The role of eye movement dysfunction in concussion

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Concussion, mild traumatic brain injury, visual and oculomotor systems, eyes, sports injuries, eye movements, visual dysfunction, concussion assessment tools, visual tools, symptom recovery, neuro-ophthalmology, orthoptics

Abstract

Introduction

The concussion epidemic is a serious concern. Affected athletes may suffer debilitating neurological sequalae, impacting both their in-game performances and quality of life. Currently, a wide range of neurocognitive tests examining memory, balance and manifesting symptomology are used to aid a physician in the diagnosis of a concussion. However, considering up to 82% of those who suffer an episode experience some form of visual dysfunction, there is very little to no assessment of this on the sideline within Australian professional sport.

Methods

Four distinct studies were conducted to explore the role of eye movement dysfunction in concussion, using various visual instruments. The first three studies (Chapters 3 to 5) involved rugby union athletes from a semi-professional club in Sydney. Chapter 6 represents a retrospective study of medical records of children referred by physicians from across New South Wales and Australian Capital Territory to a tertiary outpatient paediatric sport and exercise hospital clinic in Sydney.

Results

Evaluation of a popular visual-based assessment device, the King-Devick test, indicated up to 30 attempts are required to obtain a ceiling effect. Analysis on 183 rugby athletes show a median improvement of 4.2 seconds from a player's first

attempt at the test to their overall best score. Considering only two attempts are currently recommended to constitute a baseline score, the data reveals that six to eight are needed for greater reliability.

Using digital eye-tracking techniques, experienced rugby athletes demonstrate superior eye movements compared to the normal population. Over 78% of players exhibited faster smooth pursuits, while over 73% produce more saccades. Previous history of concussion within the last 12 months demonstrate no impact on these conjugate eye movements.

Assessment of nine concussions in the acute phase using an orthoptic tool, the Royal Air Force (RAF) Rule, demonstrated 89% with reduced accommodative amplitudes and 33% with receded convergence. In a retrospective review of 142 medical records of paediatric patients with concussion, 28% had concussion-related visual dysfunction. These patients took a mean 24.5 days longer to recover from symptoms, compared to those without visual impairment. Females took a mean 21.3 days longer to recover than males, with 32% of all episodes related to rugby.

Conclusions

This PhD research has contributed knowledge regarding the importance of eye movement assessments within the concussion paradigm. Such tools demonstrate the ability to aid physicians with pre-injury baseline testing, post-injury diagnosis and a predictor of symptom recovery in athletic cohorts. The utility of these tools and areas for future development, have all been described.

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List of Abbreviations

AC/A	Accommodative Convergence-Accommodation
ADHD	Attention Deficit Hyperactivity Disorder
ANOVA	Analysis of Variance
ATP	Adenosine Triphosphate
BESS	Balance Error Scoring System
BGC	Brainstem Gaze Centre
BMI	Body Mass Index
CI	Confidence Intervals
cm	Centimeters
CN	Caudate Nucleus
CRI	Concussion Resolution Index
CRT	Concussion Recognition Tool
CT	Computed Tomography
CTE	Chronic Traumatic Encephalopathy
D	Diopters
DEM	Developmental Eye Movement
DLPC	Dorsolateral Prefrontal Cortex
F	Focal Point
FEF	Frontal Eye Fields
fMRI	Functional Magnetic Resonance Imaging
GEE	Generalised Estimating Equation
GCS	Glasgow Coma Scale
ICC	Intra Class Coefficient

ImPACT	Immediate Post-Concussion Assessment and Cognitive Testing
KDT	King-Devick Test
LOC	Loss of Consciousness
MRI	Magnetic Resonance Imaging
Ms	Millisecond
mTBI	Mild Traumatic Brain Injury
NFL	National Football League
NMDA	N-methyl-D-aspartate
NPC	Near Point of Convergence*
NSUCO	North-Eastern State University College of Optometry
PCSS	Post-Concussion Symptom Scale
PEF	Parietal Eye Fields
RAF	Royal Air Force
RTP	Return-To-Play
SAC	Standardized Assessment of Concussion
SC	Superior Colliculus
SCAT	Sport Concussion Assessment Tool
SEF	Secondary Eye Fields
SRC	Sports-Related Concussion
TBI	Traumatic Brain Injury
USA	United States of America
VOMS	Vestibular/Ocular Motor Screening
WHO	World Health Organisation

*Referred to as convergence near point (CNP) in the ophthalmic literature. However, as papers have been published in sports medicine journals where near point of convergence (NPC) is commonly used, it will be referred as NPC throughout this thesis.

Overview of Thesis

This body of work, completed during my High Degree Research candidature, is presented in the format of thesis by compilation. In order to facilitate reading, the following overview provides an outline of my thesis's structure and brief description of each chapter. Chapter 3 has been published in the *Journal of Neurological Science* in 2020. The remaining results chapters (4 to 6) have been written in the format of articles prepared for submission. Finally, Chapter 7 provides an overall summary and conclusion to the thesis.

Chapter 1: Literature Review

The first thematic section of this thesis is a comprehensive review of the literature on concussion. It encompasses a wide range of studies identified through a search of databases, including Google Scholar, PubMed and Web of Science. Beginning with an overview of concussion as a global concern, the controversy surrounding the definition of concussion is then discussed, along with the worldwide and Australian prevalence of concussion and its pathophysiology.

The review then highlights the clinical features associated with concussion and summaries the current evidence on popular sideline diagnostic tools, before discussing the various causes of underreporting symptoms. It then focuses on the neurological impact following concussion, with a greater focus on two distinct conditions salient in the media, second impact syndrome and chronic traumatic encephalopathy.

Finally, the literature review covers the evidence for oculomotor dysfunction following concussion including describing the research of visual tools used for the detection of concussion, such as the King-Devick Test (KDT), Royal Air Force (RAF) Rule and Vestibular/Oculomotor Screening (VOMS) tool. Gaps within the literature surrounding these tools and areas for future research are addressed. A part of this chapter is an invited article with the candidate as first author, published in 2019 by the *Australian Journal of General Practice* (Appendix B).

Chapter 2: Methods

This chapter presents the methodological protocols for the subsequent studies conducted on the sporting sideline and in the field (Chapters 3 to 5) or hospital setting (Chapter 6). It discusses in detail sampling strategies and the sample size utilised, methods of data analysis and how each visual test was administered. It concludes with a brief discussion on the ethical considerations, as well as problems encountered during the project.

Chapter 3: The Learning Effect of the King-Devick Test

The next thematic section (Chapters 3 to 5) examines a number of visual tools in a cohort of rugby athletes in Sydney. Chapter 3 presents findings regarding the utility of the KDT during baseline testing. It observes the learning effect associated with repeated testing and aims to identify a point at which further repeated testing no longer improves the KDT score. There is discussion of the need for updating

standardised protocols recommended by the KDT manufacturers, to improve diagnostic procedures and patient care.

Chapter 4: Comparing the Smooth Pursuit and Saccadic Eye Movements in Rugby Players to a Normative Database

Chapter 4 evaluates the RightEye Neurovision test, a digital eye-tracking device, on top division teams from a Sydney rugby club. Normative saccadic and smooth pursuit eye movement measures in these athletes are compared to a normative database provided by the RightEye company. Associations with concussion history and age were explored. Findings highlighted the need for individual pre-injury baseline testing in order to increase reliability in the detection of concussion using this device.

Chapter 5: Post-concussive Convergence and Accommodative Dysfunction in Australian Rugby Union Athletes

In a cohort of semi-professional rugby athletes, Chapter 5 compares baseline visual functions (i.e. convergence and accommodation) to post-concussion measurements. It establishes any association with age, playing position, concussion history and previous history of double vision. This chapter aims to improve the concussion diagnostic battery with the addition of orthoptic testing on the sporting sideline.

Chapter 6: Concussion-Related Visual Dysfunction in Children: A Retrospective Study

This final results chapter explores various predictors of recovery in children with concussion, aged between 5 and 18. It examines associations of concussion-related visual dysfunction with age, sex, symptoms and history of concussion primarily using the VOMS testing. The chapter addresses possible improvements to aspects of current paediatric concussion examination protocols used by physicians and looks to aid the development of strong and targeted recovery plans.

Chapter 7: Discussion and Conclusion

This chapter summarises the findings of this thesis and addresses areas for future research.

Publications, Presentations, Awards and Honours

Publications

Gunasekaran P, Hodge C, Rose K, Fraser CL. Persistent visual disturbances after concussion. Australian journal of general practice. 2019 Aug 48(8):531.

Gunasekaran P, Hodge C, Pearce A, King D, Fraser C. A review of concussion diagnosis and management in Australian professional sporting codes. The Physician and Sportsmedicine. 2019 Jun 6:1-7.

Gunasekaran P, Fraser CL, Hodge C. The learning effect of the King-Devick test in semi-professional rugby union athletes. Journal of the Neurological Sciences. 2020 Oct 2:117168.

Conference Presentations

The list of international and domestic conference presentations has been given by the candidate. It represents data gathered during candidature.

International

Gunasekaran P, Fraser C, Cohen A, Hodge C. (2018) Comparing the smooth pursuit and saccadic eye movements in rugby players to a normative database. *The North American Neuro-Ophthalmology Society (NANOS) 44th Annual Scientific Meeting*. Waikoloa, Hawaii, USA

Gunasekaran P, Hodge C, Fraser C, Cohen A, Rose KA. (2018) Incorporating ocular assessment in diagnosis of sports-related concussion (SRC) in semi-professional rugby union players. *The Association for Research in Vision and Ophthalmology*. Honolulu, Hawaii, USA: IOVS

Gunasekaran P, Hodge C, Browne G, Fraser C, Rose KA. (2019) Concussion-Related Visual Dysfunction in Children: A Retrospective Study. *The Association for Research in Vision and Ophthalmology*. Vancouver, Canada: IOVS

Gunasekaran P, Hodge C, Browne G, Fraser C, Rose KA. (2019) Vision Problems in Children with Concussion. *American Association for Pediatric Ophthalmology and Strabismus (AAPOS)*. Sydney, Australia

Domestic Conferences

Gunasekaran P, Fraser C, Pearce A, King D, Cohen A, Hodge C. (2017) Comparing the smooth pursuit and saccadic eye movements in rugby players to a normative database. *Neuro-Ophthalmology Society of Australia (NOSA)*, 33rd Annual Meeting, Sydney, Australia.

Gunasekaran P, Hodge C, Fraser C, Rose KA. (2017) Concussion: An orthoptist's role. *73rd Orthoptics Australia Annual Scientific Conference*, Perth, Australia.

Gunasekaran P, Hodge C, Fraser C, Rose KA. (2018) "Crouch, Touch, Pause, Engage": Using a Visual Tool to Detect Concussion in Rugby Union. *74th Orthoptics Australia Annual Scientific Conference*, Adelaide, Australia.

Gunasekaran P (2019) Concussion and Ocular Consequences. 1st Orthoptics Australia (NSW Branch) *A Focus on Orthoptics in Neurology Symposium*, Sydney, Australia.

Gunasekaran P, Hodge C, Browne G, Fraser C, Rose KA. (2019) "Won't somebody please think of the children?". *75th Orthoptics Australia Annual Scientific Conference*, Sydney, Australia.

Awards and Honours

Australian Government Research Training Program Stipend - Australian Government Research Training Program Stipend, 2017

"Determining the effect of concussion on the visual and oculomotor system", Orthoptics Australia Research Grant, 2018

Emmie Russel Prize at the 74th Orthoptics Australia Annual Scientific Conference, Adelaide, Australia, 2018

Interview for MD Magazine: https://www.mdmag.com/conference-coverage/arvo-2019/concussionrelated-visual-dysfunction-linked-to-longer-recovery-time and video https://www.youtube.com/watch?v=VzaSD6eOZTk

Conference Chair at the 76th Orthoptics Australia Annual Conference (Session 6: Cataract), 2019

Statement of Original Authorship

CERTIFICATE OF ORIGINAL AUTHORSHIP

I Premkumar Gunasekaran declare that this thesis, is submitted in fulfilment of the requirements for the award of Doctor of Philosophy, in the Graduate School of Health at the University of Technology Sydney.

This thesis is wholly my own work unless otherwise referenced or acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis.

This document has not been submitted for qualifications at any other academic institution.

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Signature of Student:

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Signature removed prior to publication.

Date: 18/01/2021

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Chapter 1: Literature Review

The concussion epidemic is emerging as a serious concern. In 2016, Newcastle Knights winger James McManus was forced to medically retire from the National Rugby League after suffering up to ten episodes of concussion in his illustrious 166-game career. This led to him sustaining permanent brain damage and the consequent impairment of his mental and physical functioning which persists today.[1] Currently, Mr. McManus is heavily involved in one of dozens of longstanding legal battles, due to inadequate detection and management of concussion within the global sporting industry.[2,3] His story is not unique, however, not enough has been done to prevent such cases from reoccurring. Health professionals need to do better, and this thesis represents my attempt to address a small part of this looming crisis in the health of those who have received a concussion/s in their sporting life.

1.1 TRAUMATIC BRAIN INJURIES

The brain and its supporting structures make up a complex anatomical and physiological network. Any disruption can have a disastrous outcome on a person's overall neurological health. In recent years, traumatic brain injuries (TBI) have emerged in the scientific literature as one of the most prominent causes of such neurological disruption.[4-6] Such attention has led to advancements in detection, management and, in some cases, recovery.

TBI can be categorised into severe, moderate and mild.[7] All categories are typically caused by a blow to head or surrounding structures like the neck that can lead to the brain becoming torn, stretched, penetrated, bruised or swollen. This is commonly known to occur as a consequence of direct or indirect head injury caused by traumatic events such as personal violence, vehicle collisions, falls and sports accidents, the latter having become a more recent focus of concern.

Whilst there are several studies addressing the ramifications of these injuries on normal neurological functioning, such as in post-traumatic syndrome, traumatic encephalopathy syndrome, and chronic traumatic encephalopathy, [8-11] there is a paucity of information relating to the detection, management and recovery from such injury. The focus of this thesis is on mild traumatic brain injuries (mTBI), particularly concussion, arising from sporting activities.

1.2 CONCUSSION

1.2.1 Definition

Unlike the other forms of TBI, the definition of concussion remains controversial, with over 45 working definitions worldwide.[12] According to the Centres for Disease Control and Prevention,[13] a concussion is a "*form of traumatic brain injury caused by a hit to the head or body that causes the brain to move rapidly back and forth*". A singular concussive episode is not routinely considered life threatening or causing permanent injury and therefore it is often classified as a mTBI, although it is argued that in light of recent studies of long-term effects, this may be misleading.[14]

The terms concussion and mTBI are not considered synonymous. Kamins and Giza stated that a mTBI refers to a neurological event, historically based on the Glasgow Coma Score (GCS).[15] This a scale of up to 15, used by physicians to indicate a patient's level of consciousness and to categorise the severity of the TBI based on their score.[16] Concussion, however, is considered to be a clinical syndrome involving a variety of temporary non-specific signs and symptoms that may overlap with mild, moderate and severe TBI.[15] As opposed to TBI, concussions typically heal spontaneously over time, and in some cases, may remain completely asymptomatic.[17]

In the sporting context, the Concussion in Sport Group from the 5th International Conference on Sport refer to concussion as "*a traumatic brain injury induced by biomechanical forces*" (complete definition in Box 1).[18] While this states the mechanism of injury, the remainder of the definition focuses on defining concussion as a functional disturbance. In this context, routine neuroimaging techniques find

little in the way of structural abnormalities to the brain, yet functional deficits can occur.[18,19] While this statement provides the most well-accepted and succinct definition of concussion, there is some dispute about whether it is completely accurate.[20] Abnormal protein deposits have been detected in the brains of American football players with a history of concussion when tested port-mortem,[21] implying that there may be a structural component to the condition.

In Australia, concussion is defined in accordance with the 2016 Concussion in Sport Group's definition which is reflected in the "Concussion in Sport Australia Position Statement".[22] Supported by the Australian Institute of Sport, Australian Medical Association, Australasian College of Sport and Exercise Physicians and Sports Medicine Australia, this statement outlines the guidelines used by many Australian professional sporting organisations and provides an overview of the current literature on concussion. Despite the concordance regarding this statement, the definition of concussion used by sporting organisations differs from that used by hospital emergency and trauma departments.

According to Bazarian *et al*.[23] "*the most widely accepted clinical definition of concussion is based on definitions proposed by the Centres for Disease Control and Prevention and World Health Organization (WHO)*".[23] This definition includes in its criteria a GCS score of 13 to 15, determined 30 minutes after suffering a head injury or when presenting to a healthcare professional. In addition, the patient must manifest at least one of the following clinical features: any loss of consciousness (LOC), post-traumatic amnesia immediately after sustaining the injury, alteration in

mental state post-injury, or any neurological deficit that may or may not be transient.

With no universally accepted definition, this makes epidemiological research on the prevalence and incidence of concussion difficult. It also may affect comparability of studies with some patients who fit one study's inclusion criteria excluded in another. The definition of concussion is constantly evolving and being regularly updated in contemporary literature. Therefore, the definitions presented in this thesis may be obsolete in a decade's time. However, as this thesis is focused on concussion in sport, the Concussion in Sport Group's definition[18] will be used throughout this thesis (see Box 1).

Definition
Sport related concussion (SRC) is a traumatic brain injury induced by biomechanical forces. Several common features that may be utilised in clinically defining the nature of a concussive head injury include: • SRC may be caused either by a direct blow to the head, face, neck or elsewhere on the body with an impulsive force transmitted to the head. • SRC typically results in the rapid onset of short-lived impairment of neurological function that resolves spontaneously. However, in some cases, signs and symptoms evolve over a number of minutes to hours. • SRC may result in neuropathological changes, but the acute clinical signs and symptoms largely reflect a functional disturbance rather than a structural injury and, as such, no abnormality is seen on standard structural neuroimaging studies. • SRC results in a range of clinical signs and symptoms that may or may not involve loss of consciousness. Resolution of the clinical and cognitive features typically follows a sequential course. However, in some cases symptoms may be prolonged. The clinical signs and symptoms cannot be explained by drug, alcohol, or medication use, other injuries (such as cervical injuries, peripheral vestibular dysfunction, etc.) or other comorbidities (e.g. psychological factors or coexisting medical conditions).

Box 1. Full definition of sports-related concussion as per the Consensus statement on concussion in sport—the 5th international conference on concussion in sport held in Berlin, October 2016. Extracted from McCrory *et al.*[18]

1.2.2 Epidemiology

International Epidemiology of TBI and Concussion

Every year, an estimated 57 million people sustain a TBI worldwide,[24] with almost 75% of those diagnosed with concussion.[25] While there is poor reporting of concussions and variation in the clinical definitions used,[26-28] it is thought that more than 6 per 1,000 people are affected by concussion annually.[25] Concussion is therefore, the most common form of any TBI reported in the literature.[24,25,29,30]

In the sport context, concussion makes up roughly 5% of all sporting injuries,[31] with the majority occurring in patients aged 15 to 64 years.[32] Recreation and sports activities, such as football, rugby, basketball and hockey have high reported rates of concussion, reflecting that these sports involve a high rate of physical contact and collisions.[33-36] However, concussion is also emerging as a significant concern in non-contact sports like cricket,[37-39] equestrian events[40,41] and even cheerleading,[42] which sits at the boundary between what is seen as a sport versus an artistic display. Overall, the sports medicine literature reflects the varying degrees of head injury inherent in different sports.[43]

Despite a large focus on the more apparently vulnerable sporting groups, there remains some variation in findings between studies and the populations they sample. Some researchers have recorded higher rates of concussion in high school groups than collegiate,[44,45] while others have found the reverse.[46,47] These age-related data reveal conflicting findings in studies, probably due to differences in research methodology. For example, some studies gathered epidemiological data

through surveying athletic trainers,[48,49] while others obtain information directly from the players themselves.[47,50]

In addition to investigations on youth athletes, there is a growing body of sports literature involving concussion affecting professional athletes as well,[51-53] with 165 and 124 concussions documented over nine playing seasons in the English Premier League and Major League Soccer competitions respectively.[54] In professional rugby, the overall incidence of concussion has been calculated at 4.1 injuries per 1000 player hours, making concussion the third most common playing injury sustained by these athletes.[52]

However, there is evidence that sports-related concussions (SRC) is not always treated medically, due to the failure of athletes to seek medical attention. A study of professional Danish ice-hockey athletes indicated that only 8% of concussions sustained were actually seen by a trained physician, compared to 72% of total knee injuries.[55] This highlights the challenge many health professionals have in trying to improve poor reporting rates witnessed in SRC compared to other, more obvious, sporting injuries.

Epidemiology: Concussion in Australia

In Australia, the overall prevalence of concussion continues to remain unknown. Victorian state data suggest that between 2002 and 2011, the frequency of reported concussions increased by 60.5%, leading to an annual incidence of almost 5,000 hospitalisations from sporting events alone.[56] This equated to an estimated

total hospital cost of $18 million over the nine year period, representing a significant public health and economic concern.

In Australian contact sport research, very few studies have been conducted to calculate the incidence rates of concussion. Australian Rules Football groups have demonstrated high rates, ranging between 0.4 – 4.3 concussions per 1000 match hours.[57-59] While in rugby union, this has been recorded slightly higher at 4.7 per 1000 match hours.[60] In combat sports like boxing, concussion was found to be the second most common injury after ocular injuries (45.8%), accounting for almost 16% of injuries sustained and equating to 39.8 injuries per 1000 fight participations.[61] With a recent increase in popularity and participation in combat sports, researchers have designed structured return-to-play (RTP) protocols to minimise the risk of these athletes experiencing repeated trauma.[62]

However, despite the common misconception, the rates of concussion in non-contact sports such as elite-level of cricket are also quite substantial, ranging between 0.4 – 0.5 per 1000 match hours.[38] SRC accounted for 2.9% of the total injuries sustained over a 68 cricket match competition, although the highest rates of injury were recorded in the shoulder (12.4%), lower back (11.7%) and knee (11.7%).[37]

1.2.3 Pathophysiology

Like the definition of concussion, its pathophysiology is another aspect that has not achieved consensus within the medical literature. Following injury, the brain is recognised to undergo significant biomechanical and physiological stresses at the

neuronal level. This process represents a neuro-metabolic cascade consisting of acute changes in ion fluxes, metabolism and blood flow in the brain which ultimately lead to perturbation of neuronal homeostatic balances (Figure 1.1).[63,64]

Following the biomechanical trauma, the sudden axonal and neuronal stretching initiates a significant increase in extracellular potassium concentrations through previously regulated ion channels. This process causes the widespread release of neurotransmitters, such as excitatory amino acids, which further dysregulates ionic homeostasis.[65] These excitatory amino acids, particularly glutamate, bind to N-methyl-d-aspartate (NMDA) receptors, along with kainite and D-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid ionic channels. NMDA receptor activation results in a potassium efflux, causing cell depolarisation and neuronal activity suppression.[63,66]

This process is followed by a massive influx of calcium ions into the cell, known as "mitochondrial calcium overloading".[67-69] Disrupting mitochondrial function, the calcium overload results in the production of reactive oxidative species which induce cell-wide oxidative stress. Vagnozzi *et al*.[70] showed in rat models that this can occur within the first minute following trauma and can last for up to 48 hours post-injury. During this phase, the neural cell has less adenosine triphosphate (ATP) production, inhibiting the sodium-potassium pump and leaving it in a period of metabolic depression.[64]

To restore pre-trauma ionic homeostasis, the sodium-potassium pump must increase in activity, although this requires a high level of glucose consumption to

sustain the required energy demand. Under normal aerobic conditions, the consumption of glucose is coupled with oxygen usage for optimal ATP production. However, due to the damage sustained from calcium overloading and reactive oxidative stress, these mitochondrial functions are temporarily impaired. This leads to high lactate concentrations accumulating within the cell, while a corresponding reduction in cerebral blood flow results in a cellular "energy crisis".[71]

During the later acute stage up to 24 to 48 hours after injury, the human cerebral blood flow has been demonstrated to decrease in various regions of the brain, including the left inferior parietal lobule, right supramarginal gyrus, right middle frontal gyrus, posterior cingulate cortex, left occipital gyrus and thalamus. These changes have been correlated to poorer neurocognitive testing scores in affected individuals when compared to healthy controls.[72]

Furthermore, cerebral autoregulation has been found to be impaired following injury for up to two weeks,[73,74] suggesting neurometabolic imbalances may persist well after symptom recovery.

Studies by Yoshino *et al*.[75] and Sunami *et al*.[76] have indicated that the neuron is left in a hypometabolic state following mitochondrial dysfunction that may persist for up to one month. Further research later found that mTBI can cause meningeal vascular injury and cell death that spreads into the brain parenchyma, causing local inflammation for two to three weeks.[77] However, the research on the pathophysiology of concussion is limited with only a handful of human-based studies.

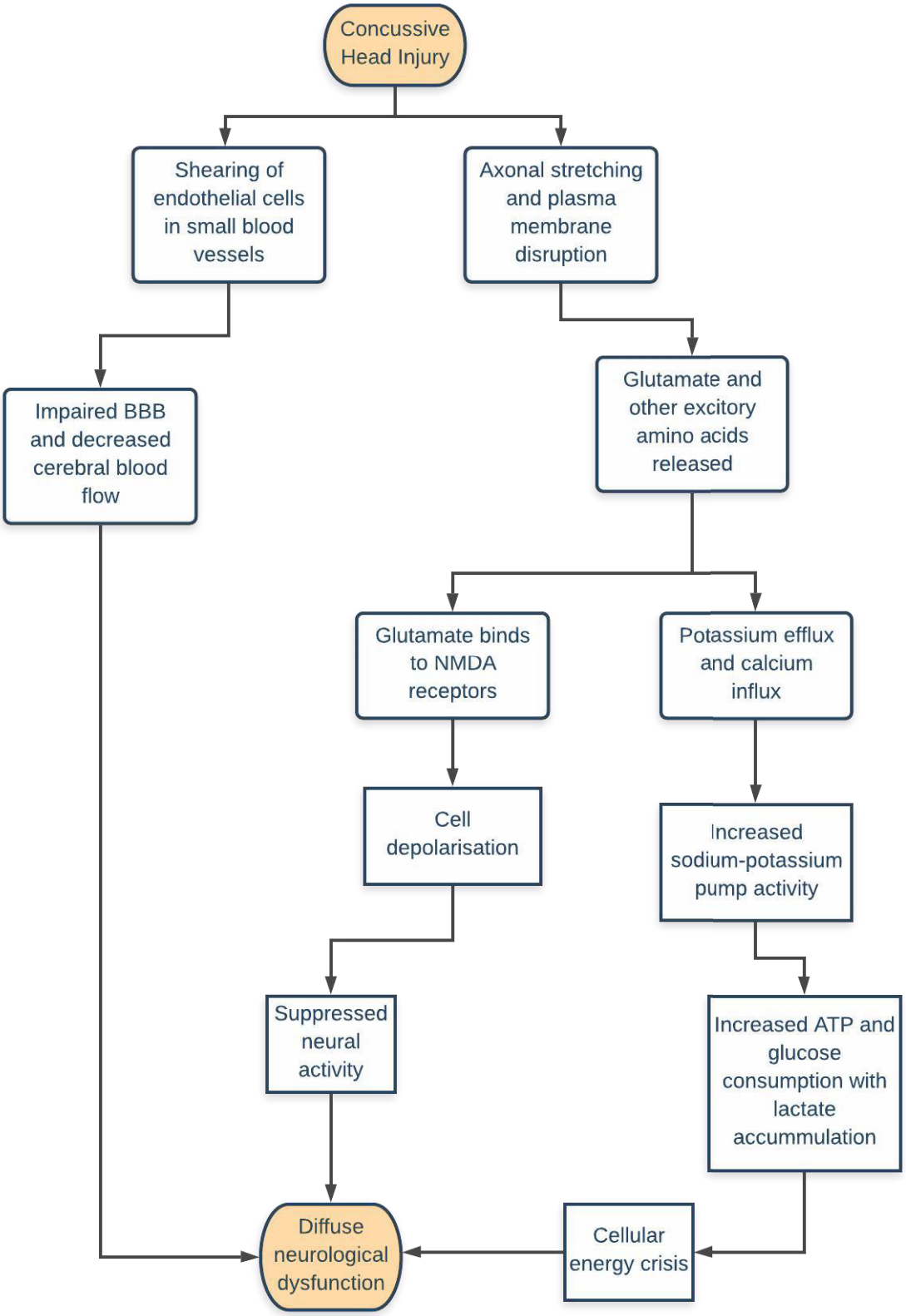


Figure 1.1. Flow diagram of the neurometabolic cascade after a concussion.

1.2.4 Neurological Impact

Neurological consequences of concussion must be viewed through the scope of both short and long-term sequelae. Although the majority of research has focused on diagnosis and treatment of concussion, it would appear that early neurological signs of concussion may represent a precursor to medium- and longer-term concerns.[78] A range of factors, including age and the repetition of head injury have been identified as contributing factors to the duration of neurological deficits.[79-81] Browne *et al*.[82] specified children between ages 13 and 16 in particular are more susceptible to cognitive changes following a concussion and this could have long-lasting impacts on their capabilities to learn and participate in sport. Especially if these changes include vestibular and oculomotor defects, which are vital for academic development during childhood and adolescence.

Neurocognitive testing on 223 high school athletes found that those who had suffered a concussion in the week prior to examination performed poorly on measures of attention and concentration when compared to the students with no concussive history.[83] In addition, those high school athletes with a history of two or more concussions but who had not been concussed within the last six months or had a recent episode within the last week, produced overall lower grade point averages compared to their peers.

Reduced academic scores in children who have suffered a concussion have also been demonstrated in a number of clinical studies, highlighting its importance to paediatric health and education systems.[84-86] Children who had experienced a concussion over two years prior to testing, demonstrated poorer academic and

neuropsychological scores when examined in areas of mental ability, neurocognition and mathematics.[84] Students who had not fully recovered from their concussive symptoms also complained of adverse academic impacts, such as difficulty studying, taking class notes and understanding learning material.[85] These effects may be prolonged as demonstrated in a cohort of high school students followed for 6 months after sustaining their injury and may impact on cortical development at such a young age,[83] although lack of further longitudinal follow-up studies is an ongoing issue.

In older age demographics, such as retired football players with a history of multiple concussions, reduced scores on cognitive function and poorer results on self-reports of physical, social, and psychological health have been found.[87,88] This has been associated with findings of depressive symptoms in retired American football athletes, with further implications to their cognition and somatosensory system through the early onset of neurological conditions, like Alzheimer's disease.[89,90] For athletes currently involved in contact sports and who may be more commonly exposed to concussive head injuries, early diagnosis and management is crucial to prevent major complications to their cognitive and psychosocial functions later in life.[91] A meta-analysis incorporating 15 case-control studies calculated a pooled odds ratio of 1.58 for the development of dementia in later-life after a single occurrence of TBI with LOC.[92]

Recently, there has been further evidence displaying the impact of concussion on long-term mental health and behaviour. Kilic *et al*.[93] observed 327 professional

male rugby players for one year and recorded the number of confirmed concussions, symptoms of distress, anxiety/depression, sleep disturbance, adverse alcohol use and eating disorders using validated questionnaires. The researchers found that the athletes who experienced a concussion were 1.5 times more likely to develop symptoms of distress and two times more likely to develop adverse alcohol usage.[93] From a clinical perspective, more needs to be done on detection and management protocols to help prevent athletes from developing these post-concussive mental health symptoms. Considering a lack of substantial data on the causality or prevalence of long-term effects amongst athletes, in the immediate, health professionals need more sensitive tools to detect SRC at the earliest possible interval.

1.2.5 Neuroimaging

When suspected of TBI, it is critical for a physician to perform additional neuroimaging to detect any abnormalities to the brain and exclude severe damage. Typically within the first 24 to 48 hours following a head injury, a computerised tomography (CT) scan is able to detect intracranial haemorrhage.[94,95] Yealy *et al*.[96] claims that CT scanning is more suitable to detect skull fractures, as well as intracranial haemorrhages, and is more cost effective, faster and easier to administer than magnetic resonance imaging (MRI). However, an MRI is able to detect cerebral contusion, petechial haemorrhages and structural changes to white matter more effectively than a CT scan.[97] It is also important to consider theradiation exposure from CT scans in subjects with repeated mTBIs or paediatric patients, due to further health risks including malignancy. Nonetheless, CT and MRI

scans commonly fail to recognise any architectural changes in concussion,[98] while multiple studies evaluating MRI scans following a concussion have revealed a low diagnostic yield.[99-101]

As noted previously, concussion is defined as a functional injury and therefore it is unlikely to be typically identifiable with an MRI.[18] An investigation on paediatric patients with persistent concussive symptoms found only 8.4% displayed anatomical changes using this neuroimaging technique, but none of these changes were deemed to be clinically significant.[99] Instead, functional MRI (fMRI) and nuclear imaging may provide better evidence of post-concussive changes for medical professionals to use as a diagnostic tool,[102,103] as they are able to measure metabolic and haemodynamic alterations in the brain following TBI.[104] Increases in the requirement of oxygenated haemoglobin to regions associated with executive functioning, such as the premotor cortex, superior and inferior parietal areas, and the cerebellum, have been observed when compared to pre-injury levels,[105] suggesting the utility of fMRI in concussion diagnostics.

Other more advanced techniques that map the brain's neural tracts, such as diffusion tensor imaging, have identified reduced white matter integrity and cerebral abnormalities in the frontal lobes, corpus callosum, and corona radiata following concussion.[106] The technique has also detected white matter changes to the cortico-spinal tract, sagittal stratum and superior longitudinal fasciculus in mTBI patients,[107] however it is unclear whether these cerebral alterations are temporary or more long-lasting as the study did not follow-up after clinical recovery.

While neuroimaging techniques have the potential to identify cerebral abnormalities related to concussion, it is still unclear which type provides the greatest diagnostic yield.[98] Churchill *et al*.[108] aimed to compare the differences between MRI, fMRI and diffusion tensor imaging on contact-sport athletes with and without a concussion history. The authors noted elevated levels of glutamate, decreased functional connectivity of the visual and motor systems, and increased fractional anisotropy in the cerebral white matter of those with a history of concussion.[108] These findings showed that all three types of neuroimaging were able to provide some evidence of long-term neurological sequelae, suggesting that using these techniques in combination would be more advisable. However, neuroimaging techniques are disadvantaged by a high financial cost. For instance, reducing the number of CT scans performed on TBI patients by 10% may provide more than $10 million in savings to hospitals per annum.[94]

It must also be considered that neuroimaging lacks in portability for sideline assessments and so are restricted to the hospital setting.[109] Professional athletes who have better access to medical services on the sidelines may benefit from these techniques through immediate referrals.[110] However, community-level and youth players who do not present to the hospital after sustaining a head injury, do not receive a complete neurological evaluation, and risk subsequent injury if prematurely returned-to-play.[15] This is especially true for those living in rural and remote communities in Australia, who can face significant geographic, socio-economic and cultural barriers in accessing these resources.[111-113]

1.2.6 Clinical Signs and Symptoms

As concussion represents a diffuse brain injury, signs and symptoms experienced on presentation may be both complex and highly variable.[114] The Centres for Disease Control and Prevention categorise these features into four main groups, physical, emotional, cognitive and sleep (Table 1.1).

Table 1.1. Common signs and symptoms experienced by patients following a concussive head injury.

Physical	Cognitive	Emotional	Sleep
Headache	Mental fogginess	Irritability	Drowsiness
Nausea	Feeling slowed down	Feeling sad	Sleep disturbance
Vomiting	Difficult concentrating	More emotional	Difficulty falling asleep
Balance problems	Difficulty remembering	Nervousness	
Visual disturbances	Forgetfulness		
Fatigue	Confusion		
Loss of consciousness	Slurred speech		
Sensitivity to noise	Repeats questions		
Dazed	Amnesia		

Immediately following the injury, the patient may experience any of the listed symptoms in Table 1.1. In one study, Collins *et al.*[81] found confusion, dizziness and post-traumatic amnesia to be more common in high school athletes with a history of three or more concussions. These athletes were found to demonstrate a 9.3 times greater risk of developing at least three symptoms than the students with a less severe concussion history. This was the first study to suggest a possible cumulative effect of concussion in young athletes, highlighting the need for more longitudinal studies on youth athletes who may experience a number of episodes. The authors also reported that post-traumatic amnesia and mental fogginess could be a potential indicator of more serious injury and longer recovery.[81] Although data in this area is quite limited, this association is supported by a number of other studies.[80,115-121]

Headache is the most common self-reported symptom.[99,115,122-125] In American high school athletes following SRC, headache was reported in up to 93.4% of the players.[126] The presence of headaches have also been correlated with increased vestibular deficits,[127] which are often noticed by the public and commentary during sporting matches as players walk from the field.[128]

These vestibular effects may also relate to dizziness, which is another frequent symptom during the acute stages of concussion and is reported in as many as 81% of cases.[129,130] Although the data is highly variable across only 114 patients, it is estimated that 1.2% of patients at six months post-injury to almost 33% at five years experience persistent vestibular dysfunction.[131]

Despite previous misconceptions, concussion does not always involve LOC. There is an abundance of evidence reporting that this clinical feature occurs in less than 10% of cases of concussion.[48,126,132-134] Considering LOC was believed to be a hallmark feature of concussion over a decade ago, these findings would imply that many cases of concussion may have previously gone undiagnosed in the past.

Evidence from multiple studies suggests that patients who experience LOC should be treated with caution and may warrant further brain imaging and intervention.[48,133,134] This was exemplified in one retrospective analysis of patients who suffered post-concussive LOC revealing 8.1% with significant findings, such as an intracranial haemorrhage and/or a skull fracture, on their CT scans.[135] For these patients, alterations to their management was required, including either surgical intervention, intensive care unit admission or increasing their length of hospitalisation. In patients without LOC, only 1.3% were identified with any significant structural changes to their brain and/or cranium.[135]

Furthermore, McCrory *et al*.[136] stated that motor phenomena, such as convulsive manifestations (or seizures) may also be associated with a concussion. This occurs when the skeletal muscles rapidly contract and relax repeatedly, resulting in uncontrolled actions of the body. One case report describes seizures in a 16 year old male wrestler after sustaining a concussion.[137] However, video analysis of over 234 concussions in professional Australian Rules Football showed that this is both a quite uncommon sign and largely benign.[138]

Additional symptoms include difficulty concentrating on tasks, sensitivity to light and visual disturbances.[139-143] However, some symptoms may be latent, manifesting several hours after sustaining the concussive head injury, as recorded in up to 23% of college athletes.[144] Other symptoms may have variable expression and may not be noticed in some patients. This makes diagnosing concussion difficult for health professionals, as many of the symptoms remain non-specific or could be related to a pre-existing condition. For example, patients with baroreflex dysfunction, such as postural orthostatic tachycardia syndrome, typically present with symptoms of fatigue, headaches, nausea, memory dysfunction, attention complaints, mental fogginess, depression, and trouble sleeping.[145,146] Therefore, good history taking is paramount to help exclude any differential diagnosis and is important for study inclusion criteria.

1.2.7 Post-Concussion Syndrome

Despite 80-90% of patients with concussion having their symptoms resolve spontaneously without medical intervention over a period of seven to ten days, some may endure ongoing symptoms.[18,147] This is referred to as post-concussion syndrome. Defined diversely amongst different sources, the most widely accepted definition is from the International Classification of Diseases, 10th edition diagnostic criteria (section F07.2).[148] Based on epidemiological findings from Great Britain, the United States of American (USA) and Scandinavia,[149] the condition is described as:

"A syndrome that occurs following head trauma (usually sufficiently severe to result in loss of consciousness) and includes a number of disparate symptoms such as

headache, dizziness, fatigue, irritability, difficulty in concentration and performing mental tasks, impairment of memory, insomnia, and reduced tolerance to stress, emotional excitement, or alcohol."

In the adult population with mTBI, post-concussion syndrome has been reported in 11 – 64%,[150] although this is estimated to be lower in children by approximately half (6 – 35%).[149,151,152] Females have also been shown to be at a higher risk of developing post-concussion syndrome than males.[153] Where indicated, treatment is essential to reduce the impact upon either schooling, work or daily activities and subsequent quality of life.[154]

1.2.8 Sideline Assessment Tools for Concussion

In order to detect post-concussive clinical features, whether acute or persistent, medical professionals use various concussion detection tools to evaluate a patient on the sideline and in emergency departments. However, in the scenario that the athlete presents unconscious, an initial assessment of the airway, breathing and circulation is vital.[155] In these cases, the athlete is assumed to have an associated cervical spine injury, with appropriate spinal precautions undertaken to support the player until they regain consciousness.[156] If a normal cervical spine is determined, and no abnormalities are detected in the four extremities, further medical assessment can be conducted. However, if the athlete remains unconscious, immediate transportation to an emergency department is required for ongoing attention.[23,157]

If the athlete is conscious, a detailed examination is conducted using concussion assessment tools. Each assessment tool involves a different criterion, variously assessing neurological, vestibular, cognitive and/or physical functions.[158] This would be performed by a medical professional with extensive training and knowledge in brain injury assessments. It is also beneficial if he or she may already know the athlete, as this would help identify subtle functional changes which might otherwise be missed. The most commonly used assessments tools for concussion are indicated in Table 1.2. However, a gold standard tool for diagnosing and for predicting the prognosis of concussion is simply lacking.

It is emphasised that an experienced clinical judgement is vital for an accurate concussion assessment.[159] Sideline concussion tools provide important information of concussive neurological function, although they should not be used as a standalone measure. Instead, various researchers have expressed that using a multimodal clinical approach to assess an athlete with suspected SRC aids the physician in their decision making.[160-162] If not rapidly removed from play, concussed athletes risk longer recovery and an increase in symptom provocation, so more reliable and well researched protocols are necessary in this field.[163]

Table 1.2. The most popular concussion assessment tools used by physicians.

Tool	Domains	Sensitivity*	Specificity*
Post-Concussion Symptom Scale	• Post-concussive symptoms	41 – 68%[160,164]	79%[164]
Standardized Assessment of Concussion	• Neurocognition	80 – 96%[165,166]	76 – 91%[165,166]
Immediate Post-Concussion Assessment and Cognitive Testing	• Memory • Visual-motor speed • Cognition	43 – 91%[160,167-170]	69 – 98%[167-171]
Concussion Resolution Index	• Neurocognition	79 – 88%[160,172,173]	Not reported
CogSport	• Neurocognition	68 – 97%[170,174]	35 – 94%[170,174]
The Standardized Concussion Assessment Tool	• Post-concussive symptoms • Balance • Physical examination • Cognition	83 – 96%[165,175,176]	76 –91%[165,175,176]

*Sensitivity and specificity rounded to the nearest whole number

The Post-Concussion Symptom Scale (PCSS)

The PCSS is a symptom checklist used by clinicians to evaluate a patient for concussion. It includes a wide range of concussion-related symptoms and signs such as headaches, vomiting and nausea, and a severity scale for each ranging between zero to six. A score of zero represents no manifestation while a score of six indicates that the symptom is most severe.[158,160]

However, the PCSS is a subjective measure due to the self-reporting nature of the questionnaire. It has been suggested that it be used in combination with other concussion tools.[177] Lau *et al*.[164] explored the need for a combination of tools in 108 male high school football athletes who had sustained a concussive head injury. The authors found that the PCSS demonstrated a sensitivity of only 41% in detecting concussion. However, when performed in combination with another testing tool, the net sensitivity increased by 23%, supporting its role within a sideline concussion battery of tests.

The Standardised Assessment of Concussion (SAC)

The SAC is a neuropsychological tool which does not require specific training in psychology for administration or interpretation.[178] It consists of a ten minute paper and pencil test, with a total score summed out of 30.[158]

Since its introduction, studies using the SAC have shown its utility in distinguishing between concussed and non-concussed athletes in various populations. Two studies have found that post-concussive scores were reduced compared to pre-injury baseline measure.[165,179] McCrea also showed that the players who sustained a concussion performed worse on the test immediately after getting injured.[165,179]

Interestingly, both studies revealed improvements to SAC scores in the concussed athletes after two days. This highlights a fairly rapid neurological recovery of the tested functions after concussion, although it is unclear whether other deficits not measured by the test were still present.

However, the SAC may not be as reliable in children. Grubenhoff *et al*.[180] performed the SAC on 165 children with concussion and 183 age-matched controls. In this study, all children with a recent episode of concussion achieved lower scores when compared to the control group, however this was determined to not be statistically significant. This aspect may require further investigation to determine if there is a true effect in children.

Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT)

ImPACT is a 25 minute computer-based concussion tool that comprises of six cognitive tests are designed to evaluate several aspects of cognitive function, including attention, memory, processing speed, and reaction time.[158,181] Developed in 2000 by Lovell *et al.*[182] it is used by the English Premier League and remains one of the most popular concussion assessment tools for sport in North America, including the National Football League, Major League Baseball, National Basketball Association, championship motorcar racing teams, and by the USA national Olympic women's hockey team.[158,168,183]

The test has been demonstrated by several studies to be highly effective in distinguishing between players with concussion and those without in the acute stages.[177,184,185] Two studies observed between 81.9 to 91.4% of concussed

participants were correctly identified by ImPACT (high sensitivity) and 69.1 to 89.4% of non-concussed participants were correctly identified (good to high specificity).[167,168] When performed on asymptomatic concussed athletes, the tool was also able to accurately identify 97.3% of cases, and distinguish them from healthy controls,[168] highlighting its suitability for the sideline assessment of concussion. The current gold-standard in diagnosing concussion is still the team physician's clinical judgement,[186] which was used in these studies. Considering many sports medicine professionals do not adopt standard clinical guidelines for concussion assessment and management,[186-188] the measures obtained could be seen as not entirely consistent or reliable.

In a further study by Iverson *et al*.[184], no significant correlation was found between the different test components of ImPACT during a pre-season baseline testing. This would suggest each module of the test assesses different functions of concussion. Having a testing battery that evaluates a variety of neurological functions, such as visual function,[161,189] as ImPACT does, may be the most suitable way for clinicians to make an accurate diagnosis of concussion and highly important in today's sports setting as concern grows about the long-term impacts on health of concussion.

Unlike other tools,[190,191] ImPACT has been demonstrated to not be influenced by large learning effects,[117] a psychological characteristic common in performance measures, where there is a change in score resulting from repetition of a particular activity. Lovell *et al*.[117] studied high school athletes with SRC over seven days and compared them to a non-concussed control group. The control participants were found to not show any significant improvements to their ImPACT memory

composite scores upon repeated testing seven-, nine- and eleven-days following their baseline measurement. Concussed players, however, revealed lower scores on their verbal memory after 36 hours and four- and seven-days post-concussion, compared to their individual baselines. Correlating to the degree of mTBI, athletes who had experienced retrograde amnesia, anterograde amnesia, or disorientation for over five minutes following their concussion, were founded to have larger decreases in their ImPACT scores and they took longer to return to baseline than the athletes who had experienced less severe symptoms.

The HeadMinder Concussion Resolution Index (CRI)

The HeadMinder CRI is an internet-based neurocognitive and neurobehavioral assessment tool that assesses an individual's information-processing speed, visual recognition and reaction time.[158] It was first developed in 1989 by Barth *et al.*[192] and has since become an accepted assessment tool for SRC in the research setting. However, there remains no available evidence that this tool is used as a part of a concussion battery for any professional sport.

Broglio *et al*.[172] found the test to have a high sensitivity of 88% in detecting concussion, however discovered that post-injury on day 45, 9% and at day 50, 33% of participants had one or more false positives on the assessment tool. More research on this tool is required to determine its utility in diagnosing a concussion before it can be reliably used as a sideline assessment tool for concussion.

The Cogstate's CogSport Test (CogSport)

The CogSport is a cognitive assessment tool, consisting of seven card tasks. It measures the person's reaction time, decision making, matching, working memory, and attention.[158] Currently, the test is used as a concussion assessment tool for the Australian Cricket Team, Hockey Australia and Surfing Australia (see Appendix A),[193] as it has been found to be a good discriminator of concussion in both non-athletic and sporting groups.[194] When conducted on non-concussed cohorts, the tool has been shown to be valuable in confirming a healthy status.[174,195]

The tool has also been shown to provide a high diagnostic yield when used as part of a multi-faceted battery of tests for concussion. In non-elite rugby players the CogSport in combination with ImPACT was able to provide an overall classification accuracy of 87.4% in distinguishing between concussed and non-concussed athletes, though there is some limitation to this study as there was no baseline measures.[170] Another study also demonstrated a high sensitivity (96.6%) and specificity (86.9%) for detecting concussion when used with baseline data.[174] However, the sensitivities achieved by both studies[170,174] were also similar to those reported previously on utilising the ImPACT test alone.[167,168] It has also been suggested that the CogSport may be affected by learning effects,[195] and it remains unclear whether this tool is also influenced by fatigue and other non-concussive injuries.

The Standardized Concussion Assessment Tool (SCAT)

The SCAT involves the assessment of concussion symptoms, cognition, and neurological signs using a variety of different measures.[196] Designed for medical

practitioners to assist in concussion diagnosis, it consists of the Maddocks score (brief questions), symptom evaluation, memory evaluation, brief neurological screening of the pupils and has return-to-play guidelines.[143] In 2008, the SCAT was revised to the SCAT-2, to reflect the current literature of that time.[197] This included a more refined tool with the addition of the GCS, modified version of the Balance Error Scoring System (BESS), integration of SAC, motor coordination examination and more detailed concussion injury advice, with each category of the test assessed individually and summed for a maximum of 100 points.[196,197]

The SCAT-2 was recommended to be a useful indicator for post-concussion assessments, capable of assessing multiple cognitive and neurological functions in a range of age demographics.[175,198] This was demonstrated on 280 university athletes over a competition season, with a 3.5 point decrease noted between baseline and post-concussion SCAT-2 measures.[175] This lead to the widespread use of the SCAT-2 and further exploration of its utility.[199-201] Another study found a difference of 1.7 points in high school athletes with and without a recent concussive history.[202] However, when the SCAT-2 was conducted on older cohorts of collegiate and professional athletes,[203,204] these previous findings by McLeod *et al*.[202] were not supported as they found no statistical difference in scores in these groups.

These discrepancies led to the revision of the tool in 2012, as part of the 4th International Consensus Conference on Concussion in Sport.[205] The newly expanded SCAT-3 now included the additions of physical/objective signs, cervical stability assessment and in addition emergency management with considerations for on-

going management and concussion advice.[206] In addition, a SCAT-3 version tailored to children under 13 years was introduced.[207,208] The total score of 100 was removed as there was no evidence supporting its validity.

This newly reformed tool was then analysed to determine its impact on normative testing for baseline concussion assessments. Snedden *et al*.[209] studied a large cohort of healthy high school athletes and found males reported an increased number of baseline symptoms, higher severity of symptoms and produced lower scores on the SAC components than females. The authors also identified that the SCAT-3 was not influenced by age. However, when conducted on brain injury patients in the outpatient setting, opposing results have been witnessed. Females and those of an older age were found to report more concussive symptoms during the SAC component of the SCAT-3.[210]

Researchers have also discovered differences in the SAC component of the SCAT-3 in cohorts with Attention Deficit Hyperactivity Disorder (ADHD) and learning disorders.[211-213] This would suggest that there is potential variation amongst population samples and potentially players that should be taken into account during diagnosis of concussion or at a study's conception.

However, when used on cohorts with a diagnosed concussion, the SCAT-3 has been proven to be highly sensitive, making it an effective tool on sporting sidelines[214] and emergency departments.[166] Galetta *et al*.[214] examined 12 athletes with SRC and demonstrated a high sensitivity of 88%. When used in combination with a visual tool, the sensitivity improved by a further 9%.

Since 2016, the concussion tool has again been reformed to the most latest edition (SCAT-5, note no 4th edition) by the Concussion in Sport Group[18] and is widely used within international professional sport.[162,183,193] This newer edition has a more detailed cognitive screening utility with a cervical spine examination and an additional ten word list option in the memory section, amongst subtle clarification and modification of the other components. Previous research established that the SAC and balance components were found to be the most useful aspects of SCAT-5 in differentiating between concussed and non-concussed athletes.[215] In particular, when using either intra-individual or normative baseline/post-injury comparisons, the SCAT-5 was also found to decrease in diagnostic utility after three to five days post-injury.[210] However, the use of the tool is limited to medically trained professionals, and therefore, not readily available for players without access to a sideline physician.[215,216]

Since its update, the SCAT-5 has been evaluated for its suitability in sideline testing, aiming to determine its superiority to earlier editions.[217] However, studies determining its capabilities to identify concussion are significantly lacking, probably due to the difficulties of obtaining large numbers of concussed patients for both baseline and post-concussive assessments. Developing a multi-faceted battery to assess the various neurological functions following brain injury would appear to be optimal.[161] However, despite significant research in the field of concussion and player welfare, researchers are yet to fully explore the potential improvements obtainable through the combination of several available tools and which combination may be the most optimal.

1.2.9 Underreporting of Concussion

For these concussion assessment tools to be effective, a suspected injury needs to be disclosed to appropriate personnel, although, as previously mentioned, there are a large portion of players who fail to report their injuries.[218]

It is estimated that as high as 90% of players in both youth and adult sports populations may not be aware of a potential concussion diagnosis and therefore go unassessed by health professionals, coaches and parents following the possible concussive event.[219,220] Other research has suggested that poor reporting rates can be attributed to players motivated by wishing to avoid being removed from play.[26,221-223] Both these reasons suggest a lack of education on the potential severity of concussion, particularly repeated concussions for both players and sports officals.[224]

Low rates of reporting concussive symptoms have been found in athletes playing different sports across a variety of ages. In a large sample of 1,532 high school football players, 41% failed to report their concussions to avoid being withheld from play.[222] This supported findings from collegiate athletes, with 43% not reporting their concussions for the same reasoning.[225] This presents particular difficulties for health professionals as their review of the patient can be markedly delayed from the concussive event, impacting the potential information available through patient history, all of which may prolong symptom recovery.[226] When McCrea's (2004) data was further analysed, 67% of players did not think the injury was serious enough to

warrant medical attention and 36% had a lack of awareness on the severity of the condition.[222]

To combat this emerging issue, it is suggested that players having access to an athletic trainer or sideline medical staff may improve the rates of concussion reporting.[227] However, when surveying high school athletes with and without access to a trainer, 55% with access still did not report their concussive injury.[223] Similar findings were discovered by Register-Mihalik *et al*.[228] who found that that only 40% of students disclosed their SRC to coaches and trainers. It is therefore vital that sporting organisations focus on changing these poor reporting cultures within sporting at the grassroots level. This could be assisted by improving access to medical resources and surveillance systems, while improving concussion education to youth athletes has also been demonstrated to be an effective method.[229]

Despite some beliefs that only youth athletes underreport concussive episodes, similar outcomes have been published on professional athletes as well.[230-232] In a survey sampling a large cohort of former National Football League (NFL) players who had previously suffered at least one concussion in their careers, it was observed that only 50% informed medical staff after sustaining an episode.[233] Similarly, in a squad of 24 current professional football players, 54% acknowledged that they would continue playing matches despite having post-concussive headaches.[231] Researchers have attributed this behaviour to the pressures applied indirectly by coaches, teammates, parents and even fans on an individual athlete, compelling them to remain on the field.[233,234] These sources of pressure have also

been recognised within younger sports cohorts as well and remain a major issue to be addressed.[222,225]

There is also some evidence suggesting team staff may also be under pressure to underreport concussions as well. In over four competition seasons of ice-hockey, there was a difference between official injury reports by the team management and the greater than 30-fold higher rate found in retrospective surveys conducted on the team personnel.[235] King *et al*.[236] suggests that these differences may be due to an overall poor understanding of concussion protocols in sporting leagues, as demonstrated in a study of a cohort of New Zealand rugby league players. As a result, there are a large number of studies aimed at improving concussion education at the youth level,[237-239] to tackle this poor culture in regards to concussion and player health.

1.2.10 Gender Differences

Along with the implications of underreporting concussive injuries, there is an increasing awareness that males and females endure a different clinical trajectory after suffering a concussion.[240] In a meta-analysis incorporating over 21 observational cohort studies, significant differences between the symptom-reporting behaviours of males and females were revealed.[241] Females reported more concussion symptoms than males, which could be attributed to difference in psychosocial behaviours with a male feeling they should simply “tough it out”.[242]

Multiple studies by Covassin *et al*.[243-247] based on self-reports have supported this finding, proposing that females also experience a higher frequency of concussive head injuries, sustain a greater number of post-concussive deficits, experience

different symptom constellations and endure a longer symptom recovery than males. However, a study of 288 high school students identified that males were four to 11 times more likely than females to avoid reporting their concussion due to perceived stigma from their peers.[248] This reporting behaviour could thereby reduce the prevalence of male concussions documented in the literature and skew previous findings.

A number of studies have also reported females sustain a higher rate of concussions compared to males in the same sports for reasons that are not clear.[41,247-250] Mansell *et al*.[249] compared the neck muscle mass and length in male and female collegiate soccer players. Following eight weeks of identical cervical resistance training, the females were found to have 7% less head-neck segment length and 26% less head-neck segment mass than the males. It is theorised that the weaker neck muscles and smaller head mass may make females more susceptible to a concussion.[241,249,250]

However, evidence from Colvin *et al.*[251] have suggested otherwise. The researchers recruited 93 male and 141 female soccer athletes and controlled for body mass index (BMI). Each participant had sustained a concussion and they performed the ImPACT testing battery to assess post-injury neuropsychological function. The data revealed that despite controlling for BMI, the female athletes still performed poorer on the ImPACT testing battery and reported more post-concussive symptoms than the males. This would imply that gender differences in concussion, that were hypothesised to be associated with differences in mass,[241,249,250] may instead be

related to other gender-specific factors. We must still consider, however that BMI does not distinguish between muscle and fat, as the authors did not directly control for muscle mass.[251]

It has also been proposed that females have an increased susceptibility to a concussion, potentially due to a lower biomechanical threshold than males.[252] Some believe this to be attributed to hormonal factors, such as oestrogen, which may elicit a different pain response in females when compared to males.[244-247,253] Wunderle *et al*.[254] demonstrated that the menstrual cycle phase influences the recovery in females possibly due to changes in their hormonal levels. In this study, the authors recruited 144 females who presented to an emergency department within four hours of sustaining a mTBI. They found that women injured during the luteal phase of their menstrual cycle had lower quality of life and neurological scores than women injured during the follicular phase.

The literature on gender and recovery rates is varied, but overall supports that females take longer than males to become symptom-free.[255-258] In one study, the recovery trajectories of 110 males and 37 females within 12 days of a concussion were closely monitored.[256] The authors observed that, on average, females took 9.3 days longer to recover from their symptoms. In fact, 65% of the females took greater than 10 days to recover, compared to only 53% of males. A further 41% of females took over 21 days to recover, compared to only 19% of the male cohort. However, the studies looking at the relationship between gender and recovery rates typically involve a much higher number of males than females.[255-258] This may be due to males being three-times more likely to attend an emergency department

after suffering a concussion.[259] More studies are thereby required to confirm these findings, which if upheld, could lead to a more detailed and specific management plan for females diagnosed with concussion.

1.2.11 Second-Impact Syndrome

Second-Impact Syndrome is a rare condition where an individual who has experienced a TBI sustains a second concussive injury before the symptoms from the first have completely resolved. This can result in cerebral oedema and haemorrhaging leading to permanent disability, and even death.[260-262] All documented cases of Second-Impact Syndrome have been reported in patients under 20 years of age.[263]

Older professional players could be less affected than younger players because they are more appropriately identified and removed from play, thereby reducing the risk of a second injury. Another factor determining a higher rate of this syndrome in younger players could be that the maturing brain is more susceptible to dysfunction following brain injury.[264,265] However, evidence from Boden *et al*.[266] shows that calamitous traumatic brain injuries occur in high school football players three times more frequently than in collegiate players, suggesting younger age groups may be more susceptible to injury per se. This also suggests that professional training may be more protective against concussive injury for players than that found at the younger amateur level.

Unfortunately, our understanding of this syndrome is still in its infancy with limited access to documented case reports. A review article in 2016 performed a systematic

review and identified 36 cases of proposed Second-Impact Syndrome documented in 15 publications, but with only 17 of those meeting accepted inclusion criteria.[267] Although quite rare, it is important for health professionals who practice in paediatric healthcare to be aware of this potentially lethal condition and to implement removal from play strategies (Figure 1.2) and rehabilitation protocols when required should such cases present. It may also be necessary to examine how coaching at the different levels of a sport differ and to identify factors that may afford professional players greater protection.

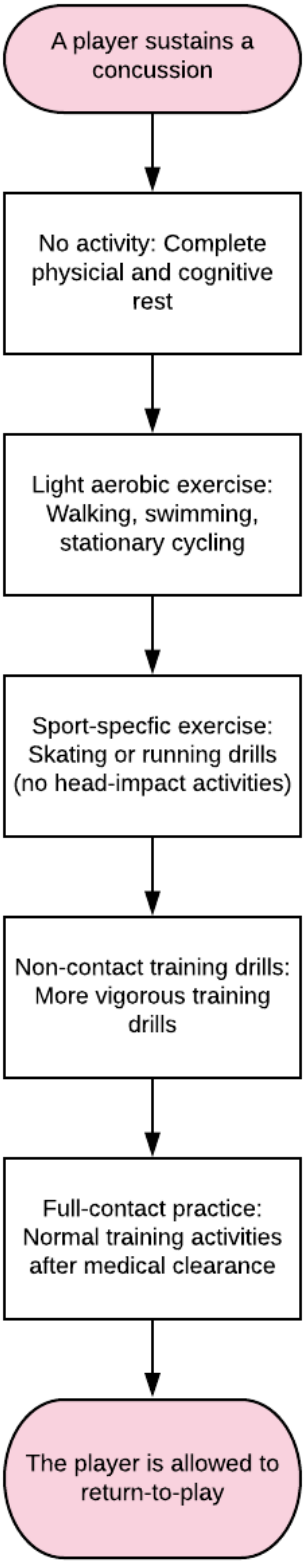


Figure 1.2. Most widely accepted graduated return-to-play protocol used in sport. Once all symptoms have completed resolved in that step, the athlete may advance to the next. Adapted from McCrory *et al.*[270]

1.2.12 Chronic Traumatic Encephalopathy

Recently, there has been an increase in publications focused on Chronic Traumatic Encephalopathy (CTE).[268-277] This is a progressive neurodegenerative disease that occurs in association with repetitive TBI. CTE is a type of tauopathy, characterised by an accumulation of phosphorylated tau protein in neurons and astrocytes, forming a pattern around small blood vessels of the cortex, typically in the sulci (Figure 1.3). [280] However, the research surrounding the topic is still very limited. This is primarily due to extremely low sample sizes and lack of good controls.[268-276,278] Although, with emerging interests in neurodegenerative brain banks around the globe, such as in USA and Australia, and an increase in contact-sport athletes donating their brains for future research, the pathophysiology of CTE is likely to become clearer in the future.

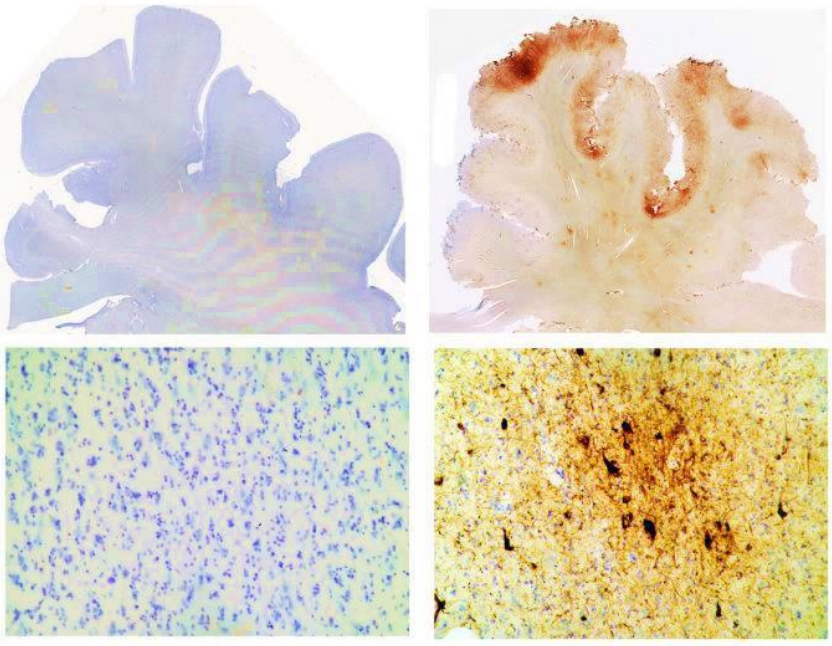


Figure 1.3. Comparison of two different brain samples. Image on the left is a normal brain from a 65 year old man. Image on the right is a corresponding brain section with evidence of CTE, from a former male NFL player who suffered eight concussions and died at age 45.[279]

Empirical research from Corsellis *et al*.[280] provided the first detailed description of CTE in 15 retired boxers. Brains from these athletes revealed cerebral atrophy, enlarged lateral and third ventricles, attenuation of the corpus callosum and cerebellar scarring. Biochemical staining in four of the boxers also demonstrated neuronal alterations to the cerebellar tonsils, substantia nigra, cerebral cortex and the presence of senile plaques. Although the neurological symptoms and signs of the boxers ante-mortem were not documented, it could be inferred from the pathological evidence that these boxers are likely to have experienced changes to their behaviour and mental health.

Since that study, six retired football players with a strong history of concussion and collisions were reported to have endured significant cognitive, behavioural and physical symptoms throughout their later lives.[278] When examined post-mortem, half of the athletes had neuropathological hallmarks of CTE, while the other three were diagnosed with Alzheimer's disease, Parkinson's disease and/or motor neuron disease. Similarly, 32% of cases from a brain bank of 66 former collision-sport athletes demonstrated p-tau staining, which is consistent with CTE.[281] Evidence from both of these studies indicates that people with a history of multiple concussions are at a greater risk of developing CTE. However, most of the research surrounding CTE involves low sample sizes and lack of pre-collision brain imaging and detailed neurological assessment.

The impact CTE has on an athlete while alive is still unknown. There is some evidence describing impairments to cognition, behaviour and mood, while others

may be completely asymptomatic.[282] However, data from 153 pathologically confirmed CTE cases in male American athletes showed the median age group of death to be between 60 – 69.[283] This represents a less than average age of death in the USA at 76.2 years.[284] According to the researchers, these athletes also had higher rates of suicide and substance abuse than the general population.[283]

1.3 VISUAL AND OCULOMOTOR DYSFUNCTION

As more than half of the brain's pathways are dedicated to vision and eye movement control, it is logical that a diffuse brain injury will impact some aspect of the visual system.[285] The presence of vision disorders following concussion, including ocular movement defects, has been recorded in as high as 69% of cases in a large prospective cohort of adolescents.[286] This has highlighted the need for a full ocular structural and visual functional assessment following a concussion, with specific attention to afferent visual dysfunction, efferent visual defects, motor dysfunction like convergence and/or higher order deficits.[287]

Although the literature describing the presence of visual symptoms in mTBI and concussion remains limited, most outcomes appear to indicate that the majority of patients will experience one or more ocular symptoms following the acute stages of a concussive episode.[288-290] Injured individuals may complain of problems performing daily activities such as reading, driving, participating in sport and coping with work. For children, adolescents and young adults with delayed recovery, this may have a detrimental outcome on their ability to complete academic activities and on their quality of life.[147,291,292] Studies in both adolescent and adult patients have described clinical features affecting vision following a concussive episode (Table 1.3).[286,289,293,294] These may include diplopia (or double vision), decreased visual attention, photosensitivity and abnormal eye tracking movements.[295,296]

Table 1.3. Signs and symptoms affecting the visual system following a concussion.[147]

Symptoms	Signs
Blurred vision	Slow eye movements
Photophobia	Anisocoria
Reading difficulties	Visual field loss
Diplopia	Impaired vestibular-ocular reflex
Headaches with visual tasks	Reduced conjugate eye movements
Loss of vision	Reduced disconjugate eye movements
Difficulty tracking	Impaired accommodation

Chronic visual problems have also been discovered in those with an extensive history of concussion and in 31% of military personnel with a history of mTBI self-reporting poor visual outcomes.[297] This suggests ocular testing may be useful in detecting latent sequelae as well.[297-299] This has been shown in a recent cross-sectional study where 85.7% of retired professional rugby league players, who were without any evident optic disease, demonstrated overall thinning to the nasal regions of their retinal nerve fibre layer using Optical Coherence Tomography.[300] These changes to the retina correlated with cerebral white matter loss and neurodegeneration on MRI in similar studies.[298,299]

Considering almost 70% of sensory processing by cerebral parenchyma is related to vision,[301] and seven of the 12 cranial nerves (II - VIII) are utilised by the visual system, assessing visual function is a necessity following any type of TBI. These assessments should include an evaluation of accommodation, convergence,

saccades, smooth pursuit eye movements and ocular movements as well as vision and visual cognition.[289]

1.3.1 Accommodation

Ocular accommodation and convergence eye movements have been implicated as affected by concussion. In order to understand these two functions, it is important to first understand their linked anatomy and physiology. Accommodation involves changing the focus of the eye to maintain a clear image of an object as it varies its distance from the observer, primarily as it approaches. This involves changing the curvature of the crystalline lens, according to the proximity of the target. Accommodation can be performed voluntarily but most frequently occurs as an involuntary response to a proximal target.

The accommodative response is initiated by a close object with its image and position on the retina stimulating the visual pathway in the brain. Information from the visual cortex is then relayed to the ciliary muscle in the eye through corticonuclear fibres and the parasympathetic innervation of the oculomotor nerve (cranial nerve III, see Figure 1.4). This efferent motor signal causes the ciliary muscles to contract, causing the shape of the crystalline lens to thicken, thus increasing the refractive power of the crystalline lens and allowing the close object to be brought into focus.

In addition, for both eyes to focus on the proximal target as it is moved closer, fixation needs to be maintained. This act of simultaneously adducting both eyes is referred to as convergence. Like accommodation, this process is also initiated by

the oculomotor nerve where the contraction of both medial recti muscles turn both eyes inwards, allowing the fovea in each eye to remain on the target. Together, accommodation and convergence work in combination and can be quantified by an accommodative convergence-to-accommodation (AC/A) ratio, with a normal value of 3:1.[302]

Considering the length and complexity of the neurological pathway involved with accommodation, this visual function is potentially susceptible to damage with resultant dysfunction after a head injury.[303,304] Affected patients would typically present with a decreased accommodative amplitude and are clinically diagnosed with accommodative insufficiency.[305,306] Accommodative lag, the difference between the accommodative demand and response, and accommodative facility, the speed of the accommodative response, are other two measures of ocular accommodation which may be impacted by concussion.[303,304] Practically, disruption to these processes may be reflected in difficulty concentrating on near visual tasks, blurry vision, asthenopia (tired eyes) or headaches following short periods of close work.[304-306]

Accommodative capacity is age dependent.[307] Healthy youth or adolescent patients retain an ability to maintain clear focus upon near objects (as close as < 10 cm) however, this capacity progressively reduces with age as the crystalline lens stiffens and gradually loses its ability to alter shape. The level of accommodation can also vary with refractive error such as myopia, where accommodative lag is commonly reported.[308] Therefore, a person's age and refractive error, which in the absence of full spectacle prescription can be partially ascertained by their history of wearing

glasses or contact lens use, and the age at which first prescribed are important information when assessing this function.[309]

Harrison (1987) first described a case study of a 20 year old male manifesting a persistent inability to accommodate in one eye, three years after sustaining a TBI.[310] The patient was noted to have a markedly receded AC/A ratio of 1.33:1, which returned to normal without intervention 18 months following his injury.

Since then, there has been two studies showing high rates of accommodative abnormalities following concussion in sporting groups (Table 1.4).[286,311] In a modest cohort of 218 athletes with concussion, 82% demonstrated some form of visual dysfunction. When the data was further analysed, 54% had accommodative abnormalities, and more specifically, 41% produced reduced accommodative amplitudes.[311] These findings were similar in an adolescent group with concussion, revealing 51% with accommodative insufficiency.[286] However, both studies lacked any baseline measure, and instead, compared recorded values to age-matched normative scores.

Table 1.4. Studies reporting the rates of accommodative dysfunction following concussion.

Author	Year	*n*	Sample	Study Design	Technique	Accommodative Dysfunction
Brahm *et al.*[312]	2009	99	War fighters	Retrospective	Push-away method	48%
Green *et al.*[313]	2010	12	Injured adults	Cross-Sectional	Auto-refractor and flipper lenses	100% (all were specifically recruited)
Capo-Aponte *et al.*[295]	2012	20	War fighters	Cross-Sectional	Phoropter	65%
Master *et al.*[286]	2016	100	Youth athletes	Cross-Sectional	Push-away method and flipper lenses	51%
Gallaway *et al.*[311]	2017	218	Youth athletes	Retrospective	Minus lenses and flipper lenses	47%

High rates of accommodative dysfunction have also been detected in military cohorts suffering blast-induced concussion (Table 1.4).[295,312] In a small group of 20 military personnel, reduced accommodative amplitudes and facility were identified in 65% and 35% of patients respectively.[295] These patients also complained of increased photosensitivity, along with impairments to hearing and balance, and onset of neuropsychiatric symptoms following their concussion. Results obtained by this study[295] mirrored findings by Brahm *et al*.[312] where almost 48% of concussed military personnel were diagnosed with accommodative insufficiency. A further 87% had self-reported complaints of reading difficulties, which may be attributed by the impaired accommodation amongst other visual abnormalities, like convergence.

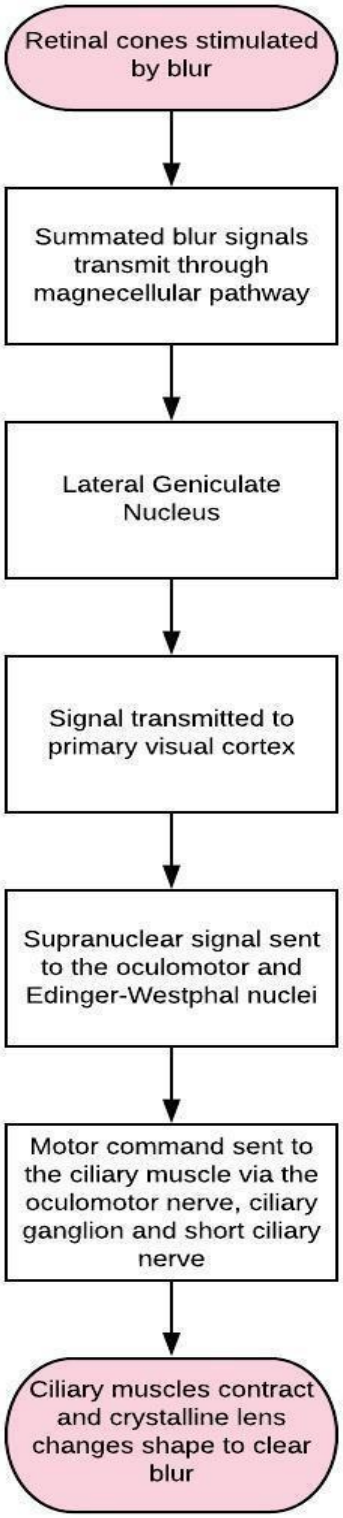


Figure 1.4. Flow diagram depicting the physiological pathway for monocular accommodation.

Despite these high rates of accommodative dysfunction reported in the literature, all studies involving post-concussive accommodative dysfunction include retrospective or cross-sectional designs.[286,295,311,313,314] This would mean that rates of accommodative insufficiency within the normal population were not taken into consideration, potentially causing an over-reporting of accommodative dysfunction. Further research is therefore warranted to determine whether there is a significant change from baseline, and if so, whether accommodative examinations could be a suitable sideline assessment.

When sustained accommodative dysfunction is suspected or noted, referral to a neuro-ophthalmologist or orthoptic clinic is recommended to help patients undertake rehabilitative exercises.[147] Accommodative and vergence therapy may also help to reduce symptoms and assist return to normal levels of near work.[315-317] This has previously been demonstrated to be effective in up to 90% of concussed patients.[318] However, further studies are required to confirm this finding as the literature encompassing visual rehabilitation after concussion is quite limited.

1.3.2 Convergence

As previously mentioned, ocular convergence refers to the inward movement of both eyes, playing a considerable role in our depth perception and refixation of eye movements. Convergence eye movements are also integrally linked with accommodation and pupil constriction with interconnections from midbrain neurons that project to the Edinger-Westphal nucleus and oculomotor nuclei.[319] The Edinger-Westphal nuclei supply preganglionic parasympathetic fibres that play

a large role in pupil constriction, crystalline lens accommodation, and ocular convergence.

The Edinger-Westphal nucleus receives its neural input from the superior colliculi (SC) and the pretectal region of the midbrain, in the brain stem. Afferent nerve signals of the pupillary light pathway arrive at the pretectal region, whereas corticotectal fibres from the visual cortex synapse in the SC for the pupillary near reflex causing miosis of the pupils. Information then travels via the oculomotor nerve to eventually synapse in the ciliary ganglion within the eye. Some fibres synapse in the sphincter muscle of the iris to initiate pupil constriction, while other fibres synapse at the ciliary muscle to enact accommodation.

Evidence has shown other cortical areas like the lateral parietal cortex, frontal eye fields, supra-oculomotor area, thalamus and cerebellum to be involved in the early stages of the pathway.[320] Lesions at the pulvinar nuclei have also been correlated with convergence disorders,[321] suggesting it has a potential role within the complex convergence pathway. Following signal exchange between these structures, there is an eventual synapse at both medial recti sub-nuclei to generate convergence eye movements.

Impairments to the convergence pathway can lead to the clinical condition known as convergence insufficiency. In order to diagnose convergence insufficiency a complete ocular examination involving measuring fusional amplitudes (extent to which binocular single vision can be maintained) and the near point of convergence (NPC). However, it is reported that around 0.1 – 0.2% of the general population

exhibit an abnormal convergence near point (>10 cm).[322] These rates have been reported to be as high as 4.2 – 6% in school[323] and clinical settings.[324]

Considering that convergence involves an expansive neurological network, it is vulnerable to the effects of concussion, with the highest rate recorded at 55% in two separate cross-sectional studies when compared to healthy controls (Table 1.5).[295,325] The literature has also shown considerably large rates of convergence dysfunction within athletic groups suffering a concussion (14 – 55%),[311,325-328] military personnel who had experienced blast-induced concussive injury (48.4 – 55%),[295,312] and other affected concussed cohorts within the hospital setting (14 – 28%).[125,326,329] However, most of these studies appear to be all cross-sectional or retrospective in design and do not compare convergence measurements to an individual's non-concussed baseline. This baseline testing is crucial for determining the role of convergence in making a proper concussion diagnosis.[330]

Table 1.5. Studies reporting the rates of convergence dysfunction following concussion.

Author	Year	*n*	Sample	Study Design	Technique	Convergence Dysfunction
Capo-Aponte *et al.*[295]	2012	20	War fighters	Cross-Sectional	Not specified	55%
Vernau *et al.*[331]	2015	11	Ice-Hockey athletes	Longitudinal	Astron Accommodative Rule	14%
Pearce *et al.*[328]	2015	78	Youth athletes	Cross-Sectional	Target and Ruler	41%
Master *et al.*[286]	2016	100	Youth athletes	Cross-Sectional	Not specified	49%
Storey *et al.*[332]	2017	275	Paediatric patients	Retrospective	Accommodative Rule	28%
DuPrey *et al.*[333]	2017	270	Youth athletes	Retrospective	Target and Ruler	50%
Gallaway *et al.*[311]	2017	218	Youth athletes	Retrospective	Accommodative Rule	47%
Howell *et al.*[325]	2018	33	Youth athletes	Cross-Sectional	Target and Ruler	55%
Gray *et al.*[125]	2020	578	Young patients	Retrospective	Target and Ruler	17%

Howell *et al*.[325] further identified that patients with convergence dysfunction following concussion also exhibited a slower gait speed and shorter stride lengths when walking, compared to the healthy controls. These findings propose that both ocular vergence and gross motor dysfunctions may be associated together after a concussion,[334] supporting the possible involvement of the frontal lobe after injury.[335,336] Health professionals examining post-concussive convergence should be aware that affected patients may need additional occupational therapy[337] and physiotherapy[338] for their gait.

Studies have also identified patients with both dysfunction to their convergence and accommodation following a concussion.[286,339] Considering the strong relationship and interconnected networks between both neurological pathways, multiple ocular functions would need to be assessed following a concussion. However, the techniques used to assess convergence have been poor and do not reflect gold-standard clinical methods. Some studies measured convergence using a target and tape measure,[125,328,333] while others used a ruler.[331,332] Others used either 5 cm,[125,325,328] 6 cm[286,311,331-333] or 7 cm[339] as a normal NPC cut-off, which continues to remain a discrepancy within the literature.

To date, there is only one study which has collected pre-injury convergence baselines and compared results following a concussion.[331] This study recruited 108 male youth ice-hockey players and monitored them for an entire playing season. Over the course of the competition, 11 had sustained a concussion from sport. NPC measurements were collected in seven of those players, with only one exhibiting an abnormal post-injury score. Despite reporting 11.5% to have convergence insufficiency, which is higher than the reported prevalence in the general population,[323,324] this study had a relatively small sample size and warrants further research comparing baseline to post-injury measurements.[331] However, there is recent evidence suggesting a reduced post-concussive NPC as not necessarily being indicative of convergence insufficiency. Instead, the diagnosis of clinically reduced convergence may indicate a range of interconnected conditions of the oculomotor system.[340] Therefore, a detailed orthoptic work-up of clinical signs, such as the

presence of asthenopia and decreased fusional amplitudes, are important to diagnose these patients accurately following a concussive episode.[323]

Recently, there have been gender differences identified in severity of oculomotor dysfunction after a concussion.[125] The study analysed medical records of 197 female and 381 male adolescents seen within 14 days post-injury. As expected, the researchers found headaches to be the most reported symptom in both males (86%) and females (93%). However, there was a significant contrast ($p = 0.017$) between the rates of convergence dysfunction in the male (14%) and female (22%) groups. In fact, females were found to be almost 1.8 times more likely to develop dysfunction to their convergence after a concussion than males,[127] again suggesting females are more susceptible to concussion and to related oculomotor deficits. These results may reflect the hormonal differences between genders as previously discussed,[244-247,253] although more research is required to explain this characteristic.

Screening for convergence deficits could help physicians distinguish patients that may require additional academic support during their recovery, especially if their ability to read and react to visual stimuli is impaired.[341-343] In some cases, visual disturbances may be chronic with ocular exercises demonstrated to be useful in symptom recovery.[332,344] Orthoptic exercises have been shown to be an effective method in alleviating convergence and fusional deficiencies.[322,345,346]

1.3.3 Saccadic Eye Movements (or Saccades)

Saccades are fast eye movements that aim to place an object of interest onto the fovea. All types of saccadic eye movements (Table 1.6) are ballistic, because the

neural pathway that generates saccades cannot respond to changes in the positioning of the target during the course of the eye movement. If the target moves during the saccade's activation, a catch-up saccade is required to correct the error. This conjugate ocular function is one of the quickest movements achievable by the human body, taking approximately 200 milliseconds (ms) to initiate from an unexpected stimulus. Its velocity, up to 500 degrees/second, is dependent on the distance of the fixation point from the fovea and takes about 50 - 100 ms to complete.[347]

Table 1.6. Types of saccades.

Type of Saccade	Definition
Visually Guided Saccade	Eyes move toward a visual stimulus
Anti-Saccade	Eyes move away from visual stimulus
Memory-Guided Saccade	Eyes move toward a remembered location
Predictive Saccade	Eyes are kept on a target moving in a predictive spatial manner
Self-Paced Saccade	Voluntary saccades between two fixation points

Generation of a saccade requires many control centres, making it highly vulnerable to TBI (Figure 1.5). The cerebral areas of the brain involved in initiating these eye movements originates from the frontal eye fields (FEF), supplementary eye fields (SEF) and parietal eye fields (PEF). These project to the SC, which integrates the visual and motor signals to recognise the direction and distance of the eye movement required. The initiation signal is then transmitted to the brainstem gaze centre (BGC) (see Figure 1.5), to either synapse at the mesencephalic reticular formation for vertical saccades, or the pontine reticular formation for horizontal saccades (not shown in Figure 1.5). The FEF also initiates saccades through a direct projection to the BGC, while the dorsolateral prefrontal cortex (DLPC) modulates

anti-saccades. The substantia nigra pars reticulata (SNPR) inhibits the SC, preventing saccade generation. However, this inhibition is inhibited by the caudate nucleus (CN), which is activated by the FEF prior to saccadic generation.

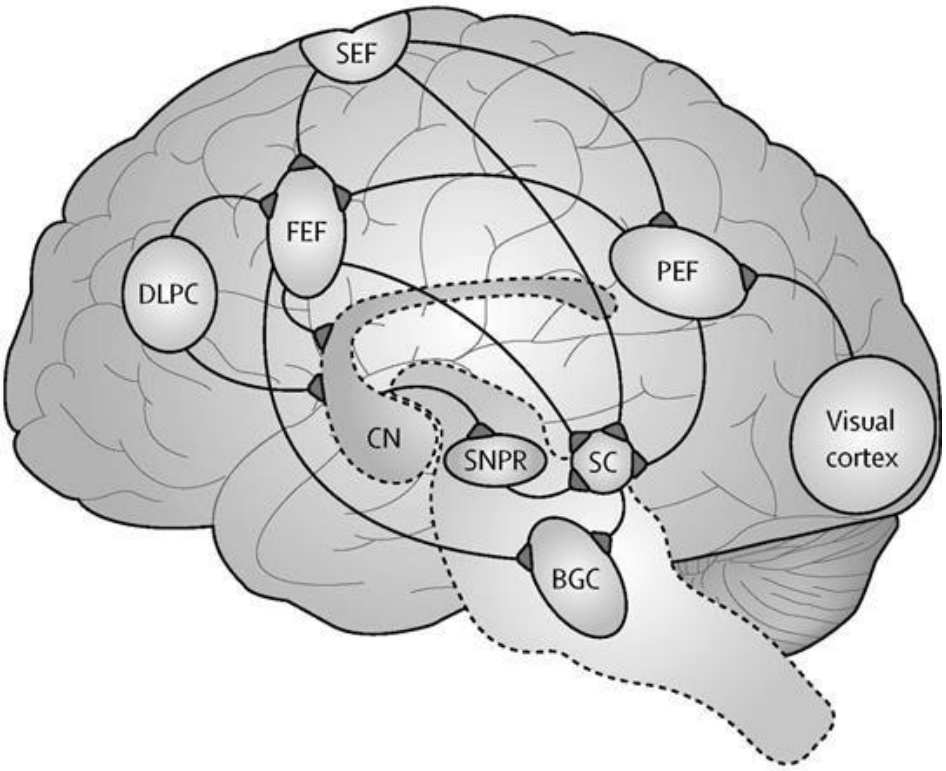


Figure 1.5. The main cortical areas and projections involved in saccadic generation. Image adapted from Ventura et al.[289]

Testing saccades, by observing the patient's eyes flick between two different targets, is a quick method to look for congruency and accuracy. In the clinic, there are several ways to assess saccadic function in patients, although they all typically involve two targets and instructing the patient to move their eyes between them. However, more recently, there is a growing interest in tracking saccades electronically using metrics as an objective marker. One example is the King-Devick test (KDT), which is used on the sidelines to detect concussive symptoms and aid in diagnosis.[348-350] This tool primarily measures saccades, but is reported to

incorporate suboptimal brain function, such as cognition and attention.[351] It involves the patient reading numbers on three testing cards as fast as possible, with the cumulative time compared with an individual baseline, if available, or an age-matched reference. Another includes the Developmental Eye Movement (DEM) Test, which is performed identically to the KDT, only read vertically.[352]

In addition, high rates of saccadic-dysfunction as a consequence of concussion (23.4% – 30%)[295,312,326] have been reported in the literature. One study found that concussed patients needed to generate more saccadic eye movements to complete the KDT, when compared to non-concussed controls.[353] Patients within the acute phase of concussion have also been found to demonstrate impairment to higher cortical saccadic tasks, such as memory-guided saccades and anti-saccades.[354-356] This type of visual dysfunction manifests with increased saccadic latencies (time between the target onset and saccade initiation) and saccadic dysmetria.[354,357-359]

Using digital eye-tracking techniques, researchers have described saccadic dysfunction following concussion in both the acute[356,359,360] and chronic stages.[355,357,361] Immediately after sustaining a concussion, Webb *et al.*[355] found patients to produce 21% more directional errors in their saccadic eye movements than healthy controls. The affected patients also demonstrated a 93 ms slower latency in generating anti-saccades and had a significantly decreased saccadic gain (accuracy) of 0.04. In another study, reduced anti-saccades post-injury were also demonstrated, but deficits to self-paced saccades, memory-guided saccades and smooth pursuit eye movements were exhibited as well.[357] Three weeks following initial assessment, anti-saccade latency was similar between both concussion and

control groups. However, saccadic gain and the number of directional errors were still notably different,[355] and have been linked to both structural and functional abnormalities to the parietal, frontal, and temporal areas and the caudate.[362]

Saccadic dysfunction following concussion have also been shown to correspond with acute changes on various neuroimaging techniques. Diffusion tensor imaging on patients with concussion displayed alterations to their corpus collosum splenium, corresponding to slower anti-saccades by a mean of 37 ms.[356] Using fMRI athletes with SRC produced longer saccadic latency times, more errors, and less self-paced saccades than a non-concussed group.[360] Results from the fMRI also showed larger activation sites and recruitment of additional brain regions upon performing these tasks, which could suggest that the injured athletes were working harder to compensate for their subtle, concussive deficits. These changes have been proposed to return to normal after one week post-injury,[363,364] however other research suggests continued hyperactivity in visual processing areas may persist for weeks after sustaining a concussion.[365]

Previous research by Master *et al*.[286] examined 100 adolescent patients diagnosed with concussion. Saccadic examination using the DEM Test detected a gross dysfunction in 29% of subjects. However, the results from this study compared the patient's measurements to a normative age-matched database, and not pre-concussive individual baselines. The DEM Test also requires some degree of cognition and attention to successfully read aloud the numbers displayed on a card. This makes it unclear as to whether the impairment within the 29 positive

participants was due to concussion-related saccadic dysfunction, cognitive dysfunction, or a mixture of the two neurological functions. Interestingly, 14 out of those 29 subjects also demonstrated deficits to their convergence and accommodation, highlighting the importance of a multi-faceted ocular battery to aid current concussion tests used on the sidelines.

1.3.4 Smooth Pursuits Eye Movements

Smooth pursuit eye movements are performed to closely track a moving target, holding the image of the moving target steady on the fovea. This is achieved by a complex feedback mechanism that continuously modifies the motor output in response to the visual input. Eliciting smooth pursuit eye movements requires high order functioning with complex neurophysiological pathways. The pursuit system cannot be initiated unless the object is moving. This conjugate eye movement has a lower latency than saccades, at approximately 140 ms. Its velocity is also much slower than saccades with a maximum of 50 degrees/second and is dependent upon the speed at which the target moves.[366] However, if the eyes are unable to keep up with the target, a series of catch-up saccades are produced to maintain fixation on the fovea.

Although the neural pathways for smooth pursuit eye movements are not quite well understood, the incorporation of multiple cortical areas in the generation of smooth pursuits makes the oculomotor function similarly susceptible to the neurological changes associated with concussion.[289,290,293] This includes the medial temporal visual area, posterior parietal cortex, dorsolateral pontine nuclei, SC, and the vermis

and paraflocculus within the cerebellum (Figure 1.6). These areas are highly involved in converting the visual information received by the visual cortex into a signal that regulates the velocity of the eye movement. For horizontal pursuits, the signal is then directed from the brainstem nuclei to the sixth nuclei and contralateral third nuclei. For vertical pursuits, the signal is directed to both third nuclei during up-gaze, and the third and ipsilateral fourth nuclei during down-gaze.[320]

Within the available literature, there is very little evidence on concussion-related smooth pursuit dysfunction. However, studies that have examined this ocular function show high rates of abnormalities.[295,312,367,368] Due to the implications it can have on a patient's safety, examining smooth pursuits is important following concussive head injury. From a clinical perspective, without extensive ophthalmological training, assessing subtle defects in smooth pursuit eye movements can be quite challenging within standard practice.

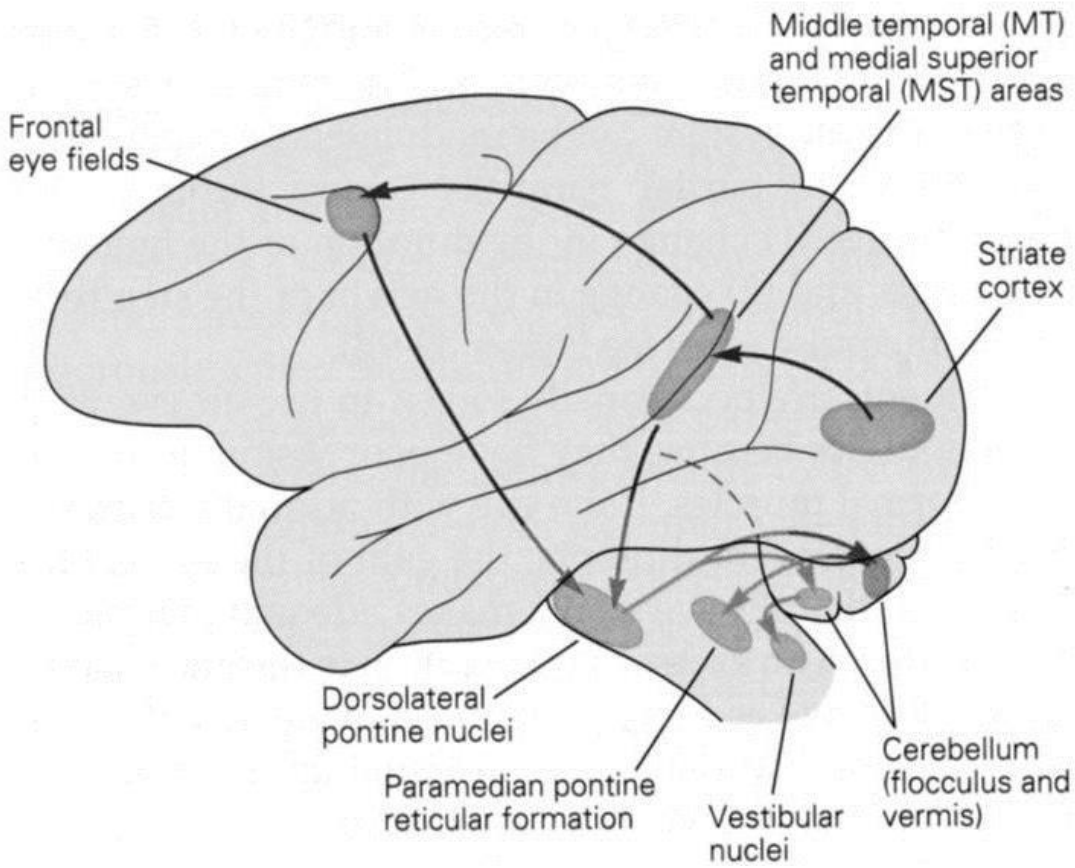


Figure 1.6. The main cortical areas and projections involved in pursuit generation.[369]

One study examined the eye movements of 36 symptomatic concussed patients three to five months after injury and compared their visual tracking abilities to 36 individually matched patients who had clinically recovered from their concussive symptoms.[357] Smooth pursuit eye movements were assessed using an infrared eye-tracking device, while the patient was instructed to follow a stimulus on a computer for 40 seconds. The authors found reduced smooth pursuits in the symptomatic group, correlating with problems performing daily living activities. This has been associated with reductions in smooth pursuit initiation latencies, position gain (eye

position/target position) and velocity gain (eye velocity/target velocity), as found in a high school athletic population.[370]

Past evidence has also shown impairments to target prediction when testing circular smooth pursuits. Studies by Suh *et al*.[371,372] found a slower phase lag in participants with concussion when tracking a target along a circular trajectory. Upon examining the other kinematics, the affected participants also exhibited an increased positional error, increased intra-individual positional variability and an increased number of catch-up saccades.[371,372]

Ideally, examining smooth pursuits using a portable concussion tool would enable health professionals to assess visual function on the sidelines.[189,373] Capo-Aponte *et al*.[295] used the North-Eastern State University College of Optometry (NSUCO) Oculomotor Test[374] to assess smooth pursuit eye movements in soldiers with concussion. The tool provides the examiner with a score out of five on pursuit accuracy and ability, along with saccadic function and the study found 60% of subjects had smooth pursuit dysfunction. However, the patient's score is dependent on the examiner's interpretation and can be seen as highly subjective.[295] Furthermore, the study did not examine eye movements before the concussions were sustained, thereby lacking individual baselines. This justifies the need for more research on comparing pre- and post-injury smooth pursuit eye movements, which would also clarify whether these impairments reported were acquired or pre-existing.

In the research setting, using video-oculography to track disconjugate eye movements is gaining popularity as a possible marker for concussion.[375-377] Maruta and co-authors examined a population with chronic concussive symptoms and found a significant decline to their predictive visual tracking capabilities.[378,379] Through diffusion tensor imaging, the researchers attributed these oculomotor impairments to white matter tract damage in the corona radiata, left superior cerebellar peduncle and genu of the corpus collosum. In combination with neurocognitive testing, these patients also showed reduced attention and working memory, highlighting the potential need for multi-faceted concussion battery involving visual assessments. However, a greater understanding of video-oculography metrics and its ability to detect an acute brain injury are firstly required to help facilitate translation of this technology into standardised concussion assessments.[189,290,380]

1.3.5 Visual Fields

Visual field anomalies have been reported following significant trauma but rarely following a concussion.[380,381] Visual field defects related to TBI include homonymous hemi- and quadrantanopia.[382] Brahm *et al*.[312] noted 3% of patients with blast-induced trauma to demonstrate reduced visual fields upon confrontation testing. For screening purposes, confrontation visual fields can be performed to provide a gross measurement. However, this type of testing provides low sensitivity.[383] Using a Goldmann or Humphrey perimeter would provide a more quantitative analysis, however would require substantial examiner training and time. Visual field loss is not expected in concussion and its occurrence should prompt further neurological examination and neuroimaging for a structural pathology.[147]

1.3.6 Cranial Nerve Palsies

The extra-ocular muscles play a vital role in normal eye movements. In particular, cranial nerves III, IV and VI innervate the six major muscles around the eye. Each nerve has a unique anatomy and neurological pathway, making them distinct in their actions (Table 1.7). Injury to these nerves through brain trauma could lead to impairments in ocular motility, causing diplopia, inadequate vergence and version eye movements.

Table 1.7. Actions of the extra-ocular muscles and cranial nerve innervation.

Extra-Ocular Muscle	Primary Action	Secondary Action	Tertiary Action	Cranial Nerve
Medial Rectus	Adduction	-	-	III
Lateral Rectus	Abduction	-	-	VI
Superior Rectus	Elevation	Incyclotorsion	Adduction	III
Inferior Rectus	Depression	Excyclotorsion	Adduction	III
Superior Oblique	Incyclotorsion	Depression	Abduction	IV
Inferior Oblique	Excyclotorsion	Elevation	Abduction	III

Oculomotor Nerve (CNIII) Palsies

The oculomotor nerve, or cranial nerve III, is derived from the basal plate of the embryonic midbrain and is involved in controlling eye movements, eye lid function and pupil constriction. It has two distinct nuclei originating from the midbrain. The oculomotor nucleus supplies the skeletal extra-ocular muscles including, the levator palpebrae superioris, superior rectus, inferior rectus, medial rectus and inferior oblique. The Edinger-Westphal nucleus innervates the ciliary ganglion via parasympathetic fibres, controlling the sphincter pupillae muscle (which allows pupil constriction) and the ciliary muscle (which allows accommodation). The nerve enters the orbit through the superior orbital fissure, where sympathetic postganglionic fibres also supply the smooth muscle of the superior tarsal, known as Mueller's muscle. It then splits into a superior and inferior branch, which supply its respective ocular muscles (see Table 1.7).

At the site of the superior orbital fissure or exit from the midbrain, the oculomotor nerve is susceptible to damage from TBI, occurring between 3 – 11% of cases.[384,385] Such damage, which would result in a third nerve palsy, is unlikely to occur in a concussion and is generally noted in more severe cases of brain injury unless associated with a pre-existing abnormality, such as a sphenoid fracture or intracranial haemorrhage.[386,387] Walter *et al*.[388] identified an oculomotor nerve palsy in a patient following a concussion, although further clinical investigation determined that this was contributed to by an underlying posterior communicating artery aneurysm.

However, upon reviewing 49 patients with blunt head injury, Coella *et al.*[389] reported seven patients were diagnosed with a third nerve palsy. Importantly, this study diagnosed brain injuries using the GCS, with all patients demonstrating abnormal CT scans. Using a modern classification of concussion, many of these may not have been included, as this study was conducted over a decade ago.

The presence of a third nerve palsy has been previously associated with mTBI. In a case report, a young woman suffered a closed head injury after falling down stairs and was diagnosed with an isolated right third nerve palsy.[390] Manifesting with completed right ptosis, pupil dilation and the typical "down and out" presentation (hypotropia and exotropia), there was no pathology revealed on MRI and CT scans to classify the TBI beyond mild. However, with such conflicting evidence on the association of a third nerve palsy and concussion, to establish such an association would warrant the need for a large multicentre collaborative study maintaining a database of all such cases with standardised clinical investigation and reporting. This could only be justified as part of a larger study on ocular motor deficits in concussion.

Trochlear Nerve (CNIV) Palsies

The trochlear nerve, or cranial nerve IV, is the smallest of the cranial nerves and solely innervates the superior oblique muscle around the eye. Like the oculomotor nerve, it derives from the basal plate of the embryonic midbrain, but instead, its function is to depress the eye during adduction and provide incyclotorsion (Table 1.7). Originating within the dorsal midbrain, the trochlear nerve decussates at the

site of the brainstem before entering the subarachnoid space. It then travels under the tentorium cerebelli and through cavernous sinus, before supplying the superior oblique muscle. Interestingly, the tendon of the superior oblique passes through a fibrous loop, called the trochlea, which acts as a pulley on the muscle.

With the longest intracranial length out of all the cranial nerves, the trochlear nerve is the most susceptible to traumatic injury occurring in between 3 – 13% of respective cohorts.[384,385,391,392] This would clinically manifest with a hypertropia and excyclotorsion, causing both vertical and torsional diplopia. However, like a third nerve palsy, this is uncommon to occur following concussion. It is more likely to be associated with the impact of the midbrain against the tentorium causing dorsal midbrain parenchymal contusions and haematomas,[393-395] or due to haemorrhaging within the subarachnoid space.[395-397]

In fourth nerve palsies, careful clinical examination including a positive Bielschowsky's Head Tilt Test and an underacting superior oblique on extra-ocular movements is diagnostic. However, they are often underdiagnosed by hospital services.[398] Therefore, these oculomotor defects may be missed on the sideline following a concussion if not carefully examined.

Fourth nerve palsies have been reported in isolated instances following concussive head injury.[187,389,393] In a case report, a young, male lacrosse player who suffered a traumatic blow to the head presented with a 10-prism dioptre hypertropia and was clinically positive of a right fourth nerve palsy.[399] In another study, seven patients reviewed were diagnosed with a fourth nerve palsy after suffering a head trauma.[389]

However, only three of those patients had normal brain imaging, suggesting the other four patients had a more severe form of TBI.

Abducens Nerve (CNVI) Palsies

The abducens nerve, or cranial nerve VI, is derived from the basal plate of the embryonic pons and is solely responsible for abducting the eye (Table 1.7). Originating from the pons, the nerve travels through the subarachnoid space and enters the dural hole. It then ascends over the ridge of the petrous bone, to reach the petrous apex. The nerve then changes direction by 120° and passes through Dorello's canal before entering the cavernous sinus and innervates the lateral rectus (Figure 1.7).

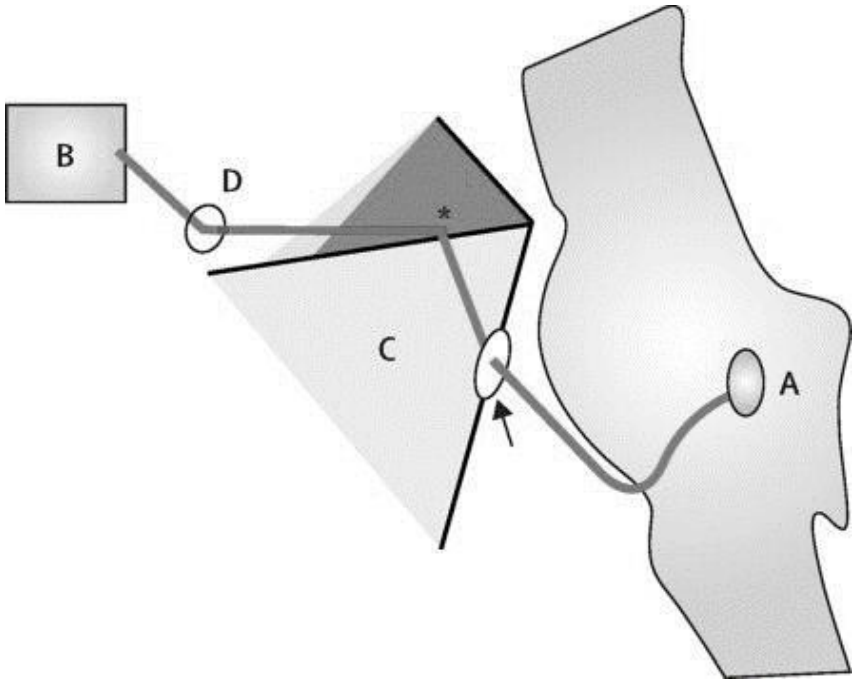


Figure 1.7. The pathway of the abducens nerve. (A) Abducens nuclei, (B) The Eye, (C) Petrous bone, (D) Supraorbital fissure, (arrow) Dural hole, (asterisk) petrous apex. Image modified from Ventura et al.[289]

Abducens nerve damage has been reported in up to 4 – 6% of patients with mTBI.[384,385] Despite not being common in mild forms of brain injury, its neurological pathway makes it highly susceptible to damage, in particular, at the apex of the petrous bone and along the base of the skull. Damage can also occur due to elevated intracranial pressure.[400] Clinically, this would manifest with the patient complaining of horizontal diplopia, worse in the distance and toward the affected side.

Asproudis *et al*.[401] reported an isolated case of abducens nerve palsy after a closed head injury in a child. In the absence of a skull fracture, haematoma or raised intracranial pressure, clinical examination revealed a 30-prism dioptre right esotropia and a restricted right lateral rectus muscle. This was similar to the presentation of eight patients with an abducens nerve palsy following minor head injury.[389] Additional brain imaging indicated that four of the patients had normal CT scans in association with a normal GCS score, which may potentially meet the contemporary diagnostic criteria of a concussion.

1.4 VISUAL TOOLS FOR DETECTING AND MONITORING CONCUSSION

Considering many of the brain's ocular pathways are susceptible to impairment following a concussion, performance measures involving visual function appear promising for post-injury assessments for diagnostics and rehabilitation.[161,189,290] These include an evaluation of an athlete's saccades, smooth pursuit eye movements, convergence and accommodation.[293] To detect abnormities to the visual and oculomotor systems, there are three popular visual tools which have been supported to be a possible addition to concussion testing batteries.

1.4.1 The King-Devick Test (KDT)

The KDT is a rapid number naming test which primarily assesses a person's saccadic eye movements. It has been widely supported by sports and neurological researchers as a reliable sideline tool for identifying concussion.[190,199,200,402] Developed in 1976 by Alan King and Steve Devick,[403] the initial use of the KDT was not for detecting traumatic brain injuries (Figure 1.8). Instead, it was originally proposed as a screening tool for eye movement abnormalities associated with reading problems.[403]

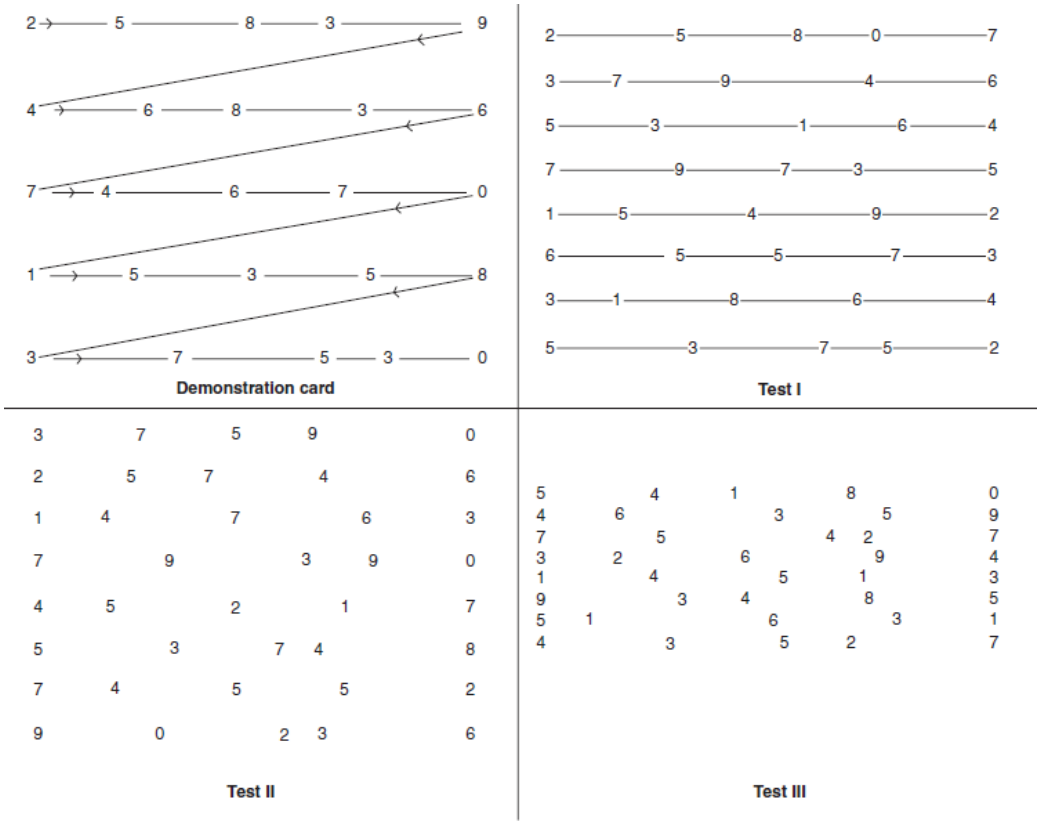


Figure 1.8. The King-Devick Test consists of one demonstration card (upper-left) and three examination cards (top-right and bottom) which increase in difficulty.[403]

In addition to providing an understanding of possible reading problems in elementary children,[404] the KDT has been used over the last couple of decades in the detection of neurological deficits affiliated with multiple sclerosis,[405] stroke,[406,407] Parkinson's Disease,[408-410] sleep deprivation and hypoxia.[411,412] For example, Stepanek *et al.*[412] induced experimental hypoxia on astronaut trainees and found a mean difference of 8.2 seconds, when compared to healthy controls. These results demonstrated that those in a sub-neurological state may manifest defective eye movements and perform poorer on the test.

More importantly, reduced performances on the KDT has been also shown to correlate with suboptimal brain function in the setting of concussion.[214,402,413-420] The tool incorporates eye movement (saccades and smooth pursuits),[421] attention and language function, and so, involves the integration of activities performed by the brainstem, cerebellum and cerebral cortex. As concussion represents a diffuse brain injury, functional damage to any cortical or subcortical areas involved with generating eye movements will likely result in abnormalties.[161,289,357,422-426] One detailed analysis of the saccadic components identified concussed participants to have prolonged intersaccadic intervals, greater numbers of saccades, and larger deviations of saccade endpoints when performing the test, but no differences in saccadic peak velocity, duration, or amplitude.[353] This may suggest that different anatomical parts of the visual and ocular motor systems may be less vulnerable to a concussion, such as the brainstem, although this has yet to be explored outside an individual case study.[427]

Considering the tool involves a high degree of visual processing, it has also been identified that there exists a strong relationship between KDT performance and visual acuity. This is important for sideline examiners who may not assess an athlete with their refractive correction. In one study, high school students with a visual acuity of less than 20/30 (6/9 equivalent) had poorer KDT scores by 4.6 seconds when compared to a control sample with a better visual acuity.[428]

This relationship has also been replicated in groups diagnosed with multiple sclerosis[429] and Huntington's disease,[430] where these patients were identified with reduced visual acuities as a result of their condition. Upon examination with the KDT, up to a 54.7 second poorer score was noted when compared to age-matched healthy controls.[429,430] This would imply that the need for a refractive correction through glasses or contact lenses upon assessment is imperative. However, it is important to also consider that those diagnosed with these systemic conditions may endure changes to other visual functions such as colour vision, visual fields, eye movements and contrast sensitivity.[431-434] More research is thereby warranted to clarify whether these reduced KDT scores are a direct result of the patient's visual acuity, secondary eye movement issues which may be subtle and not be identified during participant screening, or a combination of both factors.

Age

In addition to having better visual acuity, there is strong evidence suggesting increasing age correlates to improved scores on the KDT. This finding is supported by a variety of studies on different youth populations, including school children and

adolescents.[214,428,435,436] In one study, Alsalaheen *et al.*[436] examined the different age demographics in 157 high school football students to determine normative data for younger populations. Their results demonstrated significantly faster KDT scores in students aged 16 to 18, compared to those aged 13 to 15 (40.9 vs. 43.8 seconds; $p = 0.03$). Weise *et al.*[437] further supported this finding as students in 10th grade or higher at school performed significantly faster KDT scores than students in 9th grade or below (37.4 vs. 45.4 seconds; $p < 0.0001$). In accordance to these differences, the researchers associated the reduced scores in 9th grade or below to ongoing brain maturation,[437] as neuron growth and pruning has been found to occur at this age.[438]

In older groups of those above 30 years of age, research utilising the KDT is still quite limited. This is probably due to a greater emphasis on concussion research within the scope of youth athletic populations. A systematic review of 15 articles found faster KDT scores in non-concussed participants around the age of 18, which typically remains stable until they are 40.[190] Proceeding this age, KDT scores tend to slowly worsen, although it is unclear whether this is due to the effects of age-related conditions affecting visual acuity and/or oculomotor function.

Normative Values

The KDT protocol requires repeated baseline measurements to be performed for later comparison however this may not be possible, if used in an emergency facility. Accordingly, the use of normative population values may provide some diagnostic benefit, although is not recommended by the manufacturers of the tool. In the standard adult non-athletic population, the range of scores is from 42.2 to 54.6 seconds.[410,421,439-446] The outcomes from sports populations, on average, appears to

be faster (34.9 to 50.1 seconds, see Table 1.8). This may reflect multiple factors including faster saccadic velocities in athletic groups[447,448] or greater exposure to test procedures as likely from a competitive sports environment. Against this, at least in a contact-sports group, is the increased risk and impact of concussive episodes.[449] Further research is likely to elucidate these changes. There is some published data on the normative values of the KDT with the list of studies and values recorded in Table 1.8.

Table 1.8. Published pre-season baseline/normative KDT scores since 2011 (papers = 41). Only participants that had completed all three cards and were non-concussed were included. Age was presented as mean or range where available. Baseline scores provided as either mean ± standard deviation or median (interquartile range) and was recorded in seconds.

Author(s)	Year	Age at Baseline	*n*	Baseline Score	Study Design	Participant types
Rebchuck *et al.*[450]	2020	8 to 25	35	34.9 ± 6.4	Longitudinal	Football players
Gubanich *et al.*[451]	2019	8 to 18	483	41.7 to 72.7 (depending on age group)	Prospective observational cohort	Non-concussed children
Fuller *et al.*[452]	2019	27.6	207	44.3 (38.5 – 50.9)	Prospective cohort study	Professional rugby athletes
Elbin *et at.*[435]	2019	14 to 18	772	44.6 ± 8.2	Prospective, repeated-measures design	High school athletes
Hecimovich *et al.*[453]	2019	13.9	19	56.4 (51.2 - 61.5)	Longitudinal	Australian Football players
Clugston *et al.*[454]	2019	20	2003	42.8 (42.1 - 43.3)	Cross-sectional	Student athletes
Clugston *et al.*[455]	2019	20	2344	41.1 ± 7	Cross-sectional	Student athletes

Author(s)	Year	Age at Baseline	*n*	Baseline Score	Study Design	Participant types
Moran and Covassin[456]	2018	11.0	422	54.2 ± 11.5	Prospective observational cohort	Soccer and football players
Capo-Aponte *et al.*[439]	2018	Not specified	100	44.5 ± 8.1	Case-control correlational	Military personnel
Silver *et al.*[457]	2018	14 to 18	323	42.0 to 44.7 (depending on age group)	Prospective observational cohort	Rugby Union players
Hasanaj *et al.*[458]	2018	18 to 23	13	39.1 ± 5.4	Longitudinal	Collegiate ice hockey players
Eddy *et al.*[459]	2018	21.0	63	38.4 ± 5.7	Crossover	Collegiate students
Dhawan *et al.*[417]	2017	15.5	141	42.1	Prospective observational cohort	Youth athletes
McIntyre and Campo[460]	2017	21.1	238	41.5 ± 8.2	Cross-sectional	Dancers
Anderson and Biely[440]	2017	40.5	243	42.2 (26.2 - 76.0)	Cross-Sectional	Healthy adults
Author(s)	Year	Age at Baseline	*n*	Baseline Score	Study Design	Participant types

Author(s)	Year	Age at Baseline	*n*	Baseline Score	Study Design	Participant types
Weise *et al.*[437]	2017	Not specified	619	43.9 ± 11.6	Prospective observational cohort	School athletes
Subotic *et al.*[441]	2017	36.9	18	49.6 ± 11.2	Cross-sectional	Healthy controls
Oberlander *et al.*[442]	2017	15.4	68	48.8 - 54.6 (depending on age group)	Cross-sectional	Healthy adolescents
Molloy *et al.*[461]	2017	23.4	33	41.7 ± 8.0	Descriptive cohort	Semi-professional rugby players
Yorke *et al.*[443]	2016	15.4	105	43.3	Cross-sectional	Healthy adolescents
Rizzo *et al.*[444]	2016	32.0	42	43.8 ± 8.55	Cross-sectional	Healthy controls
MacDonald *et al.*[462]	2016	Not specified	46	40.2	Longitudinal	High school athletes
Rizzo *et al.*[421]	2016	32.0	12	51.24 ± 9.7	Cross-sectional	Adult volunteers
Alsalaheen *et al.*[436]	2016	13 to 18	157	40.9 (31.94 – 55.51)	Cross-sectional	High school football players

Author(s)	Year	Age at Baseline	*n*	Baseline Score	Study Design	Participant types
Walsh *et al.*[445]	2016	26.3	100	45.65 ± 8.31	Cross-sectional	Non-concussed military controls
Marinides *et al.*[420]	2015	Not specified	217	38.7 (37.8 - 39.6)	Prospective observational cohort	Collegiate athletes
King *et al.*[463]	2015	10.4	19	62.0 ± 9.8	Prospective observational cohort	Junior league players
Seidman *et al.*[464]	2015	15.4	328	47.4 ± 9.7	Prospective observational cohort	High school football players
King *et al.*[200]	2015	23.7	104	50.1	Prospective observational cohort	Rugby players
Vernau *et al.*[331]	2015	12.5	108	55.9	Prospective observational cohort	Youth ice hockey players
Leong *et al.*[402]	2015	19.6	127	35.9 (26.0 – 54.5)	Prospective observational cohort	Collegiate football athletes
Vartiainen *et al.*[465]	2015	23.8	185	40.0 ± 6.1	Cross-sectional	Ice hockey players
Silverberg *et al.*[446]	2014	42.0	33	47.15 ± 10.06	Cross-sectional	Non-injured controls

Author(s)	Year	Age at Baseline	*n*	Baseline Score	Study Design	Participant types
Duenas *et al.*[418]	2014	16.5	13	42.98 ± 7.3	Prospective observational cohort	High school football players
Leong *et al.*[414]	2014	Not specified	Not specified	41	Prospective observational cohort	Amateur boxers
Munce *et al.*[466]	2013	13.4	10	47.35 ± 7.41	Prospective observational cohort	Youth football players
Lin *et al.*[410]	2014	65.0	65	53 ± 13	Cross-sectional	Healthy control patients
Galetta *et al.*[413]	2013	28.0	27	40.3 ± 6.4	Prospective observational cohort	Ice hockey players
King *et al.*[199]	2013	22	37	44.9 (25.4 – 69.2)	Prospective observational cohort	Rugby players
Galetta *et al.*[416]	2011	20.3	219	37.9 (23.4 – 58.0)	Longitudinal	University athletes
Galetta *et al.*[415]	2011	24	39	44.6 (32.0 – 58.2)	Cross-sectional	Boxers and MMA fighters

According to the findings depicted in Table 1.8, it would appear that the normative value for the KDT is around 40 seconds. This would be useful information for health professionals who may assess a patient without access to a pre-injury baseline. However, the majority of normative data published (73.2% of Table 1.8) have been collected from participants from an athletic background.[199,200,331,402,413-418,420,435-437,450,452-466] Considering faster visual reaction times have been recorded in athletic populations when compared to non-athletic groups,[467-469] this may not be a true representation of the general population. In addition, this approximate normative score does not take into consideration other confounding factors such as age and visual function, with 52.5% of the studies in Table 1.8 consisting of participants between the ages of 18 to 37. Tjarks et al.[177] therefore state that a score greater than 60 seconds following a concussion can be considered universally abnormal for any age group or population type, however the need for an individual baseline score is critical in utilising this tool appropriately.

Post-Concussion Results

It is currently thought that the relationship between concussion and neurological deficits can be detected using the KDT.[214,402,413-420] Collectively, available evidence have demonstrated within various athletic populations that a worsening of over 3.2 seconds is common after a concussion.[199,200,214,402,413-420,463] In one study, King *et al.*[200] recorded a mean 6 and 5 second decrease from baseline in witnessed and unwitnessed concussions respectively, within a large sample of 104 rugby union and league athletes.

This has led to the KDT to be reported as both highly sensitive (86%)[214] and specific (94%)[200] in identifying concussion within the sports setting, making it a valuable tool for sideline medical personnel. The test-retest reliability for the KDT has also been previously researched, demonstrating high intraclass correlations between measurements in the absence of concussion of 0.96 (95% CI 0.93, 0.99) in one study[414] and 0.97 (95% CI 0.90, 1.0) in another.[415] However, some evidence has revealed that the tool may not be a reliable indicator when utilised as a standalone measure.[190,470] This is likely due to the tool only examining limited neurological functions, including cognition, language and eye movements, and may be influenced by external factors such as English language skill.[471,472] Instead, using a combination of concussion tools alongside the KDT have been able to achieve much higher diagnostic yields.[161,164,420,470] When the KDT was used alongside the SAC and BESS concussion tests (key components of SCAT-5), the sensitivity of the KDT in identifying concussion improved from 79% to 100%.[420] This would infer that the KDT would be a useful addition to current concussion testing batteries.

While there are plenty of published, peer-reviewed research establishing notable evidence in support of the KDT as a post-concussive tool,[199,200,214,402,413-420,463] one has revealed no effect.[473] The study found no statistical significant difference (p = 0.4) when comparing the scores between 12 collegiate athletes with concussion to 60 non-concussed controls.[473] However, the methodology in this paper was highly flawed with only the cumulation of two attempts used for analysis, rather than the standard and highly recommended three. In addition, the authors did not compare post-concussive scores to an individual pre-injury baseline. It is therefore possible that the negative findings witnessed in the study would heavily support the need for baseline establishments to more accurately distinguish a concussive event, as opposed to comparisons with a normative value. As such, it is widely agreed upon that the KDT is a useful concussion tool in post-injury assessments when performed correctly.[214,402,413-420]

Learning Effects

While those with a concussion demonstrate reduced times on the KDT, non-concussed control athletes, in contrast, recorded improved scores over two trials.[190,199,200,402,416] This has been described as learning effects, a common phenomenon where the speed and accuracy of completing cognitive tasks increase in correlation with the number of repetitions performed.[474] For instance, in a pooled analysis of 1048 non-concussed participants performing a baseline KDT, a mean improvement of 2.8 seconds was uncovered between first and second attempts (49.5 vs. 46.7 seconds, $p < 0.0001$).[190] These results match previous

findings, identifying a typical improvement of between 2.2 to 3.1 seconds between two attempts of a baseline establishment.[199,348,402,413,415-417,419]

However, these mild learning effects experienced during KDT baseline establishment have also been noticed when performing more than the two required attempts.[442] This emphasises the need for potentially more than two trials to establish an accurate baseline score, as currently recommended by the tool's manufacturers. A cohort of healthy adolescents produced a notable improvement of 6.9 seconds over three KDT attempts, spanning 45 days. The participants recorded an improvement of 4.3 ± 0.5 seconds between attempts one and two, and a further 2.4 ± 0.5 seconds between attempts two and three (both $p < 0.001$).[442] However, beyond this study, there is no other paper exploring this relationship. Thus, future studies are needed to determine the number of attempts required to determine a ceiling effect, a point at which there is no more learning effect obtainable. This would ensure better detection of SRC as a more accurate baseline would be used for comparison.

Fatigue

It has been additionally postulated that the KDT may be influenced by fatigue which, under playing conditions, could invalidate the test.[199,414,475] However, current evidence suggests that this does not represent an issue. Leong *et al.*[402] found a mean improvement of 2.7 seconds ($p < 0.05$) between pre- and post-workout KDT scores in men's and women's basketball teams. This is similar to prior fatigue studies performed in collegiate basketball athletes (35.0 vs. 37.9 seconds, $p < 0.01$),[476] amateur rugby athletes (43.6 vs. 44.9 seconds, $p < 0.05$)[199] and a youth

hockey study that tested non-concussed athletes before and after games (3.4 second improvement).[477] However, the aforementioned studies were conducted in athletic cohorts with pre-existing high levels of fitness which may have masked the potential impact of fatigue. Similarly, these improvements are likely indicative of a learning effect experienced by these athletes, although it is difficult to determine whether these findings are replicable in non-athletic cohorts due to the lack of studies.

Alternatively, there are a few studies that would suggest fatigue from the lack of sleep may lead to a negative effect on cognitive performance associated with the KDT.[478-480] Davies *et al.*[478] examined this in a small sample of 35 doctors, finding those who experienced less sleep (*n* = 25, median = 2 hours, range 0 to 6.5) produced poorer scores by 4.0 seconds, than those with more sleep (n = 10, median = 7.5 hours, range 6 to 8) after a working shift. While a different study noted similar results, with doctors on-call performing 0.54 seconds slower after a shift, compared to an improvement of 2.32 seconds by a well-rested control group.[480] Although not yet replicated in studies within the sport setting, medical personnel should be aware of the level of sleep deprivation in athletes before interpreting KDT results.

Future Directions

Future studies should address potential gaps in the research by appropriately determining the amount of learning effect obtainable during pre-injury assessments. This is critical to be able to identify a true baseline for athletes and for this value to be used as a more accurate measure in concussion testing and

determining the effects of fatigue. Thus, these studies should ultimately calculate the number of required trials an athlete should perform during baseline establishment.

1.4.2 The Royal Air Force (RAF) Rule

First mentioned, in 1956, by James Neely in the literature, the RAF Rule (Figure 1.9) was originally developed in the United Kingdom to assess the visual function of people conscripted into the American military.[481] Today, it is readily employed instrument in ophthalmic, optometric and orthoptic practices worldwide for the assessment of patient's NPC and NPA.[482-484]

Figure 1.9. The Royal Air Force Rule.

The instrument consists of a rotating four-sided cubical drum connected to a slider. This slider is attached to a square section metal rule, which is 50 cm long and has a cheek rest on the patient side. This cheek rest is V shaped and 6 cm in length. The four sides of the rule indicate a scale in 1 cm increments, a corresponding equivalent dioptric scale for accommodative amplitudes, an expected age scale and

a scale indicating the positions of normal and abnormal convergence. On each side of the cubical drum depicts a different black target on a white background, as shown in Figure 1.10. Sides A to C are typically used to measure accommodative amplitudes, while D is for convergence.

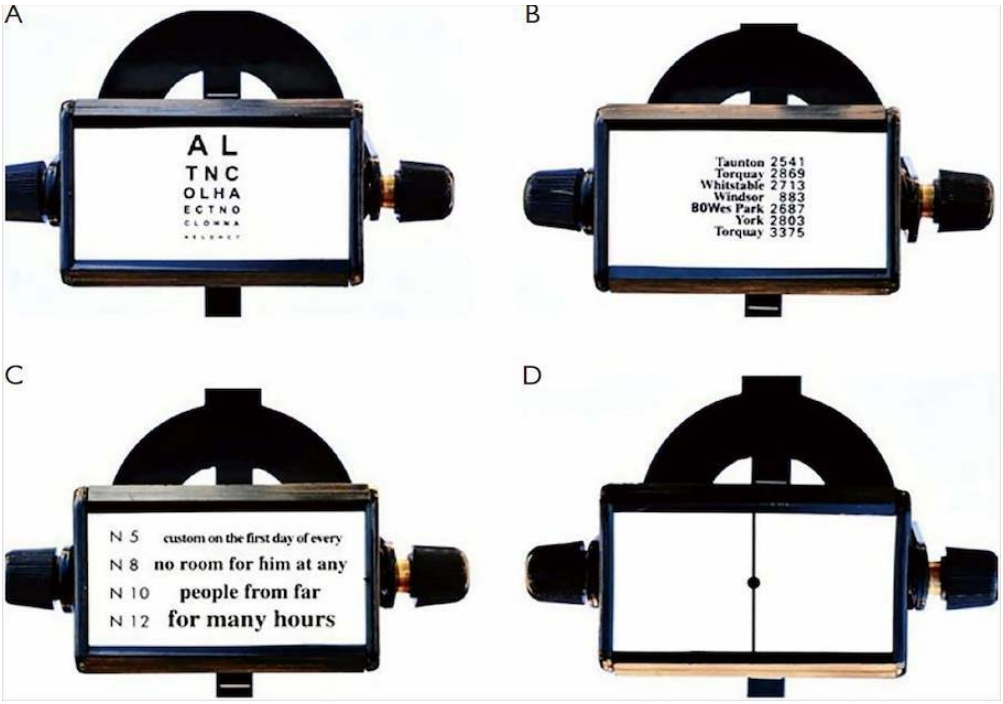


Figure 1.10. Each side of the cubical drum on the Royal Air Force Rule. Side A is a Snellen chart reduced to one-seventeenth of its actual side and is accurate at 35 cm from the patient. At this distance, the chart subtends an angle of 5 min of arc, which corresponds to a standard chart at 6m. Side B is a photographed section of the General Post Office telephone directory in 1956. Side C depicts four lines (N5, N8, N10 and N12) in "Times Roman" font. Side D is a black dot in the centre of a vertical line, used to assess NPC. Imaged adapted from Sharma (2017).[485]

According to Adler *et al.*[486] the RAF Rule produces more accurate measurements of convergence than a penlight or string with a ruler. The instrument was thereby utilised to assess a large sample of 1448 children and identified 9.6% with a receded

NPC measurement.[487] In addition, multiple studies have also demonstrated its reproducibility in measuring accommodation and convergence in cohorts of adults and children,[486,488,489] making it a preferred tool for standard ocular examinations in the clinical setting and potentially on the sideline.

Local to Australia, Cornell and Heard claim the RAF Rule is the "*most commonly used instrument to assess accommodation*", due to its advantage of comparing an individual's amplitudes with an age-related normative.[484] These normative results were determined in 1922, by Duane and plotted graphically on Duane's classical curves (Figure 1.11).[305] In the context of concussion, these normative scores could be used as a marker in the absence of a pre-injury baseline.

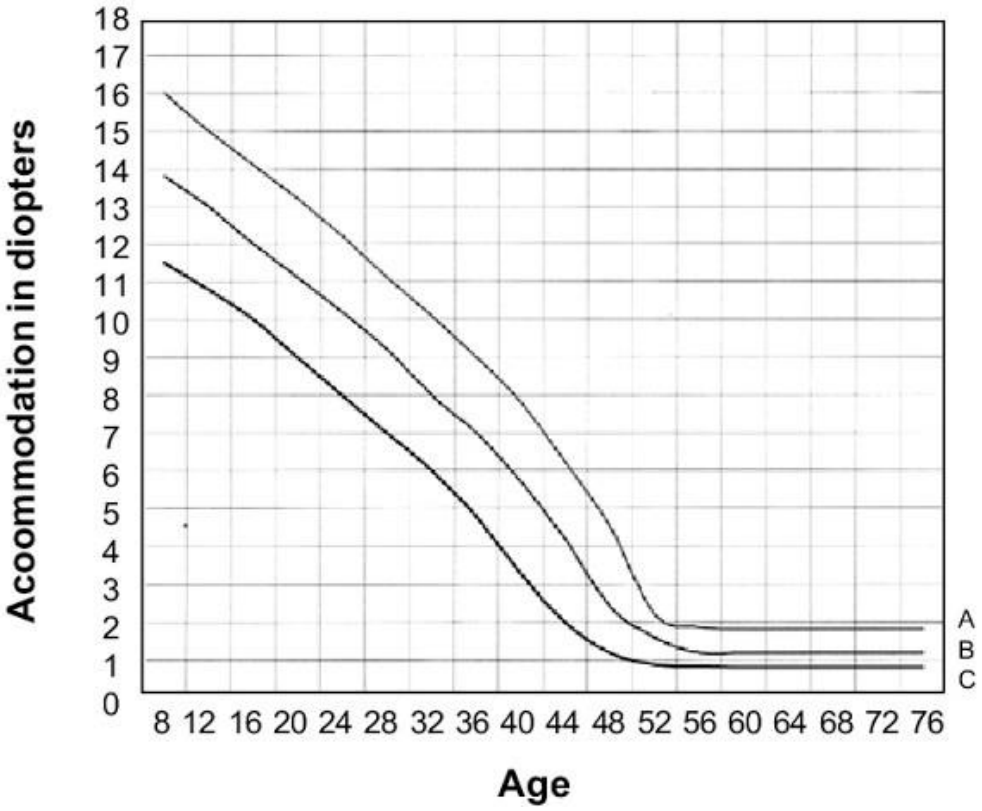


Figure 1.11. Duane's classic curve indicting the relationship between accommodative amplitudes and age. This includes the mean (B) values with the upper (A) and lower (C) standard deviations.[305]

According to Figure 1.11, accommodative amplitudes decline with age. By a person's fifth decade of life, the accommodative amplitude can decline to a near point further away from reading distance. This is clinically diagnosed as presbyopia. Once presbyopic, a person who is emmetropic (doesn't require an optical correction for distance vision) will need an optical aid, in form of a convex lens for their reading vision. Those who are myopic (nearsighted and require an optical correction for distance vision), will find that they see better at near without their distance correction. While those who are hypermetropic (longsighted), will find that they may require an optical correction for both distance and near vision. By the age of 70, a person's accommodative amplitude is approximately one dioptre (D). These are important considerations for researchers and medical staff who may use the RAF Rule to assess accommodative amplitudes following a concussion in older patients.

Post-Concussion Results

Despite being suggested,[147,439,490] there is limited evidence demonstrating the RAF Rule as an objective marker for diagnosing concussion. Capo-Aponte *et al.*[439] found post-concussive NPC measured by the RAF Rule to be useful in distinguishing between mTBI and control groups. Patients diagnosed with acute mTBI revealed an NPC of 13.25 ± 8.07 cm, compared to 8.18 ± 2.15 cm in the control group ($p < 0.001$). Although demonstrating a high sensitivity of 81%, the instrument was not

used to measure accommodative amplitudes and revealed a large false positive rate (51%).

Outside CapoAponte's work,[439] no other paper has utilised the RAF Rule in post-concussive assessments. Similar devices, like the accommodative rule, have been previously used in two other studies.[311,331] These papers have detected convergence dysfunction following a concussion in athletic groups. However, the research has been limited by either a low sample size[331] or retrospective study design,[311] suggesting the need for further clarification on the utility of the RAF Rule within a concussion assessment battery.

Future Directions

Due to the focus on convergence and accommodation testing as part of a post-concussion examination, future studies should determine the utility of the RAF Rule in identifying concussion. This would provide clinicians with an easy to use, fast and objective marker to use on the sidelines. These studies should also consist of baseline convergence and accommodation testing, with a post-injury follow up for comparison.

1.4.2.1 The Vestibular/Oculomotor Screening (VOMS) Tool

Considering the high prevalence of vestibular and oculomotor symptoms following a concussion,[286,491,492] clinicians and researchers had collaborated to develop the VOMS tool.[493] This was designed to be used in conjunction with other concussion screening tools to provide a comprehensive clinical examination.

Measuring symptom provocation after each assessment of five domains including, horizontal and vertical smooth pursuit eye movements, horizontal and vertical saccades, convergence, horizontal and vertical vestibular-ocular reflexes, and visual motion sensitivity, the tool has demonstrated strong internal consistency and the ability to differentiate between concussed and healthy samples.[493-495] Mucha *et al.*[493] found a greater mean NPC of 4 cm in the concussed group compared with the control group ($p < 0.001$). The authors also recorded a high sensitivity (89%), suggesting a positive test result is strongly indicative of a concussion. However, the tool was described to be limited by the fact it assessed subjective patient reporting of post-concussive symptoms. It has also been found to be influenced by those diagnosed with a history of motion sickness[496,497] and children with learning difficulties and ADHD.[498]

Some patients performing the VOMS tool have been reported to produced false positive rates upon completion of the test. This was in as high as 10.6% in a large sample of male youth ice hockey players from Canada.[499] In a similar-aged sample of high school athletes, these false positive rates were also revealed, although in a smaller proportion of participants (2%).[500] Concussion history has been revealed to be a contributing factor to the tool's performance with a 2.5 fold increase in false positive rates,[501] however these associations have yet to be fully understood in the literature. Clinicians using the VOMS should be aware of this proportion of false positives when making any clinical decision for concussion.

Fatigue

Considering exertion fatigue has been demonstrated to produce vascular changes,[502,503] hypoxia,[504] decreased cerebral oxygenation,[502] and changes in cerebral cortical activity in the brain,[503,505] the VOMS assessment has been hypothesised to be influenced by the effect of fatigue.[506] This would limit the accuracy of the VOMS in the sports setting, during an immediate sideline assessment. To further understand this, Ratka *et al*.[506] recruited 15 healthy participants who were absent of head injury and participated in at least three sessions of exercise per week. Each participant performed the VOMS assessment as a baseline and then following a 20-minute interval fatigue protocol consisting of sit-ups, step-ups and sprinting. From the study, the results showed worsening of the total VOMS and NPC scores following exertional fatigue. Therefore, the authors expressed caution when the tool is used as a concussion indicator immediately after sports participation.

However, additional studies exploring these effects in a larger sample are lacking. The presence of fatigue effects have also been established in other concussion tools, such as the BESS, SCAT and ImPACT.[507-510] This would mean that a physician involved in the diagnosis and management of concussion should be able to distinguish between concussive and fatigue symptoms.

Gender Differences

According to Covassin *et al.*[246] it was revealed that collegiate females reported higher baseline symptom scores than males for headaches and nausea. This has led to further research examining gender differences between VOMS testing as these

symptoms are routinely assessed by the concussion tool.[511,512] In addition to those symptoms, Covassin's study also found that females reported a high mean symptom score in fatigue, sleeping more than usual, drowsiness, light and noise sensitivity, sadness, nervousness, poorer concentration, feeling more emotional and visual problems.[246] This has implied that clinicians administering the VOMS tool should consider potential confounding factors, such as gender in clinical decision making.

Although in one study, Sufrinko *et al*.[512] investigated the gender differences of the VOMS after concussion in a sample of youth athletes ages 9 to 18 years and found that females reported a greater symptom provocation on the horizontal vestibular-ocular reflex domain when compared to the male group. However, no other gender differences were observed for any other VOMS domain. Furthermore, recent research by Moran *et al.*[511] examined if there were any gender differences in baseline VOMS testing. The authors recruited 278 male and 145 female youth football and soccer athletes aged 8 to 14 years and completed a pre-season VOMS assessment on each participant. The results revealed no relationship between each domain of the test and gender (all $p > 0.05$) suggesting that the concussion tool is not influenced by gender.[511] This is important within the clinical setting, as despite the gender differences noted by Covassin *et al.*[246] in post-concussion symptoms, it was shown to not influence VOMS testing on youth athletes.

Symptom Recovery

Recently, there has been suggestions that the VOMS tool is a good predictor of symptom recovery in young populations.[513-516] This is a critical finding for clinicians

to tailor management plans, such as specific school accommodations and individual assistance for sports. In a large retrospective study on 234 patients, those who recorded a poor VOMS outcome exhibited longer recovery times on each of test's components.[513] In particular, deficits to the vestibular-ocular reflexes and smooth components of the VOMS were highly predictive of symptom recovery, although an abnormal NPC measurement post-injury was determined to be not.[513] However, results from another study revealed the vertical saccades, horizontal saccades, and convergence components of VOMS to be the most associated with recovery time following concussion.[516] Further research is thereby required to determine the relationship between the VOMS tool and symptom recovery in various groups.

Further research by Anzalone *et al*.[514] aimed to identify these relationships with recovery in a sample of 167 youth patients with concussion. The results indicated that patients that presented with a positive VOMS outcome (i.e. symptom provocation on at least one VOMS domain) took a mean difference of approximately ten days longer to recover from their symptoms ($p < 0.001$). However, these findings contrasted to another study where the VOMS was reported to have no relationship to symptom recovery.[517] Instead, the presence of cognitive-migraine-fatigue symptoms and visual motor speed were identified as more robust predictors.

Future Directions

Overall, there is mounting evidence suggesting the role of the VOMS tool in post-concussive assessments. However, there is still room for future studies to explore the relationship the tool has with symptom recovery. Quantifying the length of time

it takes for an injured athlete to become asymptomatic would allow physicians to use the VOMS tool to construct individualised recovery and management plans.

1.5 Summary and Aims

The immediate and latent consequences of concussion have driven researchers from all over the world to explore the relationships between symptomology, diagnostics and recovery. Sideline tests are used by physicians to evaluate injured players for indications of cognitive and mobility impairment following a suspected concussion.[162] These tools demonstrate high sensitivities and specificities in detecting concussion but have also been suggested to be influenced by player fatigue, learning effects and examiner variability.[165,175,176] Therefore, there is an urgent need for supplementary assessment tools to evaluate neurological dysfunction post-concussion to ensure only those players without concussion are able to be safely returned.

It has been previously reported that visual and/or oculomotor dysfunction occurs in up to 82% of concussed patients,[311,314,518] however there are a limited number of readily available oculomotor/visual- based tools able to examine the ocular system in order to detect concussion effects. Further, the available tools are not fully validated, nor is it clear which aspects of oculomotor/visual function are most affected.[161] However, these visual tools appear to be promising for post-injury assessments for diagnostics and may provide physicians with an objective marker of an athlete's saccades, smooth pursuit eye movements, convergence and accommodation.[161] Reliable and well understood tools need to be validated to ensure that players are protected from exacerbation of concussion symptomatology by sustaining repeated head injuries.[162,519] This will remove in part the reliance on

the player's self-reported symptoms which is known to be unreliable and yet which continues to be a considerable component of current concussion assessment tools.

To date, limited research has been conducted on concussion from an ocular motility and visual perspective, which may be a representation of the paucity of studies conducted on concussion from an ophthalmic perspective. The few studies that have examined ocular movements have only documented observations in outpatient clinics following a concussion and lacked any substantial baseline information to address previous undetected oculomotor defects.[311,325,326,328] Additionally, these studies do not consider the normal prevalence rates of convergence insufficiency and accommodative insufficiency in youth populations. A better understanding of concussion's effects on the oculomotor and visual system through longitudinal follow-up studies will provide health professionals with an additional knowledge and hopefully tools to detect subtle neurological changes, improving the overall diagnostic accuracy available on the sideline and provide a standard instruments that can be used to monitor long-term side-effects.

To further enhance our understanding of concussion within the scope of visual dysfunction, with the overarching goal of preventing further stories like James McManus in the media where, after a career as a long term rugby league player, he was forced to medically retire due to having experiencing multiple concussions This body of work aims to:

- evaluate available tools that use the oculomotor/visual systems to detect and monitor concussion

- identify immediate physiological changes to the oculomotor and visual system following concussion, using standard ocular examination techniques
- identify those aspects of oculomotor and visual function that are most affected by concussion both in the short and medium term and compare these to the gold standard ocular examinations
- determine the effectiveness of ocular-based concussion detection tools and determine any modifications that may be required to improve their sensitivity.

The literature review was published on 22/03/21 and a further search of relevant literature was performed on 20/07/21. No further relevant literature was found.

Chapter 2: Methods

2.1 INTRODUCTION

The aim of this chapter is to explain, in detail, the research methodology and visual tools used in this thesis. This chapter will first describe the research approach and design for each study performed. Then the sampling strategy and sample size utilised, methods of data analysis and how each visual test was administered will be described. It concludes with a brief discussion on the ethical considerations, as well as problems encountered during the project.

2.2 RESEARCH APPROACH AND DESIGN

This thesis is divided into four distinct studies (Chapter 3 to 6), all of which make use of a quantitative research methods. The research design utilised by each study varied and are outlined in each of the respective chapter's methods sections. A quantitative research strategy was most applicable for the purposes of this thesis,[520] as it provided numerical data to evaluate each visual assessment tool in the role of concussion detection. It also allowed the determination of potential areas of improvement/modifications to each visual device and for the broader aims listed in Chapter 1 (pages 119 - 120) to be achieved.

In addition, this thesis has the advantage of utilising investigator triangulation. Triangulation provides the opportunity to approach the research aims from multiple viewpoints and creates a more nuanced perspective of the connections between the variables tested. This research project was performed in collaboration with

researchers at the University of Technology Sydney, Save Sight Institute, Vision Eye Institute, New England University, La Trobe University and the Children's Hospital Institute of Sports Medicine. Having the incorporation of different concussion experts from various academic backgrounds, for example rehabilitation, ophthalmic, medical devices and sports injuries, helped facilitate access to subjects and medical devices.

2.3 SAMPLING STRATEGY

For the purposes of this thesis, purposive sampling was performed in Chapters 3 to 5, to ensure that the subjects selected were from sporting communities with a relatively high risk of experiencing a concussive event. This was essential for the evaluation of each visual tool, determining its utility and potential for improvement of concussion detection in a sporting community. Rugby union was chosen as an appropriate sport to sample because of the relatively high incidence of concussion reported in the literature (4.73 concussions per 1000 match hours)[521] providing an opportunity to collect both pre-injury baseline and post-concussive measurements. Although higher rates of concussion are reported in fighting sports like Tae Kwon Do (8.77 per 1000 hours)[522], rugby union is a team-based sport and therefore provides a potentially larger sample size to monitor for concussion.

In Chapter 6, convenience sampling was utilised for the retrospective medical review study, through external collaboration with the sports medicine team at the Children's Hospital in Westmead. This sampling technique was used to identify and collect data on paediatric patients who had experienced a concussion through sports.

2.4 METHODOLOGY

2.4.1 Chapter 3: Evaluation of the King-Devick Concussion Tool

The KDT is emerging as a useful tool in the detection of concussion on the sports sideline. It largely assesses a person's visual function, particular saccadic eye movements, but is likely to also assess cognition, attention and language as well.[190] To explore the utility of the KDT as a sideline assessment for concussion, a total of 195 male rugby union players were recruited from an entire semi-professional club in Sydney. All athletes provided written consent (see Appendix E) to participate in the study.

During the 2017 competition pre-season, all participants performed a pre-season baseline assessment on the KDT, according to standardised protocols described by Galetta *et al.*[476]. This was conducted on the sideline, outside the rugby club gymnasium in a well-lit area. The digital version (King-Devick Technologies Inc, IL, USA) was utilised on a 9.7" iPad (iOS 10, 1024 x 768 resolution, aspect ratio 4:3). The test contains three testing cards of increasing difficulty and one demonstration card. Each card displays 40 single digit integers (refer back to Figure 1.8, pg 94).

Participants wore their reading glasses if required and held the iPad at a constant distance of 40 cm. The investigator stood next to the participant, in a spot they could see the iPad without any obstructions (Figure 2.1). Participants were instructed to read the numbers on the 'demonstration card' aloud from left to right. This was attempted as quickly as possible without any errors.

Figure 2.1. A participant performing the King-Devick Test as part of pre-season baseline testing.

Upon completion of the 'demonstration card', the examiner informed the participant that the first testing card will appear, and timing will commence. The examiner then touched the screen, commencing the start of the KDT assessment. An in-built stopwatch initiated timing and paused once the first card was completed. Timing did not occur during the changing of the cards.

Participants repeated the same procedure for the remaining two testing cards. The collective time for all three testing cards to be read comprised the person's total

KDT summary score. This was recorded in seconds. Numbers of errors made during testing were manually recorded upon test completion. An error was only deemed if the participant did not immediately correct the error, before continuing to the next number of the card. If an error was made and not immediately self-corrected by the player, the baseline measure was repeated.

Testing was completed twice for all pre-season baseline assessments. Repeated testing (post-injury or weekly updates) were only performed once (Figure 2.2). Results for this study are described in Chapter 3.

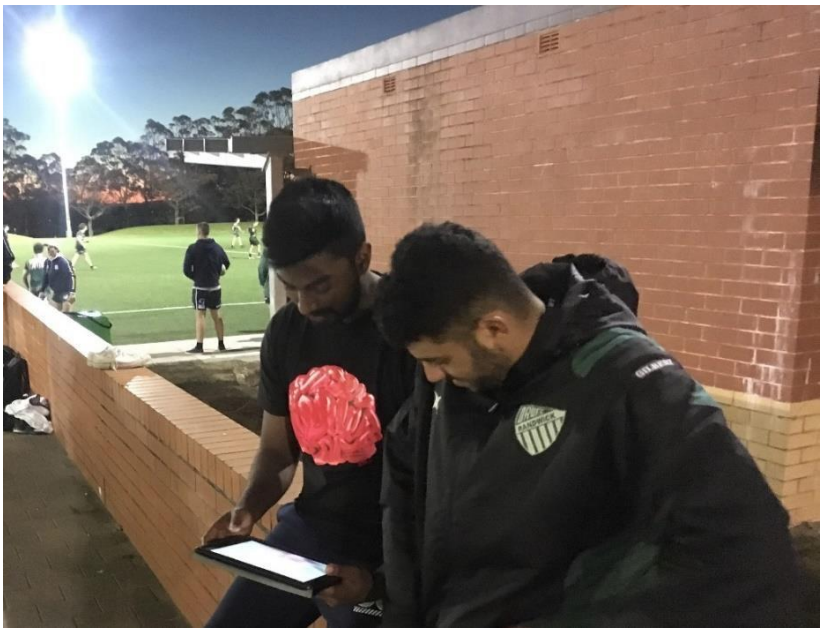


Figure 2.2. A participant performing their repeated baseline testing during the competition season.

2.4.2 Chapter 4: Saccades and Smooth Pursuit Eye Movements

To further understand the relationship between saccades and smooth pursuit eye movements in baseline concussion testing using the KDT, 42 players of the original cohort of 183 rugby club subjects from the top-division of the rugby club were selected during the pre-season for further testing of these functions. A series of ocular tests (visual acuity, cover-uncover test and ocular motility testing) were initially conducted in a quiet room at the rugby clubhouse to identify any subtle visual deficits (described below). These preliminary tests were performed by trained and registered orthoptists (Prem Gunasekaran, Christopher Hodge) in all cases.

Visual Acuity

Visual acuity assessment was undertaken according to a consistent protocol. The ESV3000 chart and light source was utilised (Good-lite, IL, USA).[523] The chart contains standardised LEDs (light emitting diodes) which automatically control background light through patented internal calibration technology to provide internal consistency. An Early Treatment Diabetic Retinopathy Study (EDTRS) LogMAR Chart was chosen for use with a 3-metre assessment lane.

Players were asked about the use of optical aids and were requested to use these during the assessment if appropriate. The right eye was tested first in all cases. The patient was instructed to cover their left eye and read the first letter on each line progressing down the left-hand side of the chart ("staircase protocol").[524] When the patient could not read or provided an incorrect answer, they were asked to begin reading the line above. If three or more letters were correctly read on this line, the player was asked to continue to the next line. Once the majority of letters (3 letters)

were incorrectly assessed on any given line, the player was asked to stop and the total number of letters recorded to provide the LogMAR score. The patient was then asked to move the occlusion device to the right eye and the test repeated to examine their left visual acuity.

Cover-Uncover Test

The cover-uncover test provides an objective indication of ocular alignment. It is traditionally performed by orthoptists and ophthalmologists in the clinically setting to detect the presence and direction of a strabismus (manifest or latent).

The procedure was completed using both far (three metre) and near (33 cm) fixation distances, as per the gold-standard methods previously described.[525] The distance fixation used the LogMAR vision chart with the fixation target a letter on the line of optotypes above their best corrected distance visual acuity (VA). An opaque occluder (Spielmann) was placed over the right eye for 1-2 seconds before removal. The examiner observed the uncovered eye during this process and recorded any movement of the uncovered eye to take up fixation and its direction, if applicable (see Table 2.1). This process was repeated twice for confirmation prior to repeating the protocol on the left eye. If no movement of the eye was seen, the examination proceeded to the alternating cover test. This procedure was then repeated while the participant fixated on an accommodative target at near.

Table 2.1. Types of strabismus and the direction of misalignment.

Position of eye	Strabismus

Outwards	Exotropia
Inwards	Esotropia
Upwards	Hypertropia
Downwards	Hypotropia
None	Orthotropia

Alternating Cover Test

The alternating cover test is performed for the detection of latent strabismus. The same near and far distance fixation targets were used. Occlusion of one eye was by alternating the occlusion to the other eye, so that the participant was unable to regain binocular fusion. The direction of any eye movement noted as the occluder was removed was recorded.

Ocular Motility

An assessment of the range and direction of the movement of the six extra-ocular muscles provides important information to researchers regarding the patency of the ocular motor system, allowing evaluation of the efficacy of the ocular cranial nerves (III, IV and VI). This procedure was conducted at 33 cm from the participant's eyes. While keeping their head still, participants were instructed to binocularly follow a LED penlight examination torch (Orthoptics Australia, AU) to examine all nine cardinal positions of gaze. At each position, the examiner observed the range, accuracy and speed of each version eye movement. This was performed an additional 1 – 2 times, if required, to confirm any abnormality. Ocular alignment was monitored throughout the testing by comparing corneal reflections and

performing a cover test at each position of gaze. Any underacting or overacting extra-ocular muscle was recorded. Duction eye movements were assessed monocularly, if any ocular movement limitation was noticed. Results of ocular motility testing were performed for pre-study visual screening and again no abnormalities were detected and therefore are not included in the analyses in Chapter 4.

Smooth Pursuit and Saccadic Eye Movements

The assessment of smooth pursuit eye movements and saccades in this study was performed using a digital eye-tracking device (RightEye Neurovision Test) and mirrored procedures from Murray *et al.*[526] Testing was non-invasive and required participants to be seated 60 cm from the screen. To align the device with a participant's height, the desk was raised or lowered. Stimuli was presented on the vision monitor/screen (NVIDIA 24" 3D, 1080p resolution) that was fitted with a remote eye tracker (Sensor Motoric Instruments 12" 120 Hz). The RightEye (Figure 2.3) was connected to an Alienware gaming system, Logitech (model Y-R0017) wireless keyboard and mouse for control (all from RightEye, LLC., MD, USA).

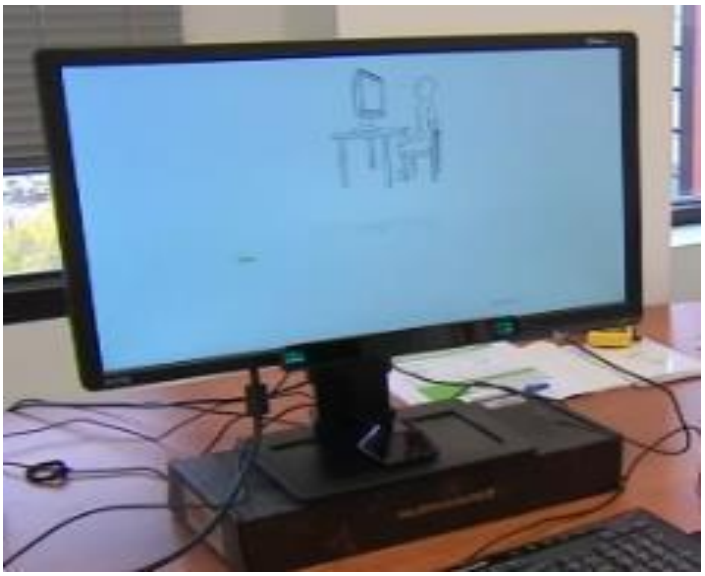


Figure 2.3. The RightEye tracking apparatus.

To begin calibration, the participants moved their eyes to the nine cardinal points around the screen. This was an important step to minimise any measurement uncertainty. Eight of the nine needed to be accurately met by the participant's eyes for the calibration to be completed successfully. The accuracy of the eye tracker was 0.4 degrees within the desired head box of 32 cm × 21 cm at 60 cm from the screen.

Circular Smooth Pursuit Test

Once calibrated, testing of circular smooth pursuits began on the RightEye apparatus. Participants were instructed to track a target stimulus, which consisted of a black dot (0.2 degrees in diameter at a 10-degree radius) as it moved in a clockwise direction (rate of 0.4 Hz) for 15 seconds. Upon completion, the system provided results on fixation percentages, saccade percentages, smooth pursuit error, and smooth pursuit target accuracy for the participant. The results of each

individual was compared to the instrument's normative population mean database, which was collected from 2500 healthy, non-concussed participants aged between 11 to 62 (provided on https://www.righteye.com/) and these results are reported in Chapter 4.

Horizontal and Vertical Smooth Pursuit Test

Using the same target stimulus, participants followed a repetitive movement from right-to-left-to-centre (horizontal testing) or up-to-down-to centre (vertical testing), for a total of 25 seconds. For the RightEye system to determine that the participant was tracking the stimulus, the participant's gaze needed to be within 2.4 degrees of the target. If fixation was lost, the examiner was immediately notified, and testing instructions were re-explained if necessary. When testing completed, the system provided measures of fixation percentages, saccade percentages, smooth pursuit error, and smooth pursuit target accuracy for analysis, which were compared to the same normative population mentioned above.

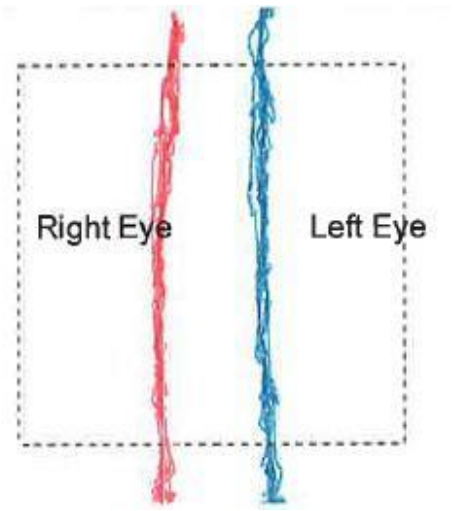


Figure 2.4. Example of a participant's vertical smooth pursuits recorded.

Horizontal and Vertical Saccades Test

Participants were instructed to watch a countdown from "3" in the centre of the screen before moving their eyes as fast as they could between two dots (1 cm in diameter) on the left and right sides. Both targets were 10 cm apart (5 cm on either side from midline). Upon commencement, the dot turned green when the participant's eye met the target's location. This was performed for a total of 10 seconds. At the end, the system displayed descriptive measures of fixation percentages, number of saccades, saccade percentages and target accuracy which were compared to the normative database provided.

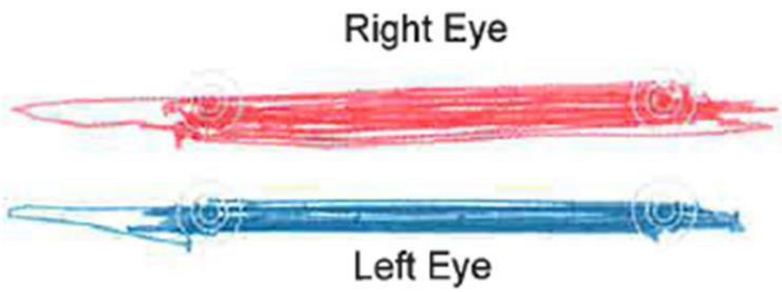


Figure 2.5. Example of a participant's horizontal saccade results.

Details of the results of these measures are also presented in Chapter 4.

2.4.3 Chapter 5: Convergence and Accommodation

To determine the utility of convergence and accommodative testing in a post-concussion assessment, the RAF Rule was utilised in the study presented in Chapter

5 as a standard orthoptic equipment for both ocular measures. Sixty athletes were sampled from the rugby club in 2019. Forty of these athletes (66.7%) were involved in the total 195 athletes recruited in Chapter 3. The other 20 players were new to the club, mostly recruited from rival Sydney rugby teams (*n* = 5) or elevated from the junior divisions (*n* =12). The three other players had been recruited to the club from other sources. All testing was performed on the sporting sideline and was conducted by an orthoptist (Prem Gunasekaran).

Convergence

An assessment of convergence using the RAF Rule was performed following a consistent protocol ("push-up method" described by Adler *et al.*[486]) and at normal outdoor illuminance. The RAF Rule (Good-lite, IL, USA) was placed on the cheek rest of the participant's inferior orbital margin. The ruler was then slightly depressed with Side D facing the participant's face (refer to Figure 1.10, pg 88). Binocularly, the participant was instructed to maintain fixation on the black dot 50 cm away, as the examiner slowly moved the target toward their nose. This was at a constant rate of 1 ± 2 cm per second (Figure 2.6).

Figure 2.6. Conducting a baseline RAF Rule on a rugby athlete.

Movement of the target ceased when either diplopia was reported, a break point (i.e. one eye manifesting an exotropia) was observed, or the slider had moved the maximal distance (5 cm from the eyes) and was stopped by the cheek rest. The point where convergence break occurred was taken as the NPC and was recorded in cm. This procedure was then repeated two more times, with the average of all three measurements used for statistical analysis.

Following a concussion during the season, convergence measurements using the RAF Rule was repeated with the exact protocol described above. Details of the results are provided in Chapter 5.

Accommodative Amplitudes

Examining accommodative amplitudes was similarly performed utilising the RAF Rule ("push-up method").[527,528] The participant's left eye was occluded using a plastic adult's eye patch (Orthoptics Australia, AU) to measure their right eye's NPA. The RAF Rule was placed on the cheek rest of the participant's inferior orbital margin (Figure 2.7), with Side A facing the participant (refer to Figure 1.10, pg 110).

Figure 2.7. Conducting binocular accommodative amplitude testing on a rugby athlete.

The participant was instructed to maintain focus on the letters printed on Side A as the examiner slowly moved the cubical drum from 50 cm away, toward their nose. This was conducted at a constant rate of 1 ± 2 cm per second. When the patient reported the first instance of blur of the letters, movement of the cubical drum was stopped. This focal point (*f*) was recorded in cm using the measurement provided

on the side of the ruler. The eye patch was then moved to the right eye and the test repeated to provide the left eye's NPA.

Upon completion of monocular accommodative testing, the eye patch was completely removed and the participant repeated the assessment binocularly. Monocular and binocular focal points were converted to diopters (D) for all analyses by taking the reciprocal of the focal point (see equation below).

$$D = \frac{1}{f}$$

Following a concussion throughout the competition season, accommodative amplitudes were re-measured using the exact protocol described above. Details of the results are provided in Chapter 5.

2.4.4 Chapter 6: A retrospective study of concussed children

To determine the relationship between duration of symptomology and concussion-related visual dysfunction, and to examine any associations with age, gender and previous history of concussion, a retrospective medical review study of children with concussion was conducted. Medical information of 142 children from a tertiary outpatient paediatric sport and exercise hospital clinic in Sydney was collected in June 2018.

All post-concussive testing (visual and vestibular) was performed by an experienced rehabilitation specialist in sports concussion (Prof. Gary Browne) within the hospital setting. This was specifically in a consultation room within the clinic under normal

room illuminance. It is important to note that visual acuity testing was not performed at this site. Results from the protocol specified below are detailed in Chapter 6.

VOMS Assessment

The VOMS assessment was performed to provide a clinical evaluation of the patient's vestibular and ocular functions. It enables the examiner with a better understanding of the eye movements involved in exacerbating concussion symptoms.

Following procedures outlined by Mucha *et al.*,[493] concussed patients were instructed to sit in front of the examiner at a distance of 1 metre. The physician scored baseline symptoms of headaches, dizziness, nausea and fogginess on a severity scale out of 10 (performed before any visual testing). A score of 0 was indicative of no symptoms while a 10 represented 'most severe'. This was recorded on the VOMS scoring sheet (Figure 2.8), which is available online for download at https://nora.memberclicks.net/assets/docs/concussion-screening.pdf and available in the appendices (Appendix H).

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

Figure 2.8. Recording sheet for the Vestibular/Ocular Motor Screening Test (unfilled).

Upon completion of each of the seven visual and vestibular components (detailed below), the patient re-scored their symptoms of headaches, dizziness, nausea and fogginess on a severity scale out of 10. If the symptom score had increased from before visual testing, this was deemed as a positive VOMS outcome.

Smooth Pursuit Eye Movements Test

With the patient remaining seated, the examiner held a pen in front of the patient's midline. The examiner then slowly moved the pen at a constant pace along the horizontal axis 50 cm to the right of the midline, then 50 cm to the left and then back to the middle. This constituted one repetition. During the repetition, the patient was instructed to maintain fixation on the pen without moving their head.

A total of two repetitions were performed. The test was then repeated along the vertical axis (50 cm up and down). After completion of this VOMS component,

symptoms of headaches, dizziness, nausea and fogginess were reported out of a maximum 10.

Horizontal and Vertical Saccades Test

The examiner held two pens, both approximately 50 cm from the patient and horizontally aligned on opposite sides of the vertical midline of the participant's eyes. This distance equates to 30 degrees of separation between both targets. The patient was then instructed to rapidly move their eyes between the top of each pen. One repetition constitutes of returning to the midline after gazing to the left and right targets. A total of 10 repetitions were performed.

The saccades test was then repeated along the vertical axis. The two pens were then held separately, one 50 cm above and the other below the horizontal midline. The patient was instructed to rapidly move their eyes between each target, with a repetition made after performing one full saccade between the higher and lower pens, before returning to the midline. A total of 10 repetitions were performed.

After completion of each saccade tests, concussive symptoms as from Figure 2.8 were re-assessed and re-reported by the patient. An increase in score on the saccade component meant saccadic dysfunction was present following concussion.

Convergence

The convergence assessment conducted in the hospital clinic was different to procedures conducted on the sporting sideline. Wearing corrective lenses if required, the concussed paediatric patient focused on the tip of a pen as it slowly moved towards the tip if their nose. The target stopped moving when the patient reported diplopia or when the examiner observed an outward deviation of one or both eyes. This constituted one repetition. The distance between the target and tip of the nose was measured using a ruler and recorded in cm. The test is then repeated and recorded another two times, with the average of all three attempts constituting the patient's NPC.

Horizontal and Vertical Vestibular-Ocular Reflex Test

The examiner held a target of 14-point font in front of the patient, in their midline. The patient was then instructed to rotate their head horizontally while maintain their fixation on the target. The head was rotated 20 degrees to each side of the midline while a metronome was used to ensure the speed of rotation is kept at 180 beats/minute. One repetition was made when the patient's head returns to the midline after rotating to the left and right. A total of 10 repetitions were performed.

The Vestibular-Ocular Reflex Test was then repeated with the patient's head moving along the vertical axis. This was moved at a position of 20 degrees above and below the midline, while a metronome was again used to keep the speed of movement constant at 180 beats/minute. One repetition was completed when the head was

moved up and down and back to a starting anatomical position of the head facing straight. A total of 10 repetitions were performed to complete the test.

At the end of the vestibular-ocular-reflex testing, concussive symptoms of headaches, dizziness, nausea and fogginess were scored out of 10. If the score on any symptom had increased from pre-testing scores, vestibular-ocular-reflexes were affected.

Visual Motion Sensitivity Test

The patients stood upright with their feet shoulder width apart while the examiner stood next to and slightly behind them. The patient held their preferred arm outstretched and fixated on their thumb. Maintaining fixation, the patient rotated their head, eyes and trunk together at an amplitude of 80 degrees to the right and left from midline. A metronome was used to maintain the speed of rotation at 50 beats/minute. One repetition was completed when the trunk returns to the midline after rotating left and right. A total of 5 repetitions were required to complete the test. Scores of concussion symptoms were then re-scored out of 10, with an increase on any symptom constituting visual motion sensitivity impairment.

2.5 Methods of Data Analysis

Measures from each four studies (Chapter 3 – 6) were initially entered into an Excel Spreadsheet (Microsoft Excel, Microsoft Cooperation, v2017). The statistical analysis of all quantitative results was performed using Statistical Package for Social Sciences software (SPSS, IBM, Chicago, IL, USA v25.0). Appropriate statistical tests and descriptive values were calculated within each study and are presented in its

respective chapter. The statistical significance level was set at $p < 0.05$ for all analysis.

The results from each study were compiled into tables and figures. The major findings of this thesis will be discussed in detail within subsequent chapters.

2.6 Ethical Considerations

This project encountered a number of ethical issues, which had to be taken into account. The most prominent issue was related with the informed consent of the rugby union athletes and paediatric patients. All of the participants recruited were informed in advance about the aims of the study and provided written consent to participate. Their identity and medical information have been kept in strict confidentiality, meeting the requirements of the Australian National Health and Medical Research Council's (https://www.nhmrc.gov.au/research-policy/ethics/national-statement-ethical-conduct-human-research) National Statement on the Conduct of Human Research applied by the Human Research Ethics Committee at the University of Technology Sydney.

Human research ethics approval was provided to the studies in Chapters 3 to 5 by the Sydney South East Local Health District Human Ethics Committee (REF 17/039), while Low/Negligible Risk approval for Chapter 6 was granted by the University of Technology Sydney Research Ethics Committee (REF 19/3748). Consent forms and ethics approval notification are provided in the Appendices section (Appendix D, E and F).

Finally, all the information collected in the course of this thesis has been used only for the purposes of the study and are kept confidential through the use of de-identified data. Data was stored in password protected server only accessible by the researchers of each study. As per university ethics requirements, the data will be stored for a further seven years after the project's completion and then destroyed.

2.7 Problems and Limitations

There were several problems encountered while conducting the research for this thesis. The first was recruiting a sufficient number of participants with concussion in Chapter 5. Gaining access to an entire rugby club for participant recruitment was difficult on its own but required the building of internal connections and relationships with coaching staff. Although the rates of concussion are considered high in rugby union,[521] the rates of TBI are substantially less common than musculoskeletal injuries to the knee, thigh and ankle.[57,529,530] Therefore, obtaining a large number of athletes who sustain a concussion and have pre-injury baseline measurements for the visual tests conducted presented significant challenges.

Secondly, the retrospective study design utilised in Chapter 6 was at times problematic. The retrospective data was prone to misclassification and only data collected by the physician could reliably be used for statistical analysis. This meant important ocular information, such as visual acuity, was not known.

Another weakness of the methodology was the large disparity between the size and narrow age range of the sample used in Chapter 4, compared to the 2500 subjects

over a wider age range used in the normative database. This made it difficult to match and therefore extrapolate the findings with complete accuracy.

Chapter 3: The Learning Effect of the King-Devick Test on Semi-Professional Rugby Athletes

This chapter comprises the following paper accepted by the *Journal of the Neurological Sciences*.

Reference: Gunasekaran, P., Fraser, C. L., & Hodge, C. (2020). The learning effect of the King-Devick test in semi-professional rugby union athletes. Journal of the Neurological Sciences, 117168.

3.1 ABSTRACT

Objective: Abnormalities of eye movement and visual processing are common in traumatic brain injury. The King-Devick test (KDT) has been widely used in the detection and recovery of concussion. Current recommendations propose performing the initial test at baseline and then repeating annually to account for potential learning effects. In practice, this may still account for large deviations. The aim of this study was to determine the number of trials needed for a player to achieve a ceiling effect and to determine the validity of the existing protocol requiring two tests at baseline.

Methods: One hundred and eighty-three semi-professional male rugby union players (median age = 22.5 (21.0-25.3) years) were recruited. Over the duration, all athletes performed the KDT on an iPad, under standardised baseline procedures and then repeated the test based on availability during weekly in-season training.

Results: The improvement through each repeated trial was 0.60 ± 0.1 seconds ($P < 0.001$). The ceiling effect was determined at 30 trials. A median difference of 4.2 seconds (range 0 to 14.9) was calculated between the initial and best trial overall, although the greatest difference occurred within the first eight attempts. There was a significant positive correlation between the initial test value and the difference between first and fastest time ($p < 0.001$, $r = 0.455$).

Conclusion: We have shown continuous improvement with repeated attempts which suggests that administrators ideally should continue to perform the KDT over the duration of the season to optimise the value of the test.

3.2 INTRODUCTION

Concussion is a diffuse neurological injury caused by a direct or indirect force to the head. The Centers for Disease Control and Prevention estimate that 1.7 million traumatic brain injuries occur annually,[531] with approximately 300 000 of those from sports-related concussions in American high school and collegiate athletes.[47] Local to Australia, state data demonstrated a substantial increase in concussion-related hospitalisations of 60.5% from 2002 to 2011.[532]

With a recent national statement within sports medicine suggesting that protective equipment such as helmets and mouthguards do not decrease the incidence of concussion,[35] effective diagnostic measures become a priority. Further, due to the potential association of early-onset neurodegenerative diseases and long-term cognitive impairment secondary to concussion,[533,534] optimal diagnosis and management is essential. Detecting concussion however can be challenging for physicians, coaches and athletic trainers, where many symptoms are either non-specific or have a high variability in presentation.

As between 69% to 82% of concussed patients have been reported to demonstrate some form of visual and/or oculomotor dysfunction,[311,326] recent studies have suggested incorporating vision-based examinations into sideline concussion assessments.[161,295,455] Visual assessment may complement existing diagnostic tools, allowing for improved clinical judgements, giving those responsible better information to remove players from ongoing play, thereby protecting them from

potential neurological sequelae. However, no visual-based tool has been integrated into sideline concussion testing, at most levels of sport internationally.[183,535]

Previous research by Heitger *et al.*[354] found greater eye-position errors, slower peak velocities and, more specifically, larger final amplitude errors in the memory-guided saccades of 36 concussed patients. These impairments to saccadic eye movements have been linked to both structural and functional abnormalities in the caudate nucleus, along with the parietal, frontal, and temporal lobes.[362] This encouraged the utilisation of a visual scanning deficit tool, the King-Devick Test (KDT), to determine a change in visual-oculomotor function post-head injury. Subsequently, the KDT has been utilised across a wide variety of contact sport populations.[415,536-538] The tool primarily measures saccadic eye movements, but is reported to also integrate other neurological functions, such as attention, language and cognition.[357]

The facility of the KDT to detect subtle changes in visual-oculomotor function has prompted its use in concussion diagnosis by comparing an individual's post-concussive score to a baseline measurement.[463,536-538] The role of baseline testing is to provide the examiner with a more accurate indicator of an individual's pre-existing neurological function for comparison. In one study, King *et al*.[536] noted a worsening of KDT scores by almost 6 seconds within a cohort of concussed rugby athletes when compared to their pre-injury baselines. Similarly, Leong *et al.*[538] witnessed this change to be 5 seconds in a sample of college football and basketball players with concussion. However, when repeated on non-concussed controls, a considerable improvement in baseline scores were observed. Although tangible

changes between scores may reflect variation in test protocol, for example KDT performed before or after physical exertion, researchers have generally identified these positive improvements as learning effects,[349,351,538] a psychological characteristic common in timed tests and performance measures, where there is a change in score resulting from repetition of a particular activity.

Due to this observed learning effect, KDT protocol requires that the tool should be performed twice during a standard baseline measurement and updated annually. However, recent evidence from Oberlander *et al.*[539] suggests more than the two recommended measurements may be required as further improvement to the score may be obtainable. In this study, the authors evaluated the test-retest reliability of the KDT and found student athletes performed better on each subsequent attempt. This included a mean 6.9 second improvement from the first to third attempt, over a period of 45 days.[539] The mean improvement of 4.3 seconds between the first and second measurements indicated a further change to the third attempt approaching two-thirds the initial difference. This would infer that more than two measurements may be needed to constitute the athlete's best score to be used as a reliable comparative measure, if a player was to prospectively suffer a concussion.

Identifying a time at which the score does not clinically improve due to estimated learning effects is essential for examiners to understand as a true marker for a player's baseline. Otherwise, standard post-concussion measurements may mask the true neurological repercussions. We hypothesise that repeated testing of the

KDT would result in a ceiling effect, a point at which the player's score can no longer improve. The aim of this study was to determine the number of trials needed for a player to achieve a ceiling effect and to determine the validity of the existing protocol requiring two tests at baseline.

3.3 METHODS

3.3.1 Participants

This study recruited 195 male rugby athletes from a rugby club in Sydney. South Eastern Sydney Local Health District Human Research Ethics Committee approval (17-039) was obtained prior to the study and all participating players provided signed consent prior to enrolment.

Players were excluded from the study if they were unable to complete their pre-season baseline measurement twice, finish all three testing cards, had been previously diagnosed with a reading disorder (e.g. dyslexia) or were continuing to experience symptoms from a concussion episode within the last month. Exclusion criteria were chosen to remove any potential bias to the results and were confirmed prior to baseline, by the team medical officer. Any previous history of concussion was also documented.

3.3.2 Testing Procedures

During the competition pre-season, each player performed all three cards of the KDT on a 9.7" iPad, according to standardised baseline procedures described by Galetta *et al.*[476] This included two trials, with the fastest without errors constituting their baseline score. Each trial consisted of the athlete reading the numbers on the

card aloud, as fast as possible. When all three cards were completed, this constituted one attempt, and the total score of each card was summated to represent that individual's KDT score. If an error was made, the participant re-performed the KDT until a trial was completed with no errors.

All assessments were performed while standing in a quiet area outside the rugby club's gymnasium, with good ambient illuminance. To account for exercise as a confounding factor, these occurred prior to training or physical contact drills and took approximately two minutes to complete per athlete. The assessments were conducted by three examiners, who were trained using an online information module supplied by the KDT manufacturers. Athletes wore near correction glasses or contact lenses if required.

During weekly elective training sessions, athletes were followed-up to repeat the KDT. This included a maximum of one attempt per week with each measurement conducted at least seven days apart. If a participant missed a follow-up due to a musculoskeletal injury or did not attend optional training, they were assessed at the next availability. Players identified with a concussion underwent a thorough medical examination and KDT assessment, as part of the management and stepwise return-to-play protocol. These post-concussive KDT results were not included within the analysis of this study due to potential bias.

3.3.3 Statistical Analysis

All statistical analyses were performed using Statistical Package for Social Sciences software (SPSS, IBM, Chicago, IL, USA v25.0). Descriptive statistics, including range,

were calculated for all outcome variables. KDT scores were presented as median with the interquartile range (IQR). A Shapiro-Wilk Test was used to determine the distribution of the data. Differences between two consecutive KDT measurements were compared using a Wilcoxon signed-rank test. To account for the loss of follow-ups, a Generalised Estimating Equation (GEE) was performed to compare the effect of repeating the KDT over the follow-up trials. A linear regression was also calculated to predict KDT score based on age. The beta coefficient ± standard error was reported for both regression models. The statistical significance level was set at $p < 0.05$ for all analyses.

3.4 RESULTS

During this study, 183 players were eligible for inclusion and successfully performed a pre-season baseline of two trials, with a median score of 42.7 (38.6 - 48.0) seconds. Ten players (5.5%) wore near correction glasses when performing the test. During the period of follow-up, there were 18 diagnosed concussions in 16 athletes.

The median age of the cohort was 22.5 years (range 17-33, IQR 21.0 - 25.3) at the time of pre-season baseline testing. Using regression analysis, a significant negative relationship between the KDT score and age was identified with a beta coefficient of -0.08 ± 0.01 seconds for each year of age ($p = 0.018$). However, no correlation was found between age and the difference between the initial attempt at the KDT during baseline establishment and the overall fastest time ($p = 0.382$, $r = 0.065$).

The number of athletes and respective median scores at each trial are displayed in Table 3.1. A median difference of 4.2 (range 0.0 - 14.9, IQR 1.5 - 7.7) seconds was

calculated between the athlete's initial trial during baseline and their overall fastest trials. There was also a significant correlation between the initial test value and the difference between first attempt during baseline establishment and overall fastest time ($p < 0.001$, $r = 0.455$). The largest improvement was witnessed within the first six to eight trials, with a significant improvement noted between the 5th and 6th attempt ($p = 0.030$).

Table 3.1. KDT scores of male rugby players in Australia. Data are reported as median with IQR (where available) at each testing point. P-value compared with previous trial.

Trial	*n*	KDT Score	p-value
1	183	46.5 (46.1-48.5)	-
2	183	43.3 (43.2-45.5)	<0.001*
3	100	42.0 (41.7-44.7)	0.129
4	82	40.6 (39.2-49.6)	0.017*
5	60	40.6 (38.7-42.4)	0.344
6	37	37.9 (34.4- 40.3)	0.030*
7	29	38.2 (34.0-40.9)	0.374
8	21	35.9 (33.8-39.2)	0.872
9	17	35.3 (32.7-39.0)	0.093
10	14	37.9 (34.5-39.3)	0.035*
11	11	35.4 (31.7-39.4)	0.091
12	8	33.1 (30.0-40.0)	0.833
13	5	35.5 (30.3-38.1)	0.588
14	4	31.8 (29.7-35.6)	0.465
15	4	34.2 (29.7-37.7)	0.465
16	4	33.7 (29.8-36.5)	0.068
17	4	34.0 (28.1-38.0)	1.000
18	4	33.0 (23.4-47.5)	0.593
19	2	39.7 (24.8-54.6)	0.655
20	2	36.0 (24.6-47.4)	0.655
21	1	35.1	-

*denotes statistically significant

The GEE describing the change in KDT score over the 21 follow-ups is depicted in Figure 3.1. There was a significant improvement of 0.60 ± 0.1 seconds upon each repeated trial ($p < 0.001$). Using information extracted from the graph, the ceiling effect was calculated to be 30 trials.

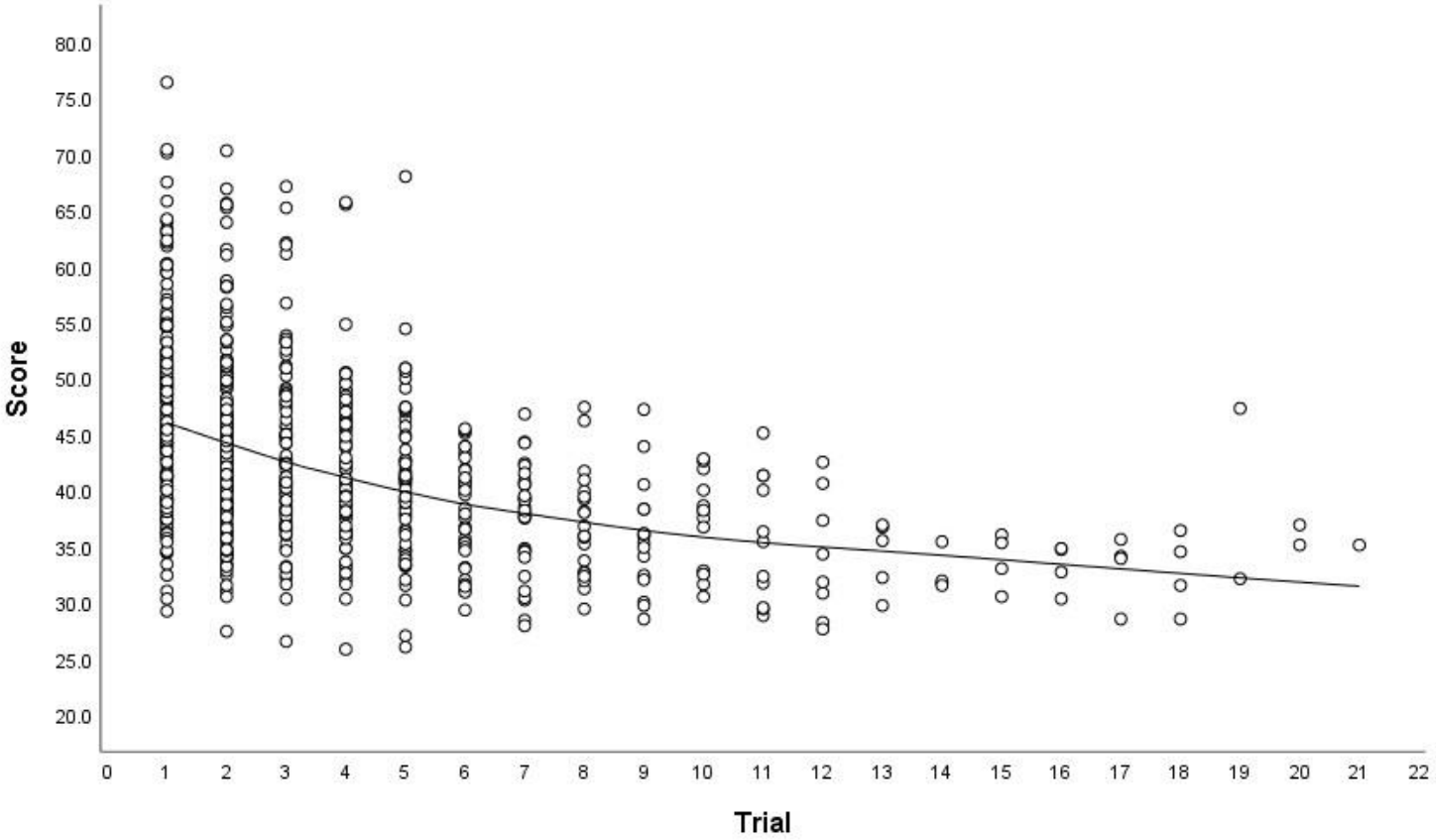


Figure 3.1. The King-Devick score and each trial interval (range = 1 to 21) for 183 rugby athletes.

3.1 DISCUSSION

In this sample of rugby players, we provide further evidence supporting Oberlander *et al.*[539] indicating multiple attempts are required to properly achieve a ceiling effect and constitute an appropriate baseline measurement. Using the polynomial data extracted from the GEE, we identified that 30 trials are needed to achieve a ceiling effect. However, performing the test this many times as part of a routine baseline protocol remains highly impractical within the clinical setting. Instead, we propose that re-performing the trial regularly, up to at least six times over the course of a competition season, would allow unmasking of a player's true baseline and provide a better pre-injury representation.

We uncovered a significant positive correlation when comparing the initial test value during baseline establishment, to the difference between this and the players' fastest times ($p < 0.001$, $r = 0.455$). Therefore, the slower the initial reading speed, the greater potential capacity of improvement to score. In a clinical context, the examiner should be more aware of the risk of a falsely high value at baseline in players achieving poor scores. This would mean encouraging them to perform the KDT as fast as possible every time the test is administered. In those that do obtain a poor baseline KDT score, undertaking additional tests prior to the season's commencement may represent a reasonable step. While there is no clinical consensus regarding an appropriate cut-off, we recommended repeating the test if a person achieves a best baseline score of slower than 60 seconds.

Between the first and second attempts of baseline establishment, this cohort of rugby athletes demonstrated a notable median improvement of 2.4 seconds. This observation matches previous research showing a decrease in overall time between 2.2 and 3.1 seconds.[348,351,413,415,420,476,477,536,538,540] Leong *et al.*[538] proposed the variation between these improvements may be attributed to the population tested and recent concussive history of the participant. However, all our athletes were tested during the pre-season and did not exhibit any signs or symptoms of concussion when assessed by the team's medical staff. Furthermore, a cross-sectional study on 691 participants by Pang *et al.*[541] found no association between KDT performance and a history of concussion ($p = 0.85$). Instead, this initial change was strongly associated with certain ethnicities, education and age (all $p < 0.001$). Unfortunately, besides ages, we did not collect further demographic information to explore the relationship of KDT scores with these variables.

In this cohort, we also found a similar association to previous studies, examining the correlation between age and KDT scores.[351,428] Our results showed a 0.08 second improvement per increasing year of age ($p < 0.001$). Research by Galetta *et al.*[351] reports these changes are likely to represent brain and ocular maturation during youth, as notable grey and white matter changes occur within the frontal eye field circuitry.[542] Professional sport, particularly contact sports, will self-select players within a small age-range, therefore this finding is unlikely to represent a clinical impact in most cohorts.

For athletes playing in non-professional levels of sport, where there may be a broader range of age groups or lack of access to regular baseline or pre-season testing, sport-specific normative scores may be more valuable. Previous findings show a normal median baseline for rugby athletes to be between 42.0 and 47.3 seconds.[452,457,536] Our data exhibited a median baseline score of 42.7 (38.7 – 48.0) seconds, which was also within the documented range found within a wide range of sporting and non-sporting cohorts.[348,351,413,415,428,463,476,536-539,543,544] This may be also beneficial for health professionals in the hospital setting, where the access to baseline testing is unlikely. However, considering a 4.2 second median improvement was noted between the cohort's initial attempt during baseline establishment and their overall fastest score, previous studies documenting normative ranges may have overestimated. Clinical decisions made by athletic trainers and health professionals should ideally be undertaken following consideration of all potential confounding factors such as age and sex.

Interestingly, we noted significant worsening to the median KDT scores between the 9th and 10th trial (35.3 vs. 37.9 seconds, $p = 0.035$) which is most likely attributed to number bias, although could reflect testing conditions. However, we tested all athletes in a quiet area at the club's gymnasium according to recommended test procedures, suggesting this anomaly was primarily due to our reduced sample size.

Despite providing a novel insight into the utility of the KDT, this study is not without methodological limitations. Ideally, a greater number of participants to have completed the test more times may have uncovered a greater change in learning

effect between the different trials. We started with 183 participants, however through the duration of the study, we were unable to assess each player on a consistent basis, due to players failing to attend their optional training sessions in an unsuccessful competition season. The use of a GEE can account statistically for this loss by providing an estimated score trajectory using the available data, although this may not fully compensate for greater sample size.

In addition, information about previous concussion history was provided by self-report, which may lack accuracy. It was also possible that some players may have previously performed the KDT at a previous club or within a clinic which may have further influenced the amount of improvement or learning effect that we encountered.

Although not plausible for widespread introduction across community or semi-professional sports which lack both the resources and access to professionals, it would be ideal if selected future research protocols could incorporate a thorough neurological and neuro-ophthalmic examination inclusive of convergence, accommodation and motility as part of baseline and post-concussive assessments. This would better determine the potential impact of concussion on cognitive capacity and possible pre-existing subtle ocular motor defects upon KDT performance, thereby further improving our understanding of the tool.

3.6 CONCLUSION

Our cohort of rugby athletes demonstrated marked improvements to their KDT baseline upon re-performing the test over a range of 21 attempts, with a median

difference of 4.2 seconds from the first baseline attempt to overall best score. Although the current results require further validation in a different and larger sample of healthy adults, we have identified that 30 trials are needed to fully achieve a statistical ceiling effect. With the largest change noted within the first six to eight attempts, administrators of the KDT should consider re-performing the tool at consistent intervals over the duration of a season, rather than just an annual update.

Chapter 4: Comparing the Smooth Pursuit and Saccadic Eye Movements in Rugby Players to a Normative Database

This chapter comprises the following paper submitted to *Clinics in Sports Medicine*.

4.1 ABSTRACT

Introduction

There is increasing evidence to suggest ocular-based tools may improve the sensitivity of sideline concussion detection protocols. Currently, normative saccadic and smooth pursuit eye movements in the general population have been documented for digital eye-tracking tests such as the RightEye Neuro Vision™ test. However, this normative database may not accurately represent athletes. This study examined the saccadic and smooth pursuit systems in premiership-grade young rugby athletes as compared to published population means. It also investigated impacts of age and previous concussion within the last 12 months on oculomotor function.

Methods

During the 2017 competition pre-season, forty-two premiership-grade male players (mean age = 20.61 ± 3.0 years) from a semi-professional rugby club were recruited. Prior history of concussion was documented including quantity and dates of medically-diagnosed concussions. Players with present symptoms of concussion were excluded. All players performed three smooth pursuit tests (horizontal,

vertical and circular) and two saccade tests (horizontal and vertical) on the RightEye apparatus. Ocular variables were calculated and recorded by the eye-tracking system.

Results

No statistical difference ($p > 0.05$) was determined when comparing between players with a history of concussion (n = 6) and those without (n = 36). No statistical difference ($p > 0.05$) was found between players below (n = 20) and over 20 years (n = 22). Faster horizontal smooth pursuits were demonstrated in 85.7% of the players than the population mean. In the vertical pursuit test, 83.3% of the rugby cohort had faster vertical smooth pursuits, while 78.6% exhibited faster circular smooth pursuits than the population. Additionally, 73.8% had greater saccade numbers in the horizontal and vertical axis than the normative mean.

Conclusion

We found that young premiership-grade rugby players possess faster smooth pursuit and saccadic ocular systems than the general population. Additionally, previous history of concussion and age have no significant impact on smooth pursuit and saccades. Future studies should include a comparative control athlete population.

4.2 INTRODUCTION

Nearly 30 years ago, Harbin and colleagues[545] noted more rapid oculomotor response times in professional athletes when compared with amateurs in the same sport, suggesting its importance in determining athletic capabilities. Although the study only identified a difference in reaction times,[545] it highlighted the possible impact of oculomotor function on an athlete's performance. More recently,[214,420] objectifying oculomotor function in athletes has influenced concussion diagnosis in young athletes. With some form of visual dysfunction, including version and vergence eye movement defects in 82% of concussed patients,[286,311] health professionals are moving towards implementing oculomotor testing to improve the sensitivity in detecting SRC.[189,290,293]

Normative oculomotor findings for saccadic and smooth pursuit eye movements in the general population have been presented for a digital eye-tracking device known as the RightEye Neuro Vision™ test (https://www.righteye.com/). However, athletes may possess a superior range of oculomotor skills.[448,546] Additionally, oculomotor function may be influenced by age, with subjects under the age of 50 years demonstrating quicker smooth pursuit eye movement initiation than those above 50 years.[547] Therefore, the RightEye normative database may not accurately represent athletic groups in community level sports. Group specific (sport and age) normative data would perhaps provide more relevant information if it were to be used in concussion assessment paradigms.

We hypothesised that identifying a normative mean for athletes would provide a more accurate reference normative measurement to use a baseline reference and

we aimed to highlight the differences, if any, between athlete's and non-athlete's oculomotor systems. This study examined the saccadic and smooth pursuit systems in top-grade senior rugby athletes and compared to published general population means. A secondary aim was to evaluate the role of eye-tracking devices as a potential concussion screening tool through determining if prior history of concussion within the last 12 months and an athlete's age has any influence on their oculomotor function.

4.3 METHODS

4.3.1 Participants

This study was conducted on a semi-professional level senior male rugby union club during the 2017 competition pre-season in Sydney, Australia. A total of 42 top-grade male players were recruited into the study with a mean age of 20.61 ± 3.0 years. Healthy rugby players over the age of 18, and registered for the 2017 season, were eligible for inclusion. Any prior history of concussion was documented, including the number and dates of medically diagnosed concussions. Players with current symptoms related to concussion, including dizziness, headaches, diplopia, nausea, photosensitivity and drowsiness were excluded. South Eastern Sydney Local Human Research Ethics Committee approval (17-039) was obtained prior to the study. All participating players provided signed consent prior to enrolment.

4.3.2 RightEye Neuro Vision™ test

The RightEye Neuro Vision™ test is a digital eye-tracking system comprising a high definition screen (NVIDIA 24-inch 3D Vision monitor), an eye movement tracking bar (SMI 12" 120 Hz remote eye-tracker connected to Alienware gaming system), a

Logitech wireless keyboard (model Y-R0017) and mouse. The reported accuracy of the eye tracker is 0.4 degrees at the required distance of 60 cm from the monitor.[526] Utilising a cloud-based platform and proprietary visual testing protocols, measures of ocular saccades and smooth pursuit eye movements in the x- and y-axis, as well as circular smooth pursuits were obtained.

4.3.3 Testing Procedures

In order to standardise testing procedures, all recruited players were seated at 60 cm in front of the remote eye tracker in a quiet, dimly lit room inside the rugby clubhouse. The chair was stationary, could not be adjusted in height and did not have a headrest. Desk height was adjusted to align the player's eyes with the monitor. Players wore their prescription glasses or contact lenses, if required. They were asked to remain as still as possible in front the computer screen. A nine-point spatial calibration procedure was initialised prior to each new subject to minimise any measurement uncertainty by ensuring the accuracy of RightEye device.

Following successful completion of the calibration, a series of five tests (three smooth pursuit and two saccade tests) commenced. The first testing component was circular smooth pursuits, followed by horizontal and vertical smooth pursuits. Following completion of these three components, horizontal and then vertical saccades were examined. Verbal and animated instructions were provided before each of the tests to model appropriate behaviour. Instructions were repeated when necessary and all tests were performed binocularly. Variables (Table 4.1) were

recorded and utilised for analysis. The full testing cycle took 15 minutes to complete per athlete.

Table 4.1. Definitions of the variables analysed during the smooth pursuit and volitional saccade tests. Variables were only used where applicable.

Variable	Definition
Smooth Pursuit (%)	The subject's following the target, within the velocity range. Calculated as a percentage of the total test time. A perfect score is 100.
Saccade (%)	Rapid eye movements which are not associated with the stimuli. Calculated as a percentage of the total test time. A perfect score is 0.
Fixation (%)	A stopping point of the eye of 100ms within 1 degree of diameter dispersion. Calculated as a percentage of the total test time. A perfect score is 0.
Target velocity error	How far the subject's eyes were away from the target. Reported as degrees per second.
Horizontal Synchronization	Ability to keep the eyes on the x-axis. A perfect score is 1.
Saccade (#)	Number of saccades recorded during the test.
Fixation (#)	Number of stopping points made by the subject gaze.
On-Target (#) - within 9mm	Number of fixations made within 9mm.
Overshot Target (#) - within 9-18mm	Number of fixations made within 9 to 18mm beyond the target.
Undershot Target (#) - within 9-18mm	Number of fixations made within 9 to 18mm closer to the centre of the screen.
Overshot Target (#) - within 18-36mm	Number of fixations made within 18 to 36mm beyond the target.
Undershot Target (#) - within 18-36mm	Number of fixations made within 18 to 36mm closer to the centre of the screen.
Missed (#) > 36mm	One or both eyes pass through the centre line twice and do not hit any other target.

Circular Smooth Pursuit Test

Players were asked to focus on a target stimulus (a black spot measuring 0.2 degrees' in diameter positioned at an 8-degree radius from the centre. The target travelled at a continuous rate of 4 Hz on the screen and the player followed its movement in a clockwise direction for 15 seconds.

Horizontal and Vertical Smooth Pursuit Test

Players were again instructed to focus and track the target stimulus in the horizontal plane. For the horizontal pursuit test, the target stimulus continuously moved to and from the centre of the screen to the far right, then to the far left and back to centre for a total duration of 25 seconds. For the vertical smooth pursuit test, the target stimulus continuously moved from the centre of the screen to the top middle then back down to the bottom middle and then to the centre of the screen for a total duration of 25 seconds.

Horizontal and Vertical Volitional Saccade Test

Players were instructed to focus at the centre of the screen for a three second countdown before rapidly scanning their eyes between the left and right circular targets on the far ends of the screen for 10 seconds in the horizontal plane. Targets turned green when the subject made fixation. This was repeated in a similar pattern in the vertical plane.

4.3.4 Statistical Analysis

Descriptive statistics (mean ± standard deviation) were calculated for all outcome variables. Bonferroni correction was used to reduce the chances of obtaining type I errors. A student *t*-test was used to discriminate between groups (age and previous history of concussion within the last 12 months). The collective cohort data was also compared to the normal population data provided by RightEye Limited Liability Company (https://www.righteye.com/). All statistical analyses were performed using Statistical Package for Social Sciences Software (SPSS, IBM, Chicago,IL, USA v24.0). The statistical significance level was set at $p < 0.05$ for all analyses.

4.4 RESULTS

Comparing players below ($n = 20$) and above age 20 years ($n = 22$), we found no statistical difference ($p > 0.05$) for all ocular test domains. No statistical difference ($p > 0.05$) was determined when comparing players with a previous history of concussion ($n = 6$) within the last 12 months to the rest of the rugby cohort ($n = 36$).

4.4.1 Smooth Pursuits

Data from the horizontal smooth pursuit test are shown in Table 4.2. Analysis of both eyes revealed that 85.7% of the rugby cohort produced greater horizontal smooth pursuit than the population mean. Additionally, 97.6% of the rugby cohort had better (lower) horizontal saccade percentages and 71.4% had better horizontal synchronisation scores than the population normative scores.

Table 4.2. Comparison of horizontal smooth pursuit test results between players (*n*= 42) and population data (*n*=2500).

Test domain	RE		LE		BE	
	Players	Popul'n	Players	Popul'n	Players	Popul'n
Smooth Pursuit (%)	94.69 ± 3.30	88 ± 8	94.24 ± 3.37	88 ± 8	95.43 ± 2.93	90 ± 8
Saccade (%)	1.54 ± 1.64	5 ± 5	1.57 ± 1.56	5 ± 5	1.50 ± 1.57	4 ± 4
Fixation (%)	3.78 ± 2.31	7 ± 5	4.19 ± 2.27	7 ± 5	3.08 ± 1.98	6 ± 5
Target Velocity Error	16.89 ± 1.15	18 ± 3	16.82 ± 1.09	18 ± 3	17.05 ± 1.10	18 ± 3
Horizontal Synchronisation (score)	0.98 ± 0.01	0.97 ± 0.03	0.98 ± 0.01	0.97 ± 0.02	0.98 ± 0.01	0.97 ± 0.02

RE = Right Eye LE = Left Eye BE = Both Eyes

The data from the vertical smooth pursuit test are shown in Table 4.3 and 83.3% of the rugby cohort had a greater vertical smooth pursuit percentage than the population mean in both eyes. All of the rugby players also had better (lower) vertical saccade percentages. However, 97.6% of the players had reduced vertical synchronisation scores when compared to the population mean.

Table 4.3. Comparison of vertical smooth pursuit test results between players (*n*= 42) and population data (*n*=2500).

Test domain	RE		LE		BE	
	Players	Popul'n	Players	Popul'n	Players	Popul'n
Smooth Pursuit (%)	62.41 ± 13.80	54 ± 12	62.53 ± 11.96	54 ± 12	81.58 ± 96.12	57 ± 13
Saccade (%)	16.14 ± 3.45	25 ± 11	16.54 ± 3.62	25 ± 11	13.29 ± 3.29	22 ± 10
Fixation (%)	20.82 ± 13.00	21 ± 10	20.47 ± 11.27	21 ± 10	19.11 ± 13.19	21 ± 11
Target Velocity Error	17.15 ± 4.32	24 ± 11	17.04 ± 4.12	24 ± 11	16.76 ± 4.53	23 ± 11
Vertical Synchronisation (score)	0.73 ± 0.04	0.83 ± 0.12	0.73 ± 0.04	0.83 ± 0.13	0.73 ± 0.04	0.83 ± 0.13

The data on circular smooth pursuits are displayed in Table 4.4 using the data for both eyes showed that 78.6% of the rugby cohort exhibited greater circular smooth pursuits than the population mean. Up to 92.4% of the athletes had better (lower) circular saccade percentages than the recorded normative mean. Additionally, 78.6% and 56.5% demonstrated better horizontal and vertical circular synchronisation scores respectively.

Table 4.4. Comparison of circular smooth pursuit test results between players (*n*= 42) and population data (*n*=2500).

Test domain	RE		LE		BE	
	Players	**Popul'n**	**Players**	**Popul'n**	**Players**	**Popul'n**
Smooth Pursuit (%)	62.41 ± 13.80	54 ± 12	62.53 ± 11.96	54 ± 12	81.58 ± 96.12	57 ± 13
Saccade (%)	16.14 ± 3.45	25 ± 11	16.54 ± 3.62	25 ± 11	13.29 ± 3.29	22 ± 10
Fixation (%)	20.82 ± 13.00	21 ± 10	20.47 ± 11.27	21 ± 10	19.11 ± 13.19	21 ± 11
Target Velocity Error	17.15 ± 4.32	24 ± 11	17.04 ± 4.12	24 ± 11	16.76 ± 4.53	23 ± 11
Vertical Synchronisation (score)	0.73 ± 0.04	0.83 ± 0.12	0.73 ± 0.04	0.83 ± 0.13	0.73 ± 0.04	0.83 ± 0.13

4.4.2 Saccades

Details of the comparison of horizontal saccades in the athletic cohort and population are shown in Table 4.5. Our results indicate that 73.8% of the rugby players had greater saccade and fixation scores than the normative means in both eyes. However, only 31% of the players had better saccadic accuracy than the normative mean, with 97.6% demonstrating a greater number of undershoots within 9 to 18 mm of the target.

Table 4.5. Comparison of horizontal saccades between players (*n*= 42) and population data (*n*=2500).

Test domain	RE		LE		BE	
	Players	Popul'n	Players	Popul'n	Players	Popul'n
Saccade (#)	24.38 ± 7.69	19 ± 7	24.48 ± 7.34	19 ± 7	24.49 ± 7.34	19 ± 7
Fixation (#)	23.38 ± 7.55	18 ± 7	23.21 ± 7.42	18 ± 7	23.07 ± 7.28	18 ± 7
On-Target (#) - within 9mm	8.29 ± 4.19	7.5 ± 4	7.93 ± 4.73	7.5 ± 4	5.52 ± 4.76	7.5 ± 4
Overshot Target (#) - within 9-18mm	1.53 ± 2.23	2 ± 2	1.73 ± 2.34	2 ± 2	1.33 ± 1.72	2 ± 2
Undershot Target (#) - within 9-18mm	5.14 ± 2.84	2 ± 2	5.40 ± 3.68	2 ± 2	9.1 ± 4.57	2 ± 2
Overshot Target (#) - within 18-36mm	0.26 ± 0.80	0.21 ± 0.21	0.12 ± 0.4	0.21 ± 0.21	0.43 ± 1.11	0.21 ± 0.21
Undershot Target (#) - within 18-36mm	6.57 ± 4.01	5 ± 3	6.67 ± 4.10	5 ± 3	5.36 ± 5.19	5 ± 3
Missed (#) > 36mm	0.45 ± 1.45	1 ± 1	0.57 ± 1.48	1 ± 1	0.36 ± 0.88	1 ± 1
Saccade (#)	24.38 ± 7.69	19 ± 7	24.48 ± 7.34	19 ± 7	24.49 ± 7.34	19 ± 7
Fixation (#)	23.38 ± 7.55	18 ± 7	23.21 ± 7.42	18 ± 7	23.07 ± 7.28	18 ± 7

Data on vertical saccades for this study are shown in Table 4.6. From our analysis on both eyes, 73.8% of the players had greater saccade numbers than the normative population. Additionally, 78.6% had better fixation and 14.3% had better fixations within 9 mm of the target. We also found 94.9% of players demonstrated greater saccadic undershoots within 9 to 18 mm of the target.

Table 4.6. Comparison of vertical saccades between players (*n*= 42) and population data (*n*=2500).

Test domain	RE		LE		BE	
	Players	**Popul'n**	**Players**	**Popul'n**	**Players**	**Popul'n**
Saccade (#)	21.43 ± 6.50	17 ± 6	21.60 ± 6.50	17 ± 6	21.21 ± 6.76	17 ± 6
Fixation (#)	20.31 ± 6.45	16 ± 6	20.57 ± 6.56	16 ± 6	20.26 ± 6.76	16 ± 6
On-Target (#) - within 9mm	7.48 ± 3.97	8 ± 4	2.43 ± 4.36	8 ± 4	5.07 ± 3.82	8 ± 4
Overshot Target (#) - within 9-18mm	1.79 ± 1.70	1 ± 1	1.79 ± 1.63	1 ± 1	1.81 ± 1.73	1 ± 1
Undershot Target (#) - within 9-18mm	5.60 ± 3.04	2 ± 2	5.95 ± 3.21	2 ± 2	8.52 ± 4.15	2 ± 2
Overshot Target (#) - within 18-36mm	0.29 ± 0.64	0.23 ± 0.23	0.43 ± 1.56	0.23 ± 0.23	0.45 ± 1.49	0.23 ± 0.23
Undershot Target (#) - within 18-36mm	4.96 ± 3.05	4 ± 3	4.14 ± 2.72	4 ± 3	3.79 ± 3.04	4 ± 3
Missed (#) > 36mm	0 ± 0	1 ± 1	1.33 ± 2.87	1 ± 1	1.00 ± 2.70	1 ± 1
Saccade (#)	21.43 ± 6.50	17 ± 6	21.60 ± 6.50	17 ± 6	21.21 ± 6.76	17 ± 6
Fixation (#)	20.31 ± 6.45	16 ± 6	20.57 ± 6.56	16 ± 6	20.26 ± 6.76	16 ± 6

4.5 DISCUSSION

We found that the top-grade rugby athletes demonstrated superior smooth pursuits and saccadic eye movements in the horizontal, vertical and circular planes compared to the normative population database. These results are similar to previous studies showing that athletes possess superior oculomotor behaviour in variables that are sport-specific.[448,548-550] This could suggest that our sample of

athletes may either develop these qualities from continuous in-game activity or naturally possess better oculomotor function than the general population.

In our study, the rugby group demonstrated reduced rates of catch-up saccades and faster levels of smooth pursuit eye movements during both the horizontal and vertical smooth pursuit tests. This corresponds to observations from Bahill & LaRitz,[551] who showed faster smooth pursuits in an elite-level baseballer tracking a pitched ball, when compared with less skilled players. Another study later showed that an increase in both fixation and smooth pursuit precision corresponds to increased perceptual performance.[552] These athletes appear to be capable of faster visual processing speeds than the average person, and in our rugby cohort, these findings support their ability to track the ball and opposition players.

However, we also noticed reduced vertical synchronisation scores in the rugby players during the vertical smooth pursuit test, with 97.6% of cohort achieving below the population mean. While it is known that trochlear nerve palsies may reduce this oculomotor variable due to its implications on vertical gaze,[553,554] it is highly unlikely that this would explain this deficit in the rugby players. Synchronisation of smooth pursuit eye movements has also been shown to be reduced in those with mTBI,[555] however in our sample we found no difference between those who had a history of concussion and those player without any history. Instead, the poor scores on vertical synchronisation may be due to the potential of effects of fatigue and boredom, leading to inattention during the vertical smooth pursuit test. As the testing components of the RightEye Neurovision

Test are completed in a specific order, future randomisation of tests is necessary to clarify this anomaly. Further testing, such as orthoptic ocular motility tests, would also be useful to uncover subtle eye movement deficits.

In rugby, and to our knowledge all professional sport, there is very little to no practical application of circular smooth pursuits. Rugby primarily involves the need for horizontal and vertical oculomotor movements to track and follow the ball, whether it has been passed, kicked or carried by another player. The rugby cohort only performed better in the variables relating to in-game oculomotor behaviour and was almost identical to the population in areas that appear not to be critical for play. Similar results have been found in a cohort of basketball players that showed that novice and expert basketball player's oculomotor skills were equivalent in general tasks, but expert players had significantly better sport-specific skills such as detecting visual cues.[550] This difference in oculomotor function may suggest either an innate or the development of oculomotor expertise in rugby players. Whether this oculomotor expertise could be trained in young players is an area for further investigation.

Lenoir *et al.*[548] and Morrillo *et al.*[556] documented superior saccadic eye movements in basketball, tennis, soccer, volleyball, handball and professional shooting athletes, compared to non-athletic controls. In both studies, the authors contributed this enhanced visual system to practice effects, as only the underlying saccadic variables required by the athletes were significantly improved.[548,556] Additionally, similar findings in Piras *et al.*[557] associated this oculomotor behaviour to faster visual

processing speeds, which advantage elite players during sport-specific tasks. Our results support these findings with the rugby players demonstrating both faster horizontal and vertical saccades than the population mean. Interestingly, subtle saccadic undershoots were noted, particularly within the range of 9 to 18 mm of the target, on both the x- and y-axis, which were outside the limits of the normal population. This was found for 94.9% of players during the Vertical Volitional Saccade Test and 97.6% during the Horizontal Volitional Saccade Test. These undershoots may be related to the enhanced visual anticipatory skills, which have been reported in athletes by Bertram *et al.*[558] We propose that this predictive behaviour is a reflection of high visuospatial awareness, as rugby players have been shown to have a greater activation of the right superior parietal lobe and lateral occipital cortex using fMRI.[559]

Since concussion has been documented to have implications on smooth pursuits and saccades,[355,359,361,560,561] we compared these variables between players with and without a history of concussion within the last 12 months. Our results showed no difference between both groups. This is suggestive of full neurological recovery and is consistent with no player reporting concussive symptoms. It is therefore possible that eye-tracking devices may be able to track a player's recovery from concussion, however, this would have to be explored in a systematic trial.

We found no association of ocular movements with age. However, this is likely due to the relatively young sample with a narrow age range (18 to 31 years) as the

decrease in oculomotor function has primarily been found in those over 40 years of age.[547,562-565]

Although this study provides an insight into one aspect of the oculomotor capabilities rugby players possess, it is not without methodological limitations. As stated, our sample had a narrower age range then the normative database (11 to 62 years), with the inclusion of older persons in the normative database likely to reduce mean scores. In addition, our sample size was relatively small and recruited from one rugby club, which as elite players these findings may not be generalizable to lower grade players.

Our findings suggest that it is important to obtain individual baseline measures of oculomotor function in order to be able to utilise the current measures in the assessment of concussion and post-concussion recovery and to determine levels of improvement in function. Identifying the influence of fatigue and psychological learning effects from repeated performances would also need to be conducted before designing appropriate studies to validate any eye-tracking device for use in the assessment of concussion.

These findings need to be replicated in other sporting codes to improve generalisability. Future studies of athletes should also include top-grade players as well as age-matched low-grade players and non-sporting populations. This would help confirm the presence of either practice effects on developing sport-specific oculomotor skills or whether predisposition to superior eye movements may have warranted identification and/or selection of players into high levels of competitive

rugby. Additional research of larger samples would be needed for older playing groups in order to determine the precise decline of oculomotor function by age. In circumstances where a similarly aged player of rugby has no recorded baseline, our results may provide health professionals with a relevant score of oculomotor function using the RightEye device for comparison before making any concussion assessment.

4.6 CONCLUSION

The results from this study suggest that young top-grade rugby players possess faster smooth pursuit and saccadic ocular systems than the general population. In addition, our results are suggestive that these athletes possess high levels of anticipatory predictive behaviour. This is advantageous in competitive sport. Therefore, a sport-specific normative database may assist non-medically trained examiners in clinical judgement of whether a player's oculomotor function is impaired following a recent potential concussion. A previous history of concussion within the last 12 months, however, appeared to have no impact on a recovered player's oculomotor function.

Chapter 5: Acute Convergence and Accommodative Dysfunction in Rugby Union Athletes with Concussion

This chapter comprises the following paper submitted to *Clinical Ophthalmology*.

5.1 ABSTRACT

Background: There is an emphasis to improve sports-related concussion (SRC) detection through the assessment of eye movements. Impairments to the near point of convergence (NPC) and near point of accommodation (NPC) are common in patients suffering an acute SRC. However, these studies do not compare to an individual pre-injury baseline. The aim of this study was to identify a change between baseline and post-concussion convergence and accommodative amplitudes.

Methods: Sixty male rugby union players (mean age = 22.1 ± 4.0 years) were recruited and completed convergence and accommodative amplitude measurements using the Royal Air Force (RAF) rule. Previous history of diplopia, concussive episodes within the past two years, playing position and use of near correction glasses was documented. If an episode of SRC was sustained during the season, these measurements were repeated (median = 3 days, IQR 3 – 8.5).

Results: The median baseline convergence was 6.0 (6.0 – 7.8) cm. Two athletes (3.3%) demonstrated abnormal baseline measures (> 10 cm). Reduced NPA measures were noted in six athletes (10.0%) No association was determined between baseline measures and previous diplopia and concussion history and playing position (all $p > 0.05$) During the season, eight athletes (13.3%) sustained a concussion, with one sustaining a second. Out of the nine episodes of SRC, a decrease from baseline monocular and binocular accommodative amplitudes were noted in 88.9% (all $p = 0.012$), while 33.3% had decreased convergence ($p = 0.686$). All players with impairments in NPC also demonstrated a reduced NPA. Only one athlete demonstrated no change to either visual function following SRC.

Conclusion: Accommodation and convergence dysfunction occur in the acute stages of SRC. Individual baseline ocular testing is important in the assessment of concussion for a true measure of neurological decline. The RAF Rule may be a useful tool in aiding concussion detection.

5.2 BACKGROUND

Over the last decade, concussion in sport has become of great public concern.[566] Representing a diffuse head injury, concussion is commonly activity-related, with a high prevalence reported in multiple contact sports, such as hockey, football, basketball and rugby.[567-569] Most symptoms are acute, typically resolving within 7 to 10 days after injury, if accompanied by adequate rest.[570] However, almost half of patients endure persistent disturbances and risk developing latent neurological sequelae, if prematurely returned to play.[571]

Recent pathological studies have found evidence of progressive neurodegenerative disease in retired contact-sport athletes who have had an extensive history of head trauma, including chronic traumatic encephalopathy and affective disorders.[273,572,573] This has evoked a strong need for health professionals to better detect concussion, in order to minimise an athlete's exposure to repeated trauma. Validated, reliable and well understood concussion detection tools are vital to protect players from exacerbation of concussion symptomatology and future possible neurodegenerative consequences, by prematurely returning to play. However, there remains no simple test to diagnose concussion in sport.

Australian professional athletes suspected of SRC are thoroughly evaluated by a sports physician using various neurological and cognitive screening tools (see Appendix A).[193] Despite demonstrating a high sensitivity for detecting post-concussive neurological decline, the use of these tools is limited to sporting games with access to medical resources. In non-professional levels of sport there remains a lack of awareness and even further, lack of trained medical support.[28,574,575] There is

an increasing need for an objective gold-standard tool that can detect SRC at the earliest possible interval post-trauma in order to prevent long-term injuries. This would remove the reliance on players self-reporting symptoms that may not accurately reflect SRC or its severity.[218,222] A simple test that can be completed by non-medical professionals that has good specificity for concussion, would be ideal.

The visual and oculomotor systems are vulnerable to traumatic brain injuries, with a wide range of visual symptoms commonly reported in patients suffering from concussion, including diplopia, impaired eye tracking, blurred vision and difficulty reading.[285,576,577] This has suggested that there may be a role for examination of ocular function following a potentially concussive event to aid the clinical assessment and diagnosis of people with concussion.[161] However, there has been limited research conducted on the relationship of concussion to eye movement and visual disorders. A better understanding of concussion's effects on the oculomotor and visual system will possibly provide health professionals with an additional tool to detect subtle neurological changes, thereby increasing our general understanding and improving the overall diagnostic accuracy available on the sideline of sporting events.

Ocular convergence and accommodation have been highlighted as two key visual functions that are commonly affected by concussion.[285,326,380] Convergence is the simultaneous movement of both eyes inwards, to maintain binocular fixation on a target. Accommodation refers to a change in the optical power of the crystalline lens of the eye to maintain a clear focus on an object, typically increasing optical

power as the object moves closer to the eye. Due to the complexities of both neurological pathways and diversity of inputs, these oculomotor functions are highly susceptible to damage, with resultant dysfunction after a concussive head injury.[285]

In one study, Master *et al.*[326] detected a receded NPC and NPA in 49% and 51% respectively of concussed adolescents, and 22% recorded both deficits simultaneously, when compared to measures in an age-matched normative sample. Similar rates of dysfunction have also been found by others, suggesting that around half of all concussions involve accommodative and/or convergence dysfunction.[295,311,312,328] However, these measures have not yet been included or rigorously studied as part of a concussion test battery. The few studies that have examined ocular movements in relation to concussion, have only documented observations in outpatient clinics following a previously detected concussion and lacked baseline information to rule out previous undetected oculomotor defects.[295,311,312,326-329] The prevalence rates of abnormal convergence and accommodative amplitudes within the general population are not well understood.[578]

To our knowledge, only one study has compared post-concussion NPC scores to individual baseline measures.[327] However, the sample was small with only 11 concussive head injuries with only one athlete manifesting reduced convergence. Of significance, no study has included baseline and post-concussive accommodative amplitudes. Therefore, there is a need for larger studies comparing NPC and NPA

values between an individual's pre-injury baseline and post-concussive score. The primary objective of this study was to identify if there was a change between baseline and post-concussion convergence and accommodative amplitudes using a more rigorous methodology.

5.3 METHODS

5.3.1 Participants

A total of 60 male rugby union players were enrolled into this study from a local rugby club in Sydney. South Eastern Sydney Local Health District Human Research Ethics Committee approval (17-039) was obtained prior to the study and all participating players provided informed consent prior to enrolment. Any history of diplopia, the number of concussive episodes within the past two years and use of near correction glasses was documented. Players with current symptoms related to concussion during baseline testing, including dizziness, headaches, diplopia, nausea, photosensitivity and drowsiness were excluded.

5.3.2 Testing Procedures

All participants completed the ocular assessment in the following order using a RAF Rule[481]:

1. monocular accommodative amplitudes
2. binocular accommodative amplitudes
3. near point of convergence assessment (a binocular assessment)

An eye patch was worn to occlude one eye during monocular testing and all measurements were conducted individually by a registered orthoptist trained in

the assessment of ocular motility. To measure convergence, the RAF Rule was centered in front of their eyes with the nose bridge resting on the player's upper cheeks. The players were instructed to follow the black spot on target with their eyes as it moved towards their nose at a rate of approximately 1 to 2 cm per second. The point at which one eye was seen to deviate outwards or diplopia was subjectively reported, constituted that player's NPC (recorded in cm). This was repeated three times with the average measure used for all analysis.

Accommodative amplitudes were measured with the player attempting to read the smallest letters (N5) on the RAF Rule accommodative target. The accommodative target was moved towards the player from 50 cm, to a point at which the letters became blurred. The target was then pulled back slightly until the N5 line became clear enough to be read. This measure known as the focal point (*f*) was recorded as the NPA in cm. The actual NPA was then converted to diopters (D) for all analyses using the following formula:

$$D = \frac{1}{f}$$

Ocular measurements were then repeated following a concussion (median = 3 days, range = 3 – 10, IQR 3 – 8.5). A concussion was defined according to the Consensus Statement on Concussion in Sport, from the fifth International Conference on

Concussion in Sport.[579] This was diagnosed by a sports physician with over 20 years' experience diagnosing concussive head injuries.

5.3.3 Statistical Analysis

All statistical analyses were performed using Statistical Package for Social Sciences software (SPSS, IBM, Chicago, IL, USA v25.0). Descriptive statistics were calculated for all outcome variables including range. Measurements were recorded as median with IQR. A worse outcome was determined if the post-injury NPA was lower and the post-injury NPC was higher than pre-injury baseline measures.

Hofstetter's equation was used to determine whether baseline NPA fit within age-matched norms.[580] The internal consistency of NPC measurements across three trials was calculated using intraclass correlation coefficients (ICCs) and a repeated-measures analysis of variance (ANOVA). This was presented as mean ± standard deviation. A Shapiro-Wilk Test was used to determine the distribution of the data. A Mann-Whitney U test was performed to calculate any difference between baseline NPC and NPA scores in association with playing position, history of concussion and/or a history of diplopia. A Wilcoxon signed-rank test was used to determine the relationship between baseline scores and age. It was also used to discriminate between baseline and post-injury NPC and NPA. The statistical significance level was set at $p < 0.05$ for all analyses.

5.4 RESULTS

Baseline testing occurred during pre-season non-contact training for the sport. The mean age of the players was 22.1 ± 4.0 years (range = 17 - 34). Of those recruited,

19 were positioned as a 'back' (31.7%) and 41 were a 'forward' (68.3%) rugby player. Six players (10%) had previously experienced transient diplopia, while 19 players (31.7%) had sustained a concussion within the last two years.

Baseline NPC and NPA are displayed in Table 5.1, including monocular and binocular measurements. The ICCs for baseline average NPC in this cohort showed a high degree of internal consistency of 0.97 (95% CI 0.95 – 0.98). There was an increase in mean NPC measurements between trials one (6.0 ± 1.6 cm), two (6.1 ± 1.7 cm) and three (6.4 ± 1.9 cm), which was found to be statistically significant ($p < 0.001$). A poor NPC (> 10 cm) was present in two players (3.3%) during baseline testing, while six (10.0%) had reduced accommodative amplitudes compared to age-related norms.

Table 5.1. Baseline NPC and NPA measurements in 60 rugby athletes and its association with playing position, history of concussion and previous history of diplopia.

			***P*-value**	
	Median (IQR)	**Playing Position**	**History of Concussion**	**History of Diplopia**
NPC (cm)	5.7 (5.0 – 6.9)	0.678	0.199	0.267
RE NPA (D)	4.3 (3.6 – 5.4)	0.504	0.956	0.596
LE NPA (D)	4.3 (3.6 – 5.5)	0.340	0.065	0.170
BE NPA (D)	4.3 (3.7 – 5.2)	0.917	0.621	0.348

RE = Right Eye, LE= Left Eye, BE = Both Eyes (assessed binocularly)

Eight athletes (13.3%) sustained a diagnosed concussion during the competition season and were followed up. One player experienced a second concussive injury. Seven (87.5%) of the injured players had a prior concussion within the last two years. An additional three players were diagnosed with concussion in the final game of the season and were lost to longer term follow up. These three players had reduced accommodative amplitudes compared to their age-norm at the initial post-concussion assessment, with one also manifesting a reduced NPC.

There was no correlation found with baseline NPC measurements and age (p = 0.064). However, there was a strong association of age with baseline accommodative amplitudes in the right eye (p = 0.011), left eye (p = 0.001) and in both eyes ($p < 0.001$).

Comparison between baseline and post-injury ocular function is displayed in Table 5.2. Out of the nine episodes of a concussion, a decrease in accommodative amplitudes was noted in eight players (88.9%), while evaluation of post-injury convergence revealed three (33.3%) had a receded NPC. All players with post-concussive impairments in convergence also demonstrated a reduced NPA. One player demonstrated no change to their baseline NPA or NPC following their concussion.

Table 5.2. Comparison between baseline and post-injury measures in nine athletes with concussion.

	Median (IQR)		Range		
	Baseline	**Post-injury**	**Baseline**	**Post-injury**	***P*-value**
NPC (cm)	6.0 (6.0 – 7.8)	6.0 (6.0 – 9.0)	5.3 – 12.0	5.3 – 34.7	0.686
RE NPA (D)	3.8 (3.3 – 4.1)	3.1 (2.6 – 3.8)	2.5 – 6.7	2.4 – 5.0	0.012*
LE NPA (D)	3.7 (2.6 – 3.9)	2.8 (2.4 – 3.4)	2.4 – 4.2	2.2 – 4.0	0.012*
BE NPA (D)	3.8 (3.3 – 4.3)	3.1 (2.7 – 3.8)	2.6 – 6.7	2.3 – 4	0.012*

*denotes statistically significant ($p < 0.05$)

5.5 DISCUSSION

To our knowledge, this study was the first to compare post-concussion accommodative amplitudes to a pre-season baseline measurement. This research suggests that a reduced accommodative amplitude is common after sustaining a concussive head injury, supporting previous findings on the relationship between accommodative dysfunction and concussion.[286,295,311] Almost 90% of the concussed rugby athletes in this cohort demonstrating a reduced accommodative capacity (median decrease of 0.7D from baseline) using the RAF Rule, which was notably higher than the 10% within the non-concussed players. The incorporation of a detailed ocular examination involving NPA testing after a concussion may be important for health professionals to improve clinical care and diagnostic batteries.

Unlike many cross-sectional studies measuring NPC who have reported high rates (up to 55%) of convergence dysfunction in athletes after a concussion,[286,295,311,325] only three of our documented nine concussions demonstrated a reduction of NPC from baseline. This coincides with results from Vernau *et al.*[327] where only one out of eleven patients had a reduced post-concussive NPC when compared to baseline.

These findings from the two studies with baseline measures suggest that post-concussive convergence dysfunction may not be as prevalent as currently thought in the literature. Although, with small sample sizes in both Vernau's and our study, further investigation is clearly warranted.

We noted a poor NPC of > 10 cm in only two athletes (3.3%) and reduced NPA in six (10.0%) during baseline testing. This matched previous findings of low rates of abnormal convergence and accommodative amplitudes within the healthy population.[322,581,582] Studies that did not include a baseline measure when assessing these visual functions may overestimate the proportion of concussion-related convergence and accommodative dysfunction by including attributing this poor convergence and accommodative function to concussion. This suggests the need for pre-season ocular screening. Any dysfunction found pre-season could then be provided ocular rehabilitation. Athletes with a pre-existing deficit of accommodation and convergence may also be at a greater risk of post-concussive symptoms, although this remains speculative as in this study no players with reduced function at baseline sustained a concussion. Further study is warranted to clarify this notion.

Our results showed no relationship between a player's position, history of concussion or a history of diplopia with any of the ocular measures made with the RAF Rule. It is likely that any previous neurological deficit sustained from a concussion in an earlier season of play would have recovered to normal levels at the time of their current pre-season assessment, making them eligible for inclusion into

this study. It is to be noted that the information extracted from the athletes in this study including their medical history was self-reported. According to findings by Kerr *et al.*[23] failure to disclose complete concussion histories to medical staff was observed in almost 50% of retired American football athletes. Therefore, it is important to consider that some athletes in our study may have also failed to report their own concussion histories prior to inclusion.

As expected NPA was influenced by age. It mirrors empirical research by Duane in 1922 that found accommodative amplitudes to decrease with increasing age.[305] This is important to note for health professionals who may use a player's NPA as a marker for concussive head injury in the future, as it again highlights the need for a pre-injury baseline assessment when diagnosing a concussion. According to Duane, there is some variability in the amount of accommodative decline per year of age.[305] Therefore, comparing the NPA of a player who is suspected of concussion to a specific age normative value may also lead to many false positives, which in the context of professional sport could have broader impact on the player's participation in games.

For the young athletes who do experience accommodative and/or convergence dysfunction after a concussion, this may manifest with headaches, diplopia, fatigue, difficulty concentrating, asthenopia and blurred vision.[147] This may lead to complications performing crucial daily activities such as reading and in the sports setting, difficulty tracking the ball. Furthermore, as our sample of rugby athletes were recruited from a semi-professional club, many of the players are also involved

with academic study and/or full-time work. Additional academic and occupational support for those with concussion-related visual dysfunction would be required to help them during symptom recovery.

Ciuffreda *et al.*[316] reported that rehabilitation in the form of eye tracking, accommodation and convergence exercises may accelerate recovery and completely alleviate symptoms in almost 90% of patients with mTBI who have chronic visual disturbances. However, research in this area is limited, with only a handful of studies reported in the literature.[311,316,317,344] In our study, we did not conduct any post-concussive ocular exercises or repeat testing when the concussion had recovered, which would be important for future studies to incorporate. This could help explore the role of ocular testing in recovery and rehabilitation.

5.6 CONCLUSION

A receded NPA occurred in almost 89% of rugby athletes with concussion while a receded NPC was detected in 33%. These deficits may impact an athlete's ability to perform at sport, cope with work and academic activities. Individual baseline ocular testing is important in the assessment of concussion-related visual dysfunction for a true measure of related neurological decline. Accommodation and convergence testing utilising the RAF Rule may be a useful adjunct for physicians aiding detection of concussion as part of a multi-faceted battery of tests.

Chapter 6: Concussion-Related Visual Dysfunction and Symptom Recovery in Children: A Retrospective Study

This chapter comprises the following paper submitted to *Brain Injury*.

6.1 ABSTRACT

Objectives: To determine the associations between duration of symptomology and concussion-related visual dysfunction, and to examine any associations with age, gender and previous history of concussion.

Methods: A retrospective study was conducted on patients (n = 142) aged 5 to 18 seen at a concussion clinic in Sydney, from November 2015 to May 2018. All had a medical diagnosis of sport or physical activity related concussion. Information extracted included age, sex, duration of symptoms, loss of consciousness, amnesia, activity withdrawal and number of previous concussions. The Vestibular/Ocular Motor Screening (VOMS) tool was used to determine concussion-related visual dysfunction.

Results: The mean age of participants was 13.17 ± 2.6 years with 103 males, 35 females. Of these 28% had a positive result on the VOMS test. Almost double the proportion females (42%) had a positive VOMS result compared to males (23%, p = 0.034). No association was found between VOMS outcome and age (p = 0.091),

occurrence of multiple concussions ($p = 0.222$), or number of previous concussions ($p = 0.187$). Ninety-three patients recovered from their concussion symptoms (mode 19-21 days) while females demonstrated a significantly longer recovery time (mean 63.15 days) than males (mean 41.88 days, $p = 0.002$). Those with a positive VOMS also had a longer mean recovery time (days=63.7) than those with a negative VOMS (39.2 days, $p < 0.001$).

Conclusion: The VOMS is a useful predictor of symptom recovery in children with concussion. Sex and visual dysfunction may be an important indicator of time-to-recovery from concussion-related symptoms.

6.2 INTRODUCTION

Concussion in sport is reported to annually affect almost 1.1 million to 1.9 million children aged 18 years of younger in the United States of America.[583] Unfortunately, it is estimated that up to 89% of patients that report to the Emergency Department with head trauma are unable to recognise their own signs and symptoms.[219] This level of oversight has led to concern from the media, parents and public,[584,585] with calls to improve the identification of concussive head injuries on the sports sideline, before consequential exacerbation of symptoms occurs.

Identifying all cases of concussion in children can be particularly challenging for medical professionals. With most sports at the junior levels not having access to a sideline physician or trainer experienced in the diagnosis of concussion, young athletes must utilise publicly available medical resources. This implies that there may be a significant proportion of children who go undetected. For those who do attend emergency departments, medical evaluation, including cognitive and neurological assessments, aid diagnosis. Post-concussive symptoms are monitored in this manner until recovery and discharge. This can be quite prolonged, with recovery taking several weeks to months in as many as 25% of children.[259,586]

Deficits in visual function have been suggested as a potential marker for improving the detection of mTBI.[286,289] In children with concussion, researchers have reported single or combined impairments of accommodation (ability to focus eyes on near objects) and eye movements such as convergence, and smooth pursuit and saccadic eye movements in up to 69% of cases.[326] These vision disorders cause functional problems such as difficulty reading and/or sustaining attention on visual tasks, in

which prolonged after-effects can affect schoolwork, sports participation, and quality of life.[587]

Master *et al.*[513] found that post-concussive visual and vestibular function in children may also be a useful predictor of potentially prolonged recovery. However, there are limited studies exploring post-concussive visual functions in children and its relationship to symptom recovery. The addition of suitable visual protocols for concussed children could help health professionals to develop better management strategies and further support full function for academic and daily life functions. In order to develop such protocols, further studies are needed to establish the feasibility and efficacy of assessing visual deficits and whether monitoring and determining recovery from concussion guides for children while amending RTP guidelines can be justified. This retrospective study aims, to determine the relationship between duration of symptomology and concussion-related visual dysfunction, and to examine any associations with age, gender and previous history of concussion.

6.3 METHODS

6.3.1 Study Design/Protocol

A retrospective study of medical records of children referred by physicians from across New South Wales and Australian Capital Territory to a tertiary outpatient paediatric sport and exercise hospital clinic in Sydney were conducted for those seen from November 2015 to May 2018. Children with a medical diagnosis of concussion in accordance with the Consensus Statement on Concussion in Sport, from the fifth International Conference on Concussion in Sport[22] were identified. Of

these, 142 cases had a concussion related to sport or other leisure physical activity. Of these, four had incomplete medical records and were excluded from the analysis. Information extracted included; age, gender, duration of symptoms, LOC, amnesia, type of activity, immediate withdrawal from activity, number of previous concussions, and concomitant injuries suffered. Children were stratified by age and schooling stage into primary school (5–13 years) and high school (14–18 years) for analysis. This follows the precedence set by Bakhos *et al.*[588]

6.3.2 Vestibular/Ocular Motor Screening test

The standard medical examination of these children included the VOMS test to screen for the presence of concussion-related visual dysfunction. VOMS includes a brief assessment of smooth pursuits, horizontal and vertical saccades, convergence, horizontal and vertical vestibular ocular reflex, and visual motor sensitivity. Symptoms including headache, dizziness, nausea and fogginess were scored between 0-10 prior to medical examination. After each component of VOMS was tested, the examiner then re-scores each symptom, with an increase in symptom severity on any of the testing domains confirming a positive VOMS result. The testing was conducted by a single paediatrician with extensive expertise in concussion and in the application of the VOMS protocol described by Mucha *et al.*[493]

This study had the University of Technology Sydney Human Research Ethics Committee approval (19-3748), with all information de-identified and study protocol adhering to the tenants of the Declaration of Helsinki.

6.3.3 Data Analysis

Descriptive statistics were calculated for all outcome variables. Pearson's Chi Square test was used to discriminate between groups (age, gender, whether the child was immediately withdrawn from activity, concomitant injury, multiple concussions suffered, LOC, and amnesia) and VOMS outcome. Mann-Whitney U test for non-parametric data was performed to determine the relationship between continuous variables (duration of symptoms and previous number of concussions) and VOMS outcome. Kaplan-Meier plots were used to determine the number of days until patients were symptom-free stratified by both gender and VOMS outcome. All statistical analysis were performed using Statistical Package for Social Sciences software (SPSS, IBM, Chicago, IL, USA v25.0). The statistical significance level was set at $p < 0.05$ for all analysis.

6.4 RESULTS

6.4.1.1 Age, Gender and Activity Characteristics

One hundred and thirty-eight medical records were suitable for inclusion in this study (103 males and 35 females). Overall, the mean age of the cohort was 13.17 ± 2.6 years, comprising of 67 children who attended primary school and 71 attending high school (see details in Table 6.1). There were 51 (76%) males attending primary school and 52 (73%) in high school. When compared to primary school students, there was a greater proportion of high school students who had sustained their concussion through contact sports (66% vs. 46%, $p = 0.035$). Only 43% of high school students were immediately withdrawn from activity upon suffering a concussion, compared to 75% of children attending primary school ($p = 0.002$).

Table 6.1. Details of patient characteristics with respect to schooling level.

Characteristic	All	Primary School	High School	*p*-value
	n = 138	*n* = 67 (49%)	*n* = 71 (51%)	
Mean age	13.2 ± 2.6	11.93 ± 2.1	15.1 ± 1.1	<0.001*
Proportion of males	75%	76%	73%	0.698
Proportion related to contact sports	57%	46%	66%	0.035*
Immediate withdrawal from activity	57%	75%	43%	0.002*
Loss of Consciousness	39%	38%	40%	0.881
Amnesia	41%	38%	44%	0.702
CT Scan performed	*47%*	46%	47%	0.499
MRI performed	*23%*	29%	24%	0.499

*Statistically significant ($p<0.05$).

The mean time from date of concussive episode to presentation at the clinic was 27.7 ± 25.8 days. Forty-nine children had a history of previous episodes of concussion ranging from 1 to 15 previous diagnoses. Seventeen children sustained repeated concussions, which, however, was not associated with having a greater prolongation of symptoms (mean 47.7 days) than those who had only the one episode (45.9 mean days, $p = 0.645$).

The characteristics of the patient, symptoms, and tests performed, with respect to gender, are described in Table 6.2. There was no statistical difference between the mean ages of males and females in this sample ($p = 0.658$). Compared to females, there was a significantly higher proportion of males who had sustained their concussion from contact sports, (62% males vs. 43% females, $p = 0.006$).

Table 6.2. Details of patient characteristics with respect to gender.

Characteristic	All	Male	Female	*p*-value
	n = 138	*n* = 103 (75%)	*n* = 35 (25%)	
Mean age	13.2 ± 2.6	13.2 ± 2.5	13 ± 2.7	0.658
Proportion related to contact sports	62%	69%	42%	0.006*
Immediate withdrawal from activity	57%	56%	59%	0.867
Loss of Consciousness	39%	34%	49%	0.089
Amnesia	41%	41%	39%	0.958
CT Scan performed	47%	47%	44%	0.763
MRI performed	23%	23%	23%	0.898

*Statistically significant ($p<0.05$).

Contact sports accounted for 60% of the concussions documented, with the highest prevalence (32%) in rugby (see Table 6.3). Non-contact sports were reported in 14% and leisure-related recorded 27% of concussive head injuries.

Table 6.3. Sports and activity characteristics of patients.

Sport/Activity	*n* (%)
Contact Sports	
Rugby (League and Union)	44 (32)
Australian Rules Football	5 (4)
Football (Soccer)	17 (12)
Basketball	6 (4)
Hockey	1 (1)
Martial Arts	1 (1)
Netball	1 (1)
Oz-Tag and Touch Football	4 (3)
Non-Contact Sports	
Cycling	2 (1)
Cricket	1 (1)
Dance	2 (1)
Golf	1 (1)
Horse Riding	4 (3)
Skateboard/Scooter	3 (4)
Motocross	4 (3)
Gymnastics	1 (1)
Leisure-Related	
Play	26 (19)
Other	9 (7)

*Percentage (%) rounded to whole number

6.4.2 VOMS Outcome

The relationship between the VOMS outcome and patient characteristics are described in Table 6.4. There was a statistically significant higher proportion of females scoring a positive VOMS result than males (23% males vs. 42% females respectively, $p = 0.034$). However, no statistical difference was found between a positive VOMS outcome and age ($p = 0.091$) or with immediate withdrawal from

activity (p = 0.832), multiple concussions (p = 0.222), concomitant injuries (p = 0.992), or the previous number of concussions experienced (p = 0.187).

Table 6.4. The relationship between VOMS outcome and patient characteristics.

VOMS Outcome	Positive	Negative
	n = 37 (28%)	*n* = 95 (72%)
Males	23%	76%
Females	42%	58%
Primary School Group	10%	38%
High School Group	18%	34%
Proportion Related to Contact Sports	30%	70%
Immediately Withdrawn from Activity	32%	68%
Loss of Consciousness	24%	76%
Amnesia	24%	72%
Multiple Concussions	41%	59%

No statistically significant relationship was determined between children who demonstrated a positive VOMS outcome and those who had experienced LOC (p = 0.373) or amnesia (p = 0.973). Nor was there any statistical association between children with amnesia and LOC (p = 0.234).

6.4.3 Time to Recovery

The duration of symptoms varied widely, with eight children recording no symptoms from the time of first presentation at the clinic. Ninety patients had recovered from their symptoms at the time data was collected. Of these, the mode period for recovery was 19-21 days, see Figure 6.1. A further 40 children were still symptomatic at the time of data collection and are therefore not included in analysis of duration of symptoms. A small number of children experienced substantially prolonged symptoms, with 97.0% recovered by 160 days. The

remaining three recovered in >200 days, with one child recovering 470 days post-concussion.

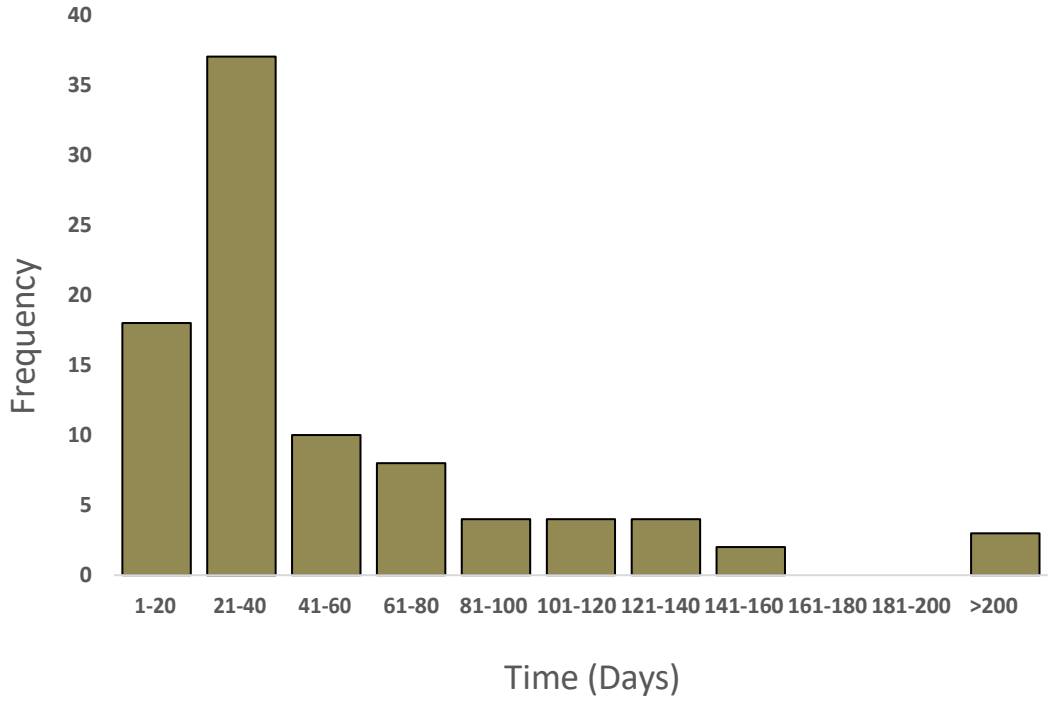
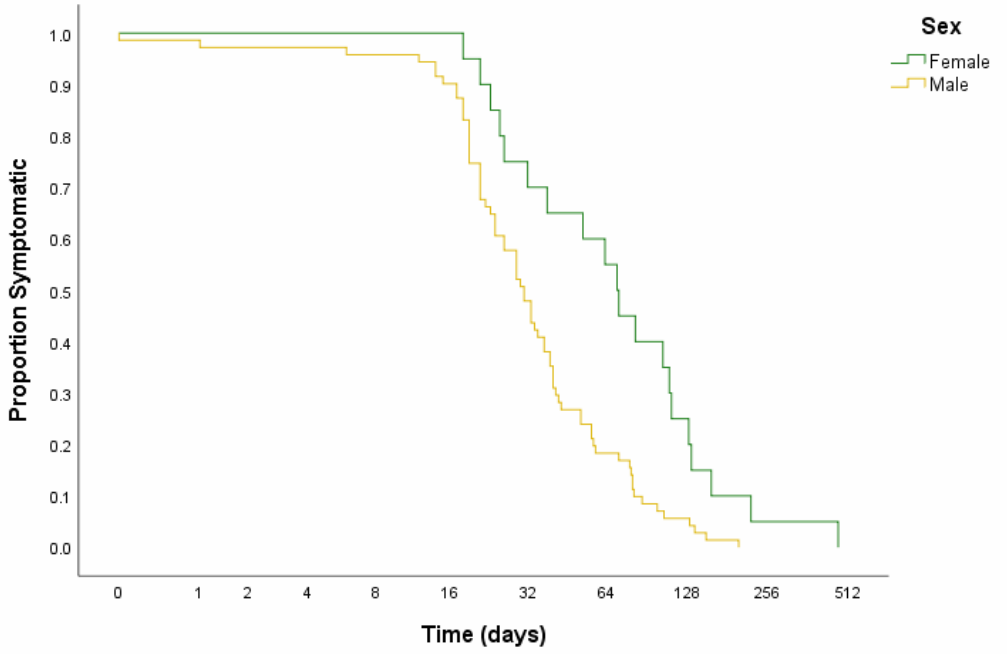


Figure 6.1. Distribution of symptom recovery in 90 children excluding those who were asymptomatic at outset (*n* = 8).

Females demonstrated a significantly longer recovery time (mean 63.15 days) than males (mean 41.88 days, $p = 0.002$, Figure 6.2). Children with a positive VOMS had a significantly longer recovery time (mean 63.67 days) than those with a negative result for VOMS (mean 39.24 days, $p < 0.001$, Figure 6.2). However, there was no association between the length of recovery and age groups ($p = 0.731$), amnesia ($p = 0.861$), LOC ($p = 0.358$) or whether multiple concussions were sustained ($p = 0.469$).



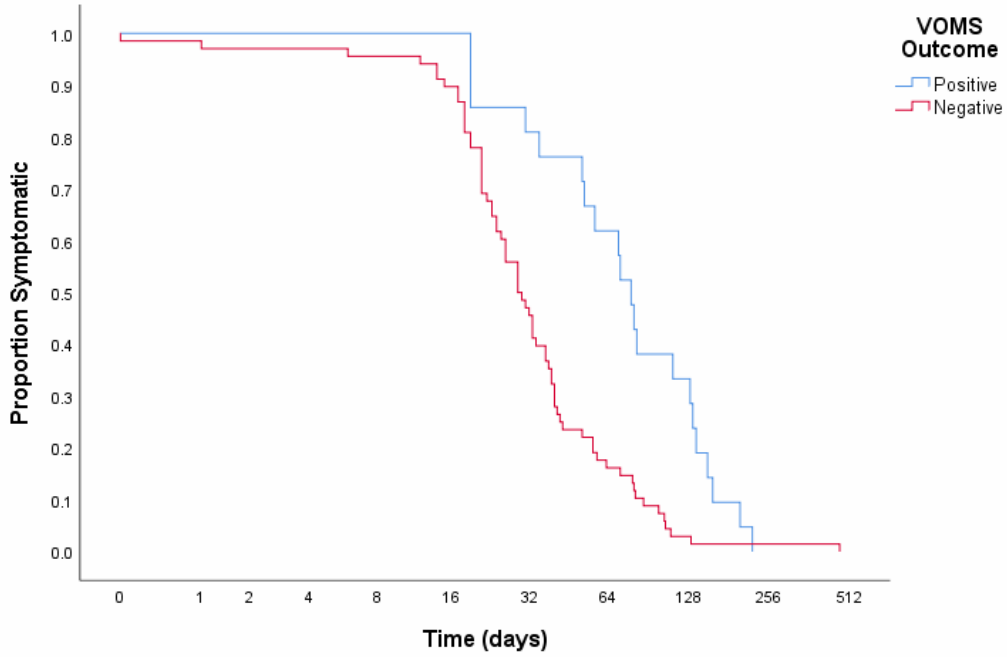


Figure 6.2. A Kaplan-Meier plot for time patients (*n* = 90) took to become asymptomatic, with respect to gender (top) and Vestibular/Ocular Motor Screening outcome (bottom).

6.1 DISCUSSION

Our findings broadly support the work of previous studies in this area, linking visual dysfunction with concussive head injury.[286,332,589] The retrospective analysis conducted in this study determined that a positive VOMS outcome in a paediatric population, was strongly associated with symptom recovery time following concussion. These results reflect those reported by Master *et al.*[513] and Anzalone *et al.*[514], which found the VOMS test to be a potential predictor for symptom recovery following sports-related concussion. This highlights the importance of vestibular and ocular testing to identify those children with concussion who may need advice regarding the potential duration of symptoms and targeted rehabilitation. Within schools and organised youth sporting activities, this could aid teachers, coaches and parents in appropriately managing affected children, as those with longer than normal recovery times may endure a prolonged negative impact on their learning and sports participation.[590]

Female children in this study took a mean difference of 21 days longer than the males to recover from their symptoms. Although there was no specific explanation of this from the data available, recent work by Baker *et al*.[256] found similar results in a sample of 117 adolescents, with 41% of females taking >21 days to recover compared to only 19% of males. This has been attributed to females exhibiting 49% less isometric neck muscle strength and 43% less lower head-neck segment mass than males,[591] potentially leading to females experiencing a greater force on the brain, compared to males, after impact. This may lead to an increase in the duration of their symptoms. However, more research is required comparing the

pathophysiology and biokinetics of concussion between males and females to clarify this characteristic, as well as possible gender-based psychosocial impacts on reporting of symptoms.[241,242]

Although empirical research by Field *et al.*[82] connected prolonged recovery times with greater deficits to memory in high school athletes, compared to collegiate and professional players, implying an age related effect, however, our data showed no significance difference in recovery time between the younger primary school children (<13 years of age) and older high school children (13 to 18 age). Similarly, we found no association by age group with prolonged recovery, nor was there an association with a poorer prognosis on the various ocular movement assessments. Future studies may need to gather larger numbers within discrete age groups to determine if there is an age-related effect on these measures in children with concussion.

In our study, the majority (75%) of concussive head injuries were documented in males. This was consistent with earlier observations showing that males are three-times more likely to attend an emergency department with concussion than females.[259,592] Whether males are fundamentally receiving more concussions than females, possibly due to the level of participation in contact sports, has not been clearly quantified. This gender-based difference may diminish as females continue to increase their participation in higher level contact sports in Australia and elsewhere.

It has previously been reported by Hurtubise *et al.*[593] that males endure a significantly higher severity of visual problems than females. However, we did not find this gender difference in this study of younger children, however, it may require a larger sample of age-matched females and males to definitively elicit this relationship. It may be also partially explained by the visual parameters tested, as Hurtubise's study analysed self-reported visual symptoms rather than signs elicited from a medical examination.

We also found that 46% of patients were not withdrawn from sports activity after suffering a concussion. Despite large bodies of research emphasising the need for vigilant RTP protocols,[18,519,535,594] these concepts seem to be lacking in practice within junior sports. Our results found only 43% of high school students were withdrawn from activity, compared to 75% of children attending primary school, highlighting a significant concern in both groups. Paediatric and adolescent athletes are at the highest risk of developing "second impact syndrome",[595] which has shown to cause diffuse cerebral swelling and death in athletes under 20 years of age.[263] Evidently, there needs to be more done to protect children from short and long-term neurological consequences of concussion. Continued education of coaches, parents and junior sporting organizations is vital to tackle this issue.

Previous work by Elbin *et al.*[596] have suggested that the continuation of play after suffering a concussion exacerbates symptoms and extends the duration of symptomology. In youth athletes, this is believed to cause alterations to synaptic plasticity and excitatory-inhibitory neuronal imbalances.[597] As demonstrated

phenotypically in an animal study, these pathophysiological changes can be expressed through impairments in cognition.[598] Ultimately, this would have a huge burden on the child's capabilities at school and in learning. However, upon analysing visual function post-injury, we found no differences in those patients that were immediately withdrawn from activity and those that had a history of previous concussions. As the VOMS test is limited in the ocular parameters it assesses, performing a more detailed ocular assessment post-injury may uncover clearer relationships between concussion history and vision.

Considering the amount of physical contact involved within different sports, the highest prevalence of concussion (32%) was documented in the rugby codes. This is consistent with a previous report,[599] and can also be attributed to the popularity of this sport in Sydney and NSW. One finding of note is the prevalence of concussion due to non-sports based "play" *(19%).* Considering the enormous financial burden concussion has on Australian emergency services,[56] these results propose that health organisations should not only focus on sport-related concussion but also those due to non-organised activities as well.

There is also evidence supporting the use of the VOMS test for concussion evaluation in the clinical setting due to its ability to discriminate, between healthy and concussed adolescent athletes.[600] However, the visual examination does contain some limitations. The test is not a specific for all concussion-related visual dysfunction. Other visual functions that are commonly reported to be affected following concussion, such as accommodative amplitudes,[326] are not evaluated.

Further, the VOMS test does not need to be performed by personnel trained in ocular motor assessment, meaning subtle eye movement abnormalities, including nystagmus and strabismus, may go unnoticed. Using a more objective tool to measure the near point of convergence and accommodative amplitude, such as the RAF Rule, may assist in providing a more comprehensive approach to assessing visual and ocular motor functions.

Despite providing an insight into the impact concussion has on the visual and oculomotor system within the paediatric population, the current study is not without some methodological weaknesses. Having a retrospective cohort study design, limits the quality of the data to the accuracy of record keeping. Our data only contained visual outcomes through the VOMS test and did not include a full ophthalmic assessment by an eye care professional. In addition, our study could benefit from a larger sample size spanning multiple concussion clinics. It is also important to note the selection bias present in this study. Patients referred to a specialist concussion clinic are likely to be symptomatic of concussion. Therefore, the sample included in this study likely represent the more injured children, excluding many concussion patients who were either asymptomatic, who did not seek further medical attention, or were discharged without referral. This would also explain the large recordings of patients experiencing LOC (39%) in our sample when compared to the numbers in the literature (< 10%).[48,126,132-134]

In the future, identifying age-based norms of different aspects of visual function, including accommodative amplitude and eye-tracking capabilities in children and

repeating measurements post-concussion would also provide a stronger understanding of the relationship between concussions and the visual system. Future research should also more thoroughly compare the visual outcomes between paediatric and adult populations, as differences by age would help sporting organisations make age-relevant amendments to concussion policies used on the sideline and in surveillance and follow-up care.

6.6 CONCLUSION

The VOMS was a good predictor of symptom recovery in these children with concussion. Gender and visual dysfunction may be important indicators of time-to-recovery from concussion-related symptoms, while further study of these factors may be required in a paediatric population.

Chapter 7: Summary and Conclusions

7.1 Summary

Developing awareness and greater availability of concussion test protocols at all levels of sports and codes of sport has led to a significant increase in the recorded incidence of concussive episodes. This heightened awareness and detection of concussion has raised the level of concern among all stakeholders including sporting organisations, team staff, medical personnel, players and their families. While the number of published studies in concussion remains limited, ongoing research is strengthening our understanding of injury detection, symptom recovery and appropriate management strategies. Traditionally, the assessment of any player suspected of concussion involved a thorough neurological examination of cognition, balance, and symptom identification by a trained physician. However, such resources are not available to all levels of sport, particularly in children and adolescent players and this judgement remains subjective. The need for reliable tools that can be used by non-medical personnel at all levels of sport to detect concussion in their players is paramount, so that players can be removed from play and avoid potential further injury.

There is emerging evidence that a high portion of athletes experience some form of visual dysfunction after sustaining a TBI. This has caused a shift towards incorporating visual-based assessments on the sideline and in specialist concussion clinics to help medical personnel in their decision making and surveillance of patients with concussion. Many of these proposed vision-based/ocular motility

tools are yet to be fully validated alongside cognitive measures, with the lack of depth provided by existing literature representing a possible obstacle to the incorporation of these tools into the routine concussion test protocols.

The aim of this thesis is to assist in broadening the knowledge base of the effects that concussion has on the human visual and oculomotor systems through a series of novel studies. Using data obtained from two different populations; semi-professional rugby athletes and children from a paediatric sports concussion clinic, this thesis focused on: (1) evaluating the available visual/ocular motor tools used to detect and monitor concussion, (2) identifying new techniques and/or modifications that may improve current sideline assessments, and (3) identifying acute physiological changes to the oculomotor and visual system following concussion, using standard ocular examination techniques.

In chapter 3, “The Learning Effect of the King-Devick Test in Semi-Professional Rugby Union Athletes”, analysis to determine the magnitude of the test learning effect for the popular KDT was undertaken. The cohort of rugby athletes demonstrated a notable median improvement in their KDT score of 2.4 seconds between their first and second attempt of the test during the pre-season assessment. A median difference of 4.2 seconds (range 0.0-14.9, IQR 1.5-7.7) was calculated between the athlete’s initial trial at baseline and their overall fastest trial. Notably, the greatest change occurred within the first six to eight attempts with a ceiling effect calculated at 30 trials. With respect to the individual participants, a negative relationship of -0.08 ± 0.01 seconds was found for each year

of increasing age even in these relatively young adults, however, this could also reflect years of play. This suggests that individual baseline measures, using at least six to eight attempts would be necessary to establish a player's optimal pre-season score.

Optimising the baseline measurement will provide the best platform for medical personnel to make their clinical decision. This study was the first paper to identify the number of attempts of the KDT needed to fully achieve a statistical ceiling effect and an optimal number of trials. With the largest change occurring within the first six to eight attempts, this paper postulates that administrators of the tool should consider re-performing the tool at consistent intervals over the duration of a season, rather than just an annual update.

In chapter 4, "Comparing the Smooth Pursuit and Saccadic Eye Movements in Rugby Players to a Normative Database", we evaluated a modern computer-based concussion tool called RightEye Neurovision Test, that has growing use as a research tool internationally. Conjugate eye movements (saccades and smooth pursuits) of 42 top-grade male rugby athletes were compared to a normative database of 2500 people from the general population, supplied by the RightEye company. Our results revealed that these rugby athletes produce superior eye movement speeds and accuracy compared to the general population as measured using the RightEye. In particular, faster horizontal and vertical smooth pursuits were demonstrated in over 80% of the rugby athletes and circular smooth pursuits were similar faster in 78.6%. The majority (73.8%) also generated greater saccade numbers in the horizontal and

vertical axis than the population data. The analysis also found that 94.9% of players during the Vertical Volitional Saccade Test and 97.6% during the Horizontal Volitional Saccade Test, made considerable undershoots. This finding was consistent with other athletic population studies and have been attributed to enhanced visual anticipatory skills.

The use of normative means has been shown to not be applicable to highly skilled athletes, therefore these findings are important for medical personnel who may use this information to help identify concussion episodes or track recovery in these athletes. Evidently, there is a strong need for an individual pre-injury baseline when making a medical decision of the neurological health of a player suspected of concussion. In the absence of a baseline, a sport-specific normative database may provide a more accurate indicator.

In chapter 5, “Acute Convergence and Accommodative Dysfunction in Rugby Union Athletes with Concussion”, post-concussive ocular measurements were compared to a pre-injury individual baseline. Over the study period, eight athletes (13.3%) sustained a concussion, with one player experiencing a second injury. A decrease in accommodative amplitudes was noted after eight of the concussive episodes, while 33.3% of these players experienced a receded NPC. All players with impairments in convergence also demonstrated a reduced NPA. Only one athlete demonstrated no change to any of these oculomotor functions following their concussive head injury.

The study determined the potential utility of measuring convergence and accommodative amplitudes through a standardised assessment (RAF Rule)

following a concussion and reinforces the likely involvement of the visual system following TBI. Further, these novel findings were able to highlight the importance of baseline testing in assisting diagnosis of immediate and short-term pathological changes to the oculomotor and visual system post-injury. Further studies in larger cohorts would be beneficial to confirming these findings.

In chapter 6, “Concussion-Related Visual Dysfunction and Symptom Recovery in Children: A Retrospective Study”, 142 medical records from a paediatric sports concussion clinic were analysed. Data showed that 28% of the concussed children experienced some form of concussion-related visual dysfunction, with a positive result on the VOMS test. Contact sports accounted for 60% of the documented concussions, with the highest prevalence (32%) in rugby. Ninety-three patients recovered from their concussion symptoms (mode 19-21 days) while females demonstrated a longer recovery time (mean = 63.15 days) than males (mean = 41.88 days). Those with a positive VOMS were found to have a longer mean recovery time (days = 63.7) than those with a negative VOMS (39.2 days) suggesting these patients may require additional support in schoolwork and learning activities through the recovery process. Of serious concern, less than half (43%) of tested high school students were immediately withdrawn from activity upon suffering a concussion, compared to 75% of those children attending primary school. This means there are still a large portion of children who risk a second episode and subsequent neurological damage. High rates of LOC (39%) and amnesia (41%) were also documented in this sample, although these were not correlated with visual symptoms.

These results show that the VOMS tool is a good predictor of symptom recovery in children and may provide an accurate indication for parents and medical personnel to develop a more appropriate pathway for observation or treatment. Gender and visual dysfunction may represent additional indicators of time-to-recovery from concussion-related symptoms, with visual dysfunction more common in females. A high rate of failure to immediately withdrawal concussed individuals from activity in youth sports warrants public health notification.

7.2 Directions for Future Research

This thesis has reported on several aspects of concussion with a focus on visual/oculomotor functions, particularly through the evaluation of various assessment tools. The chapters from this thesis combined with conference presentations (as in Appendix G), have initiated important discussions within this area. Further studies following from the topics discussed are recommended as follows:

- This thesis also provided evidence that large learning effects are evident in the use of the KDT. However, one area yet to be fully examined is the role of intentional underperformance (or “sandbagging”) during pre- and post-injury attempts. It is expected that the participant always performs the KDT as fast as physically possible, however this is only assumed by researchers. Personal experience suggests that this is difficult to accurately govern, as boredom and distractions during testing are potential confounding factors. Manufacturers of the assessment tool recommend to clearly instruct the

participant before they commence, although the effectiveness of this method has yet to be tested.

- The rugby athletes examined using the RightEye computer test demonstrated superior eye movements compared to the RightEye normative database. While this may be a true effect, the normative database contained a wider age range, particularly older, than was found in our 42 athletes. In order to confirm this difference, it would be helpful for RightEye to stratify their measures by age, perhaps in decade groups. Following that, further measures on age appropriate non-athlete adults would have to be conducted independently to verify the veracity of this finding. Further studies should also determine the utility of the digital-eye tracking device in identifying concussion by comparing post-injury measurements to pre-injury baseline scores. There may also be a role for an abbreviated version of the RightEye test translated to a tablet platform, so that it could be administered at the sideline. Until then its utility in concussion remains post-diagnostic as a monitoring tool.
- The RAF Rule was shown to be a useful tool in identifying concussion in sport. However, there is a need for this tool to be used in combination with current assessment tools. Identifying whether the RAF Rule is able to increase detection, establishing sensitivity and specificity parameters on a larger cohort would be a step forward in implementing the device as a suitable sideline concussion tool. To obtain a large number of participants

with concussion, a large multi-centre trial is needed. However, this would require additional financial support and multi-disciplinary collaborations.

- In most of the studies involving rugby athletes the examination was conducted by one researcher, with a substantial length of time to collect all measures. Although the use of one researcher ensured the same definitions of concussion and inclusion criteria were consistent throughout the data collection phase, there was no opportunity to determine examiner inter-reliability, nor were any studies able to provide Kappa values. The interpretation of a concussion was left to one sports physician and this can be seen as a limitation of the study. Future studies looking at complex conditions such as a concussion would benefit from more than one physician's reporting.
- As evident from the studies within this thesis, it is quite challenging to obtain large sample sizes of athletes with concussion. The Brain and Mind Institute, Save Sight Institute, Concussion in Sport Australia and Brain Injury Australia, are a few of many Australian organisations developing research across a plethora of aspects related to concussive injury. Collaboration between these bodies and researchers may help Australia become a leading centre of concussion research. Developing a nation-wide concussion registry poses an important step for Australian researchers to obtain data to make robust decisions in concussion detection and RTP protocols. However, obtaining government funding during a global pandemic may present difficulties in the current climate.

7.3 Conclusions

The research presented in this PhD thesis has contributed novel findings in the concussion arena, providing a deeper understanding of the role of various concussion assessment tools examining eye movements within the concussion paradigm. For the first time, the reliability in baseline KDT measures was examined and evaluated in detail, suggesting frequent updates in baseline measures are required throughout the duration of a playing season. This is supported by further findings that top-grade rugby athletes possess superior eye movements to the normal population but may also require an individual pre-injury baseline for future reliable concussion measures. The RAF Rule was found to be a useful tool in identifying concussion on the sideline and maybe a potential addition to current testing batteries. Female children suffering concussion, and those with post-injury visual dysfunction, take longer to recover from symptoms and may require careful and more prolonged detailed management from schools and parents. Together, these studies suggest a greater emphasis on concussion through a visual perspective may be an additional way to help combat this global issue.

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Appendix A

A review of concussion diagnosis and management in Australian professional sporting codes.

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REVIEW

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A review of concussion diagnosis and management in Australian professional sporting codes

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ABSTRACT

Objectives: The recognition and management of concussion has become a major health concern across all sports. Despite recent attention, concussion assessment and return-to-play protocols appear to be highly variable between leading professional sporting bodies across Australia. Without readily available guidelines, players at all levels may be at risk of suboptimal management following in-game trauma. The purpose of this study was to explore the publicly available concussion guidelines of the major Australian sporting codes with an aim to identify potential opportunities to develop a national sporting consensus.

Methods: Internet sites of the major sporting organizations within Australia were accessed between June 2018 to July 2018. Sites were reviewed for information pertaining to an available concussion protocol or guidelines including; concussion definition, player education documentation, requirement of baseline testing, standard concussion diagnostic measures, use of sideline testing and removal from play guidelines, return-to-play, minimum return-to-play intervals and the implementation of external evaluation of potential concussion cases.

Results: Twelve sites were visited. There was consensus between many of the sporting organizations in terms of concussion definition, removal of play and sideline testing protocols. A step-wise return-to-play protocol was prevalent across most sports. A number of sporting sites however did not have readily available information.

Conclusions: There is notable room for the development of concussion guidelines in Australian sport. Researchers and sporting organizations need to continuously amend current protocols to ensure this reflects best evidence-based practice.

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Appendix B

Persistent visual disturbances after concussion.

Gunasekaran P, Hodge C, Rose K, Fraser CL. Persistent visual disturbances after concussion.

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Persistent visual disturbances after concussion

CPD

Premkumar Gunasekaran,
Christopher Hodge, Kathryn Rose,
Clare L Fraser

Background
Ocular dysfunction, including eye movement defects, has been documented in up to 69% of patients with concussion. However, standard sports-related concussion assessment protocols do not typically include any clinical examination of the ocular system.

Objective
The aim of this article is to inform general practitioners (GPs) about ocular defects associated with concussion, identify test procedures and highlight the important role of GPs within the concussion paradigm.

Discussion
Ocular dysfunction that commonly occurs with concussion includes abnormalities of accommodation, convergence, saccades and smooth pursuits. This may cause blurred vision, double vision, ocular pain and difficulty with close work. Symptoms can severely affect daily work, school or play activities. Patients complaining of extended ocular symptoms following concussion should be referred to an ophthalmologist for a complete ocular assessment.

WITH AN INCREASED emphasis on awareness and diagnosis of concussion in both professional and amateur sports, the frequency of reported concussions has significantly increased over the past decade. Australian data suggest that the frequency of reported concussions increased by 60.5% between 2002 and 2011, leading to an annual incidence of >4500 hospitalisations from sporting events.[1,2] The costs associated with hospitalisation from these incidents was approximately $18 million, representing a significant burden on the health system.[2] The majority of traumatic brain injuries occur in patients aged 15–64 years during participation in sports.[1] Although most cases resolve spontaneously without medical intervention over a period of 7–10 days, a subset of patients will report ongoing symptoms.[3] Optimal diagnosis and, where indicated, treatment is therefore essential to reduce the impact on either school, work or daily activities and subsequent quality of life.[4]

Concussion is a diffuse brain injury. As such, signs and symptoms on presentation may be both complex and highly variable. Immediately following impact, the patient may have confusion, dizziness and amnesia. Additional early symptoms include headaches, difficulty concentrating on tasks, sensitivity to light and visual disturbances.[5] Despite previous misconceptions, concussion often does not involve the loss of consciousness, which is reported in <10% of cases.[6]

The widely endorsed Sports Concussion Assessment Tool 5th Edition (SCAT5) and Concussion Recognition Tool (CRT) have shown high sensitivity and specificity in detecting concussion at the sports arena. However, the use of these tests is often restricted to professional or semi-professional sporting events, where trained medical professionals are more readily available.[7,8] Accordingly, it has been reported that up to 90% of players may not be aware of a potential concussion diagnosis and go unassessed by health professionals.[9] This presents particular difficulties for general practitioners (GPs), who will often see patients at a time after the concussive event. Differentiation of non-specific concussion symptoms from pre-existing conditions is a further confounder.

As more than half of the brain's pathways are dedicated to vision and eye movement control, a diffuse brain injury such as concussion will often affect the visual system.[10] Research has found that visual disorders may occur in up to 69% of patients following mild traumatic brain injuries.[11] For children, adolescents and young adults, this may have a detrimental

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effect on their ability to complete academic activities. In adults, this may lead to difficulties performing crucial daily activities such as driving and coping with work. Early impact or sideline tests include the question, 'Have you noticed blurred or double vision?'; however, the potential impact on the visual system following concussion may require more in-depth clinical examination and investigation. This literature review aims to inform GPs about the ocular defects associated with concussion and to highlight the GPs' important role within the concussion paradigm.

Methods

A PubMed search using Medical Subject Headings (MeSH) terms including 'brain concussion', 'concussion', 'vision', 'eye movement' or 'visual dysfunction' identified 495 papers. After screening for duplicates, this was reduced to 220 papers. These were screened individually; only peer-reviewed, human-based studies published within the past 10 years were considered. Of these papers, only those that tested oculomotor dysfunction following a concussion were included in this analysis (15 papers). This search was conducted on 10 May 2019.

Oculomotor dysfunction

Studies in both adolescent and adult patients have described persistent clinical features affecting the visual system following a concussion (Table 1). These may include diplopia (double vision), decreased visual attention, abnormal pupils and an increase in abnormal eye tracking movements.[12] However, the literature in this area is surprisingly limited. The primary research focus has been on the more obvious cognitive and neuropsychological changes immediately following brain trauma. A recent study of military personnel with a past history of mild traumatic brain injury (mTBI) identified a significant relationship between visual complaints and concussion, even five years post-injury.[13] This suggests that clinicians must remain aware of possible visual dysfunction years after the event, particularly in more traumatic cases. The incidence of visual symptoms appears to remain relatively consistent across mTBI of different causes and intensities.[14]

Accommodation

Accommodation refers to a shift in the focus of the eye to maintain a clear image of an object as it varies its distance from the observer, primarily as it approaches. The neural control of accommodation requires afferent input to the visual cortex, and brainstem control of eye movements and the ciliary muscle. The complexity of this pathway makes it potentially susceptible to damage, with resultant dysfunction after a concussion. Within the clinical setting, this may manifest as complaints of blurred vision, asthenopia (tired eyes) and difficulty reading.[15]

Master et al showed reduced accommodative amplitudes in 51% of young patients with concussion when compared with age-matched normative values.[11] Similarly, Capo-Aponte et al prospectively examined 20 military personnel following mTBI and reported reduced amplitudes of accommodation and accommodative facility in 65% and 35% of patients, respectively.[12]

Accommodative capacity is age dependent. Healthy young or adolescent patients can maintain clear focus on near objects (as close as <10 cm); however, this capacity progressively reduces with age as the crystalline lens gradually becomes more rigid. Therefore, younger patients may be more affected by accommodation dysfunction of neurological origin than older patients. The level of accommodation can also vary with refractive error such as myopia, in which accommodative lag is commonly reported; therefore, a history of wearing glasses or using contact lenses is important adjunctive information.

Accommodation is tested by slowly bringing text towards the subject until the point of blur. This distance is then matched against age-related norms. Specialist equipment (Royal Air Force [RAF] Rule) is designed to measure accommodative amplitudes within ophthalmic practices. However, in the general practice setting, a finding of gross accommodation or a significant reduction through repeated measures – in conjunction with symptoms including difficulty concentrating, headaches following a relatively short period of near work or the appearance of jumbled words when reading – would necessitate referral to a neuro-ophthalmologist for further measurement and possible rehabilitation.

Convergence

Convergence is the simultaneous movement of both eyes inwards to maintain binocular fixation on a target (Figure 1). Cortical areas including the visual cortex, parietal lobe, frontal eye fields, supra-oculomotor area and cerebellum are involved in the convergence pathway.[16] This neurological pathway works closely with accommodation to provide concurrent clear focus on near objects and is highly susceptible to damage by concussion. Convergence abnormalities are reported in 14–55% of athletes,[17–19] 48–55% of military personnel[11,20] and 14–49% of

Table 1. Symptoms and signs affecting the visual system following a concussion

Symptoms	Signs
• Loss of vision	• Reduced distance or reading acuity
• Blurred vision	• Anisocoria
• Double vision	• Impaired vestibulo-ocular reflex
• Reading difficulties	• Slowed or reduced eye movements
• Photophobia	• Impaired convergence
• Headaches with visual tasks	• Impaired accommodation
• Difficulty tracking fast objects	• Decreased visual attention

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outpatient groups[11,21,22] previously diagnosed with concussion. Poor convergence will manifest clinically with double vision following near work, and blurred vision or asthenopia with prolonged near tasks such as reading.

Up to 40% of patients have ongoing visual symptoms suggestive of convergence dysfunction for at least one month following the concussive episode.[23] This suggests high visual morbidity, potentially causing significant disruption to reading and computer work. For athletes, this may affect performance such as their ability to track a ball. For military or security personnel, these symptoms could be particularly dangerous when undertaking rapid-response activities.

Convergence is tested by slowly bringing a pen (or target) closer to the patient's eyes (Figure 1). The patient is asked to maintain a single image and warned that the target may become blurred as it is brought forward (because of accommodative ability). Clinicians should look for a break in binocular fusion, which would manifest with an obvious divergence of one or both eyes from the target and/or the patient reporting diplopia. It is important to note that approximately 0.2% of the general population will have an abnormal convergence near point, clinically referred to as convergence insufficiency.[24] A diagnosis of clinically-reduced convergence may indicate a range of interconnected conditions of the oculomotor system.[25] Therefore, referral to an ophthalmologist or orthoptist is recommended.

Saccades

Saccades are rapid eye movements between two or more separate fixation points, at any angular position. Types of saccades are listed in Table 2. The saccadic pathway also involves multiple cortical, cerebellar and brainstem control areas, again making it highly vulnerable to damage following mTBI. Saccadic oculomotor impairments have been linked to both structural and functional abnormalities in the parietal, frontal and temporal areas, and in the caudate.[26]

High rates of saccadic dysfunction – which affects up to 30% of patients with a concussion – have been reported in the literature.[11,12,20] One study found that patients with a concussion needed to make more saccadic eye movements to complete a number-naming test, when compared with controls who did not have a concussion.[27] Patients with an acute concussion have been found to show significant impairment when doing higher cortical saccadic tasks, such as memory-guided saccades and anti-saccades.[28] Evidence suggests that individuals with persistent post-concussive symptoms are more likely to have saccadic dysfunction when compared with patients who had a faster recovery.[29]

Saccadic dysfunction manifests with increased latencies (time between the target presentation and saccade initiation) and dysmetria (lack of coordination of eye movements).[28,29] Practically, patients may find it challenging to read text, or complain of difficulty scanning the environment while driving.

Saccadic function (congruency and accuracy) can be readily tested by observing the patient move their eyes on command between two close targets (Figure 2). Poor saccadic accuracy requiring a secondary eye movement adjustment to the target may be seen by the clinician. In the case of significant dysfunction, the patient should be asked to abstain from critical tasks such as driving and operating machinery. Specialist referral for additional neurological deficits may be necessary at this point.

The King-Devick test has been used on the sidelines and during recovery following concussion episodes. Players are asked to read aloud a set of numbers across a page as quickly as possible. This tool primarily measures saccades; however, it also assesses cognition and

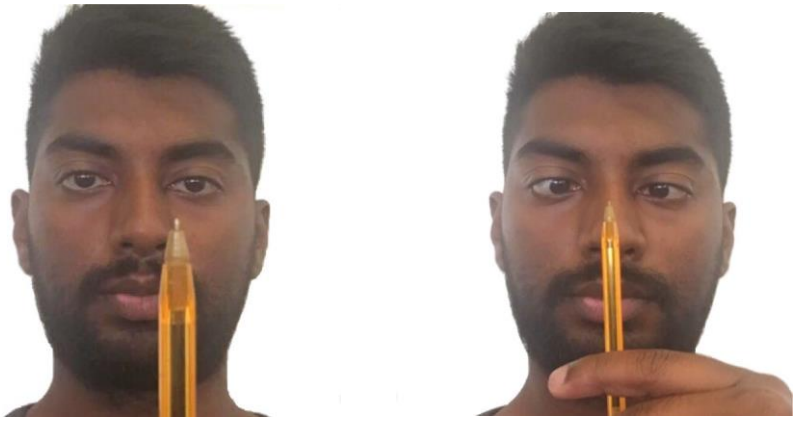

Figure 1. Eyes before (left) and after (right) converging on a pen. Convergence is tested by measuring the convergence near point.

Table 2. Types of saccades

Type of saccade	Definition
Visually guided saccade	Eyes move toward a visual stimulus
Anti-saccade	Eyes move away from visual stimulus
Memory-guided saccade	Eyes move toward a remembered location
Predictive saccade	Eyes are kept on a target moving in a predictive spatial manner

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attention faculties.[30] The test can be compared with a baseline finding if available, or to age-appropriate normative values. The King-Devick test has been increasingly used within general practice offices, particularly those with sporting associations, for diagnostic purposes and to track recovery as part of a return-to-play protocol.

Smooth pursuit eye movements

Smooth pursuit eye movements are performed to closely track a moving target, holding the image of the moving target steady on the fovea. As with other types of ocular movement, smooth pursuit requires the integration of multiple cortical areas and is similarly susceptible to concussion.

Few papers discuss concussion-related smooth pursuit dysfunction. However, those that exist report high rates of abnormalities.[12,20,31] Within the clinical setting, this would result in increased difficulty following moving objects, such as when catching a ball and tracking nearby cars while driving. Examining smooth pursuits can be achieved by asking the patient to track a pen across the vertical and horizontal planes. Jerky movements or failure to adequately follow the target may indicate problems with smooth pursuit movements. Even with extensive ophthalmological training, assessing subtle defects in smooth pursuit eye movements can be challenging in clinical practice. Specialist referral is suggested if smooth pursuit or tracking dysfunction is suspected.

In the research setting, using video-oculography to track disconjugate eye movements is gaining popularity as a possible marker for concussion.[32] Maruta et al examined a population with chronic concussive symptoms and found a significant decline in their predictive visual tracking capabilities.[33,34] Using diffusion tensor imaging, researchers attributed these oculomotor impairments to white matter tract damage in the corona radiata, left superior cerebellar peduncle and genu of the corpus collosum. These patients also showed reduced attention and working memory, highlighting the potential need for multidisciplinary referral to both ophthalmologists and neurologists for more extensive examination. A greater understanding of video-oculography metrics and the ability to provide a portable, readily accessible model will help facilitate translation of this technology into the clinic.[35]

Figure 2. For horizontal saccade testing, patients fixate continuously between a target on their right and left. The examiner observes for the complete and simultaneous movement of both eyes to each target. The same can be applied for vertical saccade testing, with a pen held high and low.

Other conditions

Visual field anomalies have been reported following significant trauma but are rare following sports-related concussive episodes.[14,35] Visual field defects related to significant trauma include homonymous hemianopia and quadrantanopia. A confrontation field test can be performed in the clinic if field loss is suspected, with referral for formal visual field testing if there are any concerns.

Cranial nerve palsy may also occur following severe trauma.[14] The patient would present with a manifest strabismus, and report diplopia.

Visual field loss and cranial neuropathy are not expected in concussion and should prompt further neurological examination and neuroimaging for a structural pathology.

Oculomotor rehabilitation

Although research is quite limited, there is some evidence supporting vision therapy/exercises as an effective strategy for rehabilitation.[36,21] Current protocols in Australian sport recommend rest and a step-wise return-to-play guideline.[37] However, recovery will be dependent on many factors including the number and severity of the existing ocular defects. Ciuffreda et al found that treatment in the form of eye tracking, accommodation and convergence exercises may expedite recovery and completely alleviate symptoms in almost 90% of patients with mTBI who have persistent oculomotor defects.[36] This can require between 10 and 30 vision therapy sessions over an eight-month period until symptoms resolve.[36]

Conclusion

Many forms of ocular dysfunction are found in acute and chronic cases of concussion. Being the primary medical contact for many patients with a concussion, either in the immediate or short-term period following the initial trauma, GPs need to be vigilant about the ocular dysfunction, as well as the behavioural, physical and emotional

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symptoms associated with concussion. Practical tips for assessment of ocular dysfunction following concussion are provided in Box 1. If the GP suspects visual and oculomotor impairment, referral to an ophthalmologist will provide patients with a complete ocular assessment and earlier implementation of treatment and rehabilitation.

Box 1. Practical tips for concussion assessments

- Subtle oculomotor dysfunction may be described by the patient as:
  - increased difficulty when completing near tasks
  - headache and eye strain after shorter duration of visual effort.
- Standard assessment of extra-ocular muscles and pupillary response can be supplemented with tests for:
  - convergence
  - accommodation
  - saccadic eye movement and smooth pursuits.
- Signs and symptoms can persist in some patients for weeks or months after concussion.
- Visual field loss and cranial nerve palsies are rare in concussion and should be investigated further.

Key points

- GPs must be alert to persistent oculomotor dysfunction following concussion including impairments to accommodation, convergence, smooth pursuits and saccadic eye movements.
- Developing strong relationships between GPs and ophthalmologists is important to provide the best evidence-based care for patients with concussion-related visual dysfunction.
- Patients with persistent visual disturbances may benefit from oculomotor rehabilitation, such as convergence, accommodation and eye tracking exercises.

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Appendix C

The learning effect of the King-Devick test in semi-professional rugby union athletes.

Gunasekaran P, Fraser CL, Hodge C. The learning effect of the King-Devick test in semi-professional rugby union athletes. Journal of the Neurological Sciences. 2020 Oct 2:117168.

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The learning effect of the King-Devick test in semi-professional rugby union athletes

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ARTICLE INFO

Keywords:
Sports-related concussion
Oculomotor function
Saccadic rhythm
King-Devick test
Vision

ABSTRACT

Objective: Abnormalities of eye movement and visual processing are common in traumatic brain injury. The King-Devick test (KDT) has been widely used in the detection and recovery of concussion. Current recommendations propose performing the initial test at baseline and then repeating annually to account for potential learning effects. In practice, this may still account for large deviations. The aim of this study was to determine the number of trials needed for a player to achieve a ceiling effect and to determine the validity of the existing protocol requiring two tests at baseline.

Methods: One hundred and eighty-three semi-professional male rugby union players (median age = 22.5 (21.0–25.3) years) were recruited. Over the duration, all athletes performed the KDT on an iPad, under standardised baseline procedures and then repeated the test based on availability during weekly in-season training.

Results: The improvement through each repeated trial was 0.60 ± 0.1 s ($P < 0.001$). The ceiling effect was determined at 30 trials. A median difference of 4.2 s (range 0–14.9) was calculated between the initial and best trial overall, although the greatest difference occurred within the first eight attempts. There was a significant positive correlation between the initial test value and the difference between first and fastest time ($P < 0.001$, $r = 0.455$).

Conclusion: We have shown continuous improvement with repeated attempts which suggests that administrators ideally should continue to perform the KDT over the duration of the season to optimise the value of the test.

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Appendix D

Ethics Approval for Chapters 3 to 5

NSW GOVERNMENT
Health
South Eastern Sydney
Local Health District

HUMAN RESEARCH ETHICS COMMITTEE
Room G71 East Wing
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05 June 2019

Dr Adrian Cohen
Attn: Mr Daryl Fong
Necksafe Ltd
231 Birrell Street
BRONTE NSW 2024

Dear Dr Cohen

HREC ref no: 17/039 (HREC/17/POWH/91)
Project title: Diagnosis of Mild Traumatic Brain Injury with Visual-Evoked Potentials

Thank you for your amendment request, dated 09 October 2018 to the above stated ethics approval. Your amendment request was initially reviewed at the Executive Committee meeting on 25 January 2019.
I am pleased to advise that with your recent correspondence dated 19 February 2019 ethics approval of the amendment has been granted.

The following documentation has been approved:

- Amendment Form dated 09 October 2018
- Protocol V1.056 dated 05 November 2018
- PISCF V1.056 dated 05 February 2019
- PGPISCF V1.056 dated 05 February 2019
- Youth Assent Form V1.056 dated 05 November 2018
- Statistical Analysis Plan V1.056 dated 05 February 2019

Ethics approval is valid for the following site(s):

- Save Sight Institute
- Necksafe Ltd

This amendment has also been reviewed by the Research Governance Officer at SESLHD. Further authorisation of the above approved documents is not required for any site that has the Research Governance conducted by the SESLHD Research Support Office. Implementation of this amendment can now proceed.

For multi-site projects reviewed by the HREC after 1 January 2011 a copy of this letter must beforwarded to all Principal Investigators at every site approved by the SESLHD HREC for

submission to the relevant Research Governance Officer along with a copy of the approved documents.

Should you have any queries, please contact the Research Support Office on (02) 9382 3587. The HREC Terms of Reference, Standard Operating Procedures, membership and standard forms are available from the Research Support Office website:
www.seslhd.health.nsw.gov.au/services-clinics/directory/seslhd-research

Please quote **HREC ref no 17/039** in all correspondence. We wish you every success in your research.

Yours sincerely

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prior to publication.

Andrew Bohlken
Executive Officer, Human Research Ethics Committee

This HREC is constituted and operates in accordance with the National Health and Medical Research Council's (NHMRC) *National Statement on Ethical Conduct in Human Research (2007),* NHMRC and Universities Australia *Australian Code for the Responsible Conduct of Research (2007)* and the *CPMP//CH Note for Guidance on Good Clinical Practice,*

Appendix E

Participant Information Sheet and Sample Consent Form for Chapters 3 to 5

The School of Aerospace, Mechanical and Mechatronic Engineering

PARTICIPANT INFORMATION SHEET AND CONSENT FORM

Diagnosis of Mild Traumatic Brain Injury Via Visual-Evoked Potentials
HREC ref no: 17/039

Invitation

You are invited to participate in a research study for a new method of testing for concussion. This is done with a short test (less than 5 minutes). It involves the shining of lights into your eyes while your brain signals are recorded non-invasively. This is done with an electroencephalography (EEG) headset. The study is being conducted by:

- Dr. Philip Boughton and Mr. Daryl Fong from the School of AMME[1] of the University of Sydney
- Dr. Clare Fraser of the Save Sight Institute
- Dr. Adrian Cohen of HeadSafe[2]
- Dr. Christopher Hodge, Mr. Premkumar Gunasekaran and Prof. Kathryn Rose from the Graduate School of Health of the University of Technology Sydney

Before you decide to participate in this study, it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish.

1. **What is the purpose of this study?**
   We are trying to devise a simple, objective and reliable concussion test. This test can be performed in any quiet environment. This study is part of a PhD thesis project for Mr. Daryl Fong and Mr. Premkumar Gunasekaran.

2. **Why have I been invited to participate in this study?**
   You have been invited to participate in this study because you are in the age group (14 and above) we are studying. After that, if you are diagnosed with concussion you can be compared to your previous state and to people who have not been diagnosed with concussion.

3. **What does participation in this study involve?**
   If you agree to participate in this study you will be provided with a questionnaire. The questionnaire will ask some basic questions and specifically whether you have a history of epileptic seizures or fits, or any other condition which would exclude you from the study
   The test will require you to view some flashing lights in a quiet environment at the sporting field, research room or a doctor's office.

   While viewing the flashes, the headset you are wearing will be recording electrical signals from your brain.

---

[1] *Aerospace, Mechanical and Mechatronic Engineering*

[2] *Headsafe is the concussion research project of Necksafe Ltd, a charity which is recognised by the Australian Charities and Not For Profits Commission (ACNC) as a Health Promotion Charity (HPC) dedicated to the elimination of preventable head and neck injuries through advocacy, awareness, education and research". The Headsafe name and Internet domain are owned by Headsafe.com.au Pty Ltd, a non-trading company with no pecuniary interest to declare in the project"*

You may choose to use one or more of the following devices:
- A commercial device
- A prototype device similar to the commercially-available devices that is not yet marketed
- A clinical research-grade device

The process is brief **(less than 5 minutes).** It is non-invasive and usually discomfort-free. No hair will need to be removed or shaven. If you experience any discomfort for any reason, you can take a moment to rest and continue, or withdraw.

If it is determined that you have abnormal test results, you may be offered further evaluation by a doctor.

If you agree to participate in this study, you will be provided with a questionnaire. The questionnaire will ask some basic questions and specifically whether you have a history of epileptic seizures or fits, or any other condition which would exclude you from the study

4. **What if I don't want to take part in this study, or if I want to withdraw later?**
Participation in this study is completely voluntary. It is completely up to you whether or not you participate. If you wish to withdraw from the study you can do so at any time without giving a reason and without penalty of any kind. If you are a student it will not influence your university grades.

5. **How is this study being paid for?**
All costs of this study are being paid for by the University of Sydney as well as the charity Necksafe and research centre Save Sight Institute.

6. **Are there risks to me in taking part in this study?**
There are minimal risks in taking part in this study. Small amounts of discomfort arising from the headset can occur. Mild headache and nausea may rarely occur as a result of continual flashing image. This should be minimised by short viewing sessions. However, if any of these do occur, you can take a rest and continue afterwards, or withdraw.

In an extremely small number of people (less than 2 in every million) flashing lights have been known to trigger a seizure in epileptic people. However, since you cannot participate in this study if you have a history of epilepsy, seizure, fits, faints or funny turns, then this risk becomes negligible. In the extremely unlikely event it occurs, doctors will be available to treat you.

7. **What happens if I suffer injury or complications as a result of the study?**
If you require treatment or suffer loss as a result of the negligence of any of the parties involved in the study you may be entitled to compensation. The cost of your treatment would have to be paid out of such compensation.

8. **Will I benefit from the study?**
This study aims to further medical knowledge and may improve future treatment of brain injury. However, it may not directly benefit you.

9. **Will taking part in this study cost me anything, and will I be paid?**
Participation in this study will not cost you anything, nor will you be paid. We are unfortunately not able to reimburse the costs of parking or transport.

10. **How will my confidentiality be protected?**
The data from the project will be coded and held in secure storage. This is the responsibility of the principal investigator of the study in accordance with the requirements of the Australian Privacy Principles (APPs) (March 2014).

All reference to participants will be by code number only in terms of the research thesis and publications. Identification information will be stored on a separate file and computer from that containing the actual data. Only the investigators will have access to computerised data.

11. What happens with the results?

If you give us your permission by signing the consent document, we plan to discuss/publish the results. This will be part of a PhD thesis submission to the School of Aerospace, Mechanical and Mechatronics Engineering at the University of Sydney. In addition, they may be used to further study and prevent concussion, and to develop concussion tests of value to athletes, clinicians, physical conditioners and coaches

In any publication, information will be provided in such a way that you cannot be identified.

12. What should I do if I want to discuss this study further before I decide?

When you have read this information, the principle investigator Dr. Adrian Cohen will be available to discuss it with you and answer any queries you may have. If you wish to withdraw from the study, the Revocation of Consent form (below) should be completed and Dr. Cohen contacted. If you would like to know more at any stage, please do not hesitate to contact him on +61 418 253 333 or email: ado@headsafe.com.au

13. Who should I contact if I have concerns about the conduct of this study?

This study has been approved by the South Eastern Sydney Local Health District Human Research Ethics Committee. Any concerns or complaints about the conduct of this study should contact the Research Support Office which is nominated to receive complaints from research participants on 02 9382 3587 or email SESLHD-RSO@health.nsw.gov.au

Thank you for taking the time to consider this study.
If you wish to take part in it, please sign the attached consent form.
This information sheet is for you to keep.

THE UNIVERSITY OF SYDNEY NECKSAFE SAVE SIGHT INSTITUTE

UTS

The School of Aerospace, Mechanical and Mechatronic Engineering

CONSENT FORM

Diagnosis of Mild Traumatic Brain Injury Via Steady-State Visual-Evoked Potentials
HREC Ref 17/039

1. I agree to participate in the study described in the participant information statement set out above.

2. I confirm that to the best of my knowledge I do not have:
   a. Epilepsy
   b. A seizure disorder
   c. A history of any fit, faint or funny turn
   d. Sensitivity to flashing lights.

3. I acknowledge that I have read the participant information statement which explains the following:
   a. Why I have been selected
   b. The aims of the study
   c. The nature and possible risks of the investigation

   The statement has been explained to me to my satisfaction.

4. Before signing this consent form, I have been given the opportunity of asking any questions relating to any possible physical and mental harm I might suffer as a result of my participation I have received satisfactory answers.

5. I understand that I can withdraw from the study at any time without prejudice to my relationship to the **University of Sydney.**

6. I agree that research data gathered from the results of the study may be published, provided that I cannot be identified.

7. I understand that if I have any questions relating to my participation in this research, I may contact the principal investigator Dr. Adrian Cohen on +61 418 253 333 or email: ado@headsafe.com.au

8. I acknowledge receipt of a copy of this Consent Form and the Participant Information Statement.

Complaints or concerns may be directed to the Research Support Office, South Eastern Sydney Local Health District, Prince of Wales Hospital, Randwick NSW 2031 Australia (phone 02-9382 3587, fax 02-9382 2813, email SESLHD-RSO@health.nsw.gov.au.

Signature of participant	Please PRINT name	Date
_____	_____	_____
Signature of witness	Please PRINT name	Date
_____	_____	_____
Signature of investigator	Please PRINT name	Date
_____		

PROTOCOL

Diagnosis of Mild Traumatic Brain Injury Via Visual-Evoked Potentials

HREC Ref 17/039

Introduction

The current state of concussion diagnostic tools is insufficient in dealing with modern health expectations. Thus, a new method utilising visual-evoked potentials (VEPs) in conjunction with electroencephalogram (EEG) is proposed as an improved and objective method of diagnosing and managing concussion.

Background

Concussion has been definitely diagnosed in this context by the International Concussion Consensus Committee over the past 16 years of its activities. The 4th International Concussion Consensus Committee [1] defined concussion as:

"a complex pathophysiological process affecting the brain, induced by biomechanical forces"

In 2014, the peak body in Australian sports, Sports Medicine Australia, in their concussion policy document, defines concussion as:

".a mild traumatic brain injury and is defined as a complex pathophysiology process affecting the brain, induced by biomechanical forces. It is characterised by a graded set of neurological symptoms and signs that typically arise rapidly and resolve spontaneously over a sequential course. The process of recovery, however, varies from person to person and injury to injury".

A doctor making the diagnosis of concussion (ideally one experienced in the condition), has already excluded more severe head injuries caused by impacts in sports such as intracranial haemorrhage, structural abnormalities, epilepsy, etc. with or without the use of radiological or other imaging. In most cases, the diagnosis is therefore clinical [1] and some of the hallmark signs of acute concussion include mental confusion, memory and balance disturbance. Over the course of the first 24 h, the most common symptoms include headache, nausea, dizziness and balance problems, blurred vision or other visual disturbance, confusion, memory loss and 'fatigue'. Symptoms such as tiredness, irritability, nervousness or anxiety, sleep disturbance and sensitivity to light or noise may be noticed in the days after injury.

An estimated 3.8 million cases of mTBI are recorded each year in the United States. However, this is estimated to include less than 50% of all cases, as it is often not detected due to lack of apparent symptoms, lack of diagnostic tools available and popular mythology. [2] Globally, sports-related concussion (SRC) accounts for an estimated 20% of cases, with cases that did not involve loss of consciousness mostly ignored. [3]

More recently, sports medicine professionals have adopted a wide range of concussion diagnosis and management tools, most of which evaluate cognitive performance (amongst other parameters) to determine the presence and severity of the concussion. Most popular according to a study in the US (and reflected in the National Athletic Trainer's Association position statement) to assess and manage SRC is the Sports Concussion Assessment Tool version 3 (SCAT3) [4] (61%) followed by the Cantu Method (28.3%). [5]

A number of current concussion diagnosis tools rely on vision assessment (among other factors) to determine the severity and presence of concussion. The King-Devick Test (KDT) [6] utilises saccadic eye movements (quick, flicking movements of both eyes) to evaluate cognitive processing. This system compares a Baseline score (pre-injury or pre-season) to the post-injury state, and if the performance on the test is significantly slower or errors are made, the individual needs to be further clinically examined for diagnosis of concussion. [6-8]

An unavoidable and limiting feature of many current concussion tests is that many are subjective to some degree: the Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT)[9], Balance Error Scoring System (BESS) [10], Standardised Assessment of Concussion (SAC) [11] and

other neuropsychological tests (such as CANTAB [12], Axon Cogstate [13], WebNeuro [14]) all have either low specificity/sensitivity in terms of diagnosis or determining recovery after a concussion event. The neurocognitive and balance tests can be influenced by both subject and observer.

Electrophysiological measures such as electromyography signals (EMG) evoked by transcranial magnetic stimulation (TMS) have shown great promise in providing objective measures of functional neuronal impairment relating to concussion. [15]

By utilising a similar objective measure, such as an electroencephalogram (EEG), surface potentials from the brain may be recorded and analysed. In particular, steady-state visual-evoked potentials (SSVEPs), a particular form of VEP, have an inherently high signal-noise ratio (SNR), allowing for more efficient and reliable data collection and analysis. The visual cortex is of particular significance as it responds to the visual stimuli that is provided which are easily recorded by surface EEG electrodes.

Aim of Study

The aim of this study is to evaluate the use of SSVEP in conjunction with EEG as a tool to diagnose concussion, as well as track an individual's recovery from concussion.

Objectives

We will initially use the system to acquire SSVEP's on participants in a control ("baseline") group.

These participants will be re-tested at regular intervals to determine a change in their SSVEP over time and in the context of the contact sports they may be playing.

Any participants diagnosed by a clinician as suffering from concussion ("concussed group") will be retested to ascertain any change in their SSVEP.

This will then be repeated one or more times until the participant is considered clinically recovered by a physician ("recovered group").

Ideally this comparison of SSVEP will illustrate a distinct, reproducible difference between the baseline/control, concussed and recovered groups.

Hypothesis

That steady state EEG response to visual stimuli (SSVEP) is clinically useful in the assessment of concussion. This SSVEP may be obtained from portable systems with high sensitivity and specificity.

Study Design

The study is of a prospective cohort observational design.

Testing will be conducted with an Emotiv EPOC+ EEG headset (a validated and commercially available, portable EEG product).

The participants will be fitted with the EEG headset and view a flashing stimulus from the same source for 30 seconds. The main study will be conducted on three groups using one or more of these systems: a control (baseline) population; a "concussed" population of participants having recently (<72 hours) experienced a concussion (as diagnosed by an experienced sports physician) and a "recovered" group (previously concussed now considered clinically recovered by the same physician.

The "concussed" population will be identified through cooperation with sporting and other groups, such as the Randwick District Rugby Union Football Club. Subjects will be diagnosed as concussed by an experienced sports physician incorporating accepted diagnostic criteria (most commonly the Sport Concussion Assessment Tool or SCAT).

The study will be conducted in an identical manner for the three groups.

Prior to testing, participants will be asked to provide informed consent as per the Patient Information Sheet and Consent Form (PISCF). If the participant is under 18, parental/guardian consent will be sought instead, and the participant provided with a youth assent form.

Participants will then fill out a Questionnaire to determine suitability against inclusion and exclusion criteria and provide some background information.

Testing with visual and cognitive tests such as the King-Devick Reading Test, RAF Rule, RightEye Neurovision Test and Cognigram may then be conducted to provide comparative data.

Visual eye-movement tests take less than 1 minute to perform each. These tests are non-invasive and participants will only be required to track the moving target with their eyes.

Participants will then be provided and properly fitted with the EEG headsets.

A visual stimulus (in the form of a flickering light emitted from a smartphone) will then be presented to the participant wearing one of the EEG headsets. This visual stimulus is displayed to the participant for 30 seconds.

This process will take less than 5 minutes in total.

After data collection, analysis will be performed in software on a Windows PC to provide visualisation of the frequency response by the participant's visual cortex in relation to the stimulus.

Study Settings

The study will take place at the University of Sydney, Necksafe and Save Sight Institute sites. Visual test information, such as from the RAF Rule, RightEye Neurovision Test and King-Devick Reading Test will be analysed at the University of Technology Sydney.

Study Duration

The study will commence in early 2017 and end in 2020.

Study Population

Any gender aged 14 and above may participate in this study.

An *a priori* analysis was performed to calculate the required sample size for the main study, and this was determined as 80 for the control/baseline group, and 20 of these for the study/"concussed" group. All calculation was performed with G* Power 3.1.9.2 [16].

The larger control/baseline group is sought to help determine normative data and standard deviations in a healthy population.

All participants are to have a history free of epileptic/seizure diagnoses and associated symptoms (characterised colloquially to participants as "fits, faints and funny turns") as determined by the questionnaire administered by the researcher performing the testing.

Control Group participants will be selected from patients of the researchers and professional associates. These will include athletes at sports clubs, as well as university students. They must be willing to participate and without structural or functional brain disease.

The Study Group population will comprise previously consented Control Group individuals referred from researchers who have sustained a recent (less than 72 hours prior) concussion as diagnosed by an experienced clinician.

They will be categorised in the study/concussed group until clinically recovered (as determined by the same physician) and then be categorised in the "recovered" group.

Risk

Very minimal risk is expected from this study: several minimally consequential risks are identified.

According to the Epilepsy Foundation [17] newly presenting seizures occur at an incidence of approximately 1.1/100,000 in the general population, with the incidence higher at younger age groups (7-19) at 5.7/100,000 and with the peak age of onset at 12-13 years. . Amongst this very small percentage of the population, the phenomenon of "clinical photosensitivity" (i.e. epileptic seizures triggered by visual stimuli, a subset of which are flickering lights) is less than 2 percent of patients of

all ages that have had seizures documented in the past. The estimated risk is therefore maximally 114/1,000,000.

To mitigate this very low risk, we will undertake screening to exclude anyone with a history of epilepsy. All participants will be interviewed and required to sign a declaration that they have no relevant seizure history, and anyone with a history of epilepsy, any other seizure disorder, or anything described as a "fit, faint or 'funny turn' will be excluded from the study.

In the extremely unlikely event that a seizure does occur, medical practitioners will be on standby to provide standard treatment for an acute seizure, and prescription medications including benzodiazepines will be available to immediately treat any seizures.

Flicker Vertigo is another very unlikely risk. According to the Vestibular Disorders Association [18], flicker vertigo is provoked by frequencies between 4-30Hz, with symptoms ranging from "vague and non-specific feelings of unease through to nausea, dizziness, migraines, unconsciousness, and even photosensitive epileptic seizures" in those prone to these. It is important to note that these symptoms are only triggered after prolonged viewing of flickers under scenarios that we will not be using. In relevant studies, it has been found that symptoms only occur after "*approximately 30 minutes of viewing strobe-like effects" [19]*). Our test stimuli display for a maximum of 30 seconds, thus reducing the likelihood of an adverse event significantly.

The EEG headset may cause minimal discomfort to the participant (similar to having a heavy pair of sunglasses in place). As it is powered by a low voltage battery with no connection to electrical mains, the danger of electrical current leakage is negligible.

Study Procedures

Recruitment

There are intended to be 3 population groups for this study, the *Control/Baseline* group, *Study/Concussion* and the *Recovered* group.

Researchers will recruit control/baseline subjects from their clinical practices, athletic clubs and university students.

These subjects will then be included in the Study/Concussed Group following a diagnosed concussion and will subsequently transfer to the Recovered group once clinically recovered.

A simple screening questionnaire will be administered by the researchers to ensure inclusion and exclusion criteria are met. No other screening tools will be used as part of the process.

Consent will be acquired by signing the Participant Information Sheet and Consent Form (or Parental Guardian form) as approved by the appropriate Ethics Committee.

Withdrawal

A Withdrawal of Consent form will be provided for the purpose of withdrawing from the study itself or any of the tests at any time.

Measurement Data

EEG data will be transferred from the headsets in the form of a European Data Format (EDF) file [20]. This file contains identifiers related to the type of participant (control/baseline, study/concussed and recovered), and will be anonymised.

The EDF format is a common file format used for EEG applications. It stores all the EEG channel data in one single file. This data will be processed in software to provide relevant measurements.

Data from visual testing will be transferred into an excel file. This will be stored and analysed by researchers from the Univeristy of Technology Sydney, who have extensive experience in eye movement research.

Study Involvement

Participants enrolled in this study are required to view a stimulus while having an EEG headset record relevant data. Multiple attempts may be performed to ensure reliability and consistency of results. This should take less than 5 minutes per study.

No follow-up is expected in the control group unless the participant subsequently sustains a concussion, in which case a comparative study or studies may be undertaken as acutely and as they recover.

No treatment guideline is to be provided although participants will be advised of their results should they request them in order to seek further professional opinion.

Participants may have subsequent studies to evaluate changes over time.

If it is determined that the participant has an abnormal test result, they may be offered further evaluation.

Safety Considerations

Participant safety is paramount to all studies. The greatest risk to a participant's safety in this study is the very minimal risk of a seizure as discussed above, and these risks have been evaluated and appropriately mitigated.

Outcomes and Significance

The outcome of this project will determine the viability of a novel method of diagnosing concussion and assisting in determining recovery.

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Appendix F

Ethics Approval for Chapter 6

May 22, 2019

To the UTS Research Committee,

I am writing to let you know that I am permitting, Mr. Premkumar Gunasekaran (SID 97126256), to use my concussion database for research purposes. I am aware that the information on my Excel database will be used towards his PhD thesis and the dissertation published in a peer-reviewed journal.

The information was gathered from The Children's Hospital Institute of Sports Medicine (CHISM), between 2016 to 2018, and all patients consented for their information to be used for research purposes. All information on this dataset is de-identified and there is no re-identifiable information, such as DOB, postcode or ethnicity.

If you have any questions, feel free to contact me at g.browne@sydney.edu.au.

Sincerely,

Production Note:
Signature removed
prior to publication.

Professor Gary Browne
Clinical Professor
Emergency Medicine, Children's Hospital, Westmead

Dear Applicant

Project title: Concussion-Related Visual Dysfunction: A retrospective study

You have declared your research as Nil/Negligible Risk and that it DOES NOT include any of the following:
* Establishment of a register or databank for possible use in future research projects
* Collection, transfer and/or banking of human biospecimens
* Any significant alteration to routine care or health service provided to participants
* Interventions and therapies, including clinical and non-clinical trials, and innovations
* Targeted recruitment or analysis of data from any of the participant groups listed in Chapter 4 of the National Statement (or where any of these participants are likely to be significantly over-represented in the group being studied) including:
  - Women who are pregnant and the human fetus
  - Children and young people (under 18 years)
  - People in dependent or unequal relationships
  - People highly dependent on medical care who may be unable to give consent
  - People with a cognitive impairment, an intellectual disability, or a mental illness
  - People who may be involved in illegal activities (including those affected)
  - Aboriginal and Torres Strait Islander Peoples
* Collection, use or disclosure of personal information (except where expert opinion is being canvased with full disclosure, consent and identification for use in the public domain)
* Collection, use or disclosure of health information
* Collection, use or disclosure of sensitive information
* Covert observation, active concealment, or planned deception of participants
* Activity that potentially infringes the privacy or professional reputation of participants, providers or organisations (except where expert opinion is being canvased with full disclosure, consent and identification for use in the public domain)
* Potential for participants to experience harm (e.g. physical, psychological, social, economic and/or legal)
* Direct contact with UTS staff/students, patients, consumers or members of the public (except where expert opinion is being canvased with full disclosure, consent and identification for use in the public domain)
* Participants who have a pre-existing relationship with the researcher (except where expert opinion is being canvased with full disclosure, consent and identification for use in the public domain)
* People unable to give free informed consent due to difficulties in understanding the Information Sheet or Consent Form
* People in other countries

PLEASE NOTE: If at any time, the scope of your research changes to include one or more of the above categories, you are immediately required to submit a new application.
To access the National Statement on Ethical Conduct in Human Research, visit the NHMRC webpage: https://www.nhmrc.gov.au/guidelines-publications/e72

Please keep a copy of your ethics application form and approval letter on file to show you have considered the risks associated with your research. You should consider this your official letter of approval.
For tracking purposes, you have been provided with an ethics application number, which is UTS HREC ETH19-3748N.

I also refer you to the AVCC guidelines relating to the storage of data, which require that data be kept for a minimum of 5 years after publication of research. However, in NSW, longer retention requirements are required for research on human subjects with potential long-term effects, research with long-term environmental effects, or research considered of national or international significance, importance, or controversy. If the data from this research project falls into one of these categories, contact University Records for advice on long-term retention.

Instructions for saving the application form can be downloaded from: https://staff.uts.edu.au/howdoi/Pages/Researching/Research%20ethics%20and%20Integrity/Human%20research%20ethics/download-a-copy-of-my-application.aspx

To access this application, please follow the URLs below:
* if accessing within the UTS network: https://rm.uts.edu.au
* if accessing outside of UTS network: https://vpn.uts.edu.au, and click on ""RM6 - Production"" after logging in.

If you have any queries about this approval, please do not hesitate to contact your local research office or Research.Ethics@uts.edu.au.

Kind regards

UTS HREC Ethics Secretariat
C/- Research & Innovation Office
University of Technology Sydney
E: Research.Ethics@uts.edu.au
https://staff.uts.edu.au/topichub/Pages/Researching/Research%20Ethics%20and%20Integrity/Human%20research%20ethics/human-research-ethics.aspx
PO Box 123, BROADWAY NSW 2007
[Level 14, Building 1, Broadway Campus]

REF: Ethics 2 -Neg Risk approved (c)

Appendix G

Poster Presentations

Comparing Smooth Pursuit and Saccadic Eye Movements in Rugby Players to a Normative Database

P Gunasekaran[1], C Fraser[2], A Cohen[2], C Hodge[1]

University of Technology Sydney[1] University of Sydney[2]

Introduction

There is increasing evidence to suggest ocular-based tools may improve the sensitivity of sideline concussion detection protocols.[1]

Athletes have been found to achieve better ocular outcomes compared to normal populations.[2]

The use of normative databases may not be optimal for researchers investigating conditions which may require comparison to standard population variables.

Aims

This study examined the saccadic and smooth pursuit systems in premiership-grade rugby athletes as compared to published population means.

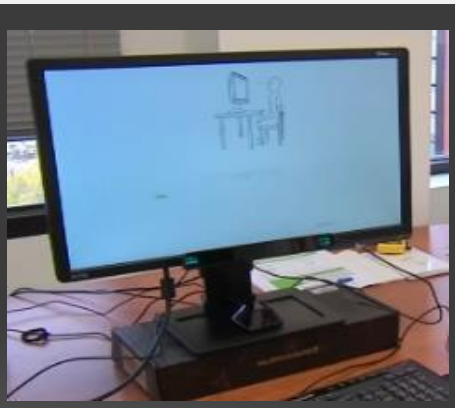

Figure 1: *RightEye apparatus*

Methods

- During the 2017 competition pre-season, forty-two premiership-grade male players from a semi-professional rugby club were recruited (mean age = 20.61 ± 3.0 years).
- Prior history of medically-diagnosed concussions was recorded.
- All players performed 2 smooth pursuit tests (horizontal and vertical) and 2 saccade tests (horizontal and vertical) on the RightEye apparatus.
- Ocular variables were calculated and recorded by the eye-tracking system.

Results

Test domain	Players	Population
Horizontal Smooth Pursuit (%)	95.43 ± 2.93	90 ± 8
Saccade (%)	1.50 ± 1.57	4 ± 4
Fixation (%)	3.08 ± 1.98	6 ± 5
Target Velocity Error	17.05 ± 1.10	18 ± 3
Horizontal Synchronization (score)	0.98 ± 0.01	0.97 ± 0.02

Table 2. *Comparison of Vertical Smooth Pursuit Test results between players (n=42) and population data (n=2500)*

- 85.7% of the rugby cohort produced greater horizontal smooth pursuit than the population mean.
- 83.3% of the rugby cohort with a greater vertical smooth pursuit percentage than the population mean.
- 100% of the rugby players have better (lower) saccade percentages.
- 92.4% of the athletes had better (lower) saccade percentages than the recorded normative mean.
- 78.6% and 56.5% demonstrated better horizontal and vertical synchronization scores respectively.
- 94.9% demonstrated greater saccadic undershoots within 9 to 18mm on the Vertical Saccade Test.

Test domain	Players	Population
Vertical Smooth Pursuit (%)	81.58 ± 96.12	57 ± 13
Saccade (%)	13.29 ± 3.29	22 ± 10
Fixation (%)	19.11 ± 13.19	21 ± 11
Target Velocity Error	16.76 ± 4.53	23 ± 11
Vertical Synchronization (score)	0.73 ± 0.04	0.83 ± 0.13

Table 3. *Comparison of Vertical Smooth Pursuit Test results between players (n=42) and population data (n=2500)*

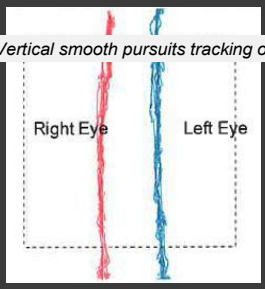

Figure 2: *Vertical smooth pursuits tracking on Player X*

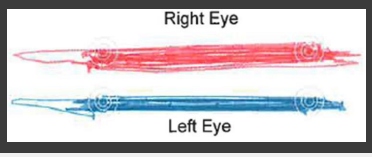

Figure 3: *Horizontal saccade tracking on Player Y*

Conclusion

- Young premiership-grade rugby players possess faster smooth pursuit and saccadic ocular systems than the general population.
- Previous history of concussion and age have no significant impact on smooth pursuit and saccades.
- Future studies should include a comparative control athlete population and compare individual baseline results to those post-concussion.

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Feel free to scan for further information

Incorporating Ocular Assessment In Diagnosis of Sports-Related Concussion in Semi-Professional Rugby Union Players

2179

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2. Save Sight Institute, Department of Ophthalmology, The University of Sydney, Sydney, NSW, Australia

Disclosures: None

BACKGROUND AND PURPOSE

Two large prospective cohort studies have reported that up to 69-90%[1,2] of concussed individuals suffer from some form of visual dysfunction, including version and vergence oculomotor defects. An objective visual tool to aid in detecting concussion may augment subjective measures currently performed in sideline assessments of concussion. This prospective observational cohort study aims to identify the incidence of sports-related concussion and related ocular manifestations in rugby union players using the King-Devick (K-D) test, in order to determine its utility in diagnosing concussion.

METHODS

Forty male rugby players (mean age 23.48 ± 3.7 years; range 18-37 years) who played more than 50% of the season in the top two divisions at a semi-professional rugby club in Sydney consented to the study. During the 2017 pre-season, players performed a baseline K-D test according to the manufacturer's recommended baseline procedures.[3] This is a rapid number-naming test eliciting predominantly saccadic eye movements and cognitive capacity (see ***Figure 1***). Participants were instructed to read aloud as quickly as possible the numbers from left to right on each card held at a constant distance of 40 cm whilst monitored by an examiner. This was repeated and the fastest of the two attempts with least errors was used to calculate the sum of the time taken to read all 3 examination cards. This provided the individual's baseline score for the K-D test. Additionally, players who made more than two errors on a single attempt were stopped and the test recommenced.

All athletes (22 forward and 18 defensive (back) players) were monitored throughout 18 rounds of the playing season and performed the K-D test following any suspected concussion. Concussion episodes were diagnosed and detailed along with all sporting injuries by an experienced sports physician using the SCAT-5 test and clinical expertise. Un-concussed players who were available were also followed-up at least once with the K-D test during the season. A Wilcoxon signed-rank test was used to compare baseline to follow-up K-D test scores.

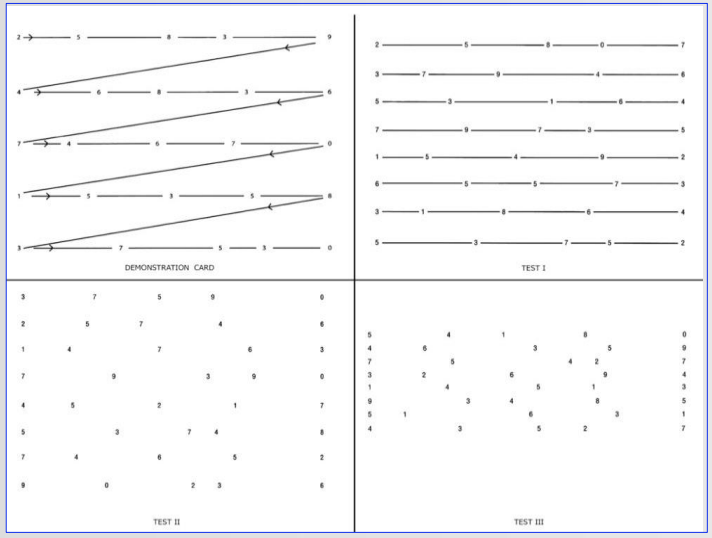


Figure 1. The King-Devick test consists of one demonstration card (upper-left) and three examination cards (top-right and bottom) which increase in difficulty.

RESULTS

- Due to 4 absentees during testing, baseline K-D test was conducted on 36 athletes resulting in an average completion time of 41.4 ± 7.9 seconds.
- There were a total of 112 injuries across the playing season. Of these 6.25% (n=7) were diagnosed as sports-related concussions, with a calculated incidence of 9.72 concussions per 1000 match hours.
- 85.71% of the concussions occurred in forward players and 14.29% in the backs.
- 28 players that repeated the K-D test during season, demonstrated significant improvement in completion time compared to their baseline scores (40.25 ± 7.1 vs. 36.41 ± 6.1 seconds, $p<0.001$) (see ***Figure 2)***.
- Concussed athletes (n=7) displayed average K-D scores that were significantly worse than baseline (33.63 ± 5.4 vs. 36.04 ± 6.0 seconds, $p=0.032$) with a mean difference of 2.41 seconds (see ***Figure 3***).
- One player with a diagnosed concussion (Athlete 4 – see ***Figure 3***) demonstrated a 2 second improvement.
- The cohort also had 3 other direct ocular-related injuries, including one orbital fracture.

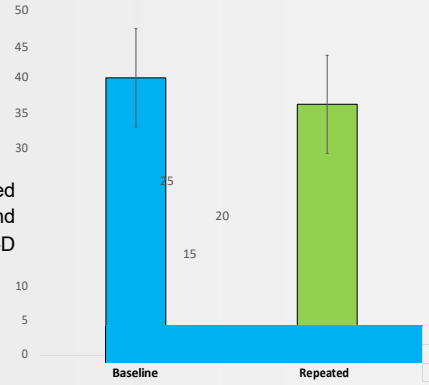
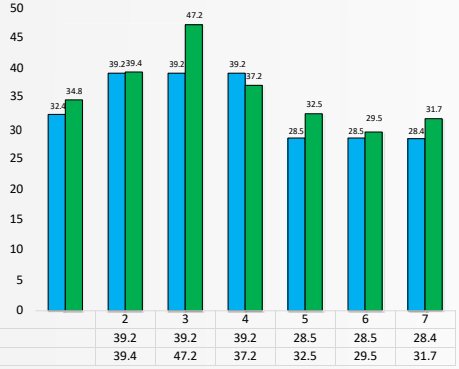


Figure 2. Baseline K-D scores (blue) vs. repeated baseline scores (green) on 28 athletes. Provided in mean ± standard deviation.



	1	2	3	4	5	6	7
	32.4	39.2	39.2	39.2	28.5	28.5	28.4
	34.8	39.4	47.2	37.2	32.5	29.5	31.7

Figure 3. Baseline K-D scores (blue) vs. their respective post-concussion scores (green) on 7 athletes.

CONCLUSIONS

Baseline K-D scores are consistent with age-matched normal values[3] while future studies using the K-D test in conjunction with other visual parameters, such as convergence and accommodation, may improve the sensitivity of concussion detection. Results from this cohort reflect over double the rate of sports-related concussion previously reported (4.73 concussions per 1000 match hours).[4] Inclusion of the K-D test may benefit sideline assessment protocols. Regular pre- and post-match K-D testing may provide a more reliable baseline.

References

1. Sussman et al. (2016) Neurosurgical Focus 40.4:E7
2. Master et al. (2016) Clinical Pediatrics 55.3:260-267.
3. King et al. (2013) Journal of the neurological Sciences 326.1: 59-63.
4. Gardner et al. (2014) Sports Med 44:1717

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Concussion-Related Visual Dysfunction in Children: A Retrospective Study

3126

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Disclosures: None

BACKGROUND AND PURPOSE

Previous researchers have reported impairments in convergence, accommodation, smooth pursuits, and saccades in up to 69% of concussed children.[1] These deficits may result in concussion-related vision disorders such as difficulty reading and sustaining attention on visual tasks, which can heavily impact on a child's learning and schoolwork. Master et al.[2] found that post-concussive visual and vestibular dysfunction in children may be a useful predictor for prolonged recovery. Better detection and management strategies involving vision may help health professionals protect children from repeated hits to the head. This retrospective study aims to establish the prevalence of concussion-related visual dysfunction in children and to examine associations with age, sex, and previous history of concussion.

METHODS

Medical records of children aged 5-18 years, who attended the concussion clinic at Children's Hospital Institute of Sports Medicine, (Westmead, NSW) from November 2015 to May 2018 were identified (n=142). Of these 138 contained sufficient information for inclusion. All had a medical diagnosis of sport or physical activity related concussion. Information extracted included age, sex, duration of symptomology, loss of consciousness (LOC), amnesia symptoms, activity withdrawal, number of previous concussions and clinical data.

The Vestibular/Ocular Motor Screening (VOMS) test was used to determine concussion-related visual dysfunction (Figure 1). A Pearson's Chi Square was used to discriminate between groups and VOMS outcome. A Mann-Whitney test for non-parametric data was performed to determine the relationship between continuous variables and VOMS outcome.

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

Figure 1. Recording sheet for the VOMS tool (unfilled)

RESULTS

- The mean age of participants was 13.17 ± 2.6 years with 103 males, 35 females and of these 28% had a positive result on the VOMS test.
- Almost double the proportion females (42.4%) had a positive VOMS result compared to males (23.2%, p=0.034).
- Contact sports accounted for 59.8% of the concussions documented, with the highest prevalence (31.7%) in rugby. Non-contact sports were reported in 13.6% of cases and non-sporting activity was recorded in 26.5% of the concussive head injuries.
- No association was found between VOMS outcome and age (p=0.091), occurrence of multiple concussions (p=0.222), or number of previous concussions (p=0.187).
- LOC or amnesia individually were not associated with visual dysfunction (p=0.373 and p=0.973, respectively), nor when combined (p=0.234). This is displayed in Figure 2.
- Ninety-three patients recovered from their concussion symptoms (median=33 days, IQR=21-71) while those with a positive VOMS had a longer mean recovery time (days=63.67) than those with a negative VOMS (39.24 days, p<0.001).

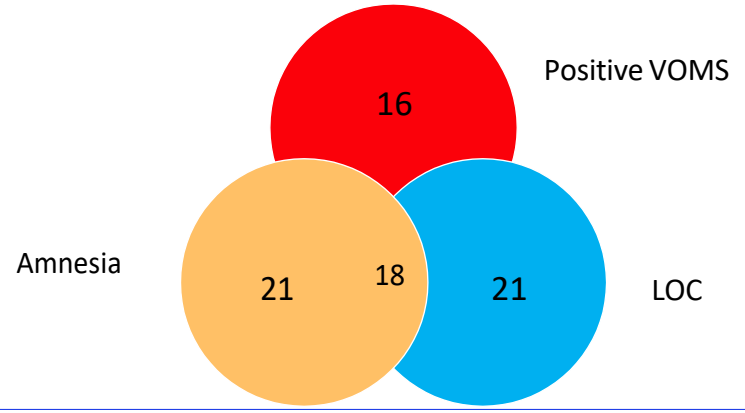

Figure 2. Signs experienced by patients. Forty-two did not experience any of the three.

CONCLUSIONS

Visual dysfunction may be an important indicator of the time to recovery from concussion-related symptoms. Visual dysfunction, as measured by VOMS, occurred in over a quarter of children suffering activity-related concussion, and may impact school work. Dysfunction was more common in females, though we are unable to speculate as to why from the data available.

References

1. Master et al. (2016) Clinical Pediatrics 55.3:260-267.
2. Master et al. (2018) Clin J Sport Med. 2018;28(2):139-145.

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Appendix H

Vestibular/Ocular Motor Screening Protocol

Vestibular/Ocular-Motor Screening (VOMS) Adapted from Mucha A[1], Collins MW[2], Elbin RJ[3], Furman JM[4], Troutman-Enseki C[1], DeWolf RM[2], Marchetti G[5], Kontos AP[6].

Total time to administer is 5 minutes

1. **Baseline Symptoms assessed via a post concussion symptom scale.**
2. **Patient rates changes in symptoms on 0 - 10 scale for symptom provocation during any of the following:**

Smooth Pursuit, Saccades Horizontal, Saccades Vertical, Convergence, VOR Horizontal, VOR Vertical and Visual Motion Sensitivity

SMOOTH PURSUIT

Patient to follow a moving target while the patient and the examiner are seated.

Examiner holds a target at a distance of 3 ft from the patient.

The patient is instructed to maintain focus on the target as the examiner moves the target smoothly in the horizontal direction 1.5 ft to the right and 1.5ft to the left of midline. One

repetition is complete when target moves back and forth to the starting position and 2 repetitions are performed.

Horizontal: Target is moved at a rate of 2 seconds for each direction (right to left and left to right).

Vertical: Repeat at the same rate (2 seconds) moving the target vertically 1.5 ft above and 1.5ft below midline for 2 complete repetitions up and down.

Record: Symptom provocation for Headache, Dizziness, Nausea, Fogginess on a 0-10 scale.

SACCADES

Horizontal and Vertical

Patient to follow a target between two points as quickly as possible.

Patient and the examiner are seated.

Horizontal: Examiner holds two single points (fingertips/ targets)

Horizontally at a distance of 3 ft from patient and 1.5 ft to the right and 1.5 ft to the left of midline so that the patient must gaze 30 degrees to the left and 30 degrees to the right. Once repetition is complete when the eyes move back and forth to the starting position. 10 repetitions are to be completed.

Vertical: Repeat the test with 2 points held vertically at a distance of 3 ft from the patient and 1.5 ft above and 1.5 ft below midline so that the patient must gaze 30 degrees upward and 30 degrees downward.

Record for each direction: Headache, Dizziness, Nausea, Fogginess ratings after each test.

NEAR POINT OF CONVERGENCE

Measure the ability to view a near target without double vision. The patient is seated and wearing corrective lenses (if needed).

Examiner sits in front of the patient and observes their eye movement during this test.

Patient focuses on a small target (approximately 14 font size) at arm's length and slowly brings it toward the tip of their nose. The patient is instructed to stop moving the target when they see two distinct images or when the examiner observes an outward deviation of one eye.

The distance in cm between the target and the tip of the nose is measured and recorded **(ABNORMAL >_ to 6cm**)

Repeat 3 times and record measures each time along with the symptom ratings for Headache, Dizziness, Nausea and Fogginess.

VESTOBULO-OCULAR REFLEX (VOR)

Horizontal and Vertical

Assess the ability to stabilize vision as the head moves.

The patient and the examiner is seated. The examiner holds a target of approximately 14 point font size in front of the patient in midline at a distance of 3 ft.

Use a metronome to help with speed at about 180 beats/min.

Horizontal VOR: Patient rotates head horizontally and maintains focus on the target.

*Amplitude of movement is 20 degrees to each side.

*Perform 10 revolutions.

Vertical VOR: Repeated with the patient moving their head vertically.

*Perform 10 revolutions.

Record after each test (Horizontal and Vertical VOR): Headache, Dizziness, Nausea and Fogginess ratings.

This test had the highest symptom provocation of 61%.

VISUAL MOTION SENSITIVITY

Test visual motion sensitivity and the ability to inhibit vestibular –induced eye movements using vision.

Patient stands with feet shoulder width apart, facing a busy area of the clinic/field/court (guard patient appropriately).

Patient holds arm outstretched and focuses on their thumb. Maintaining focus on their thumb, the patient rotates together as a unit, their head, eyes and trunk at an amplitude of 80 degrees to the left and 80 degrees to the right.

Use a metronome to ensure the speed of rotation is maintained at 50 beats/min (one beat in each direction).

5 revolutions: One revolution is from right to left to the starting position is one revolution.

Record: Headache, Dizziness, Nausea and Fogginess ratings.

VOMS SCORING SHEET

Symptoms on a 0-10 point scale

Vestibular/ Oculomotor	Type	Not Tested	Headache	Dizziness	Nausea	Fogginess	Comments
Baseline Symptoms							
Smooth Pursuit							
Saccades (Horizontal)							
Saccades (Vertical)							
Convergence (Near Point)							Score#1 cm Score#2 cm Score#3 cm
VOR Horizontal							
VOR Vertical							
Visual Motion Sensitivity							