repeatedly shown to avoid disclosing symptoms to medical professionals if it is feasible to do so, whether by withholding information or by avoiding challenging tests that would elicit the presence of symptoms [275,397]. Because gait inherently presents a greater challenge to the postural control system compared to quiet standing, the absence of significant changes in static balance is not axiomatically indicative of optimal neural functioning. Following this notion, recent developments in instrumented laboratory assessments have been conducted to assess the effects of concussion on complex movements including gait that may be evident of reductions in postural control that cannot be ascertained when solely examining static balance. In addition, research assessing rehabilitation methods for concussion have fueled a

paradigm shift away from adherence to strict bed rest and incorporating aerobic exercise to accelerate recovery from concussion. Collectively, the inclusion of gait assessments in the context of concussion has provided much needed information about the extent to which the postural control system is impaired following not only the initial injury, but also the resolution of static postural stability as determined by clinical balance testing and potentially longer than any previous assessments of balance have been able to observe.

### *2.5.1 Clinical gait testing*

Clinical diagnostic protocols are often designed to be conducted with the greatest amount of efficiency and simplicity without sacrificing an unreasonable degree of accuracy and sensitivity to detect injury or impairment. Without the use of technological instrumentation to track the body's center-of-mass during movement, clinical gait assessment protocols often focus on functionality rather than specific measures of postural stability. To assess overall function, these protocols commonly use time as a benchmark for testing and to determine how efficiently an individual can move in a given period of time. Specifically, performance can be scored based on (1) amount of distance travelled in a pre-determined amount of time, or (2) the amount of time needed to complete an objective. Predictably, this creates a paradigm in which the effectiveness of a protocol is determined by the distribution of priorities placed on the efficiency and ease with which results are obtained versus the applications and insight said results can provide clinicians treating the tested population.

One protocol utilizing a pre-determined time window that is relatively simple in design is the aptly named Six Minute Walk Test (6MWT). As the name suggests, participants undergoing the 6MWT are scored based on the amount of distance they can cover by walking in the span of

six continuous minutes. Participants can utilize adaptive equipment (i.e. cane, standing walker) and are permitted to take as many standing rests as needed, but these allowances are documented and accounted for when interpreting the results of the 6MWT. The low-impact and accommodating design of the 6MWT had made the protocol a staple for assessing the submaximal aerobic capacities of clinical populations including patients with cardiovascular disease, chronic pulmonary disease, and neurodegenerative disease that cannot withstand more strenuous bouts of exercise [394,398–400]. The 6MWT has also shown merit as a predictive tool for mortality in chronic disease populations as well as a prognostic indicator for physical inactivity in otherwise healthy populations [401,402]. However, despite its popularity and proven applications, the 6MWT is not utilized in cases of concussion. Because the procedure does not monitor the kinematics contributing to gait nor induce metabolic stress to a degree at which symptoms associated with concussion (i.e. dizziness, nausea, headache) can be elicited in an otherwise healthy cohort, the 6MWT is not considered an appropriate or useful protocol for examining postural control deficits stemming from concussion.

The amount of time required to complete a protocol has also been utilized in gait assessments as a direct measurement for performance. The Timed Up and Go (TUG) test has been utilized in numerous clinical populations as an assessment of postural transitioning and ambulation [403,404]. The protocol has a participant start seated in a chair and when instructed to begin, stand up, walk three meters, turn around an obstacle (i.e. cone), return to the starting point and sit down. Cut-off points for times to complete the protocol vary between clinical populations, but are interpreted similarly as individuals that do not complete the TUG test before the pre-determined cut-off time are classified as individuals at higher risk of sustaining a fall. The incorporation of changing postures, a change in direction, and the inherent emphasis placed on speed in order to

meet the pre-determined cut-off time gives the TUG test an advantage over the 6MWT by placing greater demands and stresses on maintaining balance during gait. However, like the 6MWT, the TUG test has shown the greatest effectiveness in applications for chronic disease populations exhibiting reduced functional capacity, in particular those presenting with a history of falls [393,405]. In the context of concussion screening, the TUG test is viewed in similar fashion to the 6MWT in that the protocol is not challenging enough to elicit physiologically meaningful results in the tested population.

The postural control deficits observed during quiet standing following concussion demonstrated that stressing the sensorimotor integration centers of the brain elicited the greatest degree of impairments [310]. These findings indicate that balance impairments associated with concussion are the result of limited access to neural resources capable of compensating for reductions in sensory feedback information (i.e. visual, vestibular and/or somatosensory) rather than decreases in musculoskeletal or aerobic functional capacities as seen in other clinical populations. Clinical assessments designed to detect such deficits in standing balance following a suspected concussion specifically target the functional capacity of the sensory feedback centers within the brain by implementing procedures in which compensatory strategies and mechanisms for injury-induced deficiencies in neural function are obstructed or eliminated [99,347]. Building upon this notion, sensorimotor integration deficits observed during static standing would predictably be evident during challenges to dynamic balance and during complex movements including gait. As a result, gait protocols for assessing concussion must be designed to challenge a tested individual sufficiently by controlling and manipulating the amount and type of sensory feedback information made available to participants during ambulation. Clinically, the most straightforward method to alter the availability of sensory information is to eliminate visual



feedback by having patients close their eyes, as is the basis for the Romberg test [307]. However, the safest and most viable means to assess gait typically involve manipulating the area of the patient's base of support during gait to challenge the vestibular system as the body moves through space without raising the risk of falls unnecessarily high.

Among the most clinician-friendly approaches to stress the postural control system during gait has been the inclusion of tandem gait performance. Heel-to-toe tandem gait substantially reduces the area of the body's base of support during gait, thus placing greater stress on the vestibular system to properly control the body's center-of-mass as well as the visual system to provide an anchored reference point to optimize stability during movement. Because of its ease of administration and considerable challenge to the postural control system in cases of neurological dysfunction, tandem gait protocols are often administered to identify cases of alcohol intoxication, as excessive ethanol ingestion transiently disrupts proper functioning of the cerebellum, resulting in slowed, uncoordinated motor function and balance impairment [406]. Because concussion is also associated with acute balance impairments following injury, tandem gait has been utilized as an efficient method to assess an individual's dynamic balance and postural control. Concussed individuals have repeatedly been shown to perform tandem gait slower and with greater difficulty (i.e. greater number of errors, increased gross postural sway) compared to their own baseline assessments and against healthy controls [280,407,408]. In addition, longitudinal clinical assessments tracking the recovery of concussed athletes have revealed that tandem gait performance gradually improves throughout the recovery process with an eventual return to baseline [409]. These findings indicate that tandem gait can provide practical value in determining the recovery of postural control following concussion when determining the progression of rehabilitation and recovery.

In addition, tandem gait was added as a component of the third edition of the Sport Concussion Assessment Tool (SCAT-3) in 2012 [410]. During the SCAT-3 protocol, the patient is instructed to walk heel-to-toe along a straight-line path exhibited by a piece of tape on the ground measuring thirty-eight millimeters (mm) wide and three meters long. After reaching the end of the three-meter path, the individual makes a one-hundred-eighty degree turn before returning to the starting point while continuing to utilize a heel-to-toe tandem gait. Four trials are performed and timed, with the best recorded time being maintained for clinical assessment. Individuals are considered to have failed the test if they (1) cannot complete the protocol in under fourteen seconds, (2) separate their feet between consecutive footfalls, (3) step off the pre-determined line path, or (4) touch or grab a nearby object or person to maintain stability. Tandem gait provided a novel addition to the standard screening protocol for concussion and the SCAT-3 became an integral component of the management plan for concussion in athletics. However, despite its practicality in the SCAT-3, studies had determined a moderate practice effect when performing tandem gait repeatedly, indicating that the fourteen-second cut-off time resulted in a high rates of false positive tests for novices and that a single cut-off point cannot be generalized across multiple age groups and clinical populations [411,412].

The most recent consensus statement on the topic of ‘concussion in sport’ held in 2016 does not place great emphasis on a specific assessment of gait following a suspected concussion, but rather names “gait unsteadiness” as a marker of balance impairment that mandates further treatment and management of the injury [4]. However, this does not exclude gait assessments from serving as a piece of a structured protocol for concussion screening. Although the modified Balance Error Scoring System (mBESS) serves as its primary module for assessing balance, the Sport Concussion Assessment Tool still includes a gait component in its most recent version

(SCAT-5) [338]. Specifically, the SCAT-5 incorporates a tandem gait task similar to the protocol outlined in the SCAT-3. The primary difference in the SCAT-5 tandem gait assessment is the elimination of the time component as a marker for failing the protocol [413]. This change made it so that the tandem gait test of the SCAT-5 is scored based on committed errors rather than the time required to complete the protocol, which could reduce the rate of false positive tests based on the findings of previous studies but leaves the criteria for passing the assessment more subjective in nature, raising concerns over false negative results instead. However, unlike other components of the SCAT-5 including the concentration and memory recall tasks, the tandem gait test is scored based on subjective observation rather than an objective evaluation of whether a response is correct, leaving the possibility of examiner error troublingly present and specificity of the assessment questionable at best. As a collective result, current standards for clinical gait assessments for concussion serve as one component of the assessment of balance following injury and thus are not meant to serve independently as a diagnostic tool.

Gait provides a useful medium for clinicians to assess an individual's physical well-being based on multiple facets including aerobic exercise capacity, musculoskeletal fitness, and execution of motor control in conjunction with feedback from the vestibular system. While screening protocols and therapeutic interventions that incorporate gait have proven to be effective for a variety of clinical populations, there is currently limited evidence supporting the efficacy of currently utilized clinical gait protocols to identify concussion patients specifically and reliably in both the acute and chronic stages of injury. Regarding the severity of symptoms, concussion can present considerably variably from case to case. However, most identified cases of concussion do not present with gross deficits in motor function or postural control comparable to those associated with neurodegenerative disease (i.e. multiple sclerosis, Parkinson's disease). As a result, postural

stability deficits during gait can be particularly difficult to detect from a clinical perspective as concussed individuals often retain an ability to compensate for their afflicted balance impairments by altering their kinematic patterns [281]. However, the presence of lingering sensorimotor integration deficits contributing to both static and dynamic postural instability following a concussion would suggest that the deficits stemming from a concussive impact are detrimental to a degree to induce changes in movement patterns and strategies during gait, but are not severe enough to be elicited and/or identified during the subpar challenges presented by standard clinical gait protocols. This distinction is indicative of a need to institute more sophisticated methods to assess the kinematic and spatiotemporal elements of gait; specifically, those that are not measured during standardized clinical protocols to identify the severity, duration of presence, and potential resolution of dynamic postural stability deficits associated with concussion.

### *2.5.2 Instrumented gait testing*

Technology has allowed research in the field of biomechanics to advance to an extent where observations and calculations of both linear and nonlinear parameters related to gait have been able to identify differences between populations based on age, sex, neurological health and previous orthopedic injury history [414–417]. Additionally, the implementation of sophisticated laboratory equipment, software, and techniques has allowed researchers to develop methods to address several components of gait from both biomechanical and physiological perspectives. Such research methods include assessing cardiorespiratory and metabolic fitness via graded aerobic exercise testing, the examination of joint and body segment kinematics using three-dimensional motion capture to build and analyze representative virtual models, and tracking of the body's center-of-mass and corresponding centers-of-pressure of footfalls during gait as representations of

dynamic postural control. Combinations of these techniques and assessments have been implemented to observe and show prospective promise to expand the understanding of the acute and chronic changes in gait stability and performance associated with concussion.

The measurement of metabolic activity and cardiorespiratory parameters (i.e. blood lactate concentration, heart rate, respiratory exchange ratio (RER)) during aerobic exercise via gait testing provides a useful method to assess functional capacity in healthy, disease, and injured populations. Graded aerobic exercise testing is conducted in environments where the intensity of each stage of the testing protocol can be precisely monitored and controlled. As such, these protocols often incorporate performing gait using remotely operated treadmills. The intensity of aerobic exercise can be manipulated based on proportions of individualized, pre-determined measures such as age-predicted maximum heart rate (APMHR) in conjunction with the Karvonen Formula to calculate heart rate reserve (HRR) [418] or estimations of energy expenditure based on the metabolic demands of gait under various levels of intensity based on speed and grade. The formulas for the estimations of volume of oxygen uptake relative to body weight ( $V_{O_2}$ , ml  $O_2$ /kg body weight/min) during walking and running are listed below in Equations 1 and 2, respectively. Using these parameters, multiple standardized testing protocols (i.e. Balke-Ware, Bruce, Naughton treadmill tests) have been developed to test the submaximal and maximal cardiorespiratory and metabolic fitness levels of a wide range of populations spanning patient in Phase I cardiac rehabilitation to elite athletes. As such, these testing protocols have shown promise in providing diagnostic, prognostic, and rehabilitative value in both clinical and research settings.

Equation 1: Walking  $V_{O_2} = 3.5 + (0.1 * speed^1) + (1.8 * speed * grade^2)$

Equation 2: Running  $V_{O_2} = 3.5 + (0.2 * speed) + (0.9 * speed * grade)$

Contrasting long-held standards of treatment promoting strict bed rest, early administration of aerobic exercise is a relatively new, yet increasingly popular facet of concussion management and rehabilitation [419,420]. The metabolic demands of gait during aerobic exercise can be utilized to identify the presence and severity of metabolic dysfunction within concussed individuals. The state of localized hypometabolism induced shortly following a traumatic brain injury can be exacerbated, and thus trigger somatic symptomology (i.e. dizziness, reductions in balance control) if metabolic resources are drawn away from the cerebral circulation [171]. This phenomenon is easily observable during vigorous exercise when blood flow is heavily redirected toward skeletal muscle. By gradually increasing the intensity and corresponding metabolic demands during graded exercise testing, parallels can be drawn between the severity of the patient's state of cerebral hypometabolism and the intensity at which concussion-related symptoms (i.e. nausea, dizziness, headache) are elicited during testing, thus revealing an incomplete recovery from injury. From there, exercise can be administered in a controlled environment and intensity can be increased in a stepwise fashion as tolerated over time until the patient can complete an entire testing protocol without symptom exacerbation. The early administration of aerobic exercise in the management for concussion has shown efficacy to accelerate recovery from injury compared to those undergoing strict rest by reducing the overall number of reported symptoms [421,422] and shortening the amount of time to receive medical clearance to return to normal levels of activity [423,424]. These findings support the notion that "exercise is medicine" when assessing patients

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<sup>1</sup> Gait speed measured in meters/minute

<sup>2</sup> Percent grade of incline expressed as a decimal (i.e. 5% = 0.05)

with concussion; that protocols incorporating gait performed at mild to vigorous intensities can elicit clinically relevant information about the severity of a sustained concussion as well as provide potential therapeutic benefits despite the long-held notion that strict bed rest and deliberate inactivity is optimal for recovery from concussion.

Although applications in exercise physiology provide excellent representations for systemic functional capacity, assessments of gait in the context of concussion are primarily conducted from biomechanical perspectives examining parameters of postural stability. Three-dimensional (3-D) motion capture has become the modern gold standard for kinematic assessments of gait. Unlike during quiet standing, gait presents a challenge for analyses of postural stability in which the body's center-of-mass is consistently changing location as the body moves through space, changes the area of its base of support between steps, and movement of the limbs transiently displaces portions of the body's total mass further off-center. 3-D motion capture procedures utilize specialized cameras to detect reflective markers placed strategically at various anatomical landmarks on the body and subsequently build representative models of the segments of the body based on the locations of each tracked marker in reference to the others throughout a collection trial. In addition, building a representative model of a human being allows for researchers to mathematically calculate the location of and track the body's center-of-mass during movement based on estimations of anthropometric proportions of mass distribution within the human body [425,426]. By observing the location of the body's center-of-mass, instrumented assessments of gait can potentially detect impairments of dynamic postural control that may not be outwardly apparent when solely assessing spatiotemporal parameters such as velocity, cadence, and average stride measurements.

3-D motion capture has recently been seeing increases in popularity when examining the effects of concussion on gait performance and postural stability. The ability to track an individual's center-of-mass is of particular interest in concussion patients because of their noted predisposition to adopt a more conservative gait pattern following injury; a precautionary movement strategy that places increased emphasis on maintaining upright postural control during gait in response to pathological instability [427]. The observed gait patterns of concussed individuals seem to prioritize maintaining control of the body's center-of-mass during motion, specifically to minimize the center's overall displacement during whole-body movement to ensure it remains within the area of the body's base of support throughout the gait cycle. As a result, acute concussion is associated with decreases in center-of-mass displacements and velocities during gait, suggesting a potentially precautionary movement strategy to ensure maintenance of postural stability [428,429]. However, the limited effectiveness of these altered kinematic patterns can be exposed by challenging the postural control system during gait by increasing the difficulty in navigating the external environment. Because maintaining upright stability during gait requires greater awareness of environmental surroundings compared to quiet standing, postural control impairments resulting from concussion can be more readily exacerbated by increasing the challenge of maintaining stability during gait with concurrent intrinsically driven tasks and/or the presence of external hazards. Under these circumstances, 3-D motion capture is able to track the center-of-mass throughout the movement patterns of concussed individuals when they are forced to stress their postural control systems beyond a range with which they may be subconsciously comfortable following injury.

Dual-task protocols have been utilized in concussion research by having concussed individuals walk while performing a concurrent cognitive task [280,430] or by having them step



around or over an obstacle [431,432] to direct cognitive and attentional resources away from solely maintaining stability during gait. Concussed individuals have been repeatedly shown to display increases in mediolateral center-of-mass displacement and velocity and overall reduced gait speed during dual-task conditions in the days and weeks following injury compared to their healthy counterparts [433–436]. While both healthy and concussed individuals demonstrate changes in their gait patterns between single and dual-task gait, concussion is associated with a greater dual-task cost to spatiotemporal gait parameters [437,438]. Specifically, concussed individuals demonstrate greater intraindividual disparities in their gait measurements (i.e. slower velocities, wider strides, greater percentage of time in double-limb support) between single and dual-task gait compared to those observed in healthy controls, suggesting a reduced capacity to optimize dynamic postural control when attentional resources are divided [280,439]. In addition, dual-task conditions have expanded the efficacy of tandem gait in clinical settings by revealing prolonged deficits in gait stability (i.e. decreased cadence, increased frontal plane center-of-mass displacement) compared to the single-task protocols commonly implemented in concussion screenings [280,409]. The inclusion of a secondary concurrent task during gait has revealed that postural control deficits resulting from concussion can persist for up to two months following the initial injury and beyond the resolution of other somatic and neurocognitive symptoms associated with concussion [440,441]. These findings are troubling because they indicate that concussion results in neurological dysfunction to a degree in which cognitive performance and dynamic postural stability cannot be optimally controlled simultaneously for an extensive period following injury. These findings further raise concerns about the chronic effects of concussion on future injury risk and whether balance impairments following concussion ever reach full resolution or if resulting deficits must permanently be accounted for using altered kinematic patterns.

Accelerometers and IMUs have also proven to be effective tools in kinematic analyses of gait. These devices hold a distinct advantage over virtual modeling and other 3-D motion capture systems in their ease of implementation and accessibility at the cost of the breadth of the scope of their potential applications in gait analysis. While accelerometry has most notably been implemented to measure the link between concussion and head impacts in sport [442–444], wireless accelerometer systems have been also been validated for use in gait analysis in both healthy individuals and pathological populations including concussion [362,416]. When affixed in strategic locations on the body, IMUs have provided an approximate estimation for the body's center-of-mass (i.e. lumbosacral spine) as well as representations of how independent segments of the body behave during gait (i.e. head, trunk, pelvis) [445]. Previous research assessing concussion patients using IMUs revealed that when changing direction during gait, previously concussed individuals demonstrate slower velocities at the level of the pelvis and more variable coordination between timings to turn the head and pelvis [446]. These observations indicate that concussion may be associated with a reduced ability to coordinate the various segments of the body during locomotion, resulting in changes in motor patterns that contribute toward the formation of a precautionary gait pattern to prioritize the maintenance of stability. In addition, accelerometers have shown utility as tools to measure progress during recovery from concussion by tracking subtle differences in average and peak accelerations at the trunk (i.e. approximate center-of-mass) during gait [447,448]. Collectively, the findings within the literature indicate that acceleration patterns during gait are altered following concussion and could potentially provide an objective marker for neurological dysfunction signaling the presence of injury and/or incomplete recovery. Accelerometers and IMUs provide an accessible means to examine segmental coordination during

gait and potentially identify changes in the complex neural networks contributing to postural control following concussion and throughout the recovery process.

One noteworthy application of accelerometry for gait analysis comes in the form of analysis of head stabilization during movement. Specifically, accelerometers affixed to the head and different segments of the spinal column (i.e. cervical, lumbar vertebrae) can measure how the body prioritizes the stabilization of the head during movement [445,449]. The visual and vestibular systems consistently work in tandem during gait to properly orient the eyes (i.e. vestibulo-ocular reflex, CN I, CN IV, CN VI) and stabilize the head as the vestibular nuclei continuously detect the motions of head created kinetic forces of foot strikes ascending from the ground throughout the body as well as the overall motion of the body being propelled through space [129,450]. Given this notion, individuals that have sustained damage to sensorimotor tissue and/or neural networks via degenerative disease or trauma may exhibit greater difficulties in stabilizing the head during gait. Notably, decreased head stabilization (i.e. excessive movement) during gait has been observed in multiple populations associated with neurological decline and dynamic balance impairment including patients with Parkinson's disease, cerebral palsy, and otherwise neurotypical elderly adults [449,451,452]. However, despite the well-documented symptomology resulting from concussion indicative of vestibular dysfunction (i.e. dizziness, balance impairment) and the noted changes in gait kinematics suggesting intrinsic reductions in postural control, the body's capability to stabilize the head during gait has not been thoroughly examined in the scope of concussion in both acute or chronic perspectives.

Rather than tracking the body's center-of-mass, ascertaining information about the center-of-pressure location for each footfall during the various stages of gait can also provide information about the sensory and motor processing areas of the brain potentially affected by injury. Despite

their stationary positions, force plates capable of tracking the center-of-pressure under one's feet have proven to be useful tools for assessing the effects of concussion on gait performance. The overall displacements of the center-of-pressure during the initiation and termination stages of gait have shown to be indicative of altered, precautionary movement strategies adopted by individuals that have sustained a concussion [453,454]. Specifically, acutely concussed patients demonstrate reductions in the posterior and mediolateral displacements of their standing center-of-pressure during gait initiation, indicating dysfunction during the planning and preparatory phases preceding gait [126,455]. Similar differences in center-of-pressure parameters have been observed during the termination stage of gait, in which concussed individuals display increases in mediolateral displacement as they begin to actively decelerate and stop walking [454]. These observations indicate that the acute stages of concussion are associated with impairments during the motor planning aspects of gait, signaling dysfunction in the premotor cortex and supplementary motor areas [456]. These findings are invaluable as they demonstrate that concussion results in not only a reduced capacity to maintain proper postural control during gait, but also an impaired ability to properly plan motor output contributing to gait. While the exact causal nature behind impaired motor planning following concussion is not thoroughly understood, the potential disconnect between perception and motor output is a growing area of interest in concussion research [457,458]. Further research is required to better understand the effects of concussion on cortical function and the resulting motor output changes indicated by alterations in changes in control of the centers of body mass and foot pressure that can be observed during gait.

The complex kinematics of gait and corresponding neurophysiology contributing to gait performance and stability inherently complicates assessments following concussion, where it can be difficult to adequately detect not only the causal source of postural control deficits, but the

presence of deficits themselves. The high number of degrees of freedom embedded in human locomotion ultimately allows for preemptive alterations of movement patterns to effectively compensate for deficits in stability whilst maintaining the overall goal of performing gait successfully. The feasibility of utilizing compensatory strategies to perform gait without demonstrating clinically apparent signs of postural instability has made using gait as a canvass to identify mild cases of traumatic brain injury, namely concussion, difficult compared to more pathologically advanced cases of trauma (i.e. stroke). Like many clinical balance assessments, protocols examining gait following concussion have proven to be lackluster in objectively identifying the presence and extent of impaired dynamic postural control in the face of mild traumatic brain injury. However, much like standing balance, gait has provided a more accurate portrayal of the temporal extents in which impairments following concussion can persist than neurocognitive assessments alone. Moving forward, kinematic assessments and nonlinear analyses of gait parameters that have been applied to various neuropathological populations can potentially be utilized in concussion patients to better understand the severity and source of dynamic postural instability during gait. As one of the most commonly performed motor tasks in humans, improving our understanding of gait stability in the context of concussion can potentially shed light on how concussion can have detrimental effects on more complex forms of locomotion and motor tasks as well.

## **2.6 Chronic Deficits Associated with Concussion**

Despite recent advances in research uncovering the alterations in neurophysiological function and improvements in expanding the scope of identifiable symptoms indicating the presence of mild TBI, the breadth of knowledge and expertise surrounding the detrimental effects

of concussion has remained troublingly shortsighted. Traditionally, concussion has often been described using colloquial terms such as “being punch drunk” or “getting your bell rung”. As a result, concussion has been widely viewed as an injury presenting with symptomology that could be overcome with willpower and perseverance rather than medical intervention. These approaches of subpar philanthropy neglect considerable scientific evidence detailing the importance of the brain for nearly all functions and regulation of the central nervous system. Unfortunately, peer-reviewed scientific evidence can take long to influence folk wisdom and cultural traditions. As a result, the long-term effects of the potential brain damage that manifests following a concussive impact can go unnoticed either because of a lack of sophisticated diagnostic and imaging techniques, or because of a lack of education about the medley of possible symptoms associated with concussion.

Approximately ten to fifteen percent of cases of concussion report persistent, long-term symptomology [459]. However, the observed problems with detecting symptoms in the acute stages following a traumatic head impact suggest that the reported rates of long-term presence of symptoms are significantly underestimated. Concussion is a uniquely difficult injury to assess from a chronic perspective in part due to the variety of possible symptoms that can arise from trauma to neural tissue and interconnecting networks. Symptoms of concussion can range in nature from cognitive, biomechanical, to physiological and can be subjective and/or outwardly evident during screening procedures. In addition, these symptoms can vary in severity considerably from case to case and thus can be difficult to objectively identify reliably across the entire population. Because of this, a disproportionate amount of attention and effort is placed between cognitive, biomechanical, and physiological symptoms. Specifically, symptoms that are the easiest to identify or gather information about are prioritized during clinical screenings. While this approach does

expedite the screening process, it can result in critical oversights, false negative diagnoses, and premature returns to normal levels of activity that can predispose individuals to a secondary and possibly more severe injury. Placing greater emphasis on symptoms that can be identified quickly has led to a lack of detailed understanding concerning the lingering effects of concussion and the detrimental consequences that a history of traumatic brain injury can have beyond the point of clinical determination of recovery.

### *2.6.1 Neurocognitive*

Among the most common symptoms associated with concussion are those that are neurocognitive in nature, such as memory loss, problems maintaining focus and attention, and confusion. Neurocognitive symptoms are prioritized in concussion screenings because they can be identified via self-reports from the patients themselves or by using a simple test that does not require technological equipment. Because of this, both the diagnosis of and determinations of recovery from concussion have traditionally been heavily reliant on the presence of neurocognitive symptoms. However, it has become more and more apparent that the short-term resolution of symptoms such as confusion, headache and emotional dysregulation are not indicative of a complete resolution of the initial injury. In recent years, the long-term neurocognitive and psychological deficits associated with prior history of concussion have been uncovered and gained a growing amount of mainstream attention [186,460]. These findings have helped clarify the foundations of post-concussion syndrome (PCS) as well as links to various neuropsychological disorders and conditions that can develop later in life [461–463]. This has also had ramifications on the development and implementation of rehabilitative protocols including defining conditions for return-to-play in athletics and return-to-learn for academics.

Cognitive impairments are often attributed to damage or dysfunction throughout the cerebrum, primarily within the frontal and prefrontal cortices where functions including abstract reasoning and decision-making originate [206,464]. The trauma induced from a concussive impact can result in widespread damage to the cortical tissue and axonal networks within the cerebrum, ultimately resulting in impaired cognitive functioning. Traditionally, recovery from concussion was thought to plateau as the tissue of the central nervous system fails to completely restore function to damaged tissue. However, recent research has observed a certain degree of plasticity within the frontal lobes following a traumatic brain injury, demonstrating a circumvention rather than a plateau to restoring function within the frontal lobes upon sustaining damage [465,466]. While plasticity of this nature seems excellent and intuitive at first glance, it is essentially a redirection of the complex networks of communication within and beyond the frontal lobes. It remains to be determined what the possible long-term effects of concussion re-wiring the circuitry of the frontal lobes can have on the function of specific areas of the cerebral cortex or on overall cognitive abilities. However, cognitive impairments observed in other neuropathological populations do exhibit alterations in frontal lobe communications [467,468], raising concerns about how a history of concussion can affect cognitive abilities and frontal lobe function throughout the lifespan.

It is well documented that concussion can manifest as a medley of neurocognitive symptoms that can vary significantly in severity, ranging from outwardly undetectable to grossly apparent [381,469,470]. Despite often serving as the primary criteria for determining recovery from concussion, recent research has revealed that these deficits can remain longer than previously believed. Specifically, concussion history has been associated with long-term impairments in visual and working memory in both young and older adults [471,472]. In addition, athletes with a



documented history of concussion have been shown to demonstrate slower and less accurate response times during numerous testing protocols that increased cognitive demand [473–475]. These deficits do not always go unnoticed by patients themselves and can result in mental stress developing from a marked inability to complete certain tasks with pre-injury levels of efficiency. Following this notion, studies implementing validated screening tools such as the Beck Depression Inventory and the 36-Item Short Form Health Survey (SF-36) have found links between concussion history and decreased emotional regulation and self-perceived quality of life [186,476]. These findings emphasize the fact that concussion is not an injury that presents with solely transient symptomology and that a holistic, comprehensive clinical approach requires the consideration of long-term consequences and impairments that may or may not ever fully reach complete resolution.

Multiple testing batteries have been developed in attempts to screen the entire possible scope and presence of neurocognitive impairment following a documented injury; perhaps the most famous of which is the Immediate Post-Concussion Assessment and Cognitive Test (ImPACT). While the ImPACT is often administered in the acute stages following a concussion to detect the presence of neurocognitive deficits [477], there are concerns about the protocol's ability to detect chronic, lingering impairments. The ImPACT is notoriously vulnerable to intentionally poor performances (i.e. sandbagging), with reports that such cases fail to be detected up to twenty percent of the time, resulting in a troublingly high false negative rate. [478]. There has also been an observed learning effect for the ImPACT, raising concerns about the efficacy of using the test multiple times to determine the progression of recovery following a concussion [479]. As a result, alternative approaches have been developed and implemented in research settings. Various cognitive testing batteries have identified deficits associated with prior history of

concussion including impaired executive function, attentional capabilities, and recall memory [186,460,480,481]. In addition, there has been an established link between concussion history and the coupling of cognitive and motor processes, which suggests that the neural damage sustained during a traumatic head impact can have long-term consequences that results in an increased cognitive demand to perform motor tasks that could previously have been executed more automatically [482]. The complexity of human cognition makes it unlikely that any single testing battery can efficiently encompass the scope of the potential neuropsychological deficits that can arise both acutely and chronically following concussion. However, this should not discourage efforts to better identify the long-term deficits of neurocognitive function associated with concussion, as this has been typically shown to be a prevalent oversight in determining the temporal extent to which concussion can negatively impact cognition. Therefore, there is still much work to be done in determining the most efficacious methods to identify and address such deficits.

Prior history of concussion has also been linked to increased incidence rates for the development of neuropsychological conditions including, but not limited to, clinical depression and dementia [193,483,484]. The development of clinical depression is associated with observed changes in metabolic rates of neurotransmitters including serotonin and dopamine throughout the frontal and prefrontal cortices [485,486]. Depressive symptoms are common in the acute stages of concussion. However, individuals with a prior history of concussion exhibit an increased risk of developing pathological, clinical depression later in life compared to those without a history of traumatic brain injury [463,487]. In addition, preliminary findings have indicated that concussion could also be linked with an increased risk of dementia onset and other biomarkers consistent with Alzheimer's disease [488,489]. These findings suggest that concussion can have chronic detrimental effects on the neural structures that contribute to proper emotional regulation and

cognition throughout the lifespan. Interestingly, despite the documented links between concussion and long-term neurocognitive pathologies, concussion history has been shown not to be associated with an increased incidence rate of malingering, nor negative behavioral tendencies including alcoholism and suicide [137,490]. Collectively, these findings suggest that the potential development of neuropsychological disorders and/or diseases associated with a history of traumatic brain injury are based on the changes in physiology rather than self-aware actions made by the patients themselves. This distinction is important to note when formulating treatment and management plans for concussion because until the pathophysiology of concussion is better understood, treatment options will be relegated to addressing symptoms as they arise rather than the root cause of the pathology.

It is currently unclear what specific factors surrounding the nature and/or sequelae of a traumatic head impact result in the extended duration of neurocognitive impairments. However, it has become increasingly apparent that current clinical protocols and standards for the determination of recovery from concussion may not be sensitive enough to accurately detect said neurocognitive impairments. From this perspective, it is also unclear if the fault of the protocols lies in the design of the tests themselves or if the thresholds for determination of recovery are too low. Furthermore, because adolescents and young adults are among the most commonly seen patients presenting with concussion, the inability to detect the chronic effects of concussion on cognitive ability and psychological regulation can have negative effects in academic and athletic environments as well as during activities of daily living [491]. Going forward, it will be of paramount importance to further clarify the associations between concussion and long-term negative effects on neuropsychological health to better identify and properly address impairments as they arise.

### 2.6.2 *Physiological*

Of all the domains of symptoms associated with concussion, physiological symptoms are the least well understood. Widespread knowledge of the physiological changes associated with traumatic brain injury is only recently becoming better understood at all levels of neurophysiology ranging from cellular to systemic. Physiological operations serve as the basis of all systemic functions throughout the human body. Therefore, it is through these perspectives that we are gaining a better and more comprehensive understanding of why concussion can potentially impact overall functional abilities of numerous neural networks throughout a much longer timeframe than was previously believed. However, physiological data often cannot be derived from subjective assessments or self-reports of symptoms from individual patients. Therefore, analyzing physiological processes is notably difficult in comparison to cognitive and biomechanical assessments because most physiological assessments require specialized equipment and training to acquire and interpret data.

Neurons communicate with one another using two methods: (1) electrical signal transmissions generated via fluctuating ion concentration gradients and (2) chemical signal transmissions moderated by the release and reuptake of neurotransmitters. Studies examining the physiological effects of concussion on brain function have primarily utilized electroencephalography (EEG) to measure electrical signals throughout the cerebrum. More advanced imaging techniques including functional magnetic resonance imaging (fMRI) and functional near-infrared spectroscopy (fNIRS) to observe oxygen consumption levels throughout the brain to indicate higher levels of metabolic activity during cognitive tasks have also been implemented in the acute stages of concussion. While not typically utilized in clinical settings,

studies utilizing these techniques have revealed chronic impairments of brain function associated with a prior history of concussion. These findings have added to the already complex sequelae associated with concussion but nevertheless provide greater, valuable details about the neurophysiology of traumatic brain injury from which more effective therapeutic and rehabilitative techniques are developed.

The non-invasive nature and relatively inexpensive cost of EEG have placed it among the most common methods of assessing physiological function of the brain. Studies utilizing EEG have shown that individuals that have sustained at least one concussion exhibit a suppressed and latent P3 response, an event-related potential (ERP) attributed to attention capacity, as well as decreased amplitudes for an N400 response, which represents the ERP component for cognitive processing speed [492–494]. In addition, studies have revealed that there appears to be a cumulative effect of concussion on electrophysiological function within the brain, demonstrated by individuals with multiple prior concussions exhibiting greater latencies within a variety of ERPs throughout the frontal cortex [495,496]. Troublingly, these deficits have been detected despite no significant differences in performance on traditional neurocognitive testing protocols. Similar changes in electrophysiology associated with concussion history have also been observed in M1 using transcranial magnetic stimulation (TMS), where attenuated P3a and P3b responses and prolonged cortical silent periods were interpreted as long-term motor system deficits independent of neurocognitive dysfunction [195]. It has been theorized that these changes may be attributable to decreases in either the extracellular concentration or metabolic rates of excitatory neurotransmitters including glutamate within the brain [497,498]. Further exploration is needed to determine if the changes in electrophysiology observed with EEG following concussion correlate with long-term changes in changes in chemical signal transmission.

Unlike electrophysiology, long-term assessments of concussion are much less well understood when examining chemical signal transmission. Chemical signal transmission is more difficult to analyze because measuring concentrations of neurotransmitters released within the brain often requires invasive procedures. For example, while Parkinson's disease is known to be associated with a loss of dopaminergic cells within the substantia nigra, diagnoses are based on the development of motor symptoms because the substantia nigra can only be closely examined to confirm the loss of available dopamine post-mortem. As such, the development of neuroimaging techniques (i.e. fNIRS, fMRI, diffusion tensor imaging) has helped researchers develop visual representations of the brain's metabolic activity indicative of neurotransmitter metabolism and chemical signaling. In the context of concussion, imaging techniques often look toward oxygen saturation within the bloodstream and various regions of the metabolically active cortex to screen for physiological impairments [499,500]. However, neuroimaging is typically only performed in the acute stages following a traumatic brain injury, whether to examine functional changes in laboratory settings or to rule out internal hemorrhaging in clinical cases. As a result, there is a limited amount of exploration that has been done looking at the chronic implications of concussion history on cortical perfusion and metabolic activity. Preliminary findings have indicated that concussion may be associated with changes in tissue perfusion within the frontal lobes, namely an increase in perfusion within white matter and a decrease within grey matter [501]. However, conflicting findings have been found when examining different areas of the cerebrum, raising additional questions about the complex, longitudinal sequelae of concussion [502]. Until these techniques are expanded to examine the cellular level and/or become more widely available, the long-term impact of concussion history on chemical signal transmission will remain somewhat ambiguous, but also an area of piqued interest for neuroscientists.

Among the physiological markers for concussion gaining in popularity during clinical screenings are examinations of oculomotor function. Because eye movements are heavily mediated by the function of three cranial nerves (CN III, IV, VI), concussion has been shown to have immediate detrimental effects on saccadic eye movements and alterations in near point of convergence [503–505]. The clinical utility of assessing eye movements in suspected cases of concussion has been growing in popularity in part due to its ease and cost of implementation. However, there is far more speculation about the feasibility of assessing oculomotor function for the detection of long-term impairments stemming from a history of concussion. There have been conflicting findings concerning the effect of concussion history on near point of convergence, where some studies claim that concussion does not result in any long-term alterations whereas others have found changes in visually evoked electrophysiological potentials associated with insufficient convergence distance [506,507]. However, there is a growing amount of evidence supporting the notion that concussion results in long-term impairments to saccadic eye movements that are commonly assessed during protocols including the King-Devick test [508,509]. These conflicting results have resulted in attempts to develop predictive models for determining the effect of multiple characteristics of oculomotor function in relation to concussion history, with mixed levels of effectiveness [510].

Additional recent developments concerning the long-term effects of concussion have centered around the cardiovascular system. Specifically, concussion has been shown to have lingering negative impacts on autonomic regulation of cardiac rhythm, suggesting dysfunction and/or uncoupling between the branches of the autonomic nervous system [511–513]. Frequency analyses of cardiac rhythm have been used to distinguish the activity of each branch of the autonomic nervous system, with lower frequencies (0.04-0.15 Hz) being attributed to the

sympathetic nervous system and higher frequencies (0.15-0.40 Hz) representing the parasympathetic nervous system [514]. While the exact physiological nature of the changes is still debated, concussion has been repeatedly shown to be associated with alterations in heart rate variability and baroreflex activity, suggesting altered modulation originating from the branches of the autonomic nervous system [515,516]. These changes have been detected monitoring the cardiovascular system via electrocardiography (ECG) during interventions such as aerobic exercise and exposure to thermoregulatory stress [103,517]. Unfortunately, the number of studies that look at autonomic dysfunction following concussion from a long-term perspective is currently limited, leaving the objective duration in which these deficits can remain speculative at best. However, these preliminary findings are invaluable to the ever-expanding scope of knowledge concerning the long-term effects of concussion, as they provide evidence that concussion can have detrimental effects outside the central nervous system. Future efforts should be directed toward examining the autonomic dysfunction associated with concussion following clinical resolution of symptoms and how these changes can affect cardiovascular function and prognosis for individuals with a history of concussion throughout their lifespan.

The neurophysiology of concussion has traditionally been viewed as so complex that it was overlooked during clinical assessments in lieu of simpler neurocognitive and balance testing. However, recent developments and discoveries have revealed that physiological approaches and analyses can be valuable tools in identifying and treating concussion. Of the three primary domains of symptoms that are associated with concussion, physiological symptoms are the least well understood and addressed in clinical assessments. Because of this, the current scope of knowledge concerning the long-term implications of concussion history on physiological functions such as cardiac rhythm and cerebral perfusion remain inconclusive. However, the preliminary findings and



trends that have been repeatedly found within concussed individuals suggest that these alterations are worth exploring for the benefit of both the individuals that sustain a traumatic brain injury and the clinicians and medical professionals that treat them without having a comprehensive understanding of the effects of the injury.

### 2.6.3 *Biomechanical*

Problems maintaining balance during standing and gait are commonly observed in the sequelae following a traumatic brain injury. As a result, assessments of static and dynamic postural stability during standing and walking have become increasingly more common and serve as integral portions of various clinical treatment approaches for concussion. Utilizing these clinical assessments, a long-standing belief states that balance deficits following a traumatic head impact are generally resolved within a few days of the initial injury [311]. However, technological instrumentation and more sophisticated analytical approaches have revealed that impairments of postural stability can persist longer than previously believed, with multiple studies revealing deficits in balance during standing and gait weeks and even months following the most recent traumatic head impact [430,518,519]. These revelations conflict with clinical standards for recovery from concussion and have likely contributed to unsettlingly high false negative rates and premature returns to activity and sport. These findings are troubling when considering the increased rates of lower-limb orthopedic injury following concussion that persist for months following a traumatic head impact [520], although this relationship remains correlational and shallowly explored to date. While the objective temporal extent in which postural stability deficits remain following a concussion remains inconclusive, there is a growing body of evidence

indicating that individuals with a history of one or multiple concussions may not reach pre-injury levels of function during standing and gait even years following their most recent injury.

Static postural stability is a common topic in research concerning the acute and chronic effects of concussion. Expanding beyond clinical assessments of balance, the extent to which deficits in postural stability during upright standing persist following a concussion have primarily been explored by examining various parameters of injured individuals' center-of-pressure (CoP) on a force plate. Specifically, alterations in CoP parameters including increased average sway displacement and decreased regularity of sway patterns have been identified in the weeks and months following a traumatic brain injury despite the resolution of observable differences in clinical balance assessments [348,355,375]. In addition, multiple studies have shown that challenging the postural control system using methods such as dual-task cognitive protocols and jumping tasks elicit observable differences in CoP parameters in individuals with a history of concussion that may not be detectable during quiet standing alone [358,521,522]. In addition, instrumented performance of the Y-Balance test to capture trunk sway measurements indicated that individuals that have sustained a concussion demonstrate greater sway displacement months following their most recent injury [523]. These findings suggest that while impairments during quiet standing may resolve to a certain degree in the acute stages following a concussive impact, the postural control system as a whole may not reach full resolution and remains susceptible to being overloaded when faced with challenges to maintaining equilibrium. However, because it has traditionally been believed that concussion symptoms resolve in a matter of days, the vast majority of studies examining the "long-term" effects of concussion history on standing balance do not extend beyond the scope of one year since the most recent injury. Therefore, it's currently unknown how long these impairments can remain in concussion patients and if these differences

are observable in all concussion patients or solely in those that have experienced more frequent and/or severe traumatic injuries. Future efforts can and should be made toward the development of studies establishing a baseline for static postural stability and tracking changes post-concussion from a longitudinal perspective.

The chronic effects of concussion history on dynamic postural stability during gait has been slightly more extensively studied compared to static stability. Much like assessments of static stability, long-term impairments during gait associated with concussion have been uncovered in the weeks and months following a concussion using instrumented assessments that are not utilized during clinical gait testing; in this context being three-dimensional motion capture and center-of-mass (CoM) displacement. Studies utilizing these methods have determined that alterations of gait patterns indicative of reduced postural control (i.e. reduced velocity, increased CoM displacement) can persist in the weeks and months following a traumatic brain injury and more importantly beyond the point in which clinical gait assessments can identify such impairments [430,524]. Furthermore, studies examining the influence of concussion history on gait have determined that concussion can potentially have detrimental effects on the stability of an individual's default gait pattern as shown by decreases in velocity and time spent in single-leg stance throughout the gait cycle several years following the most recent traumatic head injury [525,526]. These findings are indicative of the notion that concussion has long-term, possibly permanent implications on postural control during gait as individuals with a prior history of concussion demonstrate alterations in their gait patterns suggesting an impaired ability to modulate perturbations to their upright equilibrium. However, further exploration is required to better understand the neurophysiological cause of these observed impairments and efforts should be made to incorporate the instrumented methods utilized

to identify said impairments into clinical screenings to improve diagnostic techniques for concussion.

Despite promising early findings concerning the chronic effects of concussion on postural control, there are several glaring oversights in the literature. First, studies examining postural stability following concussion are often centered on external observations of quiet standing and/or gait rather than internal neural activity within the brain, thus leaving the causal root of any persisting impairments inconclusive. While evidence of chronic neurophysiological alterations following concussion have been documented [527], it remains to be seen how these changes potentially contribute to deficits in maintaining proper postural control. In addition, assessments of dynamic stability following concussion have thus far been mainly limited to observing normal, everyday gait patterns or simple alterations such as tandem gait or incorporating a pivot turn [407,446,455]. Complex movements that are utilized in athletic environments such as sidestep cutting maneuvers or braking from a full sprint have not been examined in concussed individuals in both acute and chronic timeframes. While this may have been the result of precautionary measures to avoid exacerbating postural control deficits in an injured population, this has left a considerable hole in the literature as the populations that are inclined to perform these high-impact, ballistic movements are also among those that are most likely to sustain a concussion. It has yet to be objectively determined if concussion history is a precursor to alterations in complex kinematic patterns that contribute to the increased lower-limb orthopedic injury rates that have repeatedly been observed in athletic populations [528]. However, preliminary findings assessing acutely concussed military personnel have indicated that concussion may result in neuromuscular changes that contribute to lower limb kinematics during jumping and landing movements that predispose individuals to sustaining a lower limb orthopedic injury [529]. It remains unclear if these

discrepancies remain in the months and years following a traumatic brain injury despite persisting incidence rates of orthopedic injury.

## **2.7 Limitations**

The fundamental limitations facing research examining the long-term effects of concussion on postural stability have been largely unchanged for decades. The most prominent obstacle facing any study addressing the negative effects of concussion is the difficulty of objectively identifying a concussion for diagnostic purposes. Concussion is defined as a traumatic brain injury characterized by the sequelae of symptoms that present following the injury rather than physical evidence of damage to brain tissue [4]. Many of the symptoms associated with concussion can go undetected by medical professionals as the result of an inability to objectively identify an impairment or a willful refusal to disclose the presence of symptoms by the injured individual, and thus no diagnosis will have been made. As a result, the documentation of whether an individual has a prior history of one or multiple concussions can contrast his/her actual prior experiences. This poses a potential problem when grouping participants in studies based on whether they have a prior history of concussion and/or have sustained one or multiple injuries, as mischaracterization of subjects can skew the overall outcomes and conclusions of entire projects. Until improvements are made in diagnostic techniques and screening procedures to objectively identify concussion, these problems will unfortunately remain as a speculative pitfall that any researcher examining the detrimental effects of concussion must consider and remain wary of when interpreting the findings of their work.

Another glaring limitation surrounding concussion research is the disconnect between technologically sophisticated methodology to detect neurological impairments following a

traumatic brain injury and the clinical applications of these findings. Traditionally, studies examining the aftermath of a concussion utilized the techniques and methods that were also performed by medical professionals and clinicians that treated concussion patients. These techniques are expedient and easy to administer but lack the sensitivity and specificity measures to ensure consistently and objectively accurate results concerning the presence and duration of symptoms [8,381,478]. As technology including, but not limited to, force plates, three-dimensional motion capture, metabolic testing, and neuroimaging has been incorporated into concussion research, a growing number of revelations about the more extensive extent of both the severity and complexity of symptoms and impairments associated with concussion are being shown to be overlooked or unidentified in clinical assessments following injury. However, these advanced tools and technologies are generally not available to clinicians screening for concussion due to a lack of practical application in the field, portability, financial resources, or ability to operate the equipment skillfully and properly analyze data outputs. Upon reviewing the field of concussion research as a whole, these disparities in methodology have led to conflicting conclusions about the cognitive, physiological and biomechanical changes that occur following concussion, and perhaps most pertinently, the duration with which these changes remain following an injury. Although there seems to be a recent paradigm shift toward relying more heavily on advanced technological approaches in the literature, clinicians still have been slow to implement these techniques when screening patients. Until a thorough consensus on methodology is reached between clinics and laboratories, the background and field of expertise of those contributing to the literature concerning concussion will need to be accounted for when interpreting the overall conclusions of their printed work.

A final limitation of the research examining the effects of concussion history concerns the incredibly complex and multi-faceted nature of concussion itself. There are multiple ways that one can sustain a concussion including a direct, blunt head impact, rapid linear and/or rotational head accelerations that do not result from a blunt impact, and shockwaves from blast exposures [154,530]. Troublingly, the mechanism of injury does seem to be a significant factor in the development and severity of certain symptoms, as they often do not present equally from patient to patient. Studies have also shown that the location of the focal point of a traumatic head impact (i.e. frontal bones, temporal bones, etc.) can have a significant impact on the prognosis of the severity of a concussion [531,532]. These factors and more make concussion a very complicated injury to both treat and study, and those reporting a history of concussion may not be able to accurately recall all of the details that can play a role in the development of their symptoms. While individuals that experience injuries such as ACL tears or broken clavicles have a somewhat predictable course of recovery, the experiences of concussion patients can vary wildly across the spectrum of possible outcomes. As such, it is difficult and potentially misleading to make generalizations about the effects of concussion without being extremely broad by design. Researchers must remain aware of this when examining and interpreting their findings, as their subject pool may not exhibit changes associated with their concussion history that can be applied to all individuals that have a documented history of concussion.

## CHAPTER 3

### CHRONIC IMPAIRMENTS OF STATIC POSTURAL STABILITY ASSOCIATED WITH HISTORY OF CONCUSSION

#### **3.1 Introduction**

Postural instability is a common symptom following a concussion [305,347]. In the healthy population, maintenance of upright posture requires multiple neural networks (i.e. corticospinal and vestibulospinal tracts) and structures of the brain (i.e. cerebrum, cerebellum, basal ganglia, brainstem) to facilitate parallel integration of sensory feedback information from the visual field, vestibular nuclei and somatosensory receptors in order to facilitate proper motor output to maintain stability [10,18,19,533]. Concussion is believed to result in dysfunctional sensorimotor integration stemming from disrupted neural connections in the form of axonal shearing at sensory information processing sites within the cerebral cortex or damage at the sensory receptors themselves [159,534]. Improper communication between neural structures can manifest as changes in motor output. In the context of concussion, trauma to neural tissue can potentially result in changes in motor output that can be detected beyond the determination of recovery as determined by standard clinical assessments of balance [535].

Traditionally, balance testing has been utilized in the screening process for acute concussion by challenging one or more of the sensory feedback systems to determine if a suspected injury had resulted in the implementation of compensatory actions to maintain static postural stability. Using these assessments throughout the rehabilitation process and to determine if recovery has been reached, previous research has concluded that postural instability following a



concussion typically resolves within a few days of the initial injury [311,329]. However, more sensitive methods of measuring characteristics of postural sway (i.e. center of pressure (CoP) tracing) have revealed that deficits in stability following a concussion can persist for weeks and even months after the initial injury despite injured individuals displaying no clinically detectable impairments [355,375,536]. Specifically, concussion has been shown to result in changes in CoP characteristics during upright standing indicative of reduced stability including increased sway displacement, velocity and regularity [109,359]. Troublingly, these changes cannot be accurately detected using commonly utilized screening protocols such as the Romberg Test and the Balance Error Scoring System (BESS) [9,320,335]. These changes in CoP measures are also associated with decreases in postural control, an increased falls risk, and predisposition to injury that is also seen in neurological diseases including multiple sclerosis and Parkinson's disease [61,537,538]. While concussion is widely viewed as a transient injury rather than a pathological disease, it remains to be determined whether the acute deficits in postural stability associated with the initial injury are ever fully resolved to match the measures of stability exhibited prior to experiencing a concussive impact.

Allocation of attention has been identified as a contributing factor toward proper maintenance of postural stability. In healthy individuals, maintenance of upright posture is highly automatized and does not require a significant amount of conscious effort or specifically directed attention [22]. In contrast, acute concussion has been shown to cause greater deficits in stability under dual-task conditions during quiet standing while attention is divided between the cognitive task and maintenance of upright posture in comparison to their healthy counterparts, indicating a limited capacity for allocation of attention [539,540]. In agreement with these findings, damage to the neural structures and networks that contribute to maintaining postural stability can manifest as

an increased demand for cognitive resources directed toward maintaining balance. Concussion has also been shown to result in greater deficits in both static and dynamic stability months following the initial injury and beyond the resolution of cognitive symptoms [435,439]. The exacerbation of stability deficits when performing multiple tasks at once indicates that concussion results in a reduced capability to allocate necessary cognitive resources to all the tasks being undertaken, effectively overwhelming the postural control maintenance system. When combined with the lack of objective diagnostic criteria for concussion and inability to detect subtle changes in upright standing postural sway without specialized equipment, dual-task attentional allocation deficits following a concussion present an elevated risk of injury beyond the timeline typically judged by medical professionals.

While prior studies have indicated that deficits in postural stability persist beyond the resolution of neurocognitive symptoms such as headache and dizziness, determination of recovery from concussion is still heavily influenced by self-reports of cognitive symptoms unless the initial injury results in gross impairments of postural stability [99,541]. In addition, long-term assessments of impairments associated with concussion are commonly directed toward neuropsychological and cognitive deficits rather than impairments of postural stability [136,527,542]. To date, the authors are unaware of any studies examining whether postural stability deficits in previously concussed individuals remain not only beyond the scope of recovery as determined by clinical balance assessments and self-reports of cognitive symptoms, but as a chronic impairment years after the initial injury. However, individuals that have sustained multiple concussions display incrementally greater stability deficits with each additional injury [360], indicating that the deficits in stability associated with concussion not only accumulate over time, but may persist long after an individual is deemed to have made a full recovery from concussion.

The purpose of this present study was to determine the effect of a prior history of concussion on standing postural stability after the injury has been deemed clinically resolved for a minimum of one year. Our main hypothesis was that despite all participants being deemed healthy at the time of testing, implementation of a concurrent cognitive task during standing would elicit greater deficits in postural stability in individuals with a prior history of concussion compared to those that have never sustained a concussion as evidenced by changes in multiple CoP parameters indicative of postural control (i.e. sway displacement, velocity, regularity).

## **3.2 Methods**

### *3.2.1 Participants*

Fifty-four healthy adults were recruited to participate in the present study. The participants were divided into two groups based on the number of previous diagnosed concussions they reported to the researchers. The two groups were designated as those with no reported history of concussion (NON group,  $n = 27$ ; mean age =  $28.56 \pm 5.17$  years) and those reporting one or multiple prior diagnosed concussions (CONC group,  $n = 27$ ; mean age =  $26.11 \pm 5.97$  years). Participants reporting a history of concussion reported an average of  $2.25 (\pm 1.40)$  injuries and  $6.91 (\pm 5.67)$  years since their most recent injury.

To be included in the present study, all participants had not sustained a diagnosed concussion within one year prior to their scheduled testing date. Additional exclusionary criteria included the following: (1) any orthopedic injury or condition that impaired balance or gait occurring within one year prior to testing, (2) vestibular condition that impaired participant's ability to maintain equilibrium (i.e. vertigo), (3) diagnosed neurocognitive disorder (i.e. attention deficit-hyperactivity disorder, post-traumatic stress disorder), and (4) any history of brain surgery.

Participants were also instructed to avoid vigorous exercise in the two hours before their scheduled visit to avoid the impact of musculoskeletal fatigue on balance assessments. Demographic information including age, height and weight were documented for each participant. In addition, participants were asked to report any previous orthopedic injuries at and/or inferior to the hip joints. Finally, participants were asked about the typical amount of exercise they underwent in the six months leading up to compare to the weekly recommendations for aerobic exercise determined by the American College of Sports Medicine [543]. The study was reviewed and received approval from the university's Institutional Review Board.

### 3.2.2 *Symptom assessment*

Participants were screened for concussion symptoms through the use of a symptom checklist adapted from the Sport-Concussion Assessment Tool (SCAT-5) [338]. The checklist consisted of twenty-two symptoms commonly associated with concussion rated by participants on a Likert scale ranging from 0 (no presence) to 6 (severe, debilitating). Participants were instructed to rate how they perceived each symptom during the day of testing. Participants that rated any symptom as a 4 or higher or reported a cumulative score of 20 or higher were disqualified from further participation.

### 3.2.3 *Concussion history questionnaire*

All participants were asked to report their concussion history defines as the number of prior diagnosed concussions as determined by a physician. Those reporting a history of concussion were asked to elaborate on each reported event by disclosing the amount of time since each reported injury on the day of testing.

### 3.2.4 *Postural stability assessment*

Postural stability was assessed by continuously tracking the position of the standing CoP while stressing the participants' ability to maintain upright stance on a force plate system (Model BP5050, Bertec Inc., Columbus, OH). Participants were instructed to stand upright and shoeless with their feet together on the force plate while looking straight ahead with their arms relaxed at their sides. Participants were instructed to stand in either a bipedal or unipedal stance and/or stand while concurrently performing a cognitive task, thus altering the difficulty in maintaining static stability by narrowing the participants' base of support and/or increasing cognitive demand by dividing the participants' attentional resources, respectively. Participants stood on their dominant leg during unipedal trials by flexing their non-dominant hip and knee to approximately ninety degrees. Leg dominance was determined by asking participants which leg they would use to kick a ball as far as possible. During dual-task trials, participants were instructed to maintain their balance while verbally conducting a serial subtraction task throughout the trial in order to divide their attention between the cognitive task and maintaining balance. The serial subtraction test was chosen because of the documented cognitive challenge it presents to uninjured participants as well as concussed individuals during screening [544]. The combination of the postural and cognitive components resulted in four conditions during testing administered in a random order: (1) bipedal, single-task (B-ST), (2) unipedal, single-task (U-ST), (3) bipedal, dual-task (B-DT), and (4) unipedal, dual-task (U-DT). Mistakes during dual-task conditions were defined as incorrect responses in the sequence of numbers defined by the number assigned in the serial subtraction task.

Each condition consisted of two trials measured for thirty seconds per trial with recording starting five seconds after the participant settled into the instructed position. Any trials that

included any disruptive movement as the result of external visual or auditory perturbation, excessive head movement, shifting of the feet on the force plate or a complete loss of balance during measurement were discarded and repeated until two successful trials were completed for each condition.

### 3.2.5 *Data analysis*

Raw CoP data were collected at 50 Hz for each trial and processed using a fourth-order, low-pass Butterworth filter with a cut-off at 20 Hz in a custom script written in MATLAB (MathWorks, Natick, MA). CoP parameters were calculated using the output from the force plate system indicating the position of the CoP throughout each trial about the anteroposterior (AP) and mediolateral (ML) planes. Postural sway measures derived from the CoP data included total CoP path length, mean displacement in the AP and ML planes, mean sway velocity, and elliptical area of sway tracing derived from 95 percent confidence interval. These values were chosen because increases in CoP path length, velocity, elliptical area and ranges of displacement have been shown to be indicative of poorer postural stability during upright standing in acute assessments following a diagnosed concussion [347,348,359].

In addition, sample entropy (SampEn) of each CoP position tracing was also calculated for each trial in the AP and ML planes. SampEn is a unitless measure of the regularity of a given signal with values ranging from 0 to 2. Signals with values approaching 2 are interpreted to be more irregular and unpredictable in nature (i.e. Gaussian noise), while signals closer to zero have a more regular, predictable pattern (i.e. a sinusoidal wave) [106]. In the context of CoP measurements in the present study, lower SampEn values were interpreted to be indicative of a

more regular sway pattern and a reduced capacity to properly adjust to unanticipated perturbations in postural stability [108].

### 3.2.6 *Statistical analysis*

Age, height, weight, amount of regular physical activity, lower limb orthopedic injury history and average number of mistakes during dual-task conditions were assessed between groups using independent t-tests. CoP parameters were assessed using 2 x 2 x 2 mixed-design analyses of variance (ANOVAs) to identify differences between groups (CONC v. NON) based on stance (bipedal v. unipedal) and/or number of concurrent tasks (single-task v. dual-task) during testing conditions. Effects sizes for all CoP parameters were calculated using Cohen's *d*. Planned contrasts were conducted on reported significant differences with *a priori* significance levels ( $p < 0.05$ ) adjusted for multiple comparisons using Bonferroni's correction. All statistical analyses were conducted using SAS v.9 (SAS Institute Inc, Cary, NC).

## 3.3 **Results**

### 3.3.1 *Demographics*

Demographic information for both groups are displayed in Table 1. There were no significant differences between groups based on age ( $p=0.114$ ), sex ( $p=0.054$ ), height ( $p=0.325$ ), weight ( $p=0.248$ ), level of regular physical activity ( $p=0.298$ ), or previous lower limb orthopedic injury history ( $p=0.084$ ).

### 3.3.2 Concussion symptom screening

There were no significant differences between groups based on symptom checklist scores at the time of testing ( $p=0.338$ ).

### 3.3.3 Serial subtraction performance

There were no significant differences between the NON and CONC groups based on the average number of mistakes during dual-task conditions in both bipedal stance ( $1.12 \pm 1.15$  vs.  $0.78 \pm 1.03$ ;  $p=0.246$ ) and unipedal stance ( $0.84 \pm 0.82$  vs.  $0.91 \pm 1.04$ ;  $p=0.803$ ). In addition, there were no significant differences in the total number of responses during bipedal ( $12.02 \pm 5.70$  vs.  $11.09 \pm 4.62$ ;  $p=0.509$ ) and unipedal ( $11.69 \pm 5.73$  vs.  $11.81 \pm 5.64$ ;  $p=0.935$ ) trials between groups.

### 3.3.4 Postural sway parameters

Means and standard deviations for all collected CoP parameters during single-task and dual-task conditions are displayed in Tables 2 and 3, respectively. There were no significant differences in CoP mean velocity and path length between groups across all conditions. Additionally, there were no significant group-condition interaction effects for all measured postural sway parameters.

Average sway displacement in the anteroposterior and mediolateral planes are displayed in Figures 1 and 2, respectively. There was a significant difference in anteroposterior sway displacement between groups under dual-task conditions, but notably only during bipedal stance ( $F_{1,104}=4.64$ ;  $p=0.033$ ; 95% CI= 0.836-1.19 cm vs. 1.10-1.46 cm). Significant differences between groups were found for mean mediolateral sway displacement ( $F_{1,416}=4.037$ ;  $p=0.045$ ) and elliptical



area of postural sway ( $F_{1,416}=5.114$ ;  $p=0.024$ ). Specifically, the CONC group demonstrated greater postural stability deficits under dual-task conditions in both bipedal and unipedal stance compared to the NON group. Compared to the NON group, the CONC group displayed significantly greater sway displacement in the mediolateral plane under dual-task conditions when standing on their dominant leg ( $F_{1,104}=4.29$ ;  $p=0.041$ ; 95% CI= 1.22-1.69 cm vs. 1.57-2.05 cm), but not in bipedal stance ( $p=0.210$ ). Furthermore, small effect sizes were revealed for mean postural sway displacement in the mediolateral plane (range:  $d=0.211$ - $0.408$ ) under both unipedal conditions and during U-ST trials in the anteroposterior plane ( $d=0.201$ ). In addition, the CONC group demonstrated significantly greater elliptical area of their sway under dual-task conditions compared to the NON group when assuming both bipedal ( $F_{1,104}=6.84$ ;  $p=0.01$ ; 95% CI= 1.56-3.38 cm<sup>2</sup> vs. 3.26-5.12 cm<sup>2</sup>) and unipedal stance ( $F_{1,104}=4.12$ ;  $p=0.044$ ; 95% CI= 6.51-8.94 cm<sup>2</sup> vs. 8.26-10.73 cm<sup>2</sup>). Small-to-moderate effect sizes were also found for elliptical area under dual-task conditions (range:  $d=0.397$ - $0.514$ ).

Figures 4 and 5 illustrate the SampEn measurements between groups in the anteroposterior and mediolateral planes, respectively. Significant differences in CoP SampEn were found between groups in both the anteroposterior ( $F_{1,422}=7.02$ ;  $p=0.008$ ) and mediolateral planes ( $F_{1,422}=4.81$ ;  $p=0.029$ ). Furthermore, the CONC group demonstrated lower entropy (i.e. more regular) sway patterns compared to healthy controls when performing unipedal stance under both single and dual-task conditions. Specifically, the CONC group displayed decreased SampEn values during unipedal stance in both the anteroposterior and mediolateral planes under single (AP:  $p=0.032$ ; 95% CI= 0.248-0.298 vs. 0.286-0.338; ML:  $p=0.009$ ; 95% CI= 0.433-0.500 vs. 0.373-0.437) and dual-task (AP:  $p=0.006$ ; 95% CI=0.244-0.293 vs. 0.293-0.339; ML:  $p<0.001$ ; 95% CI= 0.438-.696 vs. 0.386-449) conditions. In addition, small-to-moderate effect sizes were found for SampEn in

the anteroposterior plane in all four conditions (range:  $d=0.201-0.549$ ) while moderate-to-large effect sizes were found for SampEn in the mediolateral plane only under unipedal conditions (range:  $d=0.523-0.817$ ). Interestingly, the CONC group also demonstrated significantly reduced SampEn in the anteroposterior plane during the bipedal, dual-task condition ( $F_{1,104}=4.70$ ;  $p=0.032$ ), but reported no differences in the mediolateral plane under the same condition.

### **3.4 Discussion**

The primary findings of this study indicate that deficits in standing postural stability in those with a history of concussion are present after the determination of recovery based on current clinical screening protocols, and that these deficits can be elicited and identified with the implementation of a concurrent cognitive task during balance assessments.

#### *3.4.1 Detection of static stability impairments*

To date, there has been a limited amount of research examining long-term impairments of postural stability in previously concussed individuals beyond the scope of recovery as determined by clinical balance assessments. However, the sensitivity and reliability of clinical tests of balance commonly utilized in concussion screening have been raising concern in recent years [312,545]. For example, the BESS has seen widespread implementation in acute concussion screening. However, more technologically advanced equipment (i.e. force plates, three-dimensional motion capture) that have the capability to elicit measures of assessing postural stability (CoP displacement, SampEn, etc.) have revealed that postural stability impairments associated with concussion persist beyond the clinical determination of recovery as seen using the BESS [326,335]. Specifically, deficits in postural stability associated with concussion have been

identified in the forms of greater sway displacement and reduced entropy measures even when previously concussed individuals are tested months and even over a full year after the initial injury [358,375,376]. The present study expands on these previous findings by identifying similar trends in reductions in static postural stability in individuals reporting a prior history of one or more concussions averaging nearly seven years since their most recent injury. These findings indicate that the postural stability deficits that stem from concussion can persist beyond the scope with which clinical balance testing can accurately detect. The incorporation of technology and more sophisticated laboratory equipment during balance assessments has shown promise in detecting postural stability deficits in a variety of neurological populations including concussion patients [360,546,547]. Future efforts should be made toward providing clinicians access to these advanced methods of assessing postural stability to provide more objective and reliable means to determine if impairments stemming from a concussion have been resolved.

### *3.4.2 Chronic presence of stability impairment*

The findings of the present study demonstrated that the deficits in postural stability that are associated with the acute stages of concussion (i.e. increased sway displacement, decreased CoP SampEn) can potentially be persistent for several years following clinical resolution from the initial injury. The majority of previous studies examining the lifetime implications of prior concussion history have focused on development of neuropsychological conditions [460,472,548] and neurodegenerative disease [136,549,550]. To date, previous studies attempting to discern the duration of the presence of postural stability impairments associated with concussion have typically not exceeded the scope of eighteen months since the initial injury [429,551,552].

The individuals in the present study with a prior history of concussion reported a range of fifteen months to twenty-five years since their most recent diagnosed concussion and had all been determined to be fully recovered by a health care professional at the time of their testing visit. The comprehensive findings of the present study suggest that postural stability impairments associated with concussion linger for years after the initial injury and beyond the clinical determination of recovery. This finding is troubling because our understanding of the long-term consequences of concussion history on postural control are not as thoroughly explored or understood as the lingering effects of concussion on neurocognitive function [186,553]. While the neurological damage sustained following a concussion is widely viewed as transient and less severe in nature to neurodegenerative diseases such as Parkinson's disease, the results of this study showed similar trends in the differences in postural sway patterns between individuals with a history of concussion and Parkinsonian patients compared to healthy controls; namely by displaying persistent increases in sway displacement and reductions in sway regularity [371,554]. The observed changes in static postural stability raise concerns about the abilities of previously concussed individuals to maintain proper postural control during gait and more complex sport-related movements in the years following injury as well. Additionally, prolonged deficits in maintaining static and dynamic postural stability are likely conducive to increasing the risk of falls and secondary injuries following concussion. While these results help provide a more comprehensive understanding of the consequences stemming from concussion, follow-up studies will be required in which a cohort of concussion patients are tracked longitudinally in order to objectively determine when and if the postural stability deficits associated with concussion are fully resolved.

### 3.4.3 *Effects of divided attention*

The results presented in this study indicate that prior history of concussion is associated with deficits in static postural stability that are exacerbated by dividing attentional resources. While standing postural control is highly automatized, there is a need for attentional allocation for proper maintenance that becomes more apparent when the body is placed in more unstable, challenging positions [555,556] or when trauma, such as a concussive impact, produces damage to the structures that contribute to subconscious maintenance of stability [10,43]. Directing attention elsewhere by concurrently performing cognitive tasks provides an additional means to potentially make the maintenance of upright stability more difficult. Dual-task protocols have previously been utilized in the management of concussion by implementing a cognitive task to assess postural stability during gait, as concussed individuals display impairments under dual-task conditions for weeks and even months after exhibiting a return-to-baseline as determined by parameters measured during single-task gait [441,539,557]. However, the effect of dividing attention on static stability in the context of concussion is not as well understood.

It has been previously demonstrated that within the general, healthy population, dual-task conditions incorporating a concurrent cognitive task improves static postural stability because intentionally directing attention and effort solely on maintaining balance during quiet standing is inefficient as this strategy does not resemble typical means of functioning in daily life [558,559]. In contrast, individuals with a history of concussion demonstrated an opposite trend in the form of decreased postural stability while their attention was divided. Our findings demonstrated that there were no significant differences between groups based on the number of responses and mistakes recorded during the concurrent cognitive task, indicating that concussion history had no significant impact on performance of the cognitive task. However, the deficits in static stability represented

by CoP parameters suggest that a concurrent, increased cognitive demand had a detrimental effect on maintenance of postural control within the CONC group that was not observed in controls. Recent approaches have shown concussion is potentially associated with alterations in perception-action coupling; the continuous link between what an individual perceives in the environment and the actions taken as a result [560]. Individuals with a concussion history have previously demonstrated longer reaction and movement times in response to perceptual stimuli within the year following injury [458,561]. These deficits in perception-action coupling are believed to manifest as improper motor output responses to stimuli within the environment that can reduce postural stability and increase risk of musculoskeletal injury. The findings of the present study support the notion that concussion history is associated with a reduced capacity to perform cognitive and motor tasks simultaneously by revealing exacerbated deficits in postural control under dual-task conditions. However, the physiological basis for these changes following concussion require more extensive study.

Central nervous system tissue does not regenerate or have the capacity for repair to the same extent as the tissue of the periphery [40]. Therefore, it is reasonable to presume that damage sustained within the brain during a concussive impact can have negative influences on proper brain function that may never reach full resolution. A reduction in the number of available, functioning neural networks can result in a reduced capacity to adapt to perturbations presented to the overall system. Our findings indicate that concussion results in a long-term reduced capacity to allocate attention concurrently to multiple tasks, and that optimal performance of cognitive tasks are prioritized over motor tasks when performed concurrently. All significant differences found within the present study arose under conditions in which maintaining balance was made more difficult by either introducing a concurrent cognitive task and/or by decreasing the area of the participant's

base of support. In addition, the observed reductions in sample entropy support the notion that the postural control system is more constrained following a sustained concussion. Decreases in CoP SampEn have been interpreted as a reduced capacity to adapt to unexpected perturbations of postural stability possibly stemming from precautionary stiffening of the lower body musculature and/or reduction of the complexity of neural oscillator networks throughout the cerebrum [18,562]. Our findings demonstrate that difficulty of maintaining balance (i.e. multitasking and/or challenging position) is inversely related to complexity of CoP tracings during upright stance, and that concussion history exacerbates these changes to a degree that is potentially problematic from a clinical perspective. Future research assessing the long-term impairments associated with concussion should consider incorporating functional neuroimaging to assess activity across multiple areas of the cerebral cortex during dual-task protocols to better discern from where impairments are originating.

#### *3.4.4 Limitations*

The present study was limited in numerous ways. First, because of the lack of objective diagnostic criteria for concussion, all participants were assigned to their respective groups based on self-reported accounts of previous diagnosed concussions, thus resulting in the reported concussive events for each participant being retrospective in nature. Underreporting rates for concussion remain a widespread problem in concussion research and treatment, and this trend will persist until objective diagnostic criteria are identified and able to be detected in clinical settings outside of laboratories. Second, the study was cross-sectional in design and thus under the utilized collection format, it cannot be definitively stated that the deficits in postural stability demonstrated by the individuals reporting a history of concussion were caused by their previous injury history

and that these deficits were not consistent with their standing balance capabilities prior to sustaining their first concussion. Future studies should include a baseline assessment and follow-up testing should participants sustain a concussion in order to objectively identify the intra-individual effects of concussion on static postural stability.

Finally, there was a considerable, yet statistically non-significant difference between groups based on intra-group distribution of sex. Specifically, the NON group was represented by a group skewed toward representing females over males (21 females; 6 males) compared to the more evenly distributed CONC group (15 females; 12 males). While prior research has identified differences based on sex during clinical assessments for concussion [343,563], sex has been shown to be a poor predictor for the course of recovery of proper postural control following a concussion [336]. As such, it cannot be stated that intra-group distributions of sex contributed significantly to the differences in long-term deficits in postural stability observed in the present study. However, eliminating disparities in the demographics between groups will help minimize the potential for confounding variables in future research examining concussion within the general population.

### **3.5 Conclusion**

Overall, the present study revealed that history of concussion is associated with deficits in postural stability that remain present for years following the initial injury. Specifically, individuals that have sustained one or multiple concussions exhibit greater CoP displacement and regularity of sway under dual-task conditions compared to those that have never had a diagnosed concussion. Increasing the difficulty of maintaining upright postural stability by changing demands for allocation of attention appears to be a useful tool in identifying deficits resulting from concussion that is not currently integrated into mainstream concussion screening protocols. Collectively, these



findings indicate that concussion can result in long-term decreases in postural control indicative of reductions of complexity within the central nervous system.

Table 1: Means and Standard Deviations for Demographic Information Between Groups for Static Stability Assessment.

<i>Variable</i>	<i>NON Group (n = 27)</i>	<i>CONC Group (n = 27)</i>	<i>p-Value</i>
<i>Sex (M / F)</i>	6 / 21	12 / 15	0.054
<i>Age (years)</i>	28.56 ± 5.17	26.11 ± 5.97	0.114
<i>Height (cm)</i>	168.61 ± 8.07	171.12 ± 10.38	0.325
<i>Weight (kg)</i>	73.24 ± 13.66	77.84 ± 15.26	0.248
<i>Diagnosed concussions</i>	N/A	2.25 ± 1.40	N/A
<i>Time since concussion (years)</i>	N/A	6.91 ± 5.97	N/A
<i>PCSS Score</i>	3.15 ± 4.33	4.11 ± 3.79	0.388
<i>Lower-limb orthopedic injuries</i>	1.37 ± 2.02	2.89 ± 3.49	0.084
<i>Physical Activity (150 min/week; Y/N)</i>	20 / 7	19 / 8	0.298

Table 2: Means and Standard Deviations for CoP Parameters Between Groups Under Single-Task Conditions. Asterisks denote significant differences between groups.

<i>Variable</i>	<i>B-ST</i>				<i>U-ST</i>			
	<i>NON</i>	<i>CONC</i>	<i>p-Value</i>	<i>d</i>	<i>NON</i>	<i>CONC</i>	<i>p-Value</i>	<i>d</i>
<i>Mean velocity (cm/s)</i>	1.19 ± 0.252	1.20 ± 0.376	0.923	0.020	4.89 ± 1.08	4.57 ± 1.49	0.204	0.247
<i>Path length (cm)</i>	35.90 ± 7.59	36.36 ± 11.43	0.807	0.063	147.33 ± 32.62	138.64 ± 45.04	0.256	0.220
<i>AP sway (cm)</i>	1.14 ± 0.403	1.11 ± 0.383	0.749	0.020	2.29 ± 0.99	2.59 ± 1.85	0.312	0.201
<i>ML sway (cm)</i>	0.944 ± 0.325	0.887 ± 0.376	0.403	0.168	1.72 ± 1.13	1.99 ± 1.54	0.293	0.211
<i>Elliptical area (cm<sup>2</sup>)</i>	3.21 ± 1.55	3.07 ± 2.33	0.731	0.063	10.08 ± 7.05	11.33 ± 10.02	0.458	0.142
<i>AP SampEn</i>	0.116 ± 0.033	0.119 ± 0.047	0.660	0.201	0.312 ± 0.094	0.273 ± 0.090	0.032*	0.424
<i>ML SampEn</i>	0.156 ± 0.054	0.166 ± 0.499	0.311	0.089	0.466 ± 0.123	0.405 ± 0.114	0.009*	0.523

Table 3: Means and Standard Deviations for CoP Parameters Between Groups Under Dual-Task Conditions. Asterisks denote significant differences between groups.

<i>Variable</i>	<i>B-DT</i>				<i>U-DT</i>			
	<i>NON</i>	<i>CONC</i>	<i>p-Value</i>	<i>d</i>	<i>NON</i>	<i>CONC</i>	<i>p-Value</i>	<i>d</i>
<i>Mean velocity (cm/s)</i>	1.25 ± 0.365	1.36 ± 0.487	0.192	0.255	4.66 ± 1.13	4.35 ± 1.24	0.169	0.271
<i>Path length (cm)</i>	37.60 ± 11.03	41.21 ± 14.80	0.157	0.278	140.59 ± 34.12	131.91 ± 37.68	0.216	0.247
<i>AP sway (cm)</i>	1.01 ± 0.412	1.28 ± 0.826	0.033*	0.424	2.13 ± 0.939	2.30 ± 1.02	0.356	0.179
<i>ML sway (cm)</i>	0.817 ± 0.323	0.902 ± 0.367	0.210	0.247	1.46 ± 0.393	1.81 ± 1.18	0.041*	0.408
<i>Elliptical area (cm<sup>2</sup>)</i>	2.47 ± 1.50	4.19 ± 4.59	0.010*	0.514	7.72 ± 3.15	9.50 ± 5.55	0.045*	0.397
<i>AP SampEn</i>	0.158 ± 0.078	0.126 ± 0.049	0.015*	0.487	0.316 ± 0.084	0.269 ± 0.088	0.006*	0.549
<i>ML SampEn</i>	0.177 ± 0.060	0.172 ± 0.060	0.642	0.089	0.504 ± 0.101	0.417 ± 0.113	<0.001*	0.817

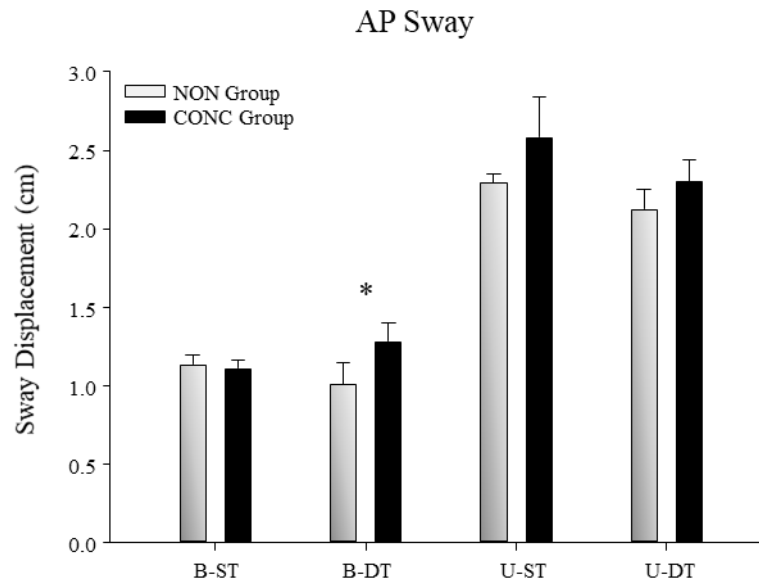


Figure 1: Group Differences in Average Anteroposterior Postural Sway Displacement Across All Four Conditions. Asterisks represent statistically significant differences between groups ( $p < 0.05$ ). Error bars represent one standard error of the mean.

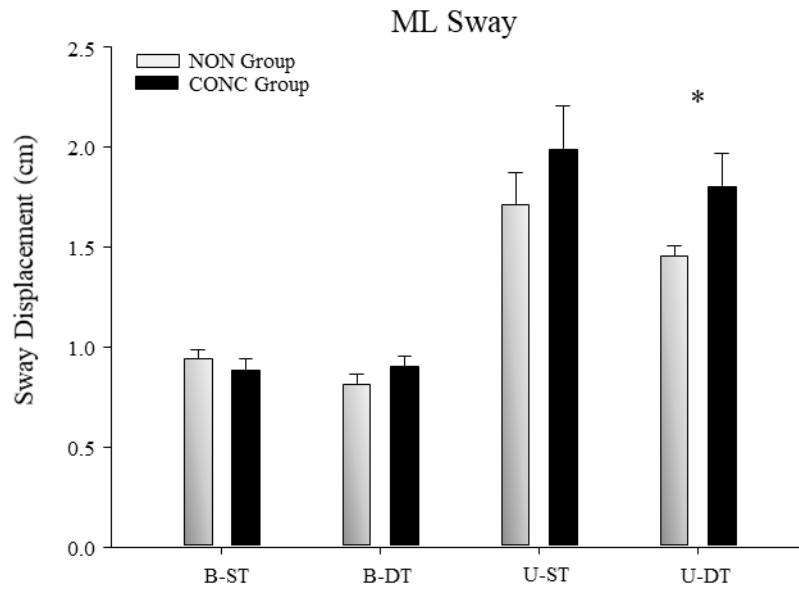


Figure 2: Group Differences in Average Mediolateral Postural Sway Displacement Across All Four Conditions. Asterisks represent statistically significant differences between groups ( $p < 0.05$ ). Error bars represent one standard error of the mean.

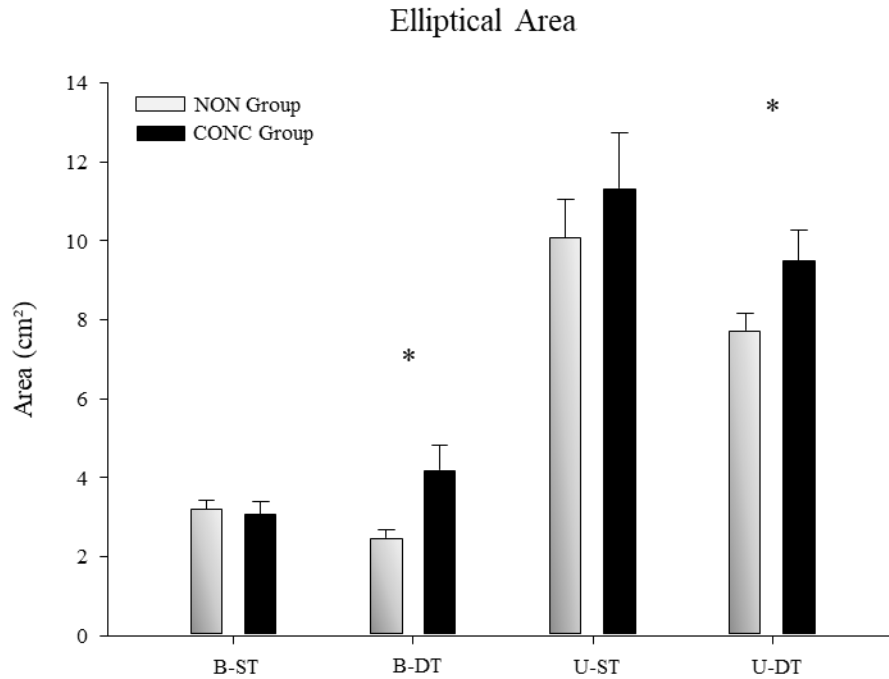


Figure 3: Group Differences in Average 95-Percent Confidence Ellipse Area for Static Postural Sway Across All Four Conditions. Asterisks represent statistically significant differences between groups ( $p < 0.05$ ). Error bars represent one standard error of the mean.

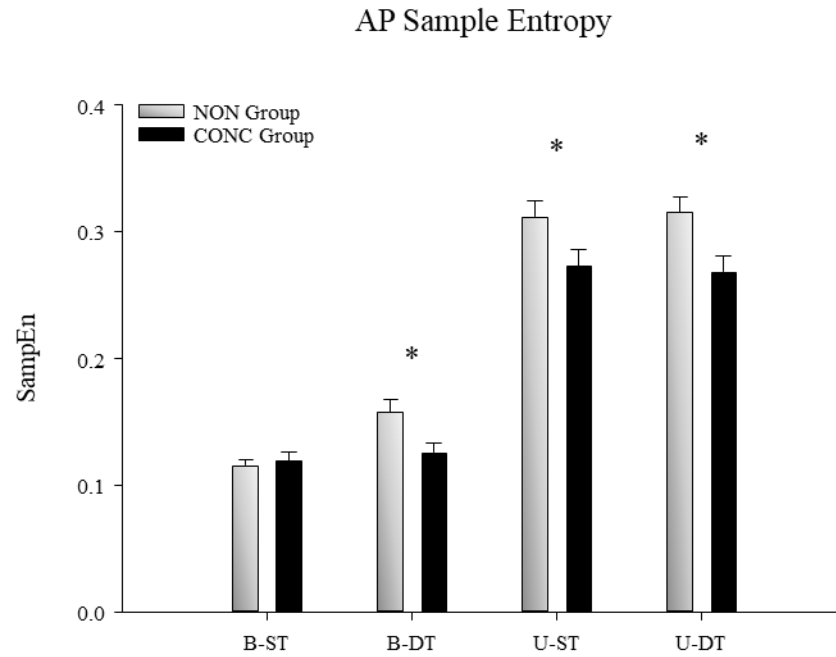


Figure 4: Group Differences in Average Sample Entropy of CoP Tracings in the Anteroposterior Plane. Asterisks represent statistically significant differences between groups ( $p < 0.05$ ). Error bars represent one standard error of the mean.



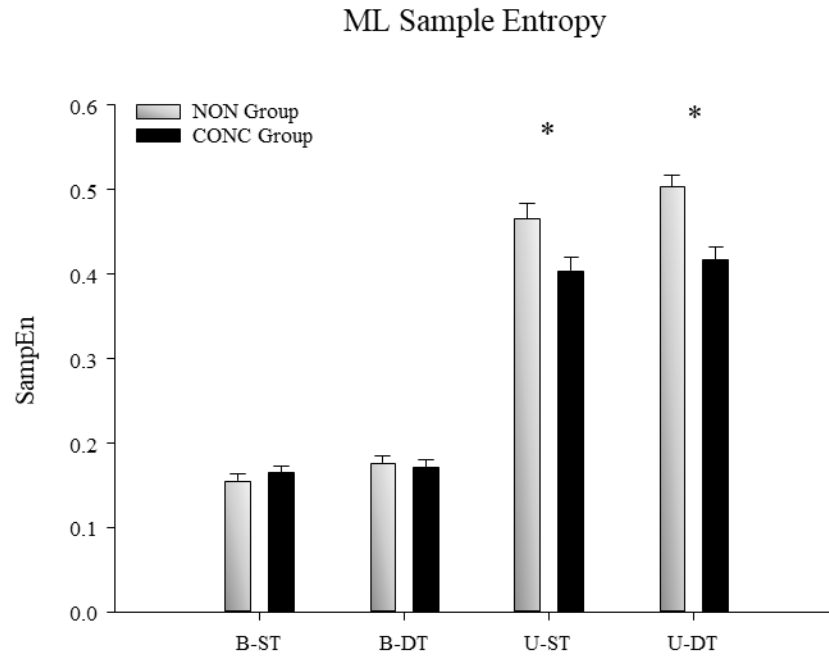


Figure 5: Group Differences in Average Sample Entropy of CoP Tracings in the Mediolateral Plane. Asterisks represent statistically significant differences between groups ( $p < 0.05$ ). Error bars represent one standard error of the mean.

## CHAPTER 4

### LONG-TERM GAIT STABILITY DEFICITS REVEAL POSTURAL CONTROL DEFICITS ASSOCIATED WITH HISTORY OF CONCUSSION

#### 4.1 Introduction

Concussion is a type of mild traumatic brain injury (mTBI) that has garnered a growing amount of mainstream attention in recent years in part due to the improvements in spreading awareness of the long-term effects of sustained head trauma [542]. In particular, concussion has been linked to the development of neuropathological diseases and conditions that can manifest beyond the point when current clinical testing measures determine the initial injury to be resolved [549,564,565]. Despite advances in understanding the pathophysiology of the injury itself, concussion continues to be among the most difficult injuries to accurately identify in a clinical setting due to the microscopic scale on which the traumatic damage is incurred [171,566]. As a result, diagnostic screenings and determinations of recovery from concussion are heavily reliant on self-reports from patients regarding somatic symptoms such as headache and nausea and/or neurocognitive impairments including memory loss and difficulties maintaining attention. Disproportionate emphasis placed on self-reported symptoms can result in oversights of objective evidence of injury including deficits in postural control during standing and walking.

Balance impairment is a commonly observed symptom following a concussion [347]. Recent consensus statements for optimal treatment of concussion include recommendations of balance assessments in addition to screening for neurocognitive symptoms to create a more comprehensive evaluation of neurological function immediately following a suspected concussion

[111,567]. Clinical assessments of balance such as the Balance Error Scoring System (BESS) and the updated modified Balance Error Scoring System (mBESS) have been designed to assess balance in a cost-effective, timely manner. Unfortunately, these protocols have demonstrated low sensitivity and specificity as a diagnostic tool that stems from poor interrater reliability and a marked learning effect that can skew performance and raise false negative rates [8,339]. In addition, clinical testing protocols assessing static balance have identified that the majority of cases of concussion are resolved within days of the sustained injury despite observable balance deficits during gait persisting for considerably longer periods of time [335,430]. The shortcomings of widely utilized balance assessments highlight the need for more reliable testing protocols to identify postural control deficits following concussion and prevent premature declarations of recovery.

Gait presents a more complex motor function in comparison to quiet standing, and thus requires a greater magnitude of neural resources to maintain stability during performance [568]. Postural stability deficits following a concussion can be exacerbated by stressing the sensorimotor networks that contribute to postural control (i.e. vision, somatosensory and vestibular feedback) [22,534]. Acutely concussed individuals attempt to compensate for deficits in stability by adopting a more protective gait pattern in the forms of slowing down (i.e. reduced velocity), widening their base of support (i.e. increased step width) and increasing the percentage of time within the gait cycle spent in double-limb support [427,545,569]. In cases of concussion, clinicians utilize protocols designed to prevent the use of these compensatory strategies to elicit objective signs of instability. As such, tandem gait is commonly utilized in concussion screenings because purposefully narrowing an individual's base of support presents a challenge to maintaining balance during gait without the need for sophisticated laboratory equipment [392]. Concussed individuals

have been shown to perform tandem gait significantly slower compared to healthy controls despite showing a return to baseline levels of velocity in their preferred gait pattern, further indicating that concussed individuals rely on compensatory strategies during gait in order to maximize stability during gait [407]. However, evaluations of tandem gait based on averages have revealed practice effects that can mask underlying impairments [411], further emphasizing the need for objective evidence of postural stability impairment during gait in order to reliably discern when a concussion has occurred and eventually has resolved.

Variability of spatiotemporal gait parameters has been shown to provide additional insight to the effects of neurological function in relation to maintenance of gait stability. Changes in variability of gait parameters have been observed in numerous neuropathological populations such as Parkinson's disease and multiple sclerosis [98,570]. It is believed that increases in gait variability are the manifestation of a reduced ability to conserve postural control during gait. While concussion is widely viewed as an injury defined by temporary dysfunction rather than a chronic disease, concussion has been shown to have potentially persistent detrimental effects on cognition, indicating that following a traumatic impact, the brain may never return to pre-injury levels of function [389,460]. In addition, concussion results in damage to areas of the brain commonly identified as sites of degeneration seen in neurological disease [571]. Despite these similarities, the effects of concussion on gait variability are not as thoroughly understood compared to average changes in spatiotemporal gait parameters. Additionally, prior research assessing gait variability changes in relation to concussion have primarily assessed acutely injured individuals' preferred gait pattern [427]. To date, there have not been any studies examining the effect of concussion on variability during tandem gait when individuals' ability to implement conservative alterations to their gait pattern are obstructed. In addition, there is currently no consensus as to whether prior

history of concussion manifests in alterations in stability during gait that remain not only past the clinical determination of recovery, but whether these changes are permanent in nature stemming from irreparable damage to central nervous system tissue and networks.

The objective of the present study was to determine the effects of a prior history of concussion on postural stability during gait after a minimum of one year since the most recent injury. It was hypothesized that (1) individuals with a prior history of concussion will demonstrate differences in average spatiotemporal gait parameters indicative of reduced gait stability compared to the control group, and (2) individuals with a prior history of concussion will exhibit changes in the variability of their gait parameters under both preferred and tandem gait patterns.

## **4.2 Methods**

### *4.2.1 Study design*

A cross-sectional experimental design was implemented to assess potential differences in gait parameter averages and measures of variability between individuals with and without a prior history of concussion.

### *4.2.2 Participants*

Fifty-three healthy adults were recruited to participate in the present study. Participants were divided into two groups based on reporting having never been diagnosed with a concussion (NON group, n=26) or whether they reported a prior history of concussion(s) diagnosed by a medical professional (CONC group, n=27). Individuals reporting a history of concussion averaged 2.26 ( $\pm 1.40$ ) previous diagnosed concussions and an average of 6.91 ( $\pm 5.67$ ) years since their most recent diagnosis. Potential participants were subjected to the following exclusionary criteria: (1)

concussion diagnosis within the last twelve months prior to the time of testing, (2) lower limb orthopedic injury or condition resulting in impairing one's ability to maintain balance and/or walk a distance of twenty-five feet sustained within one year prior to the time of testing, (3) vestibular condition impacting one's balance and/or ability to walk (i.e. vertigo), (4) neurocognitive disorder (i.e. ADHD), and (5) history of brain surgery.

All participants provided written informed consent to participate in all procedures included within the study. The study was reviewed and received approval from the university's Institutional Review Board.

#### *4.2.3 Symptom assessment*

All participants were screened for twenty-two concussion symptoms prior to conducting the gait assessment using a checklist derived from the Sport-Concussion Assessment Tool (SCAT-5) [338]. Each symptom was ranked on a Likert scale ranging from 0 (absent) to 6 (severe, debilitating). Individuals that ranked any individual symptom as a 4 or greater or reported a cumulative score of 20 or higher were disqualified from further participation.

#### *4.2.4 Gait assessment*

To account for potential confounding variables for gait variability related to health, documented information for each participant included age, sex, height, weight, medication use, self-reports of previous falls, and underlying visual and hearing impairments [572]. In addition, physical activity and lower body injury history were screened as potential contributors to gait variability. Participants were asked to report the typical amount of weekly aerobic exercise in which they partook over the course of the six months leading up to testing. These reports were

distinguished based on whether the reported regular amount of aerobic exercise met the recommendations determined by the American College of Sports Medicine (ACSM) [543]. Additionally, participants were asked to report the number of orthopedic injuries (i.e. sprains, bone fractures, strains) at the level of and inferior to the hip joints they had previously sustained.

Spatiotemporal gait parameters were measured by having participants walk across a six-meter-long, pressure-sensitive walkway (Zeno Walkway, ProtoKinetics, Havertown, PA). Participants were instructed to walk under two conditions: (1) normal, preferred gait, and (2) heel-to-toe tandem gait. For all trials, participants were instructed to walk at a self-selected comfortable pace while looking straight ahead and keeping their arms at their sides. During tandem gait trials, participants were instructed to minimize the distance between their feet with each step while avoiding direct contact between their feet with each step. Individual footfall placements were monitored in real time using ProtoKinetics Motion Analysis Software (PKMAS) [573]. If two successive footfalls were notably distant during a tandem gait trial, corrective instructions would be given as needed and the trial in question would be discarded and repeated. All participants successfully completed five trials under each condition with one trial being defined as one complete pass of the walkway in a single direction.

Individual footfalls were processed and analyzed utilizing PKMAS to calculate gait parameters over the course of each trial. Acquired variables included gait velocity, cadence, step length, stride width and percent time spent in double limb support. Mean (i.e. average) and intra-individual variability (IIV) were calculated for all collected gait parameters. IIV was calculated based on the coefficient of variation of each variable within the time series between successive footfalls with respect to the mean for each variable, making IIV a normalized value with respect to the length of each trial.

#### 4.2.5 Statistical analysis

Independent t-tests were conducted to elicit potential differences between groups based on age, height, weight, symptom checklist score, lower-limb orthopedic injury history and regular amounts of aerobic exercise. Pearson's chi-square was calculated to determine potential differences in the association between sex and group designation with an effect size represented by the odds ratio between males and females represented in each group. A 2 X 2 mixed-design analysis of variance (ANOVA) was conducted to assess differences in means and IIVs for all collected gait parameters between groups (CONC vs. NON) and walking condition (preferred vs. tandem gait). In addition, effect sizes for all collected gait parameters were calculated using Cohen's *d*. All statistical analyses were conducted in SPSS v.25 (IBM Corp., Chicago, IL) with *a priori* levels of significance set to 0.05 adjusted for multiple comparisons using Bonferonni's correction.

### 4.3 Results

#### 4.3.1 Demographic information

Table 4 displays demographic information representing both the NON and CONC groups. There were no significant differences between groups based on age ( $p=0.129$ ), height ( $p=0.415$ ), weight ( $p=0.197$ ), regular level of physical activity ( $p=0.597$ ) or lower-limb orthopedic injury history ( $p=0.057$ ). The chi-square test revealed a significant association between sex and group designation ( $\chi^2(1)=3.87$ ;  $p=0.049$ ; OR:0.278), as participants in the present study eligible for the NON group were more likely to be female rather than male. No participants reported any



medication use, falls within twelve months of their testing visit, diagnosed hearing impairment or visual impairment that could not be resolved with the use of corrective lenses.

#### 4.3.2 Concussion symptom checklist

There were no significant differences between groups based on total score reported on the concussion symptom checklist at the time of testing ( $p=0.268$ ).

#### 4.3.3 Gait assessment

Means and IIVs for all collected gait parameters during preferred and tandem gait trials are displayed in Tables 5 and 6, respectively. During preferred gait trials, there were no significant differences between groups based on average gait velocity ( $p=0.446$ ), cadence ( $p=0.150$ ), step length ( $p=0.984$ ), stride width ( $p=0.146$ ) or percent time spent in double-limb support ( $p=0.588$ ). Small effect sizes were found during preferred gait for average velocity, cadence, and stride width (range:  $d = 0.211$ - $0.414$ ). In addition, tandem gait trials elicited no observed significant differences between groups based on the means of all collected variables. Small effect sizes were found during tandem gait for average velocity, step length, and stride width (range:  $d = 0.201$ - $0.286$ ).

There was a significant difference between groups based on IIV of gait cadence during preferred gait. Specifically, the CONC group's preferred gait cadence was significantly less variable compared to the NON group ( $F_{1,51}=5.918$ ;  $p=0.019$ ; 95% CI= 1.83-2.92 steps/minute vs. 0.92-1.99 steps/minute). In addition, the CONC group demonstrated significantly decreased IIV of step length during preferred gait in comparison to the NON group ( $F_{1,51}=4.478$ ;  $p=0.039$ ; 95% CI= 2.27-2.72 cm vs. 1.94-2.38 cm). Furthermore, small effect sizes were observed during preferred gait for the IIV of gait velocity ( $d=0.454$ ) and stride width ( $d=0.403$ ) while moderate

effect sizes were found for step length ( $d=0.625$ ) and cadence ( $d=0.681$ ). In addition, tandem gait revealed small effect sizes for the IIV of gait velocity and cadence (range:  $d = 0.201-0.220$ ).

## 4.4 Discussion

The findings of this study indicate that individuals with a prior history of concussion demonstrate altered gait patterns consisting of reductions in the variability of their cadence and step length compared to those that have never sustained a diagnosed concussion. These findings support the notion that concussion can have long-term detrimental effects on dynamic postural control that extend beyond the scope of recovery as determined by clinical gait assessments and the resolution of neurocognitive symptoms.

### 4.4.1 *Gait variability and chronic neuropathology*

Changes in the variability of spatiotemporal gait parameters have been previously interpreted as indications of reduced postural control consistent with neurological decline observed with aging and more prominently with neurodegenerative disease [93,98,414]. Increases in gait variability are believed to represent a reduced capacity to control for excessive bodily movements and fluctuations of the location of the body's center-of-mass during locomotion. In contrast, reductions in gait variability are interpreted to be indicative of the adaptation of a more conservative, precautionary movement pattern in the face of impaired postural control. From a physiological perspective, successful performance of gait requires integration and coordination between multiple interconnected structures within the brain working in parallel [80]. The multitude of connections within these neural networks allow for more degrees of freedom of movement during performance; a greater number of feasible motor patterns able to be utilized to complete a

given objective. Thus, a neurologically healthy system can account for movement variability during gait while remaining optimally stable. The trauma incurred during a concussive impact can potentially damage white matter (i.e. axonal connections) between these structures, leaving fewer degrees of freedom available to ultimately produce efferent motor function, thus limiting the amount of variability during gait while remaining fully capable of achieving the overall objective of maintaining postural control as the body moves through space. This notion is supported by the present study's findings which identified that prior concussion history is associated with reductions in variability measures while demonstrating no significant differences in the averages of the same gait parameters. Further, these findings reveal that deficits in postural control evidenced by reductions in gait variability can remain following a concussion beyond the point of recovery as determined by clinical standards and resolution of neurocognitive symptoms.

The chronic nature of the present study's findings can potentially be indicative of the limited capabilities for repair and regeneration within the central nervous system [15]. Recently, a growing amount of attention has been directed toward expanding understanding of the long-term effects of concussion on postural stability [99,542]. The findings of the present study indicate that the damage sustained from a concussive impact may result in altered brain function contributing to gait stability for years following the initial injury. The collective context of these findings indicates that like neurodegenerative disease, damage to neural tissue stemming from concussion may potentially result in reductions in postural control that persist long after the emergence of the pathology. However, the observed decreases in variability demonstrated during gait suggest the presence of a compensatory mechanism to account for long-term reductions in the complexity of the postural control system. The notion that concussion history is associated with reductions in variability is also supported by prior studies indicating that concussion results in long-term

decreases in regularity of postural sway that are elicited under more challenging conditions [355,574]. Specifically, the motor control changes seen in relation to concussion history contrast those observed in neurodegenerative disease by displaying a capacity to preemptively account for deficits in postural stability rather than an inability to correct impairments brought on by the extent of tissue loss due to neurodegenerative disease. The finding that tandem gait, a condition with a greater demand for balance, elicited similar reductions in variability regardless of whether the individual had ever sustained a concussion indicates that those with a prior history of concussion adopt more protective, conservative gait patterns to account for the subtle postural stability impairments and subsequent greater demand for balance incurred following a concussion.

Gait assessments for concussion typically attempt to identify deficits in dynamic postural control by limiting the use of compensatory strategies to account for impaired balance. It has previously been established that concussion results in the adoption of a conservative gait pattern in the acute phases of injury [455,569]. While the temporal extent in which altered gait variability remains following concussion is still inconclusive, assessments of the variability of other rhythmic parameters have revealed chronic impairments associated with concussion indicative of dysfunction within the central nervous system. Concussed individuals have previously been shown to demonstrate decreased heart rate variability (HRV), a metric that has been interpreted as the uncoupling of functioning between the branches of the autonomic nervous system [105,575]. By determining no significant differences based on the averages of all measured gait parameters, the findings indicated that the acute alterations in gait patterns typically observed following concussion were resolved at the time of testing based on current clinical assessment standards. However, the results of the present study support the prior findings by Buckley et al [427] which concluded that prior history of concussion is associated with reduced variability in velocity and

step length during preferred gait. The present study expands on this revelation by demonstrating that the differences in variability of cadence and step length associated with prior history of concussion seen during preferred gait are not observed during tandem gait when constraints are placed on individuals' gait patterns. Collectively, these findings suggest that concussion is associated with long-term decreases in the complexity of the neural networks that contribute to maintaining postural stability during gait.

#### *4.4.2 Effect of concussion history on tandem gait*

Tandem gait is among the most commonly implemented testing procedures when assessing gait performance and dynamic balance in the acute stages following a suspected concussion [411,412]. The results of the present study found no significant differences based on a prior history of concussion in both the averages and variability measures of all collected spatiotemporal parameters during tandem gait. In context, the disparities in gait variability demonstrated by those with a history of concussion during their preferred gait patterns were eliminated when performing tandem gait. By its nature in minimizing the width between steps, tandem gait places a methodological constraint (i.e. reduced area of the base of support) on the postural control system during locomotion. As such, individuals innately adopt more conservative movement patterns (i.e. reduced velocity, cadence) to complete the task at hand without sustaining a complete loss of balance. When assessed alongside the observed patterns of reduced variability during preferred gait suggesting a predisposition to adopt conservative gait patterns, the present study's findings indicate that tandem gait provides an external constraint and subsequent changes in movement patterns that had already been utilized by individuals with a prior history of concussion and are readily adopted by those that have never sustained a concussion in the face of the constraint, thus

making the performance of the two groups virtually indistinguishable from one another. This distinction indicates that while individuals with prior history of concussion display decreased gait variability despite no external perturbations or constraints mandating precaution, both groups are similarly and markedly more variable during tandem gait. These findings raise concerns about the efficacy of implementing tandem gait protocols when screening for chronic balance impairments following concussion in clinical settings.

When assessing the detrimental effects of concussion, the elapsed time since the initial trauma has been shown to be a vitally important contributing factor to tandem gait performance. Tandem gait performance as measured by average velocity and time to completion has previously been shown to improve throughout the recovery process following a concussion and return to baseline levels within a matter of weeks to months [409]. The time since the most recent diagnosed concussion for the CONC group ranged from one to twenty-five years. As such, the present study found no significant differences in the averages of tandem gait parameters. However, the lack of significant differences in the variability of tandem gait parameters based on prior concussion history despite exhibiting less variability during preferred gait raises concerns about the efficacy of tandem gait protocols to examine chronic gait stability deficits associated with concussion. Based on the findings of the present study, tandem gait appears to be a more clinically valuable assessment tool for concussion to determine the presence of impairment in the acute stages following an injury as opposed to being used to determine recovery on a longitudinal scale.

#### *4.4.3 Limitations*

The authors identified several limitations in the present study. First, the study design was retrospective in nature. Therefore, it was impossible to establish a causal relationship between the

observed deficits in gait stability and a documented history of concussion due to the lack of a proper baseline assessment prior to the first sustained injury. Second, groups were divided based on self-reports of the number of sustained concussions that were diagnosed by a health care professional. Because of the lack of objective diagnostic testing for concussion [576] and documented underreporting rates for concussion [397], the reliance on self-reports of prior injury history will continue to raise concerns about properly identifying deficits associated with concussion. In addition, there is a noteworthy difference between the CONC and NON groups based on intra-group distribution of sex and number of previously sustained lower-limb orthopedic injuries. It has been previously established that sex is not a strong indicator for the progression of recovery of postural stability associated with concussion within the tested age range [577]. In addition, while concussion is associated with an increased risk of lower-limb orthopedic injury [283], these associations are observed within one year of the sustained injury. To counter this, all participants were required to have not been diagnosed with a concussion in the twelve months leading up to their testing visit.

#### **4.5 Conclusion**

Overall, the findings of the present study indicate that concussion is associated with long-term changes in maintaining stability during gait. Specifically, individuals that have a prior history of concussion demonstrate a preference to utilize a constrained gait pattern characterized by reductions in variability of cadence and step length. In addition, performing tandem gait was shown to erase observable differences in the variability of all gait parameters based on concussion history. Collectively, these findings indicate that concussion results in a chronic alteration in motor control that manifests as a locomotion pattern with which an individual maximizes gait stability

as a protective measure against the postural stability impairments brought on by a traumatic head impact. In addition, the present study's findings demonstrated the differences in the clinical applications of tandem gait in concussion screenings, namely that the utilization of tandem gait is more effective for identifying acute deficits in gait stability rather than potentially chronic postural stability impairments stemming from concussion. Future studies could build upon these findings by identifying the physiological changes within the brain that could help reveal the neurological basis of the observed chronic reductions in stability.

#### *4.5.1 Acknowledgements*

The authors report no external funding sources for the implementation of the present study. The authors report no conflicts of interest in the implementation of the present study. The authors declare that the results of the present study do not constitute endorsement by the American College of Sports Medicine. In addition, the authors declare that the results presented in the present study were done so honestly and without inaccurate or inappropriately manipulated data.



Table 4: Means and Standard Deviations for Demographic Information Between Groups for Gait Stability Assessment.

<i>Variable</i>	<i>NON Group</i> <i>(n = 26)</i>	<i>CONC Group</i> <i>(n = 27)</i>	<i>p</i>
<i>Sex (M / F)</i>	5 / 21	12 / 15	0.049
<i>Age (years)</i>	28.41 ± 5.18	26.11 ± 5.97	0.129
<i>Height (cm)</i>	169.45 ± 8.05	171.12 ± 10.36	0.415
<i>Weight (kg)</i>	73.49 ± 14.01	77.84 ± 15.26	0.197
<i>Diagnosed concussions</i>	N/A	2.26 ± 1.40	N/A
<i>Time since concussion (years)</i>	N/A	6.91 ± 5.67	N/A
<i>PCSS Score</i>	2.81 ± 4.12	4.11 ± 3.79	0.268
<i>Lower-limb orthopedic injuries</i>	1.37 ± 2.02	2.89 ± 3.49	0.057
<i>Physical Activity (150 min/week; Y/N)</i>	21 / 5	19 / 8	0.597

Table 5: Means, Standard Deviations, and Coefficients of Variation of Gait Parameters Between Groups During Preferred Gait. Asterisks denote significant differences between groups.

	<i>Variable</i>	<i>NON</i>	<i>CONC</i>	<i>p</i>	<i>d</i>
<i>Means and SD</i>	Velocity (cm/s)	129.65 ± 19.17	125.61 ± 19.07	0.446	0.211
	Cadence (steps/min)	117.43 ± 9.67	113.51 ± 9.84	0.150	0.408
	Step length (cm)	66.07 ± 6.57	66.03 ± 7.17	0.984	0.063
	Stride width (cm)	8.37 ± 1.50	8.75 ± 1.42	0.147	0.414
	Double-limb support (%)	23.59 ± 3.48	24.03 ± 2.89	0.588	0.155
<i>Coefficients of Variation</i>	Velocity	3.60	2.77	0.111	0.454
	Cadence	2.38	1.46	0.019*	0.681
	Step length	2.49	2.16	0.039*	0.625
	Stride width	20.72	17.16	0.152	0.403
	Double-limb support	3.82	3.94	0.676	0.110

Table 6: Means, Standard Deviations, and Coefficients of Variation of Gait Parameters Between Groups During Tandem Gait.

	<i>Variable</i>	<i>NON</i>	<i>CONC</i>	<i>p</i>	<i>d</i>
<i>Means and STD</i>	Velocity (cm/s)	33.66 ± 11.37	36.43 ± 11.36	0.379	0.247
	Cadence (steps/min)	68.41 ± 17.42	71.91 ± 17.41	0.493	0.191
	Step length (cm)	29.13 ± 2.87	30.08 ± 3.87	0.316	0.286
	Stride width (cm)	0.43 ± 0.98	0.63 ± 1.03	0.414	0.201
	Double-limb support (%)	38.37 ± 7.47	37.33 ± 6.69	0.596	0.110
<i>Coefficients of Variation</i>	Velocity	9.82	8.59	0.431	0.220
	Cadence	6.88	6.13	0.481	0.201
	Step length	7.45	7.42	0.965	0.063
	Stride width	29.84	41.21	0.304	0.127
	Double-limb support	12.06	10.88	0.724	0.089

## CHAPTER 5

### IDENTIFICATION OF ALTERATIONS IN HEAD STABILITY DURING GAIT ASSOCIATED WITH HISTORY OF CONCUSSION

#### 5.1 Introduction

Proper management and treatment of concussion is complex and multifaceted due to the wide spectrum of symptoms that can potentially manifest following a sustained injury [5]. Impaired postural stability is a common symptom following a head injury that is often integral in diagnosing a concussion. Clinical screenings for concussion have shown deficits in postural stability, particularly during gait, are commonly observed acutely following a suspected injury [281,578]. The aftermath of a concussive head impact is believed to damage structures within the brain contributing to postural control and the axonal networks that interconnect them, resulting in disruptions to integrations of sensory feedback and alterations in motor output [534,571]. In order to compensate for difficulties maintaining balance during ambulation, concussed individuals have been shown to alter their movement patterns in an attempt to maintain control over the body's center-of-mass when presented with challenges to maintaining proper postural control during gait [126,430]. However, clinical balance assessments are designed to identify the presence of symptoms rather than the physiological cause of impairment, leaving the causal root of observed postural control deficits indeterminate. This is particularly challenging in cases of concussion where a traumatic head impact can result in damage to a number of areas and structures within the brain (cerebral cortex, cerebellum, vestibular nuclei, brainstem, etc.) that interconnect to integrate sensory feedback information and ultimately allow for maintenance of balance. As a result, recent

approaches in studying the detrimental effects of concussion on postural control have taken novel approaches to better understand the presumed neurological changes following a sustained injury.

Stabilization of the head is an underlying priority of the postural control system during gait. Maintenance of proper postural control requires the utilization and integration of somatosensory, visual and vestibular feedback information [22,579]. During gait and other complex forms of movement, stabilizing and coordinating the head is critical for proper interpretation of spatial orientation and vestibular feedback to appropriately respond to and effectively navigate the external environment [580–582]. To facilitate proper head stability, multiple neural tracts work in parallel to mitigate the effects of gait-related oscillations of varying amplitudes and frequencies originating inferior to the level of the head in the anteroposterior (AP), mediolateral (ML) and vertical (VT) planes. These oscillations ascend the kinetic chain via the spinal column until they are attenuated by the shock-absorbing properties of the intervertebral discs and skeletal muscle, with the latter serving as a more variable component due to its capacity for changing stiffness and therefore the degree of contribution toward dampening ascending oscillations. Previous studies have noted that while walking at a preferred, self-selected speed, the head experiences acceleration patterns consisting of lower frequencies and lower amplitudes in the AP plane (i.e. direction of locomotion) compared to the accelerations observed at lower levels of the spinal column [129,449]. However, irregular head acceleration patterns consisting of increased amplitudes, reduced harmonic ratios, and decreased attenuation between segments of the spinal column between the AP and VT planes have been identified in multiple neurologically compromised populations [451,452,583]. Despite the noted associations with neurological dysfunction, changes in head acceleration patterns during gait in cases of traumatic brain injury, including concussion, have not been examined as thoroughly.

Clinical assessments following concussion, such as timed assessments of tandem gait examining balance during ambulation, are typically not heavily instrumented. Instead, these protocols rely on subjective assessments and scoring systems to detect gross reductions in stability (i.e. partial or complete loss of balance) that range considerably in sensitivity and specificity measures [99,328,407]. Despite observable signs of vestibular impairment (i.e. dizziness, problems maintaining balance) being among the most common signs of concussion, assessments of movements of the head during gait are not measured or quantified following a sustained head injury. Without instrumented measurements of the linear magnitudes and frequency domain characteristics of acceleration patterns observed at the head, the acute effects of concussion on head stability during gait are not well defined or understood. As a result, the chronic effects of gait-related oscillations of the head to elicit and/or exacerbate postural control deficits during gait following a traumatic brain injury are notably inconclusive. This ambiguity is troubling because studies have recently contradicted long-held beliefs that balance deficits following a concussion are generally resolved within a matter of days post-injury, with evidence of gait instability persisting for weeks and months following a concussive impact and well beyond the clinical determination of recovery [526,551].

To date, no prior studies have examined the chronic effects of concussion history on the ability to stabilize the head during gait as determined by acceleration patterns at multiple levels of the spinal column. The goal of the present study was to determine the effect of prior history of concussion on acceleration patterns of the head as a metric for postural control during gait. It was hypothesized that (1) individuals with a prior history of concussion will demonstrate increased amplitudes of triaxial accelerations at the head during gait compared to those that have never been

diagnosed with a concussion, and (2) individuals with a history of concussion will demonstrate a decreased ability to attenuate gait-related accelerations throughout the spinal column during gait.

## **5.2 Methods**

### *5.2.1 Participants*

Thirty-three healthy adults participated in the present study. The participants were divided into two groups based on the number of previous diagnosed concussions reported to the researchers: (1) those that reported one or multiple prior concussion diagnoses as determined by a physician or athletic trainer (CONC group,  $n = 17$ ; mean age =  $26.65 \pm 6.60$  years), and (2) those that reported having never been diagnosed with a concussion (NON group,  $n = 16$ ; mean age =  $30.56 \pm 4.79$  years). The CONC group reported an average of  $2.35 (\pm 1.45)$  previously diagnosed concussions with an average of  $7.74 (\pm 6.22)$  years since the most recent injury. The following exclusionary criteria were implemented in order to screen for potential participants: (1) diagnosed concussion within the twelve months leading up to testing visit, (2) orthopedic injury or condition that impaired normal function of gait or maintenance of balance within twelve months prior to testing visit, (3) diagnosed vestibular disorder affecting one's ability to maintain equilibrium (i.e. vertigo), (4) medication use affecting balance and/or gait, and (5) any history of brain surgery.

Upon arriving for the testing visit, demographic information including age, sex, height, and weight were documented. Participants were also asked to disclose information that could potentially serve as a confounding variable to gait stability. This included having participants report any previously sustained orthopedic injuries (i.e. sprains, strains, bone fractures) at the level of and inferior to the hip joints. Participants were also asked to disclose any hearing or visual impairments that could not be corrected with the use of hearing aids and corrective lenses, respectively. In addition, all

participants were asked to report their typical amount of aerobic exercise performed over the course of the six months leading up to the testing visit. The responses were later used to classify individuals based on whether or not they met the recommendations for physical activity as determined by the American College of Sports Medicine (ACSM) [543].

Unique subject identifiers were established to conceal the identity of all included participants. All participants provided written informed consent before participating in the testing procedures. The protocol was reviewed and received approval from the university's Institutional Review Board.

### *5.2.2 Concussion symptom checklist*

Prior to testing, participants were screened for concussion symptoms using a checklist derived from the Sport Concussion Assessment Tool (SCAT-5) [338]. The checklist consisted of twenty-two symptoms commonly associated with concussion. Participants were instructed to rate each symptom on a Likert scale ranging from 0 (absent) to 6 (debilitating, severe) based on how they were experiencing each symptom at the time of their visit. Any participants that rated one or more symptom as a 4 or higher or totaled a cumulative score of 20 or higher was disqualified from further participation in the study.

### *5.2.3 Protocol*

Segmental accelerations were collected by instrumenting participants with wireless accelerometers (Trigno Avanti, Delsys Inc., Natick, MA) affixed at the levels of the head (occipital protuberance), neck (spinous process of C7 vertebrae) and trunk (spinous process of L4 vertebrae).



Acceleration data were collected continuously in the mediolateral, anteroposterior, and vertical axes throughout the duration of each trial at a rate of 148 Hz.

Participants were instructed to walk along a six-meter path under two conditions: (1) normal, preferred gait and (2) heel-to-toe tandem gait. Under both conditions, participants were instructed to walk at a comfortable, self-selected pace to minimize the risk of sustaining a fall. For tandem gait, participants were told to minimize the distance between their feet when stepping while avoiding directly stepping on the stance leg. Individual footfall placements were tracked throughout all trials utilizing ProtoKinetics Motion Analysis Software (PKMAS, ProtoKinetics, Havertown, PA) in order to provide corrective feedback concerning foot placement during tandem gait when consecutive footfalls were placed inappropriately far apart [573]. Participants were permitted to perform one practice trial with tandem gait to familiarize themselves with the protocol. Trials in which accelerometers became detached from the participant, two consecutive footfalls overlapped and/or were notably distant during tandem gait were discarded. Each participant completed five trials under each condition with one trial being defined as a complete pass across the path in one direction.

#### *5.2.4 Data analysis*

All data processing and analyses were conducted using software written and developed in MATLAB (MathWorks, Natick, MA). Prior to all analyses, raw acceleration data were filtered using a second-order, low-pass Butterworth filter with a cut-off frequency of 30 Hz. In order to account for offset angles of the affixed sensors in reference to the vertical vector (i.e. gravity), a correction was implemented in the preliminary code using previously validated trigonometric methods conducted by Moe-Nilssen et. al [584,585]. Amplitudes of accelerations were assessed in

the ML, AP, and VT planes at the head, neck, and trunk during gait via root mean square calculations (RMS,  $\text{m/s}^2$ ). In addition, a power spectral analysis was conducted on all acceleration data using Welch's averaged periodogram (window size of 256). Outputs acquired from the power spectral analysis consisted of the frequency (Hz) at which the peak power ( $G^2$ ) occurred during each trial. Average gait velocity (m/s) was calculated using the time to complete each trial derived from laser-based timing gates positioned at the start and end points of the predetermined six-meter walking path.

A transfer function previously described by Kavanagh et al. [586] was applied to the acceleration patterns to determine the gain and/or attenuation as the signal ascending from the lower trunk to the head. The transfer function describes the relationship of accelerations at each segment in relation to the segment directly inferior to it, thus allowing for interpretation of the accelerations at each segment in relation to those adjacent to them rather than independent frequencies. For the purposes of this study, output values of the transfer function can be interpreted as gain (positive values) or attenuation (negative values). Gain and/or attenuation was calculated on the RMS of the acceleration data and the peak power output from the power spectral analysis. The acceleration gain from the neck was divided by the acceleration gain from the lower trunk to illustrate the role of the trunk in dissipating accelerations during gait. Likewise, the acceleration data from the head was divided by the acceleration data from the neck to better understand the contributions of the cervical spinal column during gait.

#### 5.2.5 *Statistical analysis*

Independent t-tests were conducted to identify differences between groups based on age, height, weight, symptom checklist score, average gait speed, lower-limb orthopedic injury history

and regular amounts of aerobic exercise. Pearson's chi-square was calculated to assess the association between sex and group designation with effect size represented by the odds ratio comparing females to males represented in each group. A generalized linear model (GLM) was implemented to distinguish whether prior history of concussion had a significant effect during gait at the levels of the head, neck, and trunk for all collected dependent variables (RMS accelerations, peak power, peak frequency). All statistical analyses were conducted in SAS v.9 (SAS Institute, Cary, NC) with *a priori* significance levels set at 0.05.

### **5.3 Results**

#### *5.3.1 Demographic information*

Table 7 displays the means and standard deviations of demographic information for the NON and CONC groups. There were no significant differences between groups based on age ( $p=0.062$ ), height ( $p=0.189$ ), weight ( $p=0.301$ ), regular amount of physical activity ( $p=0.854$ ) or lower limb orthopedic injury history ( $p=0.157$ ). Pearson's chi-square test revealed an association between sex and group designation ( $\chi^2(1)=5.48$ ;  $p=0.019$ ; OR: 10.58). Specifically, within the subject pool composing the participants in this study, individuals that reported no history of concussion were 10.58 times more likely to be female rather than male.

#### *5.3.2 Concussion symptom assessment*

There were no significant differences in concussion symptoms scores between groups at the time of testing ( $p=0.981$ ).

### 5.3.3 *Gait parameters*

There were no significant differences between groups in average velocity during both preferred (NON:  $1.254 \pm 0.164$  m/s vs. CONC:  $1.19 \pm 0.179$  m/s;  $p=0.320$ ) and tandem gait (NON:  $0.361 \pm 0.134$  m/s vs. CONC:  $0.385 \pm 0.114$  m/s;  $p=0.281$ ).

### 5.3.4 *Segmental accelerations*

Figure 6 displays the RMS accelerations at the head, neck, and trunk during preferred and tandem gait for both groups. During preferred gait, significant differences in RMS acceleration were observed between groups in at the levels of the head and neck. Specifically, the CONC group demonstrated greater amplitudes in the AP plane at the head ( $F_{1,31}=18.27$ ;  $p=0.0002$ ) as well as the level of the neck ( $F_{1,31}=17.37$ ;  $p=0.0002$ ). These findings were supported by large effect sizes (range:  $d=1.522-1.561$ ). There were no significant differences between groups in amplitudes in the ML or VT planes. In addition, there were no significant differences observed at the level of the trunk during preferred gait. However, moderate effects sizes were observed at all three body segments in the ML plane (range:  $d= 0.707-0.723$ ).

During tandem gait, the CONC group again displayed significantly greater amplitudes in the AP planes at the level of the head ( $F_{1,31}=8.04$ ;  $p=0.0081$ ) as well as the level of the neck ( $F_{1,31}=18.27$ ;  $p=0.0002$ ). In contrast to preferred gait, The CONC group also displayed significantly greater amplitudes in the VT plane at the level of the neck ( $F_{1,31}=10.04$ ;  $p=0.0035$ ). In addition, moderate effect sizes were found at the level of the head in the ML and VT planes (range:  $d=0.634-0.692$ ). There were no observed significant differences in amplitudes between groups at the levels of the trunk during tandem gait.

### 5.3.5 Power spectral analysis

Figure 7 illustrates the frequency domain profiles during preferred gait for both the NON and CONC groups. Frequency profiles revealed significant differences between groups in both the peak frequency observed during both preferred and tandem gait. Those with a prior history of concussion demonstrated an overall trend consisting of reductions in peak frequency during gait. Specifically, the CONC group exhibited significantly reduced peak frequencies in the AP plane at the head ( $F_{1,31}=5.596$ ;  $p=0.024$ ). There were no significant differences between groups in peak frequency in the ML and VT planes across all three segments during preferred gait. However, moderate effect sizes were observed in the VT plane at levels of both the neck and trunk (range:  $d=0.578-0.689$ ). In contrast, there were no observed significant differences in peak frequency between groups during tandem gait at the levels of the head and neck. However, the CONC group demonstrated a significantly greater peak frequency in the VT plane at the level of the trunk ( $F_{1,31}=4.226$ ;  $p=0.048$ ). In addition, moderate effect sizes were observed at the level of the neck in the AP and VT planes (range:  $d=0.548-0.578$ ).

Observations of peak power during preferred gait revealed no significant differences between groups at all three body segments in all three planes of motion. However, small effect sizes identified in the AP and VT planes at all three body segments (range:  $d=0.314-0.482$ ). During tandem gait, the CONC group exhibited significantly greater peak power at the level of the head in the AP plane ( $F_{1,31}=6.151$ ;  $p=0.019$ ). In addition, the CONC group also demonstrated significantly greater peak power at the level of the neck in the AP ( $F_{1,31}=4.640$ ;  $p=0.039$ ) and VT ( $F_{1,31}=7.675$ ;  $p=0.009$ ) planes. Moderate effect sizes were also observed in the ML plane at the levels of the head and neck (range:  $d=0.544-0.557$ ). There were no significant differences in peak power between groups during tandem gait at the level of the trunk.

### 5.3.6 Segmental gain

Segmental gains of RMS of triaxial accelerations during preferred and tandem gait are illustrated in Figure 8. During preferred gait, the CONC group demonstrated significantly reduced attenuation at the trunk in the AP ( $F_{1,31}=20.57$ ;  $p<0.0001$ ) and VT ( $F_{1,31}=5.91$ ;  $p=0.021$ ) planes compared to the NON group. At the neck, the CONC group also displayed significantly reduced attenuation in the ML ( $F_{1,31}=9.81$ ;  $p=0.004$ ) plane while conversely demonstrating significantly less gain in the VT ( $F_{1,31}=6.68$ ;  $p=0.015$ ) plane compared to the NON group. During tandem gait, there were no statistically significant differences between groups in attenuation of triaxial accelerations at the levels of the neck and trunk. However, moderate effect sizes were identified at the level of the trunk in all three planes of motion (range:  $d=0.717$ - $0.744$ ), an indication of a possible association that mandates further exploration and observation.

Segmental gains of peak power of triaxial accelerations during preferred and tandem gait are displayed in Figure 9. Significant differences in peak power attenuation between groups were observed during preferred and tandem gait. During preferred gait, the CONC group displayed significantly reduced attenuation in the ML ( $F_{1,31}=7.23$ ;  $p=0.012$ ) and VT ( $F_{1,31}=9.82$ ;  $p=0.004$ ) planes at the level of the neck. In addition, at the level of the trunk, the CONC group demonstrated significantly reduced peak power in the VT plane ( $F_{1,31}=7.36$ ;  $p=0.011$ ) and gain of peak power in the AP plane whereas the NON group was able to attenuate AP power at the trunk ( $F_{1,31}=24.82$ ;  $p<0.0001$ ). There were no significant differences in peak power attenuation between groups at the level of the neck during tandem gait. However, the CONC group demonstrated significantly reduced attenuation of peak power in the ML ( $F_{1,31}=6.93$ ;  $p=0.013$ ) and AP ( $F_{1,31}=7.39$ ;  $p=0.011$ ) planes at the level of the trunk during tandem gait. Moderate to large effect sizes were observed at

the trunk during both preferred and tandem gait (range:  $d=0.721-1.820$ ) while large effect sizes were identified at the level of the neck solely during preferred gait (range:  $d=0.981-1.145$ ).

## 5.4 Discussion

The primary objective of the present study was to assess the effects of a prior history of concussion on postural control during gait as a function of movement patterns at the level of the head. The findings of the study indicate that individuals with a prior history of concussion exhibit chronic alterations in their ability to stabilize the head during gait compared to individuals that have never sustained a concussion, and that these differences remain well beyond the resolution of gait instability as determined by current standards of clinical assessments for concussion.

### 5.4.1 *Evidence of precautionary gait strategy*

Previous studies have repeatedly established that acutely concussed individuals alter their gait patterns to conserve an impaired ability to maintain upright stability [280,427]. These differences have primarily been identified by observing the spatiotemporal parameters of an injured individual's gait pattern such as velocity, cadence, and stride width. Concussed individuals typically demonstrate changes in their gait pattern that indicate a constrained, precautionary movement strategy following an injury (i.e. decreased velocity and step length, increased stride width) that can remain in the weeks and months following a traumatic head impact [427,587]. It has been theorized that these changes are driven by a reduced ability to control the movement of the body's center-of-mass (CoM) following traumatic damage to the neural tissue and networks that contribute to postural control as the body moves through space [27,588]. Further, concussion is believed to result in impaired integration of multiple sources of sensory feedback information

(i.e. vision, somatosensory, and vestibular information) and thus produce inappropriate and/or insufficient motor output to optimize postural control [589]. These theories support the notion that concussion is associated with long-term neurological impairment in part due the central nervous system's limited capacity for repairing and restoring damaged tissue following a traumatic impact [15]. However, explorations of the influence of movements of the head during gait and the integration of resulting vestibular feedback they produce concerning spatial orientation have not been extensively examined from either acute or chronic perspectives following concussion. The individuals with a prior history of concussion reported a range of three to twenty-five years since their most recent diagnosed injury. The findings of the present study support the notion that concussion history is associated with persisting impairments of proper sensorimotor integration during gait and that these deficits remain despite the absence of symptoms indicating vestibular dysfunction (i.e. dizziness) and postural stability impairments as determined by clinical standards for concussion treatment and management. Future efforts examining the long-term effects of concussion should be directed at alterations in sensorimotor integration as well as the proportional utilization and conducive reliance on the specific sources of sensory feedback to better understand the compensatory strategies to maintain balance undertaken by previously concussed individuals despite a compromised postural control system.

The presence of excessive head movement during gait has previously been used to exemplify postural control deficits in multiple neurologically compromised populations [131,590]. Whereas concussion is often viewed as an injury stemming from trauma to the head with a concentrated focal point, the ensuing linear and rotational head accelerations following an impact transfer the force of the impact throughout the entire brain, resulting in the potential for widespread damage and neurological dysfunction that can manifest in a medley of symptoms, among the most



commonly observed being postural instability. Patients with neuropathological conditions typically exhibit greater amplitudes (i.e. RMS) of head accelerations in all three planes of motion during gait [451,591]. The findings of the present study indicated that individuals that have sustained one or more concussions exhibit similar patterns of increased accelerations at the superior levels of the spinal column (i.e. head and neck) during gait compared to controls, supporting the notion that concussion can manifest in the form of long-term, widespread dysfunction of the postural control system likely stemming from damage to neural tissue and axonal networks caused by shear stress induced by a traumatic head impact. Interestingly, observations of acceleration patterns at the levels of the neck and trunk revealed that the previously concussed individuals exhibited considerably smaller accelerations in the ML planes compared to controls. This distinction is particularly insightful regarding the detrimental effects of concussion because of the previously seen evidence of precautionary strategies to conserve postural control during gait following injury [427,592]. While excessive ML movement is often regarded as an indication of reduced postural control, namely an inability to properly control the movement of the body's CoM following damage and/or degeneration within the postural control system stemming from neurological disease or injury, the present findings demonstrated an opposite trend concerning concussion. These findings support the notion that prior concussion history is associated with a more constrained and precautionary movement strategy where ML stability is prioritized after injury has left behind a compromised, less dexterous postural control network rather than a systemic loss of neural function. However, despite constrained movement inferior to the head possibly undertaken to mitigate excessive movement of the head during gait, increased AP head accelerations were found in previously concussed individuals, indicating that damage sustained from a concussive impact has long-standing consequences on one's ability to stabilize

the head during gait, particularly in the direction of motion. Further exploration is required to better understand the causal roots of these deficits and the possible link they may have to the correlations previously observed between concussion history and orthopedic injury risk [246,520].

Tandem gait is often implemented in screenings for concussion because it presents a challenge to injured individuals' ability to maintain balance during gait by eliminating their ability to increase the relative area of their base of support and in turn compensate for decreased postural control. In the present study, examinations of triaxial accelerations during tandem gait revealed greater amplitudes of accelerations at the head and neck in previously concussed individuals in the AP and VT planes. Of note, the increase in VT acceleration at the level of the neck was not observed during preferred gait, indicating that the elimination of a compensatory strategy elicited greater stability deficits during gait by exacerbating a compromised postural control system. Additionally, these increases in acceleration patterns were present despite no significant differences in average velocity during tandem gait. These findings are noteworthy because implementations of tandem gait in concussion screenings are typically scored based on time to completion, which is a factor of gait velocity, whereas acceleration patterns from the trunk to the head are not considered during an assessment and can easily be overlooked. As a result, the efficacy and sensitivity of tandem gait to identify the presence and resolution of a concussion has raised concerns about the effectiveness of the assessment tool [593]. The findings of the present study provide additional evidence of the shortcomings of clinical tandem gait assessments by showing that impairments of postural stability during gait persist for years following a concussion and are indeed exacerbated by the removal of compensatory, precautionary movement strategies via implementation of tandem gait. While these findings collectively demonstrate an association between concussion history and long-term alterations in gait patterns, follow-up studies will be

required to better understand the temporal extent to which these changes remain. In addition, these findings suggest that incorporating assessments of segmental accelerations during gait can potentially provide a more comprehensive screening protocol for concussion, as current clinical standards and management plans often do not take these parameters into consideration despite documented associations with damage to the postural control structures and networks within the brain.

#### *5.4.2 Reduced complexity following concussion*

Frequency domain analyses concerning concussion have primarily been reserved for of cardiac rhythm and heart rate variability, where multiple studies have found that reductions in the high-frequency components of heart rate representing the parasympathetic nervous system's contributions to cardiac rhythm [512,594]. This pattern of reductions in frequency profiles of cardiac rhythm following a traumatic brain injury are indicative of dysfunction within the brain's autonomic regulatory centers, thus resulting in improper output and communication between the two branches of the autonomic nervous system. Considering that the force from a concussive head impact can span the entire brain and damage tissue and networks far beyond the site of the initial impact, it is plausible to presume that concussion can disrupt motor output and corresponding frequency profiles of other physiological signals, including acceleration patterns of the head during gait. The findings of the present study support the notion that damage sustained from a concussion is associated with alterations in the frequency profiles of acceleration patterns at the head and upper levels of the spinal column during gait. Of note, these findings indicate the presence of suboptimal functional capacities within the networks contributing to dynamic postural control.

However, more extensive study is required to precisely determine the physiological root of these changes in the years following one or multiple concussions.

Traditionally, postural control assessments for concussion were graded somewhat subjectively and without sophisticated technological instrumentation (i.e. Balance Error Scoring System, Clinical Test of Sensory Interaction on Balance). In addition, laboratory assessments analyzing instrumented assessments of postural control following concussion are primarily conducted within time series rather than the frequency domain. While concussion has been shown to be associated with lingering decreases in the complexity and regularity of standing CoP tracings [356,375], assessments of motor output complexity within the frequency domain during gait have not been as thoroughly explored. Recent approaches looking at various neuropathological populations have analyzed the complexity of motor output by assessing markers for postural control including nonlinear parameters of standing center-of-pressure (CoP) tracings and the frequency domain profiles of acceleration patterns [351,595]. When examining gait, decreases in the peak frequencies of acceleration patterns during gait have been interpreted as an indication for a decrease in complexity within the postural control system as damage and/or degeneration of neural tissue reduces the number of viable connections within the system, thus constraining motor output and leaving an individual more vulnerable to sustaining a fall or injury [131]. The findings of the present study demonstrated that the changes in frequency profiles of those with a prior history of concussion (i.e. reduced peak frequency, increased peak power) are similar in nature to those observed in neuropathological populations including Parkinson's disease, indicating a similar pattern of reduced complexity within the postural control system throughout the brain. This finding is noteworthy because it has been theorized that concussion can give rise to problems with proper motor output in response to sensory stimuli [458,596]. Reducing complexity within the

neural networks contributing to sensorimotor integration would reduce the degrees of freedom and subsequently the number of possible motor responses to a given stimulus, leaving one more vulnerable to unfavorable outcomes in the face of unexpected perturbations. Damage to the central nervous system via injury or disease often results in permanent impairment or loss of function because of the limited capacity for repair and regeneration of the tissue [14]. Hence, the findings of the present study support the notion that concussion can have negative effects on postural stability for years after the initial trauma that may never reach full resolution despite no grossly apparent, clinically observable signs of dysfunction.

#### *5.4.3 Attenuation of gait-related oscillations*

The ability to dissipate the oscillatory movements that ascend the kinetic chain during gait is a key component in properly stabilizing the head as the body moves about the external environment. Minimizing the movements of the head allows for optimal stability required for proper function and integration of visual and vestibular sensory feedback information [19]. A reduced capacity to attenuate gait-related oscillations throughout the spinal column and minimize accessory movements of the head has been observed in numerous neuropathological populations and has been interpreted as an indication of decreased postural control and an increased risk of injury [451,452]. However, the ability to stabilize the head during gait via attenuation at multiple levels of the spinal column have not been extensively studied in the context of concussion from either acute or chronic perspectives. The results of the present study indicated that individuals that have sustained one or more concussions demonstrate an impaired capacity to properly attenuate gait-induced accelerations as they ascend the spinal column, with the most prominent differences being identified in the AP and VT planes. By demonstrating a reduced capacity to control for

movements of the head both vertically and in the direction in which the body is moving, individuals with a history of concussion are exhibiting movement patterns indicative of impaired sensorimotor integration. It is reasonable to presume that these excessive head movements are causing dysfunctional communication between the visual processing centers and the vestibular nuclei as the head moves excessively during gait, ultimately producing efferent motor signals that may place the body in positions that predispose the individual to sustaining a fall or injury. Further studies should be directed at examining the movements of the head in concussed individuals and how they may contribute to kinematic patterns that could potentially predispose an individual to a lower-limb orthopedic injury [282,597].

A possible explanation of the alterations in segmental acceleration attenuation following concussion may be attributable to improper muscle activation and/or coordination within the skeletal musculature of the trunk. The musculature of the trunk holds a crucial role in stabilizing the spine during gait and controlling for excessive movements in all three planes of motion [598,599]. It has been shown that increasing muscle stiffness throughout the trunk results in increases in acceleration amplitudes observed at the head as the shock-absorbing properties of the skeletal muscle of the trunk are inversely related to the stiffness of the muscle at a given moment. Increasing the stiffness throughout the trunk also artificially yields similar results, suggesting that the trunk plays a crucial role in dampening the oscillations arising from the heel strikes performed during gait [600]. The present study found the most prominent differences in attenuation of triaxial accelerations at the level of the trunk with individuals that had previously been concussed showing a remarkably reduced ability to attenuate accelerations in the AP and VT planes during preferred gait. Concussed individuals have been shown to alter the spatiotemporal parameters of their gait suggestive of a precautionary movement strategy to avoid losing balance [281]. Among these

tactics includes widening their strides during gait, which may be a subconscious effort to prioritize mediolateral stability during gait. This notion is supported by the findings of assessments of tandem gait in concussion screenings when the ability to widen strides is eliminated and thus greater instability is elicited. The findings of the present study support the notion that the trunk plays an important role in mitigating gait-related accelerations ascending the kinetic chain, and that individuals with a history of concussion seem to prioritize mediolateral stability at the expense of excessive movements in the AP and vertical planes in order to maintain postural control during gait. It is plausible that individuals with a history of concussion increase the stiffness of certain musculature of their trunk to ensure ML stability as they move, which could potentially explain why these individuals seem to have much more success at attenuating accelerations at the trunk in the ML plane compared to the AP and VT planes and thus culminates at overall greater movement of the head during gait. Future studies assessing muscle activity could be invaluable in interpreting the findings of the present work more concisely and better understand the consequences of concussion history on motor output.

#### *5.4.4 Limitations*

The present study was not exempt from limitations. First, the groups were divided based on self-reports of the number of previously diagnosed concussions. The subjective nature of self-reports and documented trends of underestimates of reporting rates raises concerns about the accuracy of the group designations [397]. Second, because the study design was cross-sectional and retrospective in nature, it cannot be definitively stated that prior history of concussion was the sole causal factor for the observed findings of the study. In addition, the distance traversed for each trial during the protocol did not record a sufficient number of strides during gait to conduct

nonlinear analyses such as measures of regularity (i.e. sample entropy) of acceleration patterns at each body segment [601]. Future analyses can expand the protocol by increasing the distance and therefore number of strides per trial to properly address additional gait characteristics including regularity and variability measures. Analyses incorporating assessments of activity (i.e. EMG) of the musculature of the trunk can help provide further insight toward possible changes in skeletal muscle stiffness and the physiological nature of the observed differences in segmental acceleration patterns between the two tested groups and further uncover altered facets of postural control stemming from concussion. Lastly, there was a statistically significant difference between groups based on intra-group distribution of sex, with the controls being much more heavily skewed toward representing females over males compared to the individuals with a history of concussion, which was much more evenly distributed. While previous research has found differences in post-concussion assessments based on sex [343,602], sex has also been shown not to have a significant effect on the recovery of postural control following a concussion [336]. As a result, it cannot be definitively stated that sex had a significant effect on the patterns of head accelerations observed in the present study. However, a larger sample size and the subsequent elimination of confounding variables would benefit future efforts to understand the effects of concussion within the general population.

## **5.5 Conclusion**

In summary, the findings of the present study revealed that concussion history is associated with alterations in the ability to stabilize the head during gait and that these deficits can remain present for years after the initial trauma. Specifically, individuals with a prior history of concussion demonstrated greater head accelerations during gait compared to healthy controls, most



prominently in the anteroposterior plane, and were exacerbated when performing tandem gait. This suggests that concussion history is associated with a persistent alteration in gait patterns designed to circumvent an ultimately impaired ability to maintain stability during gait. In addition, the patterns of gain concerning the amplitude and frequencies of acceleration patterns ascending the spinal column rather than attenuation provides a useful perspective of the changes in motor output following concussion and how these alterations can have long-standing consequences on postural control during gait. Collectively, these findings illustrate persistent detriments following concussion that may be attributable to alterations of complexity within the networks of the brain that contribute to the ability to stabilize the head and ultimately optimize upright postural stability during ambulation.

Table 7: Means and Standard Deviations for Demographic Information Between Groups  
for Head Stability Assessment

<i>Variable</i>	<i>NON Group (n = 16)</i>	<i>CONC Group (n = 17)</i>	<i>p</i>
<i>Sex (M / F)</i>	1 / 15	7 / 10	0.019
<i>Age (years)</i>	30.56 ± 4.79	26.65 ± 6.60	0.062
<i>Height (cm)</i>	166.41 ± 5.43	170.48 ± 10.88	0.189
<i>Weight (kg)</i>	73.48 ± 14.16	79.06 ± 16.20	0.301
<i>Diagnosed concussions</i>	N/A	2.35 ± 1.46	N/A
<i>Time since concussion (years)</i>	N/A	7.74 ± 6.22	N/A
<i>PCSS Score</i>	3.38 ± 5.18	3.41 ± 3.68	0.981
<i>Lower-limb orthopedic injuries</i>	1.00 ± 1.15	3.29 ± 3.99	0.157
<i>Physical Activity (150 min/week; Y/N)</i>	9 / 7	8 / 9	0.854

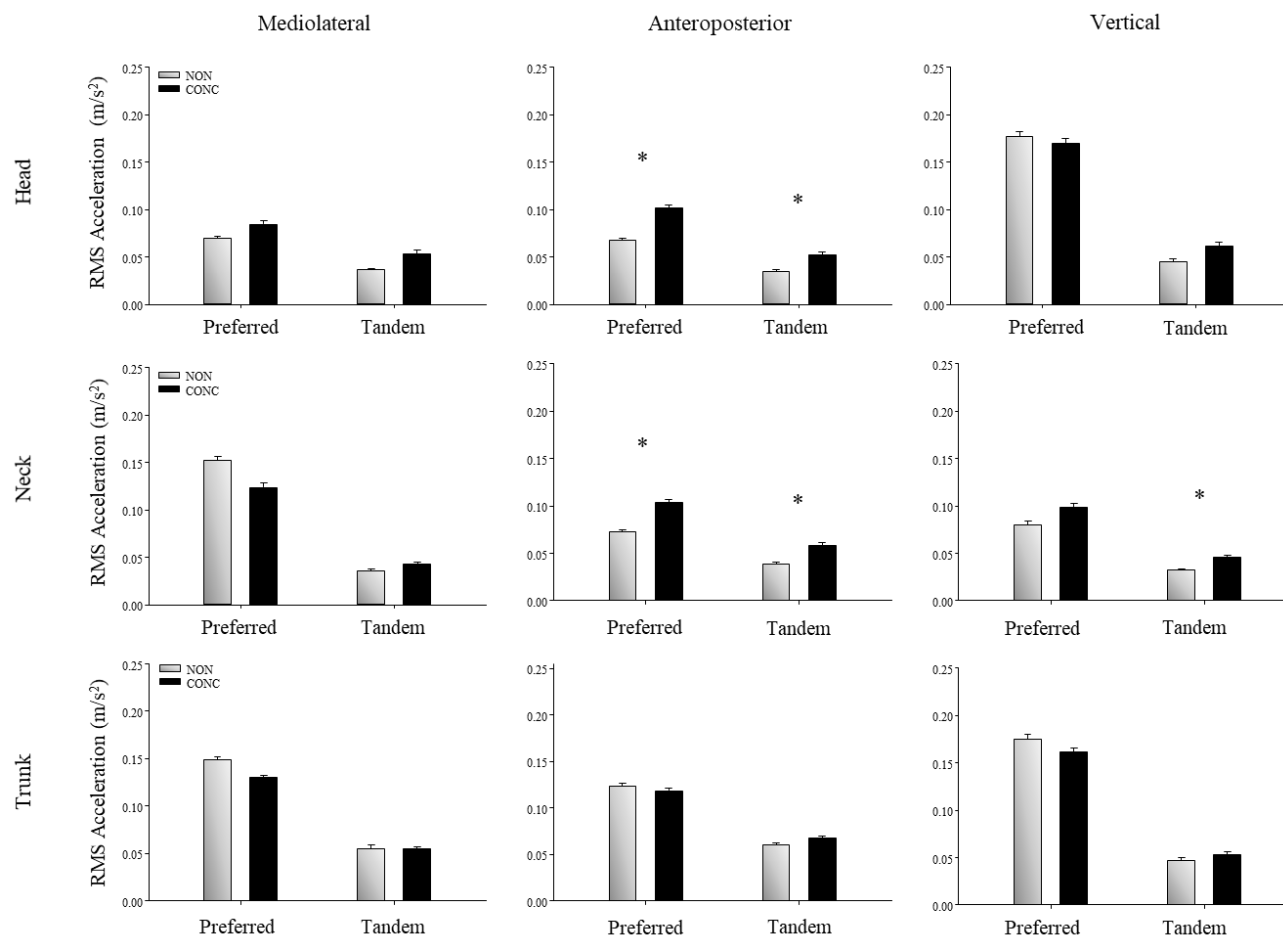


Figure 6: Average Root Mean Square (RMS) of Segmental Triaxial Accelerations During Preferred and Tandem Gait. Asterisks represent statistically significant differences between groups ( $p < 0.05$ ). Error bars represent one standard error of the mean.

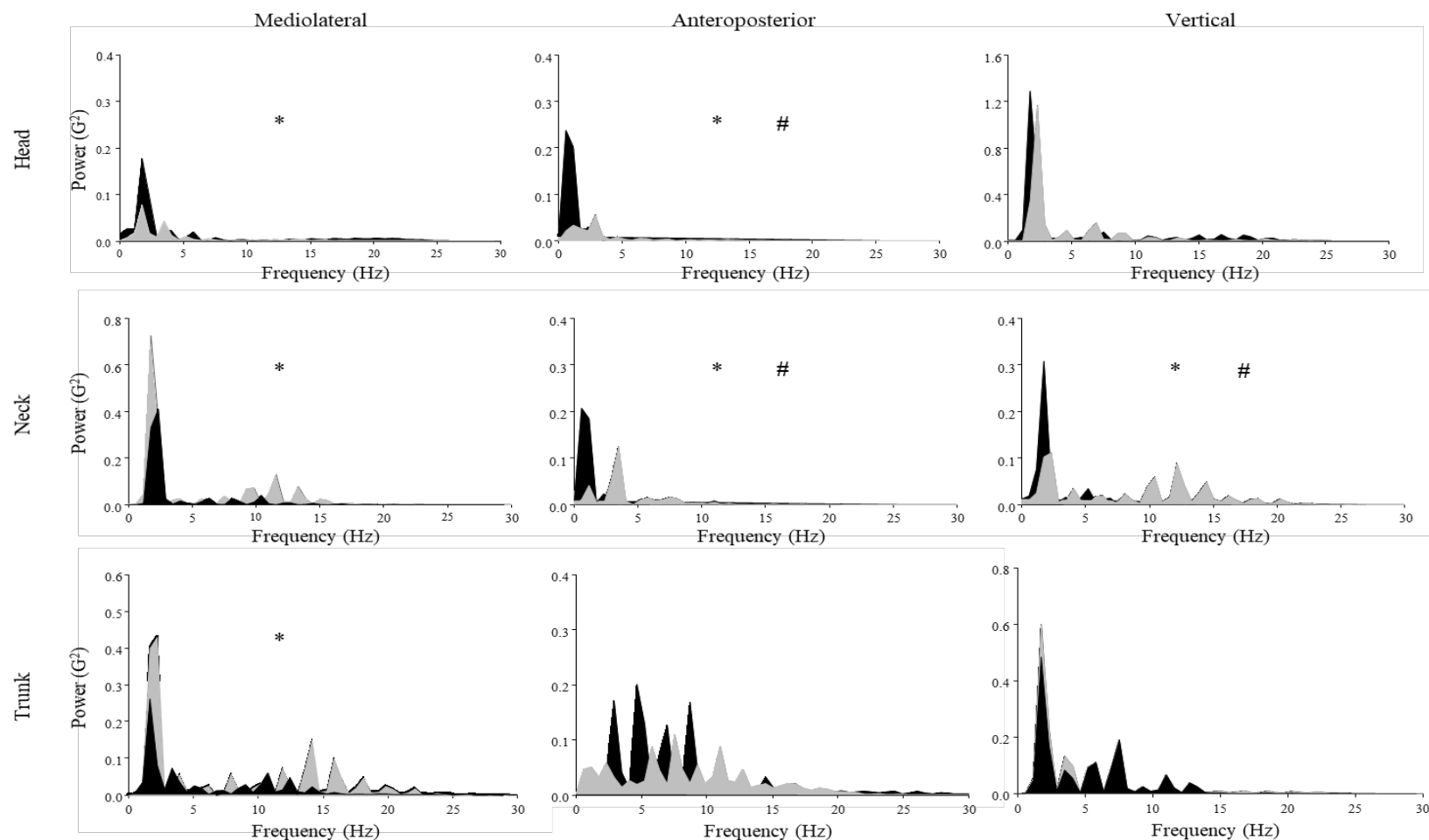


Figure 7: Comparisons of Representative Power Spectral Analyses of Triaxial Accelerations at the Head, Neck, and Trunk During Preferred Gait. Each group's data is represented by the average of five trials performed by a single subject in each group. Asterisks denote significant differences in peak frequency between groups

<i>Variable</i>	<i>NON Group</i> ( <i>n</i> = 16)	<i>CONC Group</i> ( <i>n</i> = 17)	<i>p</i>	<i>d</i>
<i>Head</i>				
<i>ML</i>	1.63 ± 0.10 Hz	1.50 ± 0.88 Hz	0.531	0.229
<i>AP</i>	1.54 ± 0.05 Hz	0.95 ± 0.28 Hz	0.024*	0.850
<i>VT</i>	1.91 ± 0.45 Hz	2.01 ± 0.49 Hz	0.549	0.220
<i>Neck</i>				
<i>ML</i>	1.91 ± 0.31 Hz	1.79 ± 0.50 Hz	0.363	0.333
<i>AP</i>	1.74 ± 0.05 Hz	1.29 ± 0.84 Hz	0.119	0.578
<i>VT</i>	2.97 ± 0.11 Hz	1.82 ± 0.34 Hz	0.117	0.578
<i>Trunk</i>				
<i>ML</i>	1.92 ± 0.19 Hz	2.01 ± 0.80 Hz	0.601	0.191
<i>AP</i>	3.58 ± 0.08 Hz	2.99 ± 2.83 Hz	0.566	0.211
<i>VT</i>	1.96 ± 0.42 Hz	1.94 ± 0.35 Hz	0.813	0.089

Table 8: Means and Standard Deviations for Segmental Peak Frequencies During Preferred Gait for Head Stability Assessments. Asterisks denote significant differences between groups.

<i>Variable</i>	<i>NON Group</i> ( <i>n</i> = 16)	<i>CONC Group</i> ( <i>n</i> = 17)	<i>p</i>	<i>d</i>
<i>Head</i>				
<i>ML</i>	0.79 ± 0.56 Hz	0.82 ± 0.65 Hz	0.963	0.020
<i>AP</i>	0.69 ± 0.31 Hz	0.59 ± 0.13 Hz	0.652	0.168
<i>VT</i>	3.21 ± 1.27 Hz	3.01 ± 1.48 Hz	0.646	0.168
<i>Neck</i>				
<i>ML</i>	2.51 ± 1.23 Hz	2.43 ± 1.56 Hz	0.676	0.155
<i>AP</i>	0.77 ± 0.62 Hz	0.59 ± 0.06 Hz	0.117	0.578
<i>VT</i>	1.19 ± 1.08 Hz	1.90 ± 2.16 Hz	0.138	0.548
<i>Trunk</i>				
<i>ML</i>	1.14 ± 0.44 Hz	1.63 ± 1.46 Hz	0.260	0.414
<i>AP</i>	1.42 v 1.66 Hz	1.64 ± 1.68 Hz	0.727	0.127
<i>VT</i>	2.31 ± 1.27 Hz	3.23 ± 1.57 Hz	0.048*	0.739

Table 9: Means and Standard Deviations for Segmental Peak Frequencies During Tandem Gait for Head Stability Assessments. Asterisks denote significant differences between groups.

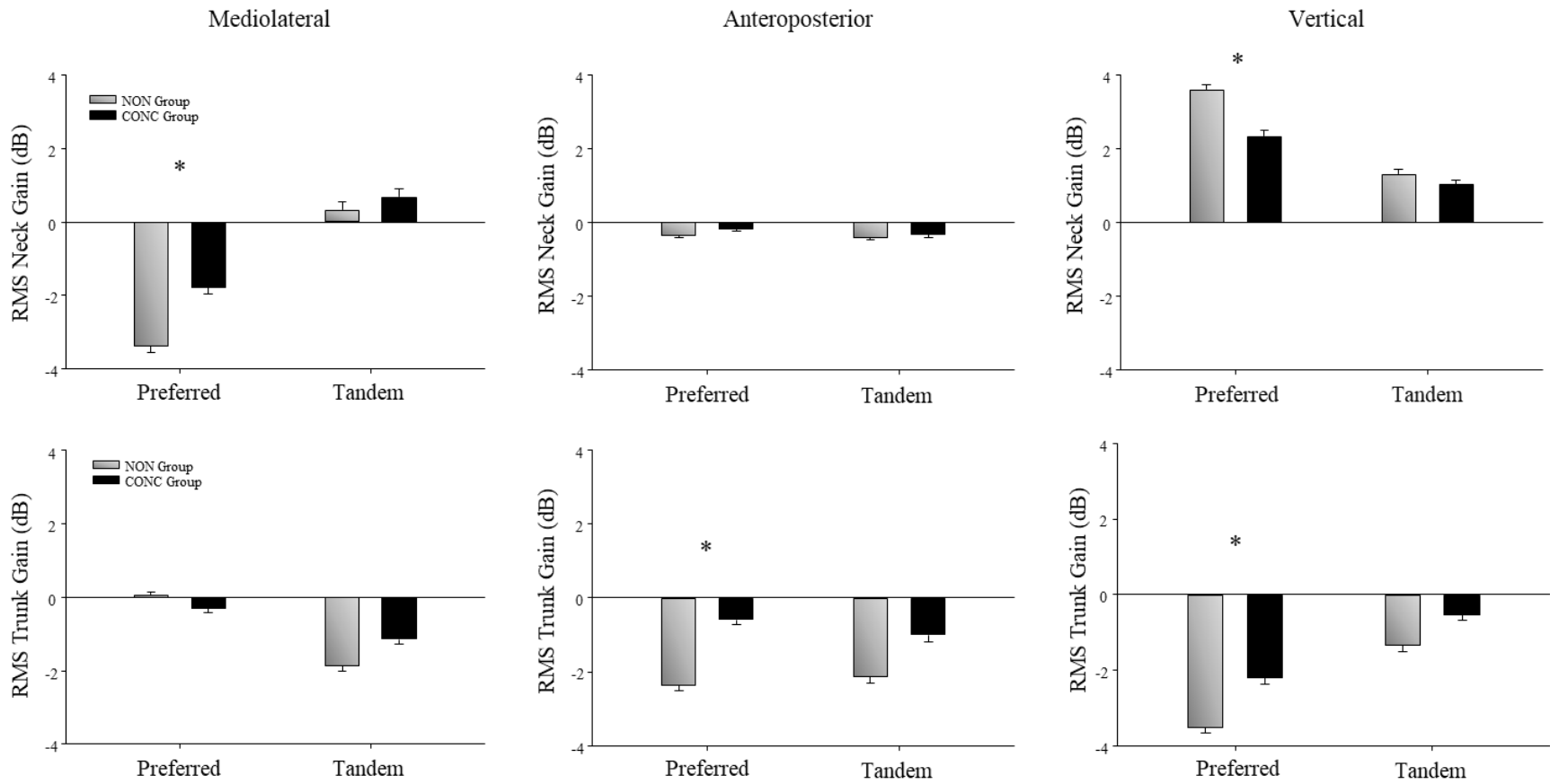


Figure 8: Group Differences in Segmental Gain of Acceleration Root Mean Square at the Neck and Trunk. Significant differences in RMS gain between groups are designated by asterisks. Error bars denote one significant error of the mean.

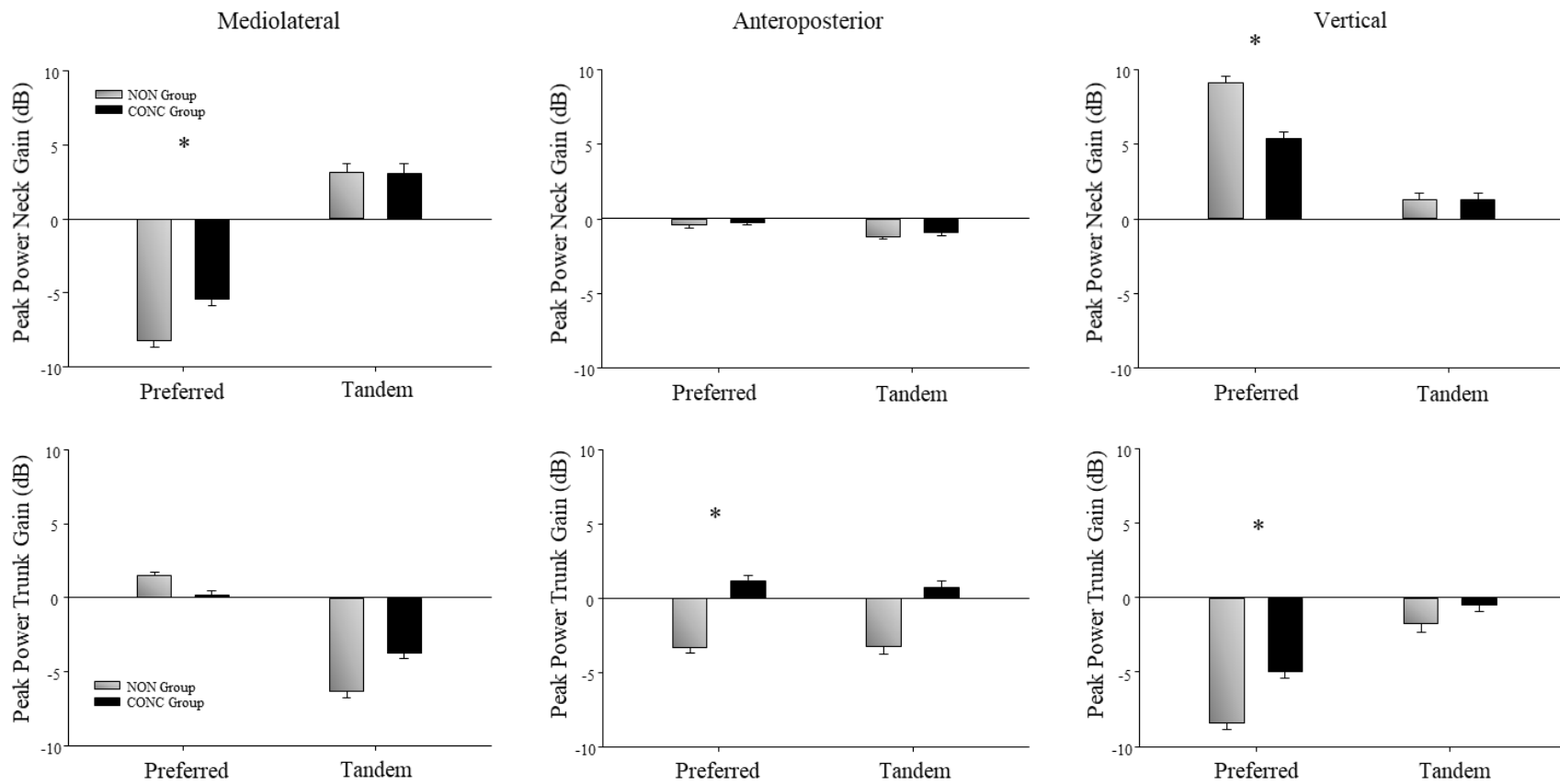


Figure 9: Group Differences in Segmental Gain of Peak Power of Acceleration Patterns at the Neck and Trunk. Significant differences in peak power gain between groups are designated by asterisks. Error bars denote one significant error of the mean.



## CHAPTER 6

### SUMMARY

Navigating the external environment can be chaotic and outright dangerous. As such, very few human beings, if any, have never experienced trauma to their body in the form of an injury. Proper treatment and management of all forms of injury requires a thorough and comprehensive approach to understand the pathophysiology of the sustained damage and the multi-faceted consequences that can potentially arise following a sustained trauma. Despite improvements in understanding the complex neurophysiology of concussion, technological advances in improving the performance of safety equipment, and institutional changes designed to improve safety during athletics, concussion remains among the most prominent and commonly seen injuries in the United States. Even more troubling is the lack of detailed knowledge about the consequences of concussion that can persist beyond the clinical determination of recovery. Injuries that are thought of as temporary hinderances can potentially have persistent, even lifelong consequences, such as the development of chronic ankle instability following a lateral ankle sprain or the development of hyposmia and/or anosmia following a nasal bone fracture. This notion is particularly pertinent in cases of concussion as the tissue composing the central nervous system is notoriously poor at regenerating following trauma, making hinderance and/or loss of function a more likely possibility in the face of damage. However, most of the research directed at examining the long-term deficits associated with a history of concussion have primarily focused on cognitive function and the potential development of neuropsychological conditions despite a medley of additional symptoms, including decreases in postural control during standing and walking. The objective duration in

which the presence of postural instability remains following a concussion is largely undetermined, and it is inconclusive as to whether these deficits ever reach full resolution or if impaired postural control is a lifelong consequence following a traumatic brain injury. The primary objective of the experiments composing this dissertation was to examine the chronic detrimental effects of concussion on static and dynamic postural stability despite the determination of recovery based on current standards of clinical practices and medical guidelines.

Experiment 1 focused on the effects of concussion history on postural stability during quiet standing. Both individuals with and without a prior documented history of concussion(s) had their standing CoP traced while having their equilibrium challenged using four combinations of conditions created by making their posture more challenging (i.e. bipedal vs. unipedal stance) and/or incorporating a concurrent cognitive task (i.e. serial subtraction). It was hypothesized that compared to healthy controls, individuals with a history of concussion would (1) exhibit greater deficits in CoP parameters including sway displacement, velocity, and regularity (i.e. SampEn), and (2) have their postural control deficits exacerbated under dual-task conditions. The first hypothesis was partially correct. While individuals with a history of concussion demonstrated significantly greater AP and ML sway displacement and elliptical area and significantly reduced AP and ML sway regularity, there were no observed significant differences in sway velocity and path length. It was theorized that the patterns of velocity and path length may have resulted from increases in muscle stiffness in the lower extremities, which would have constrained and slowed the previously concussed individuals' sway patterns at the expense of a decreased ability to correct for perturbations, resulting in increases in sway area and reduced regularity and complexity of their sway patterns. The second hypothesis was supported by the findings of the study. All significant differences in linear CoP found between groups were elicited under dual-task

conditions. In addition, significant differences in sway regularity were also elicited under dual-task conditions, but also unipedal conditions as well, suggesting that sway regularity can potentially serve as a more sensitive metric for determining the long-term presence of postural instability following concussion. Collectively, these findings indicate that individuals that have sustained one or more concussions exhibit impaired static postural control that can remain present for years following the initial trauma and well beyond the clinical determination for recovery based on current standards for assessing balance following concussion. In addition, these deficits have been shown to be exacerbated under dual-task conditions indicative of a decreased capacity to allocate attention toward multiple concurrent tasks, which may predispose a concussed individual's ability to return to normal levels of athletic participation and even academic programs without facing functional deficits.

Experiment 2 looked to examine the effects of a history of concussion on dynamic postural stability during gait. Both individuals with and without a prior history of concussion were instructed to walk across a six-meter, pressure-sensitive gait mat under two conditions: (1) normal, preferred gait pattern, and (2) heel-to-toe tandem gait, a task that is often incorporated in concussion management protocols. It was hypothesized that in comparison to healthy controls, individuals with a history of concussion would (1) demonstrate gait patterns indicative of decreased postural control marked by slower velocities and wider strides, and (2) demonstrate reduced variability in their gait patterns during both preferred and tandem gait. The first hypothesis was not supported by the findings of Experiment 2, which showed no significant differences based on concussion history in the averages of all collected spatiotemporal gait parameters. The second hypothesis was partially supported, with previously concussed individuals displaying reductions in the variability of their cadence and step length compared to healthy controls. Reduced gait

variability has been identified in numerous neuropathological populations and is interpreted as a reduction in the complexity of the numerous neural networks within the brain that contribute to postural control. While studies assessing gait variability often look at hundreds of consecutive strides and conduct nonlinear analyses to better understand the complexities of gait, Experiment 2 utilized a middle-ground approach between these advanced analytical techniques and the potential for clinical applications when assessing gait following a concussion. The findings of Experiment 2 suggest that a history of concussion may have chronic consequences on dynamic postural stability stemming from a potential reduction in the complexity of the postural control system spanning throughout the brain, and that tandem gait, one of the most common gait assessments for concussion, may be a less effective tool for identifying chronic impairments compared to the acute stages following injury. Critically, the lack of significant differences in the averages of spatiotemporal gait parameters highlights the dangers of falsely concluding that an individual has achieved a full recovery from concussion, as significant differences in the variability of these parameters have been shown to remain years following the initial trauma and possibly contribute to an increased risk of falls and orthopedic injury. Future efforts can expand on these findings by implementing nonlinear analyses to thoroughly assess the effects of concussion on gait variability.

Experiment 3 looked to examine the effect of a prior history of concussion on stabilization of the head during gait. Triaxial accelerometers were affixed to the posterior aspect of the head, neck, and lower trunk to assess the patterns of gait-related accelerations in both individuals with and without a history of concussion during (1) normal, preferred gait and (2) heel-to-toe tandem gait. It was hypothesized that compared to healthy controls, individuals with a history of concussion would (1) exhibit greater amplitudes of accelerations at the head, and (2) demonstrate decreased attenuation of gait-related accelerations at the levels of the neck and trunk. The first

hypothesis was supported by the findings in Experiment 3, with previously concussed individuals displaying greater head accelerations, most notably in the AP plane and to a lesser extent the ML plane. These findings were also supported by the findings observed during tandem gait, in which a more challenging gait pattern elicited greater vertical head accelerations compared to healthy controls despite walking at an overall slower velocity compared to preferred gait. The second hypothesis was supported by the findings of Experiment 3, as individuals with a prior history of concussion demonstrated decreased attenuation of the amplitudes and peak frequencies of acceleration patterns ascending the spinal column in the AP and vertical directions. Individuals that have sustained one or more concussions also exhibited significantly reduced attenuation in all three planes of motion. Specifically, concussed individuals demonstrated reduced attenuation at the trunk in the AP and vertical planes as well as the neck in the ML plane during preferred. It has been well established within the scientific literature and clinical practices that concussion is associated with reductions in postural stability during gait. However, the physiological cause of said deficits is intensely debated and currently inconclusive. The findings of Experiment 3 support one of the more common theories concerning postural control and concussion, namely that concussion results in alterations in sensory feedback integration and corresponding motor output to correct perturbations of upright stability. In these particular findings, excessive head movement during gait can alter feedback from both the visual and vestibular systems as the body moves through space. As a result, concussed individuals have been shown to adopt a conservative, protective gait strategy to compensate for this dysfunction, a strategy that is confirmed by assessments of tandem gait that eliminate the use of certain protective strategies and elicit greater deficits in the patterns of head accelerations. In addition, examinations of the frequency profiles of the acceleration patterns of the head reaffirm the notion that a reduction in the complexity of

the postural control system following concussion can remain for years following the initial injury and leave an individual with a history of concussion with a predisposition to have trouble maintaining postural stability despite no clinically apparent outward signs of dysfunction. Assessments of the stabilization and acceleration patterns of the head are relatively novel in the scope of concussion. However, these analyses provide a promising new approach to better understand the pathophysiology of concussion from a different, non-invasive perspective.

## **6.1 Future Directions**

Paradoxically, concussion is a maddeningly complex, pathophysiological puzzle of an injury despite its relatively high epidemiological incidence rate. Perhaps the paramount problem facing research concerning any aspect of concussion is the lack of definitive, objective diagnostic criteria. As of the time of writing this dissertation, international consensus statements continue to define concussion broadly and there are no widely available neuroimaging techniques to accurately identify the presence of neural trauma that would result in the sequelae widely interpreted as a concussion. If the primary goal of researchers studying concussion is to advance the understanding of the pathophysiology of concussion and the corresponding deficits following injury, the most crucial step would be to develop an objective means to diagnose the presence of a concussion as well as determine if the markers for injury remain post-impact, indicating the resolution of injury. Objective diagnostic criteria would eliminate the need to rely on subjective self-reports from injured individuals themselves who may withhold from being completely transparent about their symptomology because of fear of being removed from athletic competition, internal self-drive and resilience, or the sheer fact that their brain has been damaged and they lack a clear grasp on reality following an injury.

Regarding the effects of concussion on postural control, it is important to take note of the most vulnerable populations to sustain a concussion, namely athletes and military personnel. Studies examining concussion have focused primarily on quiet standing, dynamic balance tasks, and gait. While these are all fundamentally important motor tasks to give insight about the effects of concussion on postural stability, the findings of this dissertation have shown evidence that the detrimental effects of concussion history can remain for years following a traumatic head impact. In that timespan, most individuals that do sustain one or multiple concussions return to their normal levels of physical activity despite a known association between concussion and increased rates of lower-body orthopedic injuries including lateral ankle sprains and ACL tears. Athletes and soldiers regularly perform high-intensity, ballistic movements (i.e. jumping, sidestep cut maneuvers, rapid decelerations) that can result in high levels of strain being placed on the ligaments, tendons, and bones of the lower body. These movements can also result in catastrophic structural failures if performed with improper kinematic patterns. Recent efforts to better understand the relationship between concussion and long-term orthopedic injury risk have directed attention toward visual-motor output, reaction time, and clinical balance testing performances, but not analyses of the actual ballistic movements themselves. While there is an inherent risk in having previously concussed individuals perform actions that potentially raise the chances of sustaining a secondary injury, analyses of the kinematic patterns of previously concussed individuals could potentially provide invaluable insight into the long-term biomechanical changes and alterations in postural control that may contribute to an increased orthopedic injury rate. In addition, the Belmont Report of 1979 fundamentally states that as long as human research subjects are made aware of the potential risks and voluntarily agree to accept those risks, this is an avenue worth pursuing to advance the breadth of knowledge concerning concussion.

It is becoming more and more apparent that the long-term effects of concussion history are being uncovered using instrumentation and analytical procedures that are not commonly available to the clinicians that are primarily responsible for treating and managing concussion. Clinicians do not have ready access to equipment such as force plate systems to track an individual's standing center-of-pressure or three-dimensional motion capture systems to assess joint kinematics during gait, nor do they often possess the coding and analytical skills required to properly interpret data concerning physiological signals. In addition, researchers have identified deficits associated with concussion that are simply not addressed in clinical screenings for concussion, such as alterations of cardiac rhythm and attenuated baroreceptor reflex activity. This disconnect has undoubtedly contributed to the high rates of false negatives, underreporting, and premature return to activity for concussion observed in the field. Moving forward, it will become imperative to bridge the gap between clinical and laboratory practices to harness a more comprehensive approach toward treating concussion and improve the overall understanding of the scope of the injury itself. Until then, clinicians will continue to work with an incomplete toolbox and researchers will continue to have their findings reported in the literature without influencing clinical practices.

It is the nature of science that there will never be a lack of questions to answer. Every answer, whether a hypothesis is confirmed or nullified, raises further questions that pique our interest. Occasionally, answers can show that widespread beliefs and practices have been abhorrently misleading or incorrect. There is still much to learn about the neurophysiological nature of concussion and the various complex associations the injury has on postural control throughout the lifespan. The findings presented in this dissertation advance our knowledge in this field, if only slightly in the grand scopes of neuroscience and pathophysiology. Knowledge is the light that guides us through the darkness we must navigate in the world, and scientific study is our



torch. It is imperative that we continue to explore the questions that remain, dare to advance the scope of our knowledge, and provide more light to improve the health and well-being of the millions of people that persevere through the impairments that are brought on by concussion. The challenges that face this line of research will not be easy to overcome, but the prospect of decoding the function and pathology of the brain and how to comprehensively understand changes in function following an injury that affects millions of people annually is enough to spark motivation and drive to find answers that we so relentlessly pursue. Above all else, it's for science.

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## APPENDIX A

## DATA COLLECTION SHEET

## Old Dominion University

**Assessment of long-term biomechanical and physiological changes associated  
with history of concussion**

Subject ID \_\_\_\_\_

Date \_\_\_\_\_

<b>I: Demographic Information</b>
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Age: \_\_\_\_\_ Sex: M / F Height: \_\_\_\_\_ Weight: \_\_\_\_\_

Physical Activity Levels: \_\_\_\_\_

Light

Moderate

Vigorous

Orthopedic Injury History:

Surgery: N/A \_\_\_\_\_

Bone fracture: N/A \_\_\_\_\_

Ligament tear: N/A \_\_\_\_\_

Strain: N/A \_\_\_\_\_

Other: N/A \_\_\_\_\_

Substance Intake:

Alcohol: \_\_\_\_\_ Caffeine: \_\_\_\_\_ Other: \_\_\_\_\_

Medications:

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#### IV: Physiological Assessments

##### A. Reaction Time

1.	6.	11.	16.
2.	7.	12.	17.
3.	8.	13.	18.
4.	9.	14.	19.
5.	10.	15.	20.

##### B. Postural Hemodynamics

Posture	Heart Rate	Blood Pressure
Supine		
Seated		
Standing		

##### C. Dive Reflex Response

Baseline HR: \_\_\_\_\_ Baseline BP: \_\_\_\_\_

Skin Pre-Test: \_\_\_\_\_ Skin Post-Test: \_\_\_\_\_

##### Cold Exposure

Time	Heart Rate	Blood Pressure
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		

##### Return to Baseline

Time	Heart Rate	Blood Pressure
1		
2		
3		
4		
5		

**APPENDIX B**

**CONCUSSION HISTORY FORM**

**Old Dominion University**

**Assessment of long-term biomechanical and physiological changes associated with history of concussion**

**Concussion History**

**Subject ID:** \_\_\_\_\_

**Date:** \_\_\_\_\_

Number of previous concussions: \_\_\_\_\_

Timeline:

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Mechanism of Injury:

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Symptoms:

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Treatment:

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## APPENDIX C

## CONCUSSION SYMPTOM CHECKLIST

**Post-Concussion Symptom Checklist**

Name: \_\_\_\_\_

Date: \_\_\_\_\_

Please indicate how much each symptom has bothered you over the past 2 days.

	Symptoms	None	Mild	Moderate	Severe			
<b>PHYSICAL</b>	Headache	0	1	2	3	4	5	6
	Nausea	0	1	2	3	4	5	6
	Vomiting	0	1	2	3	4	5	6
	Neck Pain	0	1	2	3	4	5	6
	Dizziness	0	1	2	3	4	5	6
	Blurry or double vision	0	1	2	3	4	5	6
	Sensitivity to Light	0	1	2	3	4	5	6
	Sensitivity to Noise	0	1	2	3	4	5	6
	Balance Problems	0	1	2	3	4	5	6
	Pain other than headache	0	1	2	3	4	5	6
<b>THINKING/ COGNITIVE</b>	Feeling "in a fog"	0	1	2	3	4	5	6
	Feeling Slowed Down	0	1	2	3	4	5	6
	Difficulty concentrating	0	1	2	3	4	5	6
	Difficulty Remembering	0	1	2	3	4	5	6
<b>SLEEP ISSUES</b>	Trouble Falling Asleep	0	1	2	3	4	5	6
	Fatigue or low energy	0	1	2	3	4	5	6
	Drowsiness	0	1	2	3	4	5	6
<b>EMOTIONAL</b>	Feeling more Emotional	0	1	2	3	4	5	6
	Irritability	0	1	2	3	4	5	6
	Sadness	0	1	2	3	4	5	6
	Nervousness	0	1	2	3	4	5	6

Do symptoms worsen with physical activity? Yes \_\_\_\_\_ No \_\_\_\_\_ Not Applicable \_\_\_\_\_

Do symptoms worsen with thinking/cognitive activity? Yes \_\_\_\_\_

Applicable \_\_\_\_\_

## VITA

### Nicholas G. Reilly

School of Rehabilitation Sciences  
Old Dominion University  
4211 Monarch Way, Suite 275  
Norfolk, VA, 23508

#### EDUCATION

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2017-2021	PhD	Old Dominion University Major: Kinesiology and Rehabilitation
2016-17	MS	University of Delaware Major: Exercise Science
2012-16	BS	Pennsylvania State University Major: Kinesiology Minor: Biology

#### RESEARCH AND PUBLICATIONS

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##### Referred Publications

1. **N. Reilly**, J. Prebor, J. Moxey, E. Schussler, Chronic impairments of static postural stability associated with history of concussion, *Exp Brain Res.* 238 (2020) 2783–2793. <https://doi.org/10.1007/s00221-020-05934-4>.

##### Published Abstracts

1. **N. Reilly**, J. Moxey, J. Prebor, E. Schussler, Gait variability alterations in relation to prior history of concussion. *Journal of Sport and Exercise Psychology*. Volume 42(S):56, August 2020.
2. A. Firoved, **N. Reilly**, D. Russell, Changes in cervical position modulate slow gait speeds. *Journal of Sport and Exercise Psychology*. Volume 42(S):38, August 2020.
3. **N. Reilly**, J. Prebor, J. Moxey, E. Schussler, Persistent gait stability deficits associated with history of concussion. *Medicine and Science in Sports and Exercise*. Volume 52(7S):733, July 2020.

#### PROFESSIONAL CERTIFICATIONS

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2017-PRESENT	American College of Sports Medicine	Clinical Exercise Physiologist (ID# 1051571)
2017- PRESENT	American College of Sports Medicine	Exercise is Medicine Credential