The role of eye movement dysfunction in concussion

Premkumar Gunasekaran

BMedSci, MOrth

Primary Supervisor: Prof. Kathryn Rose

Co-supervisor: Dr. Christopher Hodge

Submitted in fulfilment of the requirements for the degree of

Doctor of Philosophy

Discipline of Orthoptics

Graduate School of Health

University of Technology Sydney

2021

Keywords

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.

Table of Contents

Keywords i
Abstract ii
List of Figures vii
List of Tables viii
List of Abbreviations ix
Overview of Thesis xi
Publications, Presentations, Awards and Honours xv
Statement of Original Authorship xix
Acknowledgements xx
Chapter 1: Literature Review 1
1.1 Traumatic Brain Injuries 1
1.2 Concussion 3
1.2.1 Definition 3
1.2.2 Epidemiology 7
1.2.3 Pathophysiology 9
1.2.4 Neurological Impact 13
1.2.5 Neuroimaging 15
1.2.6 Clinical Signs and Symptoms 18
1.2.7 Post-Concussion Syndrome 21
1.2.8 Sideline Assessment Tools for Concussion 22
1.2.9 Underreporting of concussion 33
1.2.10 Gender Differences 35
1.2.11 Second-Impact Syndrome 38
1.2.12 Chronic Traumatic Encephalopathy 41
1.3 Visual and Oculomotor dysfunction 44
1.3.1 Accommodation 46
1.3.2 Convergence 51
1.3.3 Saccadic Eye Movements (or Saccades) 56
1.3.4 Smooth Pursuits Eye Movements 61
1.3.5 Visual Fields 65
1.3.6 Cranial Nerve Palsies 66
1.4 Visual Tools for detecting and monitoring concussion 71
1.4.1 The King-Devick Test (KDT) 72
1.4.2 The Royal Air Force (RAF) Rule 87
1.4.2.1 The Vestibular/Oculomotor Screening (VOMS) Tool 91
1.5 Summary and Aims 97
Chapter 2: Methods 100
2.1 Introduction 100

2.2 Research Approach and Design....100
2.3 Sampling strategy....101
2.4 Methodology....102
2.4.1 Chapter 3: Evaluation of the King-Devick Concussion Tool....102
2.4.2 Chapter 4: Saccades and Smooth Pursuit Eye Movements....105
2.4.3 Chapter 5: Convergence and Accommodation....111
2.4.4 Chapter 6: A retrospective study of concussed children....115
2.5 Methods of Data Analysis....120
2.6 Ethical Considerations....121
2.7 Problems and limitations....122
Chapter 3: The Learning Effect of the King-Devick Test on Semi-Professional Rugby Athletes....124
3.1 Abstract....124
3.2 Introduction....126
3.3 Methods....129
3.3.1 Participants....129
3.3.2 Testing Procedures....129
3.3.3 Statistical Analysis....130
3.4 Results....131
3.5 Discussion....135
3.6 Conclusion....138
Chapter 4: Comparing the Smooth Pursuit and Saccadic Eye Movements in Rugby Players to a Normative Database....140
4.1 Abstract....140
4.2 Introduction....142
4.3 Methods....143
4.3.1 Participants....143
4.3.2 RightEye Neuro Vision™ test....143
4.3.3 Testing Procedures....144
4.3.4 Statistical Analysis....147
4.4 Results....147
4.4.1 Smooth Pursuits....147
4.4.2 Saccades....150
4.5 Discussion....152
4.6 Conclusion....157
Chapter 5: Acute Convergence and Accommodative Dysfunction in Rugby Union Athletes with Concussion....158
5.1 Abstract....158
5.2 Background....160
5.3 Methods....163
5.3.1 Participants....163

5.3.2 Testing Procedures 163
5.3.3 Statistical Analysis....165
5.4 Results....165
5.5 Discussion 168
5.6 Conclusion....171
Chapter 6: Concussion-Related Visual Dysfunction and Symptom Recovery in Children: A Retrospective Study 172
6.1 Abstract....172
6.2 Introduction 174
6.3 Methods....175
6.3.1 Study Design/Protocol 175
6.3.2 Vestibular/Ocular Motor Screening test....176
6.3.3 Data Analysis 177
6.4 Results....178
6.4.1.1 Age, Gender and Activity Characteristics 178
6.4.2 VOMS Outcome 181
6.4.3 Time to Recovery....182
6.5 Discussion 185
6.6 Conclusion....190
Chapter 7: Summary and Conclusions....191
7.1 Summary....191
7.2 Directions for future research....196
7.3 Conclusions 199
Bibliography 201
Appendix A....202
Appendix B 202
Appendix C 202
Appendix D....202
Appendix E 202
Appendix F 202
Appendix G....202
Appendix H....202

List of Figures

Figure 1.1. Flow diagram of the neurometabolic cascade after a concussion 12

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] 40

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] 41

Figure 1.4. Flow diagram depicting the physiological pathway for monocular accommodation 50 58

Figure 1.5. The main cortical areas and projections involved in saccadic generation. Image adapted from Ventura et al.[289] 58

Figure 1.6. The main cortical areas and projections involved in pursuit generation.[369] 63

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] 70

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] 72

Figure 1.9. The Royal Air Force Rule 87

Figure 1.10. Each side of the cubical drum on the Royal Air Force Rule 88

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] 90

Figure 2.1. A participant performing the King-Devick Test as part of pre-season baseline testing 103

Figure 2.2. A participant performing their repeated baseline testing during the competition season 104

Figure 2.3. The RightEye tracking apparatus. 109

Figure 2.4. Example of a participant's vertical smooth pursuits recorded 110

Figure 2.5. Example of a participant's horizontal saccade results. 111

Figure 2.6. Conducting a baseline RAF Rule on a rugby athlete 113

Figure 2.7. Conducting binocular accommodative amplitude testing on a rugby athlete 114

Figure 2.8. Recording sheet for the Vestibular/Ocular Motor Screening Test (unfilled) 117

Figure 3.1. The King-Devick score and each trial interval (range = 1 to 21) for 183 rugby athletes. 134

Figure 6.1. Distribution of symptom recovery in 90 children excluding those who were asymptomatic at outset (*n* = 8) 183

Females demonstrated a significantly longer recovery time (mean 63.15 days) than males (mean 41.88 days, *p* = 0.002, Figure 6.2) 183

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) 184

List of Tables

Table 1.1. Common signs and symptoms experienced by patients following a concussive head injury 18
Table 1.2. The most popular concussion assessment tools used by physicians. 24
Table 1.3. Signs and symptoms affecting the visual system following a concussion (Extracted from Appendix B) 45
Table 1.4. Studies reporting the rates of accommodative dysfunction following concussion 49
Table 1.5. Studies reporting the rates of convergence dysfunction following concussion 54
Table 1.6. Types of saccades. 57
Table 1.7. Actions of the extra-ocular muscles and cranial nerve innervation 66
Table 2.1. Types of strabismus and the direction of misalignment 106
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 133
Table 4.1. Definitions of the variables analysed during the smooth pursuit and volitional saccade tests. Variables were only used where applicable 145
Table 4.2. Comparison of horizontal smooth pursuit test results between players (*n*= 42) and population data (*n*=2500) 148
Table 4.3. Comparison of vertical smooth pursuit test results between players (*n*= 42) and population data (*n*=2500) 148
Table 4.4. Comparison of circular smooth pursuit test results between players (*n*= 42) and population data (*n*=2500) 150
Table 4.5. Comparison of horizontal saccades between players (*n*= 42) and population data (*n*=2500) 151
Table 4.6. Comparison of vertical saccades between players (*n*= 42) and population data (*n*=2500) 152
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. 166
Table 5.2. Comparison between baseline and post-injury measures in nine athletes with concussion 168
Table 6.1. Details of patient characteristics with respect to schooling level 179
Table 6.4. The relationship between VOMS outcome and patient characteristics. 182

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.

This research is supported by an Australian Government Research Training Program Scholarship and the Orthoptic Australia Research Grant.

Signature of Student:

Production Note:
Signature removed prior to publication.

Date: 18/01/2021

Acknowledgements

There are many people who have guided and supported me throughout some of the toughest years of my life. Without them, I would have never completed this project. These are just but a few.

Many thanks to McDonalds, KFC, Hungry Jacks and Guzman Y Gomez for supplying me with the adequate nutrients and energy to collect data and write this thesis.

On a serious note, I would like to firstly thank Dr. Vincent Nguyen, Dr. Amanda French and (soon-to-be Drs.) Michelle Courtney-Harris and Felicia Adinanto for their ongoing guidance. You are all amazing people who have always looked after me, even when you never had to.

I would also like to thank the rest of the faculty members in the Discipline of Orthoptics, at the University of Technology Sydney, for their ongoing support, encouragement and friendship. In particular my fellow PhD colleagues, Sahar and Mythili, who have been there since day one. I will treasure the numerous laughs, cries and international adventures we shared over the last few years.

To Sue, Donna, Julie and the rest of the team at Gordon Eye Surgery. I honestly, cannot thank you all enough for your ongoing support.

To my brilliant supervisor, Prof. Kathryn Rose, you are honestly the most intelligent person I have ever met. I will always be truly indebted to you for your time and energy. For this I am truly grateful and completely honoured that you believed in me. To Dr. Christopher Hodge, you are simply amazing. You were a leading light and I cannot thank you enough for the guidance and encouragement. To A/Prof. Clare Fraser, I cannot thank you enough for the amount you taught me in both the clinical and research settings. Although you were never officially my supervisor, this thesis could not have been completed without you. I definitely owe you many rounds of buffalo wings.

To my friends who have helped me along this journey, I thank you. You know who you all are. To my loving family, you all mean the world me. Forever I am in debt to the time, support, patience, cooked meals, lifts, hugs and kisses you have given me.

And lastly this thesis is dedicated to my fiancé (now wife) and best friend, Dr. Rachel Yeong. Since the day we met, you have been my soulmate and one true love. Your support throughout the last few years has been second-to-none.

xx