Spring 2016

Assessment of Anti-Saccades Within 24 to 48 Hours Post-Concussion

Nathan D'Amico
Georgia Southern University

ASSESSMENT OF ANTI-SACCADES WITHIN 24 TO 48 HOURS POST-CONCUSSION

by

NATHAN D'AMICO

(Under the Direction of Nicholas Murray)

ABSTRACT

INTRODUCTION: Oculomotor control dysfunction is present in about 90% of concussed athletes, with anti-saccades being the most prominent. PURPOSE: To investigate anti-saccades, reflexive gaze deviations from a fixed point or area of interest, between NCAA Division I athletes 24 to 48 hours post-concussion (PC) and healthy, matched controls (MC). METHODS: 10 PC (4 female, 6 male; age: 18.9 ± 0.9 years) and 10 MC (4 female, 6 male; age: 18.3 ± 0.6 years) wore a monocular eye tracker (240Hz) while performing 2 trials of the 60-second WiiFit Soccer Heading game. During play, participants were instructed to not deviate their gaze away from the center area of interest. Ocular raw point of gaze coordinates were tracked during play for specific areas of interest (left, right, and center) to determine gaze deviations away from the center area of interest. RESULTS: One-way ANOVAs revealed significantly greater anti-saccades ($p = 0.031$) in PC (15.2 ± 7.1) when compared to MC (5.4 ± 5.2), significantly greater anti-saccade durations ($p = 0.023$) in PC (11.2 ± 8.8s) when compared to MC (1.2 ± 1.3 s), and significantly greater average anti-saccade durations ($p < .0001$) in PC (0.671 ± 0.205s) when compared to MC (0.133 ± 0.042s). CONCLUSIONS: These results suggest that anti-saccades are significantly more prevalent in PC compared to MC. The great number and duration of anti-saccades could suggest a major deficiency in oculomotor control and could be a candidate marker for concussion.

INDEX WORDS: Concussion, Oculomotor Control, Anti-Saccades, Eye Tracking, WiiFit

ASSESSMENT OF ANTI-SACCADES WITHIN 24 TO 48 HOURS POST-CONCUSSION

by

NATHAN ROY D'AMICO

B.S., James Madison University, 2014

M.S., Georgia Southern University, 2016

A Thesis Submitted to the Graduate Faculty of Georgia Southern University in

Partial Fulfillment of the Requirements for the Degree of

MASTER OF SCIENCE

STATESBORO, GEORGIA

DEDICATION

I dedicate this thesis to my loving family and undergraduate Athletic Training family at James Madison University

ACKNOWLEDGEMENTS

Words cannot express how appreciative I am towards the several people who have contributed to this thesis, my academic training, my professional development, and my personal well-being. This would not have been possible without your continuing love and support. I would like to offer my sincerest thanks to:

- My mother and father: Annette and Matthew D'Amico.
- My three brothers: Adam, Eric, and David.
- My Committee Chair and Mentor: Dr. Nicholas Murray.
- My Committee Members: Dr. Barry Munkasy and Dr. Brandonn Harris.
- My Georgia Southern Athletic Training Professors: Dr. Tamerah Hunt, Vicky Graham, Dr. Jessica Mutchler, Erin Jordan, and Dr. Steve Patterson.
- My Georgia Southern Athletic Training Preceptor: Brandy Clouse.
- My Georgia Southern H&K Professors: Dr. Barry Joyner, Dr. Jim McMillan, Dr. Li, Dr. John Dobson, Dr. Steve Rossi, Dr. Jody Langdon, and Dr. Adam Wells.
- My Georgia Southern Secretaries: Jody Rushing, Beth Sammons, and Laura Wilson.
- My Georgia Southern Biomechanics Laboratory Colleagues: Megan Mormile, Peter Chrysosferidis, and Chaz Kilgore.
- My JMU Athletic Training Preceptors: Dr. Paula Maxwell, Dr. Connie Peterson, Dr. Jamie Frye, Dr. Kent Diduch, Tom Kuster, Lisa Friesen, and Chuck Wenger.
- My JMU ATEP Family: Calleigh Fangmeyer, Kala Young, Elizabeth Bird, Ashley Lopez, Mark Heintzleman, Kelsey Harney, Katelyn Grimes, Timothy Huynh, Laura Bepko, Tanner Howell, Kaitlyn Grossman, Nic Wadsworth, Molly Maffei, Melanie Collier, Daniel Hanson, Shana Sherman, Alyssa McCarron, and Paul Roberson.

TABLE OF CONTENTS

CHAPTER 1: INTRODUCTION AND PURPOSE STATEMENT

1.1 CONCUSSION EPIDEMIOLOGY

1.6 to 3.8 million sports-related concussions are reported annually in the United States,[1-3] which account for 5% to 9% of all sports-related injuries.[4-6] Concussions also account for approximately one-third of all injuries in high school and collegiate athletics.[7-9] The prevalence of concussion in sport is expected to be even higher as undiagnosed sport-related concussions range from 50% to 85%.[10,11] This is primarily due to the reliance on the clinical presentation of signs and symptoms following concussion because very little, if any, physical damage is able to be detected by imaging devices.[10] As such, concussion is a growing health concern, particularly among athletic populations.

Concussion is defined as a complex pathophysiological process affecting the brain, induced by traumatic biomechanical forces that result in transient neurologic signs or symptoms, and reflect a functional disturbance of the brain rather than a structural injury.[11-13] Dizziness is the second most commonly reported symptom, following headache, after sustaining a concussion.[9] Dizziness may represent an underlying impairment of the vestibular system, which is directly linked with the visual system.[14,15] About 81% of concussed athletes complain of dizziness[7,16-20] and over 30% of concussed athletes complain of visual issues.[6,15,16,20-25] However, about 90% of concussed athletes would be diagnosed with at least one visual impairment if they were to be assessed, regardless of whether the athlete complained of having a visual issue.[26-33]

Visual impairments are one of the most robust discriminators for the identification of concussion.[34-36] Injury to the brain can negatively affect sensory processing, and 70% of all sensory information is collected by the eyes.[37] Impairments to the visual system following

concussion is associated with a 6.4-times greater risk in protracted recovery (>21 days) and further risk of injury,[16,25,34-36,38,39] a 1.5-times greater risk for depression,[37] and a 4.5-times greater risk for Alzheimer's-like symptoms.[40-42] There is also a direct correlation between visual impairments and neuropsychological deficits,[43] short-term and long-term cognitive impairments,[44] and self-reported quality of life[37,45] following concussion.

Impairment of the visual system refers to a general disorder pertaining to the eye, and oculomotor dysfunction is the most common form of visual impairment.[35,36,38,39] Oculomotor dysfunction involves the inability to control and coordinate eye movements rapidly, accurately and smoothly, and may manifest as blurred vision, diplopia, impaired eye movements, difficulty in reading, dizziness, headaches, ocular pain, and poor visual-based concentration.[31] The eyes are considered to be windows into the brain,[29,46,47] with more than 50% of the brain being directly or indirectly involved in visual processes.[21,48-52] Over 30 areas of the brain[53-55] and over half of the cranial nerves[26,53-57] are responsible for vision. Thus, oculomotor dysfunction is prevalent following concussion and, therefore, may play an integral role in the assessment of concussion.

1.2 OCULOMOTOR CONTROL

Success and safety in sport requires oculomotor control (robust vision tracking, substantial intake of visual information, and rapid analysis of visual information).[58-60] Oculomotor control is closely related to the functional integrity of the brain[46,61,62] and provides insights into the neural control of volitional, reflexive, and anticipatory processes.[63,64] Concussions can cause oculomotor control dysfunctions[13,44] and have direct and measurable impacts on the oculomotor control system.[46,61] Oculomotor control dysfunctions are independent of intellectual ability and occur independently of neuropsychological impairment after a

concussion.[34] There are several different types of oculomotor control such as vergence, vestibular ocular reflex, smooth pursuit, and saccades.

Saccades are the rapid, accurate, ballistic shifting of eye movements to bring an object of interest into the center of sight and are important for safely navigating through the environment.[46,50,65-67] Saccades require complex coordination and timing in several different areas of the brain, including primarily the frontal lobe, basal ganglia, superior colliculus, and the cerebellum.[65,68] The network involved in saccades includes cortical (frontal, parietal, and supplementary cortices) and subcortical (thalamus, pons, superior colliculus, midbrain, brainstem, and cerebellum vermis) structures.[23,43,46,50,51,69] Saccade dysfunctions are present in over 30% of patients with concussion,[6,22,23,70] and are correlated with brain injury severity.[71,72]

Anti-saccades are the most common oculomotor dysfunction following concussion and may play a key role in the assessment of concussion.[6,30,34,50,65] There are several advantages in the assessment of anti-saccades following concussion. Anti-saccades are easily recorded, can be precisely quantified, their neural substrates are well understood, and they provide information about both low-level, subcortical function and high-level, executive functions.[66,72] Patients with anti-saccades cannot safely navigate through their environment and are susceptible to more severe impacts.[46,50,65-67]Anti-saccades also have the benefit of providing valuable information and correlations with aspects of executive function including: memory, attentional processes, impulse control, decision making, and initiation and control of behaviors.[73]

1.3 OCULOMOTOR ASSESSMENTS

Eye tracking is a user friendly, low cost, non-invasive, quantitative assessment of oculomotor control that may provide a fast, accurate, and reliable way to screen for

concussion.[61,65,66,74] This oculomotor control assessment provides a neuro-ophthalmological method of assessing the integrity of cortical and subcortical areas and pathways that are important for the successful execution of saccades.[75,76] Successful execution requires the ability to inhibit anti-saccades, gaze deviations away from a fixed point or area of interest and towards a peripheral or distracting target.[43,59,61,74,75,77] Good eye tracking is characterized by overall tight clustering of gaze around the area of interest (saccades).[66,75] Poor eye tracking is characterized by a wide distribution of unwanted, reflexive eye movements away from the area of interest (anti-saccades).[64,66,75,78-80]

There is previous literature that has assessed anti-saccades in concussed individuals, but not without several limitations. Many of these studies included a wide age range of sedentary individuals, did not assess anti-saccades until well after 48 hours post-concussion, compared concussed participants to volunteers, included a broad spectrum of traumatic brain injury patients, did not investigate anti-saccades during a dual task. The investigators of this study tried to address these limitations and investigated anti-saccades in concussed student-athletes 24-48 hours post-concussion using a dual task, and the anti-saccade data was reduced by hand.

There was a very wide age range of participants included in these previous studies that have assessed anti-saccades in concussions. Participants were as young as 13 years old[9,81] and as old as 70 years old.[61] No previous research has specifically looked at college-aged individuals and all the studies included an age range of at least 20 years. The great differences in the ages of the participants in these studies is a limitation that may have impacted the results of the studies. Our study only looked at college students, with all of our participants being between the ages of 18 and 21 years old.

The previous studies also did not necessarily assess anti-saccades in active individuals. Only 2 studies assessed anti-saccades in concussed collegiate athletes.[9,46] One study assessed anti-saccades in military veterans,[65] one study assessed anti-saccades in recreational athletes,[82] and all the other studies assessed anti-saccades in sedentary individuals.[61,67,74,75,81,83,84] Oculomotor control is important for sport and for being active.[58-60] Therefore, the execution of oculomotor control may be different between active and inactive individuals. Also, many of participants in these previous studies were healthy volunteers for the controls or were recruited from clinics for the concussed group. This method led to the participation of both sedentary and active individuals. Our study only included elite collegiate athletes for both the concussed and control participants.

Previous literature that has investigated anti-saccades in concussed participants also did not define concussion very well. Anti-saccades were assessed in participants with mild traumatic brain injury,[67,83,84] moderate traumatic brain injury,[75] traumatic brain injury,[75] and in participants with post-concussion syndrome.[61,65,74] These are more severe head injuries and may not accurately represent findings in a concussed participant. Many of these participants were also recruited from concussion clinics, further supporting that these studies may have studied anti-saccades in participants with more severe cases of concussion. This also led to several different mechanisms of injury including motor vehicle accidents and falls. Only two studies investigated anti-saccades in participants with a sport-related concussion.[9,46]

Even if participants with concussion were assessed, they were assessed well after 48 hours post-injury. Only two studies assessed anti-saccades within a week following concussion.[9,83] All of the other studies did not assess anti-saccades until at least one week post-concussion. Some studies did not assess anti-saccades until several months post-

concussion.[61,65,81,84] One study did not assess anti-saccades until 5 years following concussion.[74] Understanding the pathophysiology of concussion and the neurometabolic cascade of events following injury, the brain is most vulnerable within the first 48 hours after injury.[85-87] Therefore, our study assessed anti-saccades within 48 hours following concussion.

Additionally, the previous studies only assessed either the amount of anti-saccades or the duration of anti-saccades. Seven only assessed the amount of anti-saccades[9,61,65,74,75,81,83] and three only assessed the duration of anti-saccades.[67,82,84] Only one other study has assessed both the amount and the duration of anti-saccades in concussed individuals.[46] All of these studies reduced the anti-saccade data by hand frame-by-frame, typically in Microsoft Excel. The anti-saccade data in our study was reduced automatically by Applied Science Laboratories, which helped reduce human error.

1.4 PURPOSE STATEMENT

Therefore, the purpose of this study was to investigate anti-saccades, anti-saccade durations, and average anti-saccade durations between NCAA Division I athletes 24 to 48 hours post-concussion and healthy, matched NCAA Division I athletes during an environmentally-relevant dynamic postural assessment using an eye tracker.

1.5 QUESTIONS AND HYPOTHESES

Question 1: Is there a significant difference in the total amount of anti-saccadic eye movements between athletes with concussion and healthy athletes?

Hypotheses 1: It is expected that there will be significantly greater anti-saccadic eye movements in athletes with concussion when compared to healthy athletes.

Question 2: Is there a significant difference in the total time spent outside of the center area of interest during all anti-saccadic eye movements between athletes with concussion and healthy athletes?

Hypotheses 2: It is expected that there will be significantly longer total time spent outside of the center area of interest during all anti-saccadic eye movements in athletes with concussion when compared to healthy athletes.

Question 3: Is there a significant difference in the average time spent outside of the center area of interest during each individual anti-saccadic eye movement between athletes with concussion and healthy athletes?

Hypotheses 3: It is expected that there will be significantly longer average time spent outside of the center area of interest during each individual anti-saccadic eye movement in athletes with concussion when compared to healthy athletes.

CHAPTER 2: LITERATURE REVIEW

2.1 INTRODUCTION

Every year in the United States 1.6-3.8 million sports-related concussions occur,[1-3] which accounts for 5% to 9% of all sports-related injuries.[4-6] Additionally, concussions account for approximately one-third of all injuries in high school and collegiate athletics.[7-9] The prevalence of concussion in sport is expected to be even higher with undiagnosed sport-related concussions ranging from 50% to 85%.[10,11] Clearly concussion is a growing concern, especially among athletic populations, and is increasing.[46] Unfortunately, concussion cannot be detected by any imaging devices and the assessment of concussion is reliant upon the presentation of clinical signs and symptoms.[10]

Dizziness is the second most commonly reported symptom following headache after sustaining a concussion.[9] About 81% of concussed athletes complain of dizziness[7,16-20] and over 30% of concussed athletes complain of visual issues.[6,15,16,20-25] Dizziness is directly linked with the visual system,[14,15] and 6.4-times greater risk in protracted recovery (>21 days) and further risk of injury,[16,25,34-36,38,39] a 1.5-times greater risk for depression,[37] and a 4.5-times greater risk for Alzheimer's-like symptoms.[40-42] There is also a direct correlation between visual impairments and neuropsychological deficits,[43] short-term and long-term cognitive impairments,[44] and self-reported quality of life[37,45] following concussion.

It is estimated that about 90% of concussed athletes would be diagnosed with at least one oculomotor dysfunction if they were to be assessed, regardless of whether the athlete complained of having a visual issue.[26-33] Anti-saccades are the most common oculomotor dysfunction following concussion and may play a key role in the assessment of concussion.[6,30,34,50,65,74,79] Oculomotor dysfunction is one of the most robust discriminators for the identification of

concussion.[34-36] Greater than 50% of the brain,[21,48-52] more than 30 areas of the brain[53-55] and over half of the cranial nerves[26,53-57] are directly or indirectly responsible for vision. Therefore, it is no surprise that visual disturbances are so prevalent following concussion.

2.2 ANATOMY AND PHYSIOLOGY

Diffuse axonal injury is considered to be a key underlying cause of the more lasting signs and symptoms of concussion, including oculomotor dysfunction.[28] This injury involves the stretching, twisting, and tearing of the axons, which results in microscopic lesions, axonal swelling/degeneration, myelin loss, compromised cerebral vasculature, and even neuronal cell death.[21,28,30,78] Both cortical and sub-cortical pathways are disrupted[43,75] and the most common sites of injury include the corpus callosum and the superior colliculi in the frontal region of that brain at the white-gray matter junctions.[26,88] The frontal region of the brain is highly susceptible to deformation, which may impair concentration, attention, memory, and high-level executive functions such as planning and decision making.[74] Diffuse axonal injury also disrupts the overall speed, efficiency, and integration of mental and central nervous system function.[42]

The disrupted white matter integrity caused by diffuse axonal injury reduces the strength, number, and organization of the neural synapses. This causes the neuronal synchrony and firing rate to be compromised, which results in inaccurate, variable, and slowed executive functioning. In particular, motor functioning is lost, causing the concussed patient to not respond in a time-optimal manner. Therefore, patients with diffuse axonal injury following concussion will need to constantly exert considerable effort to try to perform simple lower-level tasks, such as saccades, and will most likely exhibit an oculomotor dysfunction.[30,72]

Cerebral structures concerned with oculomotor control are well-mapped and form extensive and highly complex networks that encompass the entire brain spanning cortical and subcortical structures.[42,44,59,61,69] The widespread architecture of these neural networks makes them vulnerable to the diffuse and pervasive nature of concussion,[25,43,46,50,51,75,89] with the frontal cortex (specifically the prefrontal cortex) being the most susceptible to dysfunction following concussion.[75,90] The cortical structures involved in oculomotor control and saccades include: primary visual cortices, dorsolateral prefrontal cortices, extrastriate cortices, middle temporal area, occipital lobe, striate cortices, posterior parietal cortices, and frontal eye fields, and supplementary eye fields.[23,43,46,50,51,75,79,83,89] The subcortical structures include: thalamus, pons, superior colliculus, midbrain, brainstem, and cerebellum vermis.[23,43,46,50,51,69,75,79,83,89]

The frontal and parietal cortices of the brain play crucial roles in the execution of oculomotor control and saccades.[62,75,83] The dorsolateral prefrontal cortex is the central site for the synthesis of executive functions including: saccades, attention, cognition, working memory, and the suppression of anti-saccades.[23,72,74,77,83,90-92] The posterior parietal cortex and supplementary eye fields connect information between sensory and motor structures to play an important role in the integration of oculomotor control and postural control coordination.[83,91-93] The supplementary motor area is also directly involved in planning and execution of oculomotor control.[93] The functional integrity of all of these neural networks could be damaged following concussion and may compromise the execution oculomotor control.[83] Additionally, the most affected regions of the central nervous system following concussion are the diencephalon and midbrain, which is where the cranial nerves responsible for oculomotor control originate.[13]

The pathways for the execution of oculomotor control starts in the occipital lobe when it receives the visual information from the optic tract.[52,69,79] This information travels from the

occipital lobe to posterior parietal cortex for further processing.[50,52] Saccades are then generated by the frontal eye fields and executed through subcortical circuits.[50,52,79] The dorsolateral prefrontal cortex (area highly vulnerable to concussion) is the highest cortical area responsible for motor planning and working memory, and has an established link with saccades.[23,52,75,79] The dorsolateral prefrontal cortex is responsible for three primary oculomotor control functions: inhibition of anti-saccades, production of voluntary saccades, and maintaining memorized visual information for ongoing saccades.[50,52,62,79,91]

Generating saccades requires coordinated actions between many control centers.[50,79,84] Successful completion requires the inhibition from higher cognitive systems in the frontal and parietal areas of the brain, which is compromised during anti-saccades.[50,52,79,84,91] Saccades assess frontal function (especially of the prefrontal cortex), which requires inhibition of anti-saccades and the deliberation, planning, and initiation of voluntary saccades.[75,76] Anti-saccades are generated from the parietal eye field, unlike saccades which are generated from the frontal eye fields, and involve hyperactivation of the cerebellum and V5/V1 cortical areas.[50,52,84] Literature has suggested that concussed patients exhibit deficits in the generation of saccades and difficulty inhibiting eye movements toward a distracting stimulus (anti-saccades).[50,52,79,84,91]

Other areas involved in oculomotor control that are susceptible to injury following concussion include: anterior cingulate gyrus, orbital frontal gyrus, hippocampus, anterior corona radiate, superior longitudinal fasciculus, uncinate fasciculus, genu of the corpus callosum, forceps major, superior cerebellar peduncle, and cingulum bundle.[43,72,74,75,81,84,90] The anterior cingulate gyrus and the orbital frontal gyrus (as well as the dorsolateral prefrontal cortex) are important prefrontal sites of executive and cognitive functions including oculomotor control.[72,90] The forceps major and superior cerebellar peduncle are also correlated with oculomotor

control.[74] The corpus callosum is important for many cognitive functions, especially in the transfer and coordination of information between the prefrontal cortices.[81,84] These cognitive functions are important in sustaining attention and working memory, which oculomotor control is dependent upon.[74,81,82]

2.3 OCULOMOTOR CONTROL

Oculomotor control is responsible for stabilizing and optimizing vision relative to the movement of the visual world,[66] and is achieved through extensive and complex networks that encompass the entire brain.[42,44,59,61,69] The networks responsible for oculomotor control and executive functioning (attention, concentration, cognition, working memory, planning, decision making) all overlap in these cortical and subcortical structures.[23,43,46,50,51,75,83,89,94] With over 30 areas of the brain[53-55] and over half of the cranial nerves[26,53-57,94] being responsible for vision, oculomotor control is closely related to the functional integrity of the brain.[46,61,62] All of these structures are vulnerable following concussion and diffuse axonal injury to these networks may be imminent.[25,42,43,46,50,51,89,94] In fact, some form of oculomotor control dysfunction is present in about 90% of concussed athletes.[26-33,94]

There are several types of oculomotor control including: vergence, vestibular ocular reflex, smooth pursuit, and saccades. Vergence is the ability to coordinate and focus both eyes on a single point in space moving toward or away from the eyes.[50,52,95] Vergence dysfunctions are detected in up to 90% of patients with concussion.[96] Convergence abnormalities have been reported in 64% of concussed patients.[33,51] Vestibular ocular reflex allows the eyes to maintain steady focused gaze on a fixed visual point while the head is moving.[9,95,97] The vestibular ocular reflex is a fast-acting reflex that keeps the eyes stable by generating compensatory eye

movements in the precisely and proportionally opposite direction of the head movement.[50,98] Smooth pursuit is the ability to accurately and smoothly pursue a slowly moving target[50,52,99] and requires attention, anticipation, working memory, and saccades to continuous stabilize the eyes on a moving target.[51,66,92] Some form of smooth pursuit dysfunction is present in up to 60% of concussed patients.[33]

However, saccade dysfunctions are the most common oculomotor dysfunction following concussion.[6,30,34,50,65,74,79] Saccades are the rapid, accurate, ballistic shifting of eye movements to bring an object of interest into the center of sight and are important for safely navigating through the environment.[46,50,65-67,94] Saccades require voluntary control of eye movements and the successful inhibition of reflexive saccades toward the periphery (anti-saccades).[43,59,61,74,75,77,100,101] Concussed patients have difficulty inhibiting anti-saccades, specifically with releasing attention from one visual target and/or difficulty locking onto another target.[102] These inaccurate and interruptive saccades are considered abnormal and are indicative of central nervous system dysfunction.[103] Detecting anti-saccades may provide a fast, accurate, and reliable way to screen for concussion.[66]

Anti-saccades are the most common oculomotor dysfunction following concussion and may play a key role in the assessment of concussion.[6,30,34,50,65] Anti-saccades are present in over 30% of patients with concussion,[6,22,23,70] and are correlated with brain injury severity.[71,72,94] There are several advantages in the assessment of anti-saccades following concussion. Anti-saccades are easily recorded, can be precisely quantified, their neural substrates are well understood, and they provide information about both low-level, subcortical function and high-level, executive functions.[66,72] Patients with anti-saccades can't safely navigate through their environment and are susceptible to more severe impacts.[46,50,65-67,102] Anti-saccades also have the

benefit of providing valuable information and correlations with aspects of executive function including: memory, attentional processes, impulse control, decision making, and initiation and control of behaviors.[73]

Successful completion of saccades is directly related to attention.[66] Saccades require the rapid disengagement of attention on a fixation point, the movement of attention to the area of interest, and the reengagement of attention on that fixation point.[96] These processes have been shown to engage a diffuse network of cortical (primary visual, extrastriate, parietal cortices, and frontal and supplementary eye fields) and subcortical (thalamus, superior colliculus, striatum, and cerebellum vermis) structures of the brain.[46,69,104,105] These neural networks overlap the structures responsible for both saccades and attention, suggesting that visual attention and saccades are closely associated.[23,43,46,50,51,75,79,83,89,94,98] Therefore, quantitative and objective measurements of anti-saccades may important information regarding the health and integrity of the brain.[13,62,65,66,74,92,93,106]

2.4 OCULOMOTOR ASSESSMENTS

Quantification of eye movements can provide valuable information related to the function of the brain following concussion.[36,61,65,66,74] Recent technological advances have produced non-invasive eye tracking measures capable of recording eye positions with high resolution.[66,94] Three-dimensional rotation of the eye is captured using changes in the locations of two specific landmarks. The pupil can be quickly identified, frame-by-frame, using a computer because is a dark and elliptical in shape.[50-52,66] The other landmark is a bright spot produced by the reflection of a light source called a corneal reflection point, and it moves in relation to the eye's rotation.[50-52,66] Therefore, when the dots created from these two landmarks are connected, there is a straight

line pointing directly to where the eye is looking. The coordinates are then mapped to physical coordinates created by a motion capture system.[66,94] With proper calibration, combined tracking of the pupil and corneal reflection can produce a very precise measurement.[50-52,66,94]

Eye tracking involves the combination of both smooth pursuit and saccades, and collectively they stabilize the moving object of interest onto the fovea and into the center of sight.[50-52,66,94] Good eye tracking is characterized by overall tight clustering of gaze around the area of interest (saccades).[66,75] Poor eye tracking is characterized by a wide distribution of reflexive eye movements away from the area of interest (anti-saccades).[66,75,78,79] Eye tracking is a user friendly, low cost, non-invasive, rapid, convenience, portable, definitive approach for the objective assessment of the brain after a concussion.[61,65,66,74]

There are several emerging measures for the assessment of oculomotor control including: infrared oculography (OBER-2 system),[76] infrared videography and dynamic retinoscopy (Power Refractor II, GA),[45] a head mounted video-based binocular eye tracker (Eyelink II, Canada),[65,74] DIOPSYS NOVA-TR system (Diopys Inc., NJ),[106] EyeLink 1000 eye tracker,[107] IRIS infrared limbus tracker (Skalar Medical, Netherlands),[61] infrared corneal reflection device (Iris Skalar),[77,82] infrared scleral reflection oculography technique (Skalar Medical, Netherlands),[83] MRI compatible eye tracking system (PC-60, AZ),[46] integrated stimulus presentation-eye tracking apparatus (EyeLink CL, Canada),[81] head-mounted eye-tracker (SensoMotoric Instruments, Germany)[72] Vistagraph reading eye movement system (Taylor Associates, NY),[30] Arrington eye movement recording system,[89] Saccadometer Advanced (Ober Consulting),[84] and monocular eye tracking system (Applied Science Laboratories, MA)[9].

Eye tracking has quantified that patients have a higher amount of oculomotor dysfunction following concussion.[9,30,46,61,65,67,74,75,81-84,89,106] Anti-saccades were all measured differently in

each study, but were generally characterized by amount, duration, accuracy, and velocity. More, longer, larger, and faster anti-saccades were indicative of diffuse axonal injury and oculomotor dysfunction. Literature has shown that concussed patients have significantly more anti-saccades,[9,46,61,65,74,75,81,83] significantly longer anti-saccade durations,[46,67,82,84] significantly larger anti-saccades,[46,61,65,74,83] and significantly faster anti-saccades[61] when compared to controls. Previous studies have also revealed that concussed patients have significantly more anti-saccades when compared to sleep-deprived individuals,[81] and that oculomotor training improves most visual impairments following concussion.[30,89,106]

Other emerging visual assessments include the King-Devick test, the Vestibular Ocular Motor Screening (VOMS), and the Display Enhance testing for Concussion and mild traumatic brain injury system (DETECT). The King-Devick test is an innovative reading efficiency test that has been recently recommended and utilized for sideline diagnosis of sport-related concussion.[35,108-110] The VOMS compares oculomotor tasks to clinical signs and symptoms, and has recently been suggested to be a sensitive marker for identifying patients with concussion.[108] DETECT is a virtual reality oculomotor test that creates an immersive environment free from visual and auditory distractions.[111] More research is needed to evaluate these measures. All of these oculomotor tests show promise; however, more objective and accurate measurements of oculomotor control dysfunction following concussion are still warranted.

2.5 POSTURAL ASSESSMENTS

The second most commonly reported symptom following concussion is dizziness with over 75% of concussed athletes complaining of dizziness.[7,9,16-20,34] Dizziness may represent an underlying impairment of the vestibular system, which is neurologically related and directly

linked to dysfunction of the oculomotor and vestibular systems.[9,14,15,97,112] The vestibular system is a complex network that includes small sensory organs of the inner ears (utricle, saccule, and semicircular canals) and connections to the brainstem, cerebellum, cerebral cortex, oculomotor system, and postural system.[16,61] The vestibular system is also organized into two functional units: the vestibulo-ocular system (oculomotor control) and the vestibulo-spinal system (postural control).[16,61] Due to the organization and neurophysiology of the vestibular system, dysfunction to this system manifests as symptoms of dizziness, visual instability, and balance deficits,[16,61] so postural assessments following concussion may also be warranted.

Postural assessments have been used extensively to assess the health and integrity of the vestibular system because balance provides an ideal model for determining vestibular dysfunctions following concussion.[113,114] Balance is the ability to stand with upright posture without deviating outside the limits of the base of support.[19,112,114] Postural control requires the continuous complex integration of several sensory feedback and feedforward sources (vision, proprioception, and vestibular function) and regulation of motor responses to ensure that the center of mass of the body maintains within its base of support for upright posture.[19,110,112-115] Scientific-grade force plates quantify postural control based on measured changes in body sway during standing and are considered the gold standard for the assessment of posture.[113,116-119]

Unfortunately, force plates are expensive (up to $15,000), difficult to set up, and cumbersome to transport.[113,118] Therefore, the BESS and SOT have been implemented in most sport-related concussion assessment batteries.[80,113,120] Although the BESS is more cost-effective and more portable than the force plate, evidence regarding its validity and reliability are poor.[113,121-124] Additionally, these measures are only reprehensive of the vestibulo-spinal aspect of the vestibular system and are quiet, static stance assessments. Postural control involves the

integration of three separate entities: the individual, task, and environment.[112] The BESS and SOT do incorporate an environmental component; however, the environment is not heavily weighed because the examiner controls for environmental variables that may affect the results. An assessment that more heavily weighs the environmental component, such as in sport, may provide a better understanding of the health and integrity of the vestibular system.

There is convincing evidence that a low-cost ($50) Wii Balance Board (WBB) has been determined to be a valid and reliable force plate alternative.[113,118,119,121,125,126] Comparably, the WBB proved to be superior to the BESS[19,113] and had an almost perfect agreement with the gold standard force plate.[113,118,119,121,125,126] The WBB is inexpensive, portable, and contains four transducers to assess force distribution and resultant movement just like a laboratory-grade force plate.[113,118,119,127] Originally designed as a video game controller, the WBB can be isolated from the Wii gaming system and wirelessly interfaced with a computer as a peripheral device as a clinical balance test.[113,118]

The WBB is an enjoyable postural assessment that provides instant feedback and enhances motivation levels.[118,127,128] These benefits have advocated for this assessment to be integrated into rehabilitation program for neurologically-impaired patients with balance deficits.[118,129] In addition, the WBB is a virtual reality gaming system, which is defined as the use of interactive simulations created with computer hardware and software to present users with opportunities to engage in environments that appear to be, and feel familiar to, real world objects and events.[127,130] Therefore, the WBB may provide a more heavily weighed environmental component to the postural assessment when compared to the BESS and SOT.

CHAPTER 3: METHODOLOGY

3.1 RESEARCH SETTING

Two groups of NCAA Division I athletes were evaluated in this cross-sectional design. This design allowed the researchers to evaluate the gathered data between each of the two cohorts. The cohorts in this study included athletes with concussion and healthy, matched athletes without concussions. All participants were student-athletes at a university located in southeast Georgia and the university's certified Athletic Trainers assessed for each concussion. Athletes with concussion reported to the Athletic Training Room for initial evaluation and were referred to the Biomechanics Laboratory where all assessments were conducted for this study.

3.2 PARTICIPANTS

Ten athletes with concussion (4 female, 6 male; age: 18.9 ± 0.9 years) and ten position-matched, healthy athletes (4 female, 6 male; age: 18.3 ± 0.6 years) participated in this study (Table 1). The healthy and concussed athletes were matched based off of age, gender, and sport. The healthy athletes were not currently participating in their sporting season to decrease the risk of sustaining sub-concussive hits during the respective season.

Table 1. Participant Demographics

	Gender		Age				Sport			
Participant	Male	Female	18	19	20	21	Football	Soccer	Cheer	Track
Concussed Athletes	6	4	4	4	1	1	6	1	1	2
Healthy Athletes			7	2	1	0				

Notes. 6 male and 4 female athletes with concussion were matched to healthy controls based on gender, age, & sport

The primary investigator recruited all of the healthy athletes and the athletes with concussion that participated in this study. After an athlete sustained a concussion, the attending

certified Athletic Trainers would inform the athlete about the study and would ask if he/she would like to participate. If the athlete agreed to participate, the Biomechanics Laboratory staff was notified and set up a time for the athlete to be tested. All healthy athletes were tested in the preseason during pre-participation physicals. This was to allow for testing to occur while athletes were not physically engaged in their respective sporting season, decreasing the risk of sustaining any hits that may cause a concussion or negatively impact the results of this study. All participants in this study satisfied all of the following inclusion and exclusion criteria (Table 2):

Table 2. Inclusion and exclusion criteria for healthy controls and concussed athletes

Participation Criteria	
Inclusion Criteria	Exclusion Criteria
• Between the ages of 18-30 • Athletes under care of athletic training staff • Free of musculoskeletal/neuromuscular injury • No diagnosis of learning disorders or ADHD • No history of psychiatric illnesses or seizures * Documented concussion (concussed athletes)	• Documented head injury (including concussion) within past 12 months • Loss of consciousness within past 6 months • Report any symptoms during healthy questionnaire and interview * In current sporting season (concussed athletes)

Notes: All participants were student-athletes at a NCAA Division I university in southeast Georgia. The controls were assessed during pre-participation physicals and the concussed athletes were assessed 24 to 48 hours following a diagnosed concussion. Participants were free of pathologies or previous injuries that may impact oculomotor control.

All concussions were confirmed by the head certified Athletic Trainer at a NCAA Division I university in southeast Georgia and/or a medical doctor on staff. Athletes with concussion that agreed to participate in this study were referred to the Biomechanics Laboratory to be tested within 48 hours of their concussion. No athletes with concussion reported experiencing an additional concussion injury or any increase in concussion symptoms during the time of testing. If the attending certified Athletic Trainers determined that the athletes with concussion were too symptomatic 48 hours after concussion, as determined by the university's policies and procedures, they did not participate in this study. All participants signed informed written consent to participate in the study as approved by the Institutional Review Board.

Figure 1. Dynamic, Environmentally-Relevant Postural Assessment: 60-second assessment of the participant playing the WiiFit Soccer Heading game while wearing the ASL Eye Tracker, which sampled the anti-saccade data at a frequency of 240 Hz.

3.3 STUDY DESIGN

As stated previously, two groups of athletes (healthy and concussed) were evaluated in this study. All participants performed a total of 3 trials of a dynamic, environmentally-relevant postural assessment (WiiFit Soccer Heading game) in the Biomechanics Laboratory (Figure 1.) while wearing the Applied Science Laboratories (ASL) Eye Tracker. The first trial was a practice trial and the following 2 trials were data collection trials. The healthy athletes performed the postural assessment during their pre-participation physicals and the athletes with concussion performed the postural assessment 24-48 hours following their concussion.

3.4 PROCEDURES

Participants completed a dynamic, environmentally-relevant postural assessment, the WiiFit Soccer Heading game. This dynamic assessment was performed barefoot on the WiiFit board while playing the WiiFit Soccer Heading game. The athlete swayed his/her body in the mediolateral direction to move his/her associated avatar in a similar fashion to head soccer balls coming down the center, left, and right of the screen. No anteroposterior movement is necessary to head the soccer balls; the avatar's head making contact with the soccer balls is all that is needed to be successful. The duration of the WiiFit Soccer Heading game lasts about 60 seconds with a total of 80 soccer balls being kicked.

While playing the WiiFit Soccer Heading game, the athletes wore the ASL Desktop 7 Eye Tracker. ASL was founded in 1962 in Bedford, Massachusetts and is the recognized leading authority in eye tracking. The ASL Eye Tracker is user friendly, low cost, non-invasive, definitive, rapid, and convenient.[61,65,66,74] There are currently two versions: the Desktop 7 Eye Tracker, which is more accurate; and the Mobile Eye, which is portable. The Desktop 7 Eye Tracking System is ASL's latest high speed, head mounted optics. This headgear fits like a baseball cap and quantitatively assesses the athlete's eye movement while they performed the dynamic, environmentally-relevant balance assessment on the WiiFit board.

The ASL Eye Tracking Software works in coordination with the Vicon Nexus 1.8.5 8-camera motion capture system in the Biomechanics laboratory. The Vicon cameras use infrared light to detect reflectors on the back of headgear to track head position and determine its orientation in space. The ASL Eye Tracking System also uses infrared light with its two cameras on the headgear. One camera points forward to see the orientation of the head. The other camera points down and reflects off an optical lens into the eye. Once calibrated, the infrared light from

the camera pointing down reflects off of the eye and directly onto where the eye is looking using the pupil and the corneal reflection point.[50-52,66] During the postural assessment, infrared light will reflect onto the specific point of the TV screen that the eye is looking while playing the WiiFit game. This point where the eye is looking is seen on the forward facing camera and picked up by the Vicon Nexus motion capture system, allowing for eye-head integration and the collection of gaze coordinates in real time.

The ASL Eye Tracker captures the oculomotor control movements of the eye in conjunction with the Vicon Nexus motion capture system. The researchers analyzed saccades (rapid eye movements toward a fixed point or area of interest) and anti-saccades (reflexive gaze deviations away from a fixed point or area of interest). The specific variables of interest were the total amount of anti-saccades and the total duration of anti-saccades spent away from the fixed point or area of interest, and the average duration of anti-saccades spent away from the fixed point or area of interest. The TV screen was divided into center, left, and right areas of interest using the soccer goal posts (Figure 2). The center area of interest is from where all of the soccer balls were being kicked and is where the participants were instructed from which to not deviate their gaze.

The researchers tracked how frequently and how long the eyes of the participants deviated away from the center area of interest. The goal posts served as the boundaries between areas of interest because they were from where the next soccer ball was being kicked during the game. Once the soccer ball coming towards the avatar hit the plane of the goal post, the next soccer ball to be headed was kicked from the center area of interest. When this happened, the participant would have to make a rapid eye movement toward that soccer ball (saccade) to determine its direction and velocity so it can be headed.

Every gaze deviation away from the center area of interest was considered an anti-saccade. At that point, the soccer ball being tracked had gone outside of the goal posts and the next soccer ball was kicked from within the center area of interest. Participants should inhibit their gaze on the current soccer ball and make a rapid eye movement toward the new incoming soccer ball. If this did not occur, then the participants were making a reflexive gaze deviation away from this new soccer ball by continuing to track the current soccer ball (anti-saccades). The ASL Eye Tracker sampled these anti-saccade data at a frequency of 240Hz.

Figure 2. WiiFit Soccer Heading game: the TV screen is broken into center (blue), left (red), and right (yellow) areas of interest to determine gaze deviations away from the center (total amount of anti-saccades, total duration of anti-saccades, and average duration of each anti-saccade) between PC and MC. Each green dot represents a gaze fixation point (points in which the eye is focusing) and the blue lines represent the path of the participant's eye movements.

3.5 DATA REDUCTION

Raw oculomotor data was coded for each area of interest using ASL Results Plus (Bedford, MA). Areas of interest included the center, left and right of the screen (Figure 2). Anti-saccadic eye movements were measured using three variables: the total amount of gaze

deviations away from center (anti-saccades), the total duration of gaze deviations away from center (anti-saccade durations), and the average duration of each gaze deviation away from center (average anti-saccade durations). ASL Results Plus coined these variables as: non-center dwells (anti-saccades), non-center dwell durations (anti-saccade durations), and average non-center dwell durations (average anti-saccade durations).

ASL Results Plus calculated each of these variables using the information gathered from the Vicon Nexus 1.8.5 8-camera motion capture system. While playing the WiiFit Soccer Heading game, infrared light from the ASL Eye Tracker was reflected off of the participant's eye (using the pupil and the corneal reflection point) and onto the specific area of interest that his/her eye was focusing. This point where the eye is looking is seen on the forward facing ASL Eye Tracker camera and picked up by the Vicon Nexus motion capture system, allowing for eye-head integration and the collection of gaze coordinates in real time. The ocular raw point of gaze coordinates were calculated at a sampling frequency of 240 Hz with a set threshold of 25 Hz to control for eye blinks during the data analysis.

3.6 DATA ANALYSES

One-way Analyses of Variances (ANOVAs) were utilized to determine total amount of anti-saccadic eye movements (anti-saccades), total time spent outside of the center area of interest during all anti-saccadic eye movements (anti-saccade durations), and average time spent outside of the center area of interest during each individual anti-saccadic eye movement (average anti-saccade durations) between the two cohorts (healthy, matched athletes vs. athletes with concussion). This examined if there is a significant difference between the 10 healthy, matched control (MC) and the 10 athletes 24-48 hours post-concussion (PC). A sample size of 8-10 was

deemed sufficient by G*Power with a beta level of 0.80 and an alpha level of 0.05. It was expected there would be significantly more anti-saccadic eye movements, significantly longer anti-saccadic eye movement durations, and significantly longer average anti-saccadic eye movement durations in the PC group when compared to the MC group.

CHAPTER 4: RESULTS

4.1 ONE-WAY ANOVAS

One-way ANOVAs revealed significantly greater anti-saccades ($F_{(1,18)} = 19.339$, $p < 0.001$, $\eta^2 = 0.680$) in the PC group (11.85 ± 6.89) when compared to the MC group (2.00 ± 1.67), significantly greater anti-saccade durations ($F_{(1,18)} = 11.459$, $p = 0.003$, $\eta^2 = 0.438$) in the PC group (8.90 ± 7.88 seconds) when compared to the MC group (0.45 ± 0.43 seconds), and significantly greater average anti-saccade durations ($F_{(1,18)} = 12.479$, $p = 0.003$, $\eta^2 = 0.547$) in the PC group (0.83 ± 0.64 seconds) when compared to the MC group (0.12 ± 0.08 seconds).

Table III: One-Way ANOVA for Anti-Saccadic Eye Movements

Anti-Saccadic Eye Movement	Group	N	F	Mean	Standard Deviation	p-value
Anti-Saccades	PC	10	19.339	11.85	6.89	<0.001*
	MC	10		2.00	1.67	
Anti-Saccade Durations	PC	10	11.459	8.90	7.88	0.003*
	MC	10		0.45	0.43	
Average Anti-Saccade Durations	PC	10	12.479	0.83	0.64	0.002*
	MC	10		0.12	0.08	

Notes: Athletes with concussion (PC) demonstrated significantly more anti-saccades ($p < 0.001$), anti-saccade durations ($p = 0.003$), and average anti-saccade durations ($p = 0.002$) when compared to healthy, matched controls (MC) while playing the WiiFit Soccer heading game.

CHAPTER 5: DISCUSSION

5.1 REVIEW OF THE PURPOSE

The purpose of this study was to investigate oculomotor dysfunctions (anti-saccades, anti-saccade durations, and average anti-saccade durations) between NCAA Division I athletes 24 to 48 hours post-concussion and healthy, matched NCAA Division I athletes during an environmentally-relevant dynamic postural assessment, the Wii Soccer Heading game, using the ASL Eye Tracker. Anti-saccades were defined as the total amount of reflexive gaze deviations away from the fixed center area of interest. Anti-saccade durations were defined as the total time spent outside of the fixed center area of interest during these reflexive eye movements. Average anti-saccade durations were defined as the average time spent outside of the fixed center area of interest during each individual reflexive eye movement.

5.2 DISCUSSION OF THE RESULTS

Our results found significant differences in anti-saccades, anti-saccade durations, and average anti-saccade durations between NCAA Division I athletes 24 to 48 hours post-concussion and healthy, matched NCAA Division I athletes during an environmentally-relevant dynamic postural assessment, the Wii Soccer Heading game, using the ASL Eye Tracker. Therefore, athletes with concussion may not have sufficient gaze stability to adequately navigate through a dynamic, environmentally-relevant environment and may be at further risk for injury if returned to play. The great number and duration of anti-saccades suggests a major deficiency in oculomotor control and could be a candidate marker for concussion.

These results are in agreement with previous literature, which suggest that concussed patients have a significantly higher degree of oculomotor dysfunction compared to healthy controls.[9,30,46,61,65,67,74,75,81-84,89,106] Anti-saccades were all measured differently in each study, but were generally characterized by amount, duration, accuracy, and velocity. More, longer, larger, and faster anti-saccades were indicative of diffuse axonal injury and oculomotor dysfunction. Our study looked at the amount and the duration of anti-saccades in athletes with 24 to 48 hours post-concussion using a dynamic, environmentally-relevant postural assessment.

Concussed patients have significantly more anti-saccades,[9,46,61,65,74,75,81,83] significantly longer anti-saccade durations,[46,67,82,84] significantly larger anti-saccades,[46,52,61,65,74,83] and significantly faster anti-saccades[61] when compared to controls. Previous studies have also revealed that concussed individuals have significantly more anti-saccades when compared to sleep-deprived individuals,[81] and that oculomotor training improves most visual impairments following concussion.[30,89,106] However, all of these studies had several limitations that our study tried to address. Anti-saccades were assessed in participants with a wide age range, in sedentary participants, in participants with several different severities of brain injury, in concussed participants well after 48 hours post-injury, by comparing concussed participants to volunteers, using a seated assessment, and the anti-saccade data was reduced by hand.

There was a very wide age range of participants included in these previous studies that have assessed anti-saccades in concussions. Participants were as young as 13 years old[9,81] and as old as 70 years old.[61] No previous research has specifically looked at college-aged individuals and all the studies included an age range of at least 20 years. The great differences in the ages of the participants in these studies is a limitation that may have impacted the results of the studies.

Our study only looked at college students, with all of our participants being between the ages of 18 and 21 years old.

The previous studies also did not necessarily assess anti-saccades in active individuals. Only 2 studies assessed anti-saccades in concussed collegiate athletes.[9,46] One study assessed anti-saccades in military veterans,[65] one study assessed anti-saccades in recreational athletes,[82] and all the other studies assessed anti-saccades in sedentary individuals.[61,67,74,75,81,83,84] Oculomotor control is important for sport and for being active.[58-60] Therefore, the execution of oculomotor control may be different between active and inactive individuals. Also, many of participants in these previous studies were healthy volunteers for the controls or were recruited from clinics for the concussed group. This method led to the participation of both sedentary and active individuals. Our study only included elite collegiate athletes for both the concussed and control participants.

Previous literature that has investigated anti-saccades in concussed participants also did not define concussion very well. Anti-saccades were assessed in participants with mild traumatic brain injury,[67,83,84] moderate traumatic brain injury,[75] traumatic brain injury,[75] and in participants with post-concussion syndrome.[61,65,74] These are more severe head injuries and may not accurately represent findings in a concussed participant. Many of these participants were also recruited from concussion clinics, further supporting that these studies may have studied anti-saccades in participants with more severe cases of concussion. This also led to several different mechanisms of injury including motor vehicle accidents and falls. Only two studies investigated anti-saccades in participants with a sport-related concussion.[9,46]

Even if participants with concussion were assessed, they were assessed well after 48 hours post-injury. Only two studies assessed anti-saccades within a week following

concussion.[9,83] All of the other studies did not assess anti-saccades until at least one week post-concussion. Some studies did not assess anti-saccades until several months post-concussion.[61,65,81,84] One study did not assess anti-saccades until 5 years following concussion.[74] Understanding the pathophysiology of concussion and the neurometabolic cascade of events following injury, the brain is most vulnerable within the first 48 hours after injury.[85-87] Therefore, our study assessed anti-saccades within 48 hours following concussion.

Additionally, the previous studies only assessed either the amount of anti-saccades or the duration of anti-saccades. Seven only assessed the amount of anti-saccades[9,61,65,74,75,81,83] and three only assessed the duration of anti-saccades.[67,82,84] Only one other study has assessed both the amount and the duration of anti-saccades in concussed individuals.[46] All of these studies reduced the anti-saccade data by hand frame-by-frame, typically in Microsoft Excel. The anti-saccade data in our study was reduced automatically by Applied Science Laboratories, which helped reduce human error.

Anti-saccades following concussion may be explained due to the damage of the cortical and subcortical networks responsible for attentional disengagement and inhibition caused by diffuse axonal injury.[43,59,61,74,75,77,100,101] Furthermore, increased anti-saccade durations are a dysfunction of saccade initiation. The time required for the integration and calculation of anti-saccades reflects the time needed to process the task involving higher brain structures.[84] Therefore, the concussed patients in our study had a higher amount of anti-saccades and a longer duration of anti-saccades because they needed more time to determine the direction and the velocity of the soccer balls to carry out the appropriate motor control response to head them. Anti-saccades require a high recruitment of cerebral resources at both the cortical and sub-cortical levels and are directly related to the functional integrity of the brain.[9,14,15,46,61,75,84,97,112]

5.3 LIMITATIONS AND DELIMITATIONS

This study had some limitations and delimitations. One limitation to this study was that the data collection methods of this study included a novel assessment of postural control. There is convincing evidence that a low-cost ($50) WBB has been determined to be a valid and reliable force plate alternative.[113,118,119,121,125,126] Comparably, the WBB proved to be superior to the BESS[19,113] and had an almost perfect agreement with the gold standard force plate.[113,118,119,121,125,126] The WBB is inexpensive, portable, and contains four transducers to assess force distribution and resultant movement just like a laboratory-grade force plate.[113,118,119,127] Originally designed as a video game controller, the WBB can be isolated from the Wii gaming system and wirelessly interfaced with a computer as a peripheral device as a clinical balance test.[113,118]

Second, the sample included a convenience sample that was drawn from the surrounding NCAA Division I students-athletes at a university located in southeast Georgia. This presents a possible threat to the external validity of the study. The study design did not require blinding for the researchers and it is possible that previous injuries may have gone unreported or undiagnosed. All previous injuries were accounted for as best as possible and the longitudinal cohort study design will help reduce internal validity of the study. The athletes who participated in this study were from a variety of sports and were matched healthy controls instead of the gold standard baseline comparison. Future research should look at the comparison of oculomotor dysfunction following concussion when compared to baseline measures.

A delimitation of this study was that the instrumentation used in this study potentially presented a concern for the internal validity of the research. The ASL Eye Tracker is user friendly, low cost, non-invasive, definitive, rapid, and convenient.[61,65,66,74] Three-dimensional

rotation of the eye is captured using changes in the locations of two specific landmarks. The pupil can be quickly identified, frame-by-frame, using a computer because is a dark and elliptical in shape.[50-52,66] The other landmark is a bright spot produced by the reflection of a light source called a corneal reflection point, and it moves in relation to the eye's rotation.[50-52,66] Therefore, when the dots created from these two landmarks are connected, there is a straight line pointing directly to where the eye is looking. The coordinates are then mapped to physical coordinates created by a motion capture system.[66,94] With proper calibration, combined tracking of the pupil and corneal reflection can produce a very precise measurement.[50-52,66,94] We used the most accurate ASL Desktop 7 Eye Tracking System, which also happens to be the latest high speed, head mounted optics.

Second, the sample of this study was delimited to NCAA Division I athletes from a university located in southeast Georgia. This study is also delimited to the current concussion assessment and return-to-play protocol set in place by the athletic department of the university located in southeast Georgia. This is a potential threat to the internal validity of the study if an athlete returns to play after a concussion and receives sub-concussive blows. However, inclusion and exclusion criteria will attempt to recruit athletes out of their athletic season during pre-participation physicals to reduce this threat.

5.4 ASSUMPTIONS

This study had some assumptions that could limit the accuracy of the study. First, it was assumed that all participants gave 100% effort during the entire duration of this study. Total effort is an assumption of almost every study. However, if effort was compromised in any matter during testing, it could have potentially skewed and impacted the results of this study. Second, it

was assumed that all participants demonstrated complete honesty with respect to their injuries. Again, honesty is an assumption of almost every study. Lying about additional injuries, medications, diseases/illnesses, or even sleep could have negatively impacted the results of this study. Third, injuries and visual disturbances requiring glassware could worsen oculomotor control. Medications or drugs such as alcohol or caffeine could influence oculomotor control. History of any nerve, inner ear, eye, metabolic, neuromuscular, or balance disorders and even AD/HD could impair oculomotor control. Poor/little sleep, high stress levels, and psychosocial factors could negatively affect oculomotor control. It is important that as many variables were considered as possible for inclusion into this study. These factors could have contributed to the results and pose as a limitation to this study.

5.5 CONCLUSIONS

In conclusion, athletes 24 to 48 hours post-concussion had significantly more anti-saccades, longer anti-saccade durations, and longer average anti-saccade durations when compared to healthy, matched controls. These findings suggest that athletes with concussion are presented with an abnormal oculomotor dysfunction when compared to their matched controls during a dynamic, environmentally-relevant postural assessment, the WiiFit Soccer heading game. Anti-saccades require a continuous inhibitory signal to be present to maintain stable gaze and prevent reflexive gaze deviations away from a fixed point or area of interest. These results may imply that athletes with concussion do not have sufficient gaze stability to adequately navigate through a dynamic environmentally-relevant environment and may be at further risk for injury if returned to play. The assessment of anti-saccades may provide important information

regarding the healthy and integrity of the brain following concussion and could be a candidate marker for concussion.

REFERENCES

1. Bakhos LL, Lockhart GR, Myers R, Linakis JG. Emergency department visits for concussion in young child athletes. *Pediatrics.* 2010;126(3):e550-e556.
2. Langlois JA, Rutland-Brown W, Wald MM. The epidemiology and impact of traumatic brain injury: a brief overview. *The Journal of head trauma rehabilitation.* 2006;21(5):375-378.
3. Meehan WP, 3rd, d'Hemecourt P, Comstock RD. High school concussions in the 2008-2009 academic year: mechanism, symptoms, and management. *The American Journal Of Sports Medicine.* 2010;38(12):2405-2409.
4. Gessel LM, Fields SK, Collins CL, Dick RW, Comstock RD. Concussions among United States high school and collegiate athletes. *Journal Of Athletic Training.* 2007;42(4):495-503.
5. Powell JW, Barber-Foss KD. Traumatic brain injury in high school athletes. *Jama.* 1999;282(10):958-963.
6. Poltavski DV, Biberdorf D. Screening for lifetime concussion in athletes: importance of oculomotor measures. *Brain Injury.* 2014;28(4):475-485.
7. Marar M, McIlvain NM, Fields SK, Comstock RD. Epidemiology of concussions among United States high school athletes in 20 sports. *The American Journal Of Sports Medicine.* 2012;40(4):747-755.
8. Slobounov S, Slobounov E, Sebastianelli W, Cao C, Newell K. Differential rate of recovery in athletes after first and second concussion episodes. *Neurosurgery.* 2007;61(2):338-344.
9. Murray NG, Ambati VNP, Contreras MM, Salvatore AP, Reed-Jones RJ. Assessment of oculomotor control and balance post-concussion: a preliminary study for a novel approach to concussion management. *Brain Injury.* 2014;28(4):496-503.
10. McCrea M, Hammeke T, Olsen G, Leo P, Guskiewicz K. Unreported concussion in high school football players: implications for prevention. *Clinical Journal of Sport Medicine.* 2004;14(1):13-17 15p.
11. Leong DF, Balcer LJ, Galetta SL, Liu Z, Master CL. The King-Devick test as a concussion screening tool administered by sports parents. *The Journal of sports medicine and physical fitness.* 2014;54(1):70-77.
12. McCrory P, Meeuwisse WH, Aubry M, et al. Consensus statement on concussion in sport: the 4th International Conference on Concussion in Sport held in Zurich, November 2012. *British Journal Of Sports Medicine.* 2013;47(5):250-258.
13. Braun PA, Kaminski TW, Swanik CB, Knight CA. Oculomotor Function in Collegiate Student-Athletes With a Previous History of Sport-Related Concussion *Athletic Training & Sports Health Care.* 2013;5(6):7.
14. Shumway-Cook A, Woollacott MH. *Motor Control: Translating Research into Clinical Practice 4th ed.*: Lippincott Williams & Wilkins; 2012.
15. Broglio SP, Collins MW, Williams RM, Mucha A, Kontos AP. Current and Emerging Rehabilitation for Concussion: A Review of the Evidence. *Clinics In Sports Medicine.* 2015;34(2):213-231.
16. Mucha A, Collins MW, Elbin RJ, et al. A Brief Vestibular/Ocular Motor Screening (VOMS) assessment to evaluate concussions: preliminary findings. *The American Journal Of Sports Medicine.* 2014;42(10):2479-2486.

17. Alsalaheen BA, Whitney SL, Mucha A, Morris LO, Furman JM, Sparto PJ. Exercise Prescription Patterns in Patients Treated with Vestibular Rehabilitation After Concussion. *Physiotherapy Research International.* 2013;18(2):100-108.
18. Guskiewicz KM, Mihalik JP, Shankar V, et al. Measurement of Head Impacts in Collegiate Football Players: Relationship Between Head Impact Biomechanics and Acute Clinical Outcome After Concussion. *Neurosurgery.* 2007;61(6):1244-1253.
19. Murray N, Salvatore A, Powell D, Reed-Jones R. Reliability and validity evidence of multiple balance assessments in athletes with a concussion. *J Athl Train.* 2014;49(4):540-549.
20. Kontos AP, Elbin RJ, Schatz P, et al. A revised factor structure for the post-concussion symptom scale: baseline and postconcussion factors. *The American Journal Of Sports Medicine.* 2012;40(10):2375-2384.
21. Alvarez TL, Kim EH, Vicci VR, Dhar SK, Biswal BB, Barrett AM. Concurrent vision dysfunctions in convergence insufficiency with traumatic brain injury. *Optometry And Vision Science: Official Publication Of The American Academy Of Optometry.* 2012;89(12):1740-1751.
22. Ciuffreda KJ, Kapoor N, Rutner D, Suchoff IB, Han ME, Craig S. Occurrence of oculomotor dysfunctions in acquired brain injury: a retrospective analysis. *Optometry.* 2007;78(4):155-161.
23. Master CL, Scheiman M, Gallaway M, et al. Vision Diagnoses Are Common After Concussion in Adolescents. *Clinical pediatrics.* 2016;55(3):260-267.
24. Thiagarajan P, Ciuffreda KJ. Effect of oculomotor rehabilitation on vergence responsivity in mild traumatic brain injury. *Journal of rehabilitation research and development.* 2013;50(9):1223-1240.
25. Pearce KL, Sufrinko A, Lau BC, Henry L, Collins MW, Kontos AP. Near point of convergence after a sport-related concussion: measurement reliability and relationship to neurocognitive impairment and symptoms. *American journal of sports medicine.* 2015;43(12):3055-3061.
26. Thiagarajan P, Ciuffreda KJ, Ludlam DP. Vergence dysfunction in mild traumatic brain injury (mTBI): a review. *Ophthalmic & Physiological Optics: The Journal Of The British College Of Ophthalmic Opticians (Optometrists).* 2011;31(5):456-468.
27. Muir B, Lynn A, Maguire M, et al. A pilot study of postural stability testing using controls: the modified BESS protocol integrated with an H-pattern visual screen and fixed gaze coupled with cervical range of motion. *The Journal of the Canadian Chiropractic Association.* 2014;58(4):361-368.
28. Tjarks BJ, Dorman JC, Valentine VD, et al. Comparison and utility of King-Devick and ImPACT® composite scores in adolescent concussion patients. *Journal Of The Neurological Sciences.* 2013;334(1-2):148-153.
29. Hua LV, Laukkanen HRV, Hayes J, Andre M. Tolerability and effectiveness of contact lenses in mild traumatic brain injury with visual discomfort: A case series. *Optometry & Visual Performance.* 2014;2(1):17-25.
30. Thiagarajan P, Ciuffreda KJ, Capo-Aponte JE, Ludlam DP, Kapoor N. Oculomotor neurorehabilitation for reading in mild traumatic brain injury (mTBI): an integrative approach. *Neurorehabilitation.* 2014;34(1):129-146.
31. Ciuffreda KJ, Ludlam D, Thiagarajan P. Oculomotor diagnostic protocol for the mTBI population. *Optometry (St. Louis, Mo.).* 2011;82(2):61-63.

32. Kaufman DR, Puckett MJ, Smith MJ, Wilson KS, Cheema R, Landers MR. Test-retest reliability and responsiveness of gaze stability and dynamic visual acuity in high school and college football players. *Physical therapy in sport : official journal of the Association of Chartered Physiotherapists in Sports Medicine.* 2014;15(3):181-188.
33. Capó-Aponte JE, Tarbett AK, Urosevich TG, Temme LA, Sanghera NK, Kalich ME. Effectiveness of computerized oculomotor vision screening in a military population: pilot study. *Journal of rehabilitation research and development.* 2012;49(9):1377-1398.
34. Heitger MH, Jones RD, Anderson TJ. A new approach to predicting postconcussion syndrome after mild traumatic brain injury based upon eye movement function. *Conference Proceedings: ... Annual International Conference Of The IEEE Engineering In Medicine And Biology Society. IEEE Engineering In Medicine And Biology Society. Annual Conference.* 2008;2008:3570-3573.
35. King D, Brughelli M, Hume P, Gissane C. Concussions in amateur rugby union identified with the use of a rapid visual screening tool. *Journal Of The Neurological Sciences.* 2013;326(1-2):59-63.
36. Lau BC, Kontos AP, Collins MW, Mucha A, Lovell MR. Which on-field signs/symptoms predict protracted recovery from sport-related concussion among high school football players? *The American Journal Of Sports Medicine.* 2011;39(11):2311-2318.
37. Goodrich GL, Kirby J, Cockerham G, Ingalla SP, Lew HL. Visual function in patients of a polytrauma rehabilitation center: A descriptive study. *Journal of rehabilitation research and development.* 2007;44(7):929-936.
38. Brahm KD, Wilgenburg HM, Kirby J, Ingalla S, Chang CY, Goodrich GL. Visual impairment and dysfunction in combat-injured servicemembers with traumatic brain injury. *Optometry and vision science : official publication of the American Academy of Optometry.* 2009;86(7):817-825.
39. Cockerham GC, Goodrich GL, Weichel ED, et al. Eye and visual function in traumatic brain injury. *Journal of rehabilitation research and development.* 2009;46(6):811-818.
40. Gavett BE, Stern RA, Cantu RC, Nowinski CJ, McKee AC. Mild traumatic brain injury: a risk factor for neurodegeneration. *Alzheimer's Research & Therapy.* 2010;2(3):18-18.
41. Plassman BL, Havlik RJ, Steffens DC, et al. Documented head injury in early adulthood and risk of Alzheimer's disease and other dementias. *Neurology.* 2000;55(8):1158-1166.
42. Leong DF, Balcer LJ, Galetta SL, Evans G, Gimre M, Watt D. The King-Devick test for sideline concussion screening in collegiate football. *Journal of optometry.* 2015;8(2):131-139.
43. Kraus MF, Little DM, Wojtowicz SM, Sweeney JA. Procedural learning impairments identified via predictive saccades in chronic traumatic brain injury. *Cognitive And Behavioral Neurology: Official Journal Of The Society For Behavioral And Cognitive Neurology.* 2010;23(4):210-217.
44. Galetta KM, Barrett J, Allen M, et al. The King-Devick test as a determinant of head trauma and concussion in boxers and MMA fighters. *Neurology.* 2011;76(17):1456-1462.

45. Szymanowicz D, Ciuffreda KJ, Thiagarajan P, Ludlam DP, Green W, Kapoor N. Vergence in mild traumatic brain injury: a pilot study. *Journal of rehabilitation research and development.* 2012;49(7):1083-1100.
46. Johnson B, Zhang K, Hallett M, Slobounov S. Functional neuroimaging of acute oculomotor deficits in concussed athletes. *Brain Imaging And Behavior.* 2014.
47. Wade NJ. Pioneers of eye movement research. *i-Perception.* 2010;1(2):33-68.
48. Kaas JH. The evolution of the complex sensory and motor systems of the human brain. *Brain Research Bulletin.* 2008;75(2-4):384-390.
49. Okonkwo O. King of the Field. *Neurology.* 2014;13.
50. Ventura RE, Balcer LJ, Galetta SL. The Concussion Toolbox: The Role of Vision in the Assessment of Concussion. *Seminars in neurology.* 2015;35(5):599-606.
51. Ventura RE, Jancuska JM, Balcer LJ, Galetta SL. Diagnostic tests for concussion: is vision part of the puzzle? *Journal of neuro-ophthalmology : the official journal of the North American Neuro-Ophthalmology Society.* 2015;35(1):73-81.
52. Ventura RE, Balcer LJ, Galetta SL. The neuro-ophthalmology of head trauma. *The Lancet. Neurology.* 2014;13(10):1006-1016.
53. Ciuffreda KJ, Ludlam DP, Thiagarajan P, Yadav NK, Capo-Aponte J. Proposed objective visual system biomarkers for mild traumatic brain injury. *Mil Med.* 2014;179(11):1212-1217.
54. Suter PS, Harvey LH. *Vision Rehabilitation: Multidisciplinary Care of the Patient Following Brain Injury.* New York: Taylor & Francis Group; 2011.
55. Truong JQ, Ciuffreda KJ, Han MH, Suchoff IB. Photosensitivity in mild traumatic brain injury (mTBI): a retrospective analysis. *Brain Inj.* 2014;28(10):1283-1287.
56. Suchoff IB, Kapoor N, Ciuffreda KJ. Visual & vestibular consequences of acquired brain injuries. Santa Ana, CA :: Optometric Extension Program Foundation; 2001.
57. Zasler ND, Katz DI, Zafonte RD. *Brain Injury Medicine: Principles and Practice.* New York: Demos Medical Publishing; 2007.
58. Clark JF, Graman P, Ellis JK, et al. An Exploratory Study of the Potential Effects of Vision Training on Concussion Incidence in Football. *Optometry & Visual Performance.* 2015;3(2):116-125 110p.
59. Hayes A, Chen CS, Clarke G, Thompson A. Functional improvements following the use of the NVT Vision Rehabilitation program for patients with hemianopia following stroke. *NeuroRehabilitation.* 2012;31(1):19-30.
60. Honaker JA, Criter RE, Patterson JN, Jones SM. Gaze Stabilization Test Asymmetry Score as an Indicator of Previous Concussion in a Cohort of Collegiate Football Players. *Clinical journal of sport medicine : official journal of the Canadian Academy of Sport Medicine.* 2015;25(4):361-366.
61. Heitger MH, Jones RD, Macleod AD, Snell DL, Frampton CM, Anderson TJ. Impaired eye movements in post-concussion syndrome indicate suboptimal brain function beyond the influence of depression, malingering or intellectual ability. *Brain: A Journal Of Neurology.* 2009;132(Pt 10):2850-2870.
62. Pierrot-Deseilligny C, Rivaud S, Gaymard B, Müri R, Vermersch AI. Cortical control of saccades. *Annals Of Neurology.* 1995;37(5):557-567.
63. Lin TP, Adler CH, Hentz JG, Balcer LJ, Galetta SL, Devick S. Slowing of number naming speed by King-Devick test in Parkinson's disease. *Parkinsonism & related disorders.* 2014;20(2):226-229.

64. Murray NG, Ponce de Leon M, Ambati VNP, Saucedo F, Kennedy E, Reed-Jones RJ. Simulated visual field loss does not alter turning coordination in healthy young adults. *Journal of Motor Behavior.* 2014;46(6):423-431 429p.
65. Cifu DX, Wares JR, Hoke KW, Wetzel PA, Gitchel G, Carne W. Differential eye movements in mild traumatic brain injury versus normal controls. *The Journal of head trauma rehabilitation.* 2015;30(1):21-28.
66. Maruta J, Ghajar J. Detecting eye movement abnormalities from concussion. *Progress In Neurological Surgery.* 2014;28:226-233.
67. Mullen SJ, Yücel YH, Cusimano M, Schweizer TA, Oentoro A, Gupta N. Saccadic eye movements in mild traumatic brain injury: a pilot study. *The Canadian Journal Of Neurological Sciences. Le Journal Canadien Des Sciences Neurologiques.* 2014;41(1):58-65.
68. Ramat S, Leigh RJ, Zee DS, Optican LM. What clinical disorders tell us about the neural control of saccadic eye movements. *Brain: A Journal Of Neurology.* 2007;130(Pt 1):10-35.
69. McDowell JE, Dyckman KA, Austin BP, Clementz BA. Neurophysiology and neuroanatomy of reflexive and volitional saccades: evidence from studies of humans. *Brain And Cognition.* 2008;68(3):255-270.
70. Capó-Aponte JE, Urosevich TG, Temme LA, Tarbett AK, Sanghera NK. Visual dysfunctions and symptoms during the subacute stage of blast-induced mild traumatic brain injury. *Military Medicine.* 2012;177(7):804-813.
71. Williams IM, Ponsford JL, Gibson KL, Mulhall LE, Curran CA, Abel LA. Cerebral control of saccades and neuropsychological test results after head injury. *Journal Of Clinical Neuroscience: Official Journal Of The Neurosurgical Society Of Australasia.* 1997;4(2):186-196.
72. Phillipou A, Douglas J, Krieser D, Ayton L, Abel L. Changes in saccadic eye movement and memory function after mild closed head injury in children. *Developmental Medicine And Child Neurology.* 2014;56(4):337-345.
73. Hutton SB. Cognitive control of saccadic eye movements. *Brain And Cognition.* 2008;68(3):327-340.
74. Maruta J, Suh M, Niogi SN, Mukherjee P, Ghajar J. Visual tracking synchronization as a metric for concussion screening. *The Journal of head trauma rehabilitation.* 2010;25(4):293-305.
75. Kraus MF, Little DM, Donnell AJ, Reilly JL, Simonian N, Sweeney JA. Oculomotor function in chronic traumatic brain injury. *Cognitive And Behavioral Neurology: Official Journal Of The Society For Behavioral And Cognitive Neurology.* 2007;20(3):170-178.
76. Crevits L, Hanse MC, Tummers P, Van Maele G. Antisaccades and remembered saccades in mild traumatic brain injury. *Journal Of Neurology.* 2000;247(3):179-182.
77. DeHaan A, Halterman C, Langan J, et al. Cancelling planned actions following mild traumatic brain injury. *Neuropsychologia.* 2007;45(2):406-411.
78. Maruta J, Lee SW, Jacobs EF, Ghajar J. A unified science of concussion. *Annals of the New York Academy of Sciences.* 2010;1208(1):58-66.
79. Galetta MS, Galetta KM, McCrossin J, et al. Saccades and memory: baseline associations of the King-Devick and SCAT2 SAC tests in professional ice hockey players. *J Neurol Sci.* 2013;328(1-2):28-31.

80. Guskiewicz KM. Postural stability assessment following concussion: one piece of the puzzle. *Clinical Journal Of Sport Medicine: Official Journal Of The Canadian Academy Of Sport Medicine.* 2001;11(3):182-189.
81. Maruta J, Heaton KJ, Maule AL, Ghajar J. Predictive visual tracking: specificity in mild traumatic brain injury and sleep deprivation. *Mil Med.* 2014;179(6):619-625.
82. Drew AS, Langan J, Halterman C, Osternig LR, Chou L-S, van Donkelaar P. Attentional disengagement dysfunction following mTBI assessed with the gap saccade task. *Neuroscience Letters.* 2007;417(1):61-65.
83. Heitger MH, Anderson TJ, Jones RD. Saccade sequences as markers for cerebral dysfunction following mild closed head injury. *Progress In Brain Research.* 2002;140:433-448.
84. Ting WK, Schweizer TA, Topolovec-Vranic J, Cusimano MD. Antisaccadic Eye Movements Are Correlated with Corpus Callosum White Matter Mean Diffusivity, Stroop Performance, and Symptom Burden in Mild Traumatic Brain Injury and Concussion. *Frontiers in neurology.* 2015;6:271.
85. Giza CC, Difiori JP. Pathophysiology of sports-related concussion: an update on basic science and translational research. *Sports Health.* 2011;3(1):46-51.
86. Giza CC, Hovda DA. The Neurometabolic Cascade of Concussion. *Journal Of Athletic Training.* 2001;36(3):228-235.
87. Giza CC, Kutcher JS, Ashwal S, et al. Summary of evidence-based guideline update: evaluation and management of concussion in sports: report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology.* 2013;80(24):2250-2257.
88. Biscaldi M, Fischer B, Stuhr V. Human express saccade makers are impaired at suppressing visually evoked saccades. *Journal Of Neurophysiology.* 1996;76(1):199-214.
89. Thiagarajan P, Ciuffreda KJ. Versional eye tracking in mild traumatic brain injury (mTBI): effects of oculomotor training (OMT). *Brain Injury.* 2014;28(7):930-943.
90. Halbauer JD, Ashford JW, Zeitzer JM, Adamson MM, Lew HL, Yesavage JA. Neuropsychiatric diagnosis and management of chronic sequelae of war-related mild to moderate traumatic brain injury. *Journal of rehabilitation research and development.* 2009;46(6):757-796.
91. Benedict PA, Baner NV, Harrold GK, et al. Gender and age predict outcomes of cognitive, balance and vision testing in a multidisciplinary concussion center. *J Neurol Sci.* 2015;353(1-2):111-115.
92. Abrams RA, Oonk HM, Pratt J. Fixation point offsets facilitate endogenous saccades. *Perception & Psychophysics.* 1998;60(2):201-208.
93. Forbes K, Klein RM. The magnitude of the fixation offset effect with endogenously and exogenously controlled saccades. *Journal Of Cognitive Neuroscience.* 1996;8(4):344-352.
94. Sussman ES, Ho AL, Pendharkar AV, Ghajar J. Clinical evaluation of concussion: the evolving role of oculomotor assessments. *Neurosurgical focus.* 2016;40(4):E7.
95. Briggs F, Mangun GR, Usrey WM. Attention enhances synaptic efficacy and the signal-to-noise ratio in neural circuits. *Nature.* 2013;499(7459):476-480.
96. Posner MI. Orienting of attention. *The Quarterly Journal Of Experimental Psychology.* 1980;32(1):3-25.

97. Mucha A, Collins MW, French J. Augmenting neurocognitive assessment in the evaluation of sports concussion: how vestibular and ocular issues impact recovery. *Brain Injury Professional.* 2012;9(1):12-16.
98. Corbetta M. Frontoparietal cortical networks for directing attention and the eye to visual locations: identical, independent, or overlapping neural systems? *Proceedings Of The National Academy Of Sciences Of The United States Of America.* 1998;95(3):831-838.
99. Pratt J, Bekkering H, Abrams RA, Adam J. The Gap effect for spatially oriented responses. *Acta Psychologica.* 1999;102(1):1-12.
100. Suh M, Kolster R, Sarkar R, McCandliss B, Ghajar J. Deficits in predictive smooth pursuit after mild traumatic brain injury. *Neuroscience Letters.* 2006;401(1-2):108-113.
101. Hanes DP, Carpenter RH. Countermanding saccades in humans. *Vision Research.* 1999;39(16):2777-2791.
102. Barnett BP, Singman EL. Vision concerns after mild traumatic brain injury. *Current Treatment Options In Neurology.* 2015;17(2):329-329.
103. Lei-Rivera L, Sutera J, Galatioto JA, Hujsak BD, Gurley JM. Special tools for the assessment of balance and dizziness in individuals with mild traumatic brain injury. *Neurorehabilitation.* 2013;32(3):463-472.
104. Nobre AC, Sebestyen GN, Gitelman DR, Mesulam MM, Frackowiak RS, Frith CD. Functional localization of the system for visuospatial attention using positron emission tomography. *Brain: A Journal Of Neurology.* 1997;120 (Pt 3):515-533.
105. Posner MI, Petersen SE. The attention system of the human brain. *Annual Review Of Neuroscience.* 1990;13:25-42.
106. Yadav NK, Thiagarajan P, Ciuffreda KJ. Effect of oculomotor vision rehabilitation on the visual-evoked potential and visual attention in mild traumatic brain injury. *Brain Injury.* 2014;28(7):922-929.
107. Samadani U, Ritlop R, Reyes M, et al. Eye tracking detects disconjugate eye movements associated with structural traumatic brain injury and concussion. *Journal Of Neurotrauma.* 2015;32(8):548-556.
108. King D, Clark T, Gissane C. Use of a rapid visual screening tool for the assessment of concussion in amateur rugby league: a pilot study. *Journal Of The Neurological Sciences.* 2012;320(1-2):16-21.
109. Smith DH, Meaney DF, Shull WH. Diffuse axonal injury in head trauma. *The Journal of head trauma rehabilitation.* 2003;18(4):307-316.
110. Galetta KM, Brandes LE, Maki K, et al. The King-Devick test and sports-related concussion: study of a rapid visual screening tool in a collegiate cohort. *Journal Of The Neurological Sciences.* 2011;309(1-2):34-39.
111. Barker JM, Wright DW, Goldstein FC, Ockerman J, Ratcliff JJ, Laplaca MC. The DETECT system: portable, reduced-length neuropsychological testing for mild traumatic brain injury via a novel immersive environment. *Journal Of Medical Engineering & Technology.* 2007;31(3):161-169.
112. Shumway-Cook A, Horak FB. Assessing the influence of sensory interaction of balance. Suggestion from the field. *Physical Therapy.* 1986;66(10):1548-1550.
113. Chang JO, Levy SS, Seay SW, Goble DJ. An alternative to the balance error scoring system: using a low-cost balance board to improve the validity/reliability of sports-

related concussion balance testing. *Clinical Journal Of Sport Medicine: Official Journal Of The Canadian Academy Of Sport Medicine.* 2014;24(3):256-262.
114. Guskiewicz KM. Balance assessment in the management of sport-related concussion. *Clinics In Sports Medicine.* 2011;30(1):89.
115. Goble DJ, Coxon JP, Van Impe A, et al. Brain activity during ankle proprioceptive stimulation predicts balance performance in young and older adults. *The Journal Of Neuroscience: The Official Journal Of The Society For Neuroscience.* 2011;31(45):16344-16352.
116. Guskiewicz KM, Perrin DH, Gansneder BM. Effect of mild head injury on postural stability in athletes. *Journal Of Athletic Training.* 1996;31(4):300-306.
117. Cavanaugh JT, Guskiewicz KM, Stergiou N. A nonlinear dynamic approach for evaluating postural control: new directions for the management of sport-related cerebral concussion. *Sports Medicine (Auckland, N.Z.).* 2005;35(11):935-950.
118. Clark RA, Bryant AL, Pua Y, McCrory P, Bennell K, Hunt M. Validity and reliability of the Nintendo Wii Balance Board for assessment of standing balance. *Gait & Posture.* 2010;31(3):307-310.
119. Huurnink A, Fransz DP, Kingma I, van Dieën JH. Comparison of a laboratory grade force platform with a Nintendo Wii Balance Board on measurement of postural control in single-leg stance balance tasks. *Journal Of Biomechanics.* 2013;46(7):1392-1395.
120. Nashner LM, Black FO, Wall C, 3rd. Adaptation to altered support and visual conditions during stance: patients with vestibular deficits. *The Journal of neuroscience : the official journal of the Society for Neuroscience.* 1982;2(5):536-544.
121. Bell DR, Guskiewicz KM, Clark MA, Padua DA. Systematic review of the balance error scoring system. *Sports Health.* 2011;3(3):287-295.
122. Finnoff JT, Peterson VJ, Hollman JH, Smith J. Intrarater and interrater reliability of the Balance Error Scoring System (BESS). *PM & R: The Journal Of Injury, Function, And Rehabilitation.* 2009;1(1):50-54.
123. Hunt TN, Ferrara MS, Bornstein RA, Baumgartner TA. The reliability of the modified Balance Error Scoring System. *Clinical Journal Of Sport Medicine: Official Journal Of The Canadian Academy Of Sport Medicine.* 2009;19(6):471-475.
124. McCrea M, Barr WB, Guskiewicz K, et al. Standard regression-based methods for measuring recovery after sport-related concussion. *Journal Of The International Neuropsychological Society: JINS.* 2005;11(1):58-69.
125. Yamada M, Aoyama T, Nakamura M, et al. The reliability and preliminary validity of game-based fall risk assessment in community-dwelling older adults. *Geriatric Nursing (New York, N.Y.).* 2011;32(3):188-194.
126. Holmes JD, Jenkins ME, Johnson AM, Hunt MA, Clark RA. Validity of the Nintendo Wii® balance board for the assessment of standing balance in Parkinson's disease. *Clinical Rehabilitation.* 2013;27(4):361-366.
127. DeMatteo C, Greenspoon D, Levac D, Harper JA, Rubinoff M. Evaluating the Nintendo Wii for assessing return to activity readiness in youth with mild traumatic brain injury. *Physical & occupational therapy in pediatrics.* 2014;34(3):229-244.
128. Ramchandani A, Carroll A, Buenaventura R, Douglas J, Liu J. Wii-habilitation increases participation in therapy. Paper presented at: 2008 Virtual Rehabilitation; 25-27 Aug. 2008, 2008.

129. Deutsch JE, Borbely M, Filler J, Huhn K, Guarrera-Bowlby P. Use of a low-cost, commercially available gaming console (Wii) for rehabilitation of an adolescent with cerebral palsy. *Phys Ther.* 2008;88(10):1196-1207.
130. Weiss PL, Rand D, Katz N, Kizony R. Video capture virtual reality as a flexible and effective rehabilitation tool. *Journal Of Neuroengineering And Rehabilitation.* 2004;1(1):12-12.