Eye tracking as a diagnostic and monitoring tool for sports-related concussion.

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DECLARATION

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This dissertation includes two original papers published in peer-reviewed journals and one submitted publication. The development and writing of the papers (published and submitted) were the principal responsibility of myself and, for each of the cases where this is not the case, a declaration is included in the dissertation indicating the nature and extent of the contributions of co-authors.

ABSTRACT

Background: Eye movements have become an easy-to-quantify biomarker for a range of disorders; however, the potential for concussion assessment still needs to be validated. The aim of this prospective cohort study was to establish whether eye tracking technology (ETT) would be a clinically useful, reliable, and valid method to diagnose and monitor youth and adult athletes who have sustained a sports-related concussion (SRC).

Methods: To investigate the clinical utility of ETT, an online survey amongst sports medicine clinicians (n = 171) was conducted. For determination of reliability and validity, a testing battery with selected eye tracking metrics (n = 47) was implemented three times (3.0 ± 1.4, 26.1 ± 47.2 and 45.8 ± 19.3 days post-injury) on concussed adult and youth athletes (n = 70) and twice on non-concussed age-and-sex matched athletes (n = 92) with 7.0 ± 3.9 days between sessions.

Results: There was insufficient awareness among surveyed clinicians that concussion could lead to abnormal eye movements. Thus, with the exception of abnormal pupil light reflex (examined by 68%), eye movement deficits were inspected by less than half of the respondents (46.3 ± 12%). Only 11% clinicians had actually worked with ETT. Self-paced saccade (SPS) count in the adult group, and the blink duration in the memory-guided saccade (MGS) task, proportion of antisaccade errors, and gain of diagonal smooth pursuit (SP) in the youth group indicated good reliability (ICC > 0.75). Concussed youth athletes had a higher blink duration in the fast MGS task (p = 0.001, $\eta^2 = 0.17$) and a tendency for higher blink duration in the sinusoidal SP task (p = 0.016, $\eta^2 = 0.06$) compared to non-concussed youths, as well as to their own subsequent post-concussion values (blink duration decreased over time by 24%, p = 0.35, and 18%, p = 0.48, accordingly).

Conclusion. Overall, this study was not able to confirm the findings of previous research on eye tracking metrics for SRC assessment, due to insufficient reliability of described protocols when applied to athletes participating in contact sports. Clinicians can make use of the SPS count as indicator of a concussion among adult athletes, while longer blink durations in MGS or sinusoidal SP tasks might indicate a concussion in youth athletes. Increasing educational opportunities and practical experience of clinicians regarding the use of ETT for SRC assessment to encourage its broader use

is advocated, since most deficits in saccades or smooth pursuit are missed during un-instrumented examination. Finally, serial comparison within the same individuals over time is more likely to detect the effect of a SRC than comparison to healthy controls.

OPSOMMING

Agtergrond: Oogbewegings het 'n maklike kwantifiseerbare biomerker geword vir 'n verskeidenheid van siektes; alhoewel die potensiaal vir harsingskudding assessering moet nog bekragtig word. Die doel van hierdie voornemende kohortstudie was om vas te stel of oogvolgingstegnologie (OVT) 'n klinies nuttige, betroubare en geldige metode kan wees om jeug- en volwasse atlete wat 'n sportverwante harsingskudding (SVH) opgedoen het, te diagnoseer en monitor.

Metodes: 'n Aanlyn-opname was gedoen onder sportsgeneeskundiges (n = 171) om die kliniese nuttigheid van OVT te ondersoek. Om die betroubaarheid en geldigheid te bepaal, was 'n toetsbattery met geselekteerde oogvolgingsmetings (n = 47) drie keer (3.0 ± 1.4, 26.1 ± 47.2 en 45.8 ± 19.3 dae na besering) uitgevoer op volwasse- en jeugatlete met SVH (n = 70), en twee keer op ouderdoms-en geslagsooreenstemmende atlete sonder harsingskuddings (n = 92) gedoen met 7.0 ± 3.9 dae tussen sessies.

Resultate: Volgens die aanlyn-opnames het sportsgeneeskundiges onvoldoende kennis gehad dat harsingskudding kan lei tot abnormale oog bewegings. Minder as die helfte van die respondente (46.3 ± 12%) het oogbewegings-tekortkominge geïnspekteer, met die uitsondering van abnormale pupille-ligrefleks (ondersoek deur 68%). Slegs 11% van die geneeskundiges het al met OVT gewerk. Die teling van self-tempo saccades (STS) in die volwasse groep, asook die oëkniptydsduur in die geheue-geleide saccade-taak (GGS), die hoeveelheid antisaccade-foute en die diagonale gladde agtervolging (GA) wins in die jeuggroep het op goeie betroubaarheid gedui (ICC > 0. 75). Jeugatlete met harsingskudding het 'n langer oëkniptydsduur in die vinnige GGS taak ($p = 0.001$, $\eta^2 = 0.17$) en 'n neiging vir langer oëkniptydsduur in die sinusvormige GN taak ($p = 0.016$, $\eta^2 = 0.06$) getoon in vergelyking met nie-harsingskuddings jeugatlete, sowel as teenoor hul eie daaropvolgende post-harsingskuddingswaardes (oëkniptydsduur het afgeneem oor tyd met 24%, p = 0.35, en 18%, p = 0.48, dienooreenkomstig).

Afsluiting: In die geheel kon hierdie studie nie die bevindinge van vorige navorsing oor oogvolgingsmetings vir SVH- assessering bevestig nie, as gevolg van onvoldoende betroubaarheid van die beskryfde protokolle wat toegepas word op atlete wat aan kontaksport deelneem. Geneeskundiges kan gebruik maak van die SPS-

telling as 'n aanduiding van 'n harsingskudding by volwasse atlete; terwyl langer oëkniptydsduur in GGS of sinusvormige GA-take op 'n harsingskudding by jeugatlete kan dui. Die bevordering van opvoedingsgeleenthede en praktiese ervaring van geneeskundiges word voorgestaan ten opsigte van die gebruik van OVT vir SVH-assessering om die breër gebruik daarvan aan te moedig, aangesien die meeste tekorte in saccades of gladde agtervolging tydens ondersoeke sonder instrumentasie gemis word. Laastens is daar ‘n neiging vir agteropvolgende vergelykings binne dieselfde individue om meer die effek van 'n SVH op te spoor as die vergelyking met gesonde kontrole groep.

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GLOSSARY & ABBREVIATIONS

Abbreviation	Term	Definition
AS	Antisaccades	Antisaccades are voluntary saccades made in the direction opposite to the stimulus (Pierrot-Deseilligny et al. 2004).
ADD / ADHD	Attention Deficit (and Hyperactivity) Disorder	Brain disorder characterised by frequent inattention and/or hyperactivity. It tends to affect certain types of eye movements (Munoz et al. 2003).
BESS	Balance Error Scoring System	Clinical balance test that requires the patient to perform three static stances on two different surfaces (Sussman et al. 2016; Kontos et al. 2017).
CTE	Chronic Traumatic Encephalopathy	A complex of symptoms presumably resulting from repeated sublethal blows to the head that include disorientation, depression, as well as decline in memory, attention and concentration (McKee et al. 2009).
CT	Computerised Tomography	A neuroimaging technique that uses a combination of several computer-processed X-ray scans.
DTI	Diffusion Tensor Imaging	A neuroimaging technique based on magnetic resonance imaging that measures the diffusion of water in tissue.
EEG	Electroencephalogram	Electrophysiological test that detects electrical activity in the brain.
EFSMA	European Federation of Sports Medicine	Main Europe-wide sports medicine organisation.
ERP	Event-related potentials	Electrophysiological response to a specific event or stimulus, usually measured using EEG (Sur and Sinha 2009).
ETT	Eye Tracking Technology	Camera-based technology that detects and processes eye movements in order to analyse visual information processing (Mele and Federici 2012).
FIFA	Fédération Internationale de Football Association	**International governing body of football.**
	Fixation	The state of the eye when it is relatively still for some time, during which the fixated object is cognitively processed by the participant (Holmqvist et al. 2011).
FDA	Food and Drug Administration	Federal agency of the Department of Health and Human Services responsible for safety of medical and food products in the United States.
fMRI	Functional Magnetic Resonance Imaging	A neuroimaging technique that detects changes in blood oxygenation and flow.

HREC	Health Research Ethics Committee	**Committee that reviews the ethics of a health research study.**
ImPACT	Immediate Post-concussion Assessment and Cognitive Test	Computer-based test battery for assessing concussion symptoms and neurocognitive function (Covassin et al. 2009).
FIMS	International Federation of Sports Medicine	International organisation comprising national sports medicine associations worldwide.
K-D	King-Devick Test	A concussion test that requires a participant to read quickly and aloud three cards of irregularly spaced numbers (Sussman et al. 2016). It simultaneously evaluates the ability to concentrate and the saccadic eye movements (Yorke et al. 2017).
MRI	Magnetic Resonance Imaging	A medical imaging technique that uses magnetic fields to generate images of the organs.
MGS	Memory-Guided Saccades (also referred to as memory-based saccades)	Saccadic eye movements that are directed towards remembered locations of objects without the presence of a visual stimulus (Kori et al. 1998).
MoCA	Montreal Cognitive Assessment	A simple, stand-alone cognitive screening tool that is used to detect cognitive impairment or Alzheimer's disease (Nasreddine et al. 2005).
MOOSE	Meta-analysis of Observational Studies in Epidemiology	A reporting checklist for authors and reviewers of meta-analyses focused of observational studies (Stroup 2000).
NCAA	National Collegiate Athletic Association	**Association that regulates student athletes from United States and Canada.**
NFL	National Football League	Professional American football league.
NIH	National Institute of Health	Federal agency of the Department of Health and Human Services in the United States; the largest biomedical research agency in the world.
OKR	Optokinetic Reflex	A type of eye movement intended to stabilise a moving scene while the head is kept steady (Liversedge et al. 2011).
PHQ-9	Patient Health Questionnaire	Self-administered screening instrument for depression disorders (Kroenke et al. 2001).
PET	Positron Emission Tomography	A medical imaging technique that uses a radioactive drug (tracer) to measure metabolic activity of the cells.
PCSS	Post-Concussion Symptom Scale	Concussion symptom checklist that is intended to be filled and rated by a patient. It constitutes part of several concussion assessment tests (Chen et al. 2007).

PCS	Post-Concussion Syndrome	Prolonged presence of a number of symptoms, such as headache, fatigue, poor concentration or disturbed sleep that may last from several weeks to years (Messé et al. 2013).
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses	A checklist for authors of systematic reviews and meta-analyses (Moher et al. 2009).
RS	Reflexive Saccades	Saccadic eye movements that occur in response to a sudden appearance of an object of interest (Hutton 2008).
RED	Remote Eye Tracking Device	A non-invasive device called the eye tracker placed under a computer screen without contact to the participant. It is capable of viewing the participant's eyes from a distance, and keeping track of the eyes as they move within a certain volume (Holmqvist et al. 2011).
RTS	Return-to-Sport	A multi-step process of returning a concussed athlete back to active participation in sport after recovery (Menta and D'Angelo 2016).
RoBANS	Risk of Bias Assessment Tool for Non-randomised Studies	Test for assessing the risk of bias which is recommended for reviewing observational non-randomised studies (Kim et al. 2013).
	Saccade	A fast movement of the eyes from one fixation to the next. Many eye movement paradigms assume that we do not acquire information consciously during most of the saccade (Holmqvist et al. 2011).
SAC	Sideline Assessment of Concussion	A tool for on-site evaluation of the mental status of an athlete with a suspected concussion (McCrea et al. 1998).
SCAT	Sport Concussion Assessment Tool	A standardised neuro-cognitive concussion test suitable for individuals above the age of 12. It consists of the Glasgow coma scale, Maddocks questions (set of 5 questions that assess game-specific orientation and recent memory), symptom checklist, verbal cognitive tests, a physical examination, a modified BESS, and a SAC (Echemendia et al. 2017). The latest version is referred to as SCAT5.

Child- SCAT	Sport Concussion Assessment Tool for Children	A standardised neuro-cognitive concussion test suitable for children 5-12 years of age. It is similar to the SCAT5, with the adjusted wording according to the comprehensive abilities of young children and parental/guardian input (Davis et al. 2017a).
SP	Smooth Pursuit Eye Movements	A type of eye movement as the eye follows an object moving smoothly across a stationary background, such as an airplane in the sky. The main purpose is to keep the fovea steadily focused on the object (Robinson et al. 1986).
SPS	Self-Paced Saccades	Voluntary saccades usually made between two stationary targets in a fixed amount of time; the decision when to start a saccade and where to move the eyes next is intentional and planned (McDowell et al. 2008; Berchicci et al. 2012).
SRC	Sports-Related Concussion	A complex pathophysiological process that takes place in the brain caused by biomechanical forces and typically resulting in a fast onset of short-term neurologic impairment (McCrory et al. 2017a).
	Sub-Concussive Head Impacts	Head impacts (from falls, head-to head or head-to body impacts, etc.) that are below the concussion symptom threshold and thus do not meet the criteria for diagnosis of concussion, but possibly have long-term consequences (Shultz et al. 2012; Belanger et al. 2016).
VOMS	Vestibular/Ocular-Motor Screening	A test that provokes concussion symptoms and then evaluates smooth-pursuit and saccadic eye movements, vestibular ocular reflex, convergence, and visual motion sensitivity (Anzalone et al. 2017; Kontos et al. 2017; Yorke et al. 2017).
VOR	Vestibular-Ocular Reflex	A type of eye movements that allows the eyes to remain stable and compensate for the head and body movement by moving the eyes in the direction opposite to the motion of the head. (Liversedge et al. 2011).

PREFACE

This dissertation follows an article format. The first chapter provides a brief introduction to the research topic, followed by the problem statement and the motivation and rationale for the study. Chapter 2 (the first published article) provides an overview of the existing literature and key concepts of the research topic. Thereafter, Chapter 3 (the second published article) addresses the first research objective, whereas the following Chapter 4 (the submitted third article) covers the of the remaining research objectives of this dissertation. The final chapter (Chapter 5) comprises an overall discussion and conclusion, as well as study limitations and recommendations for future studies.

Since this is an article-format dissertation, there is no specific methodology chapter. Methodology is explained in each article and is condensed to accommodate word limitations in the selected journals. The dissertation follows the author-date referencing format (Harvard style).

CHAPTER 1. INTRODUCTION

1.1. Background Information

Sports-related concussion (SRC) is a frequently occurring and potentially serious traumatic brain injury caused by biomechanical forces (Carroll and Rosner 2011; McCrory et al. 2017a). The past decade has seen a growing recognition of the possible consequences of concussion and its severity. In most cases, with proper and timely treatment, the patient with concussion will recover fully, however if unrecognised, there may be serious implications for the health of the athlete: not only can the immediate concussive symptoms be debilitating, but there is also an elevated risk of subsequent concussive and musculoskeletal injuries in the first week following a SRC, and a spectrum of further possible implications later in life, including depression or cognitive deterioration (Dashnaw et al. 2012; Hubertus et al. 2019).

The awareness and management of SRC have improved substantially in the past few years, yet there is still no uniform tool to assess concussion and reliably monitor its progression (Pusateri et al. 2018; Garcia et al. 2019; Smith et al. 2019). Hence, clinicians have to rely on the description of symptoms provided by the patients; yet the symptom presentation not only varies between individuals and evolves rapidly but is also not specific for a concussion and can be caused by other reasons (e.g. fatigue or systemic illness such as influenza). Moreover, these patients are often young and motivated athletes who sometimes misjudge their condition and thus under-report their symptoms (Register-Mihalik et al. 2013; Scolaro Moser and Schatz 2017; Wallace et al. 2017).

Due to the complexity of this injury and the number of potential presentations of symptoms, the best strategy to obtain the complete clinical picture might be to utilise a battery of several tools, consisting of the Sports Concussion Assessment Tool (SCAT5), neurocognitive tests, in certain cases advanced neuroimaging (for example, head CT, if a more serious intracranial pathology is suspected, or an MRI examination if the concussion symptoms are not improving along an expected clinical course, aimed to look for such findings as diffuse axonal injury or cerebral contusion), as well as vestibular and eye movement assessments. The assessment of eye movements using computerised eye tracking technology (ETT) for the diagnosis and monitoring of a SRC is the major focus of this study, since a close relationship is known to exist between the ability to properly generate eye movements and brain dysfunction (Ting et al. 2014).

Abnormal eye movements have previously been found in several neurological disorders, such as Parkinson's (Kitagawa et al. 1994), Huntington's disease (Patel et al. 2012), or schizophrenia (Subramaniam et al. 2018). The promise of ETT for concussion diagnostics is supported by several empirical studies (Diwakar et al. 2015; DiCesare et al. 2017; Bin Zahid et al. 2018; Danna-Dos-Santos et al. 2018; Webb et al. 2018) and reviews (Greenwald et al. 2012; Ting et al. 2014; Hunt et al. 2016; Ventura et al. 2016; Kontos et al. 2017; Snegireva et al. 2018). Nevertheless, it is not yet possible to properly compare the findings and thus draw definite conclusions due to a number of limitations of these studies: inconsistencies between eye movement metrics and experimental designs, high variability in the time elapsed after the injury at the moment of testing, and lack of uniformity in participant selection.

Therefore, further research that involves developing consistent eye tracking protocols for SRC assessment in clearly defined populations is required (Hunt et al. 2016; Ventura et al. 2016). The group of studies described in this dissertation was initiated to establish whether ETT would be a clinically useful, reliable, and valid tool to diagnose SRC in the early symptomatic stage (which typically lasts approximately a week after the injury (Williams et al. 2015)), and to monitor athletes in the recovery stage (typically up to two weeks in adult and four weeks in youth cohorts (Iverson et al. 2017; McCrory et al. 2017a), although the duration of this stage varies between individuals).

1.2. Rationale

Sports-related concussion is one of "the most complex injuries in sports medicine to diagnose, assess and manage" (McCrory et al. 2017a), yet its accurate detection and management for each individual athlete is crucial. Current clinical tools may not be sufficiently sensitive to identify minor neurocognitive and neuromuscular impairments that extend beyond observable signs and may still be present at the time of return-to-sport (Brooks et al. 2016; Herman et al. 2017; Reams et al. 2017). These impairments, including more conservative gait strategies, deficits in dynamic balance, increased postural sway, reduced cognitive processing speed or deficits in attentional resource allocation, are likely exacerbated during demanding sporting activities, thus placing the athletes at risk of sustaining a further injury (Lynall et al. 2015; Brooks et al. 2016; Herman et al. 2017).

Major concerns regarding the risk of repeat concussion have been expressed (Harmon et al. 2013; Register-Mihalik et al. 2013; Giza and Hovda 2014). After a concussion, there is a period of neurometabolic vulnerability that typically lasts approximately a week (as shown in animal models) and is associated with increased (up to three-fold) risk for sustaining a repeat concussion (McCrea et al. 2009; Giza and Hovda 2014; Brooks et al. 2016; Schneider et al. 2017). The probability of sustaining such repeat concussion in football (soccer) was found to be as high as 50% (Nordström et al. 2014), and in rugby even 60% (Cross et al. 2016). Repeat concussion has been associated with the potential for acute and severe exacerbation of symptoms, prolonged recovery, and possibly development of chronic sequelae including clinical depression, cognitive deterioration, persistent concussion symptoms, early onset of neurodegenerative disorders, or the well-publicised neuropathological features of chronic traumatic encephalopathy (CTE) (McCrea et al. 2009; Makdissi et al. 2010; Carson et al. 2014; Ellis et al. 2015b; Brooks et al. 2016; Manley et al. 2017). Among the most severe, but rare, consequences is the life-threatening second-impact syndrome (Wetjen et al. 2010).

Furthermore, due to impaired neuromuscular and neurocognitive control potentially leading to worsened judgment and coordination, athletes who experienced a concussion are almost twice as likely to sustain an injury to the muscular or skeletal system within the following year compared with non-concussed athletes (Nordström et al. 2014; Lynall et al. 2015; Brooks et al. 2016; Herman et al. 2017).

Acknowledging the need for an accurate and objective biomarker for SRC assessment documented in the Berlin Consensus Statement on Concussion in Sport (McCrory et al. 2017a), the research community has been investigating a broad range of tools (please refer to Section 2.1.6 for detailed analysis). Among others, there has been an increase in experimental research involving eye movements, both with and without eye tracking technology (Lavoie et al. 2004; Ellis et al. 2015a; Howitt et al. 2016; Snegireva et al. 2018; Webb et al. 2018). However, further dedicated research is essential in order to determine whether eye tracking can be a valuable clinical tool to add to the concussion diagnostic toolbox.

1.3. Research Question, Aim, Objectives and Hypothesis Statement

1.3.1. Statement of the Problem

Generation of eye movements requires the integration of signals from nearly every part of the brain, and the damage to any of these areas may negatively influence the individual's ability to perform eye tracking tasks (Leigh and Zee 2015). Indeed, eye movements have already been successfully established as biomarkers for disorders ranging from schizophrenia to muscular dystrophy (Kitagawa et al. 1994; Patel et al. 2012; Leigh and Zee 2015; Subramaniam et al. 2018), but definitive conclusions regarding the suitability of eye tracking for SRC assessment are yet to be drawn. The current study was set to investigate which eye tracking metrics are most indicative of SRC in youth and in adult athletes at different periods following the injury using a broad range of established eye tracking tasks and variables.

1.3.2. Research Question

Would computer-interfaced ETT be a clinically useful, reliable, and valid method to diagnose and monitor youth and adult athletes who have sustained a SRC?

1.3.3. Research Aims

The primary aim of this prospective cohort study was to evaluate the clinical utility, reliability, and validity of technology-supported eye tracking metrics of saccades, smooth pursuit, and fixation stability, as diagnostic and monitoring tests for SRC by comparing concussed adult and youth athletes (latter referring to young children (6-12 years) and adolescents (13-18 years), as stipulated in the Berlin Consensus Statement (McCrory et al. 2017a)) to healthy age-and-sex matched controls, as well as to the athlete's own post-recovery values, i.e. after deemed fit and cleared to return to sport by a medical specialist according to the international consensus criteria (McCrory et al. 2017a).

The secondary aim of this study was to determine whether repeat concussions or concussions with presentation of more severe symptoms would manifest in a higher extent of eye movement impairment.

1.3.4. Research Objectives

The objectives of the study were to establish the:

1. Clinical utility of eye tracking; by investigating the awareness of eye movement deficits associated with SRC amongst sports medicine clinicians and determine the utilization and perceptions of the value of ETT for concussion diagnosis (Chapter 3).

2. Reliability of eye tracking metrics; by comparing the eye tracking metrics between the two sessions conducted with healthy athletes (control group) whilst stratifying by age group (youth and adult) (Chapter 4).

3. (Criterion) validity of eye tracking metrics; by comparing selected eye tracking metrics between concussed and control groups, as well as between the sessions within the concussed group, whilst stratifying by age group (Chapter 4).

4. Relationship between selected eye tracking metrics and (a) the severity of concussion symptoms and (b) number of previous concussions (Chapter 4).

These objectives were achieved by the means of the following steps:

- Collect the demographic information and medical history of all participants (such as previous concussion history, age, years in current sport), as well as SCAT5 / Child-SCAT5 scores.

- Implement a computer-interfaced eye tracking testing battery on adult and youth athletes who have experienced a concussion (concussed group) in the early stage of a concussion (typically approximately one week post-injury, the period within which the concussion symptoms are present but gradually resolve (Henry et al. 2010; Gardner et al. 2015)), in the recovery stage (two to four weeks post-injury, usually sufficient for a full neurobiological recovery to take place, however the exact timeframe is yet to be established (Iverson et al. 2017; Pusateri et al. 2018)) and finally at approximately 3 months post-injury, subject to being cleared to return to sport by a clinician, in order to obtain their post-factum baseline values.

- Implement the same testing battery on healthy age-and-sex matched athletes (control group) twice with a one-week interval between the sessions.

1.3.5. Hypothesis Statement

It was hypothesised that:

1. Sport medicine clinicians would be aware that in diagnosing a SRC, assessing the eye movements can be useful; however, since the technology is relatively new and still needs more extensive validation, only a few clinicians would utilise the ETT in their practice.

2. Due to the ability of ETT to measure eye movements objectively, in quantifiable manner, and with minimal operator influence, thus leading to repeatable results, it was expected to be a reliable tool for assessing SRC in athletic cohorts.

3. Owing to a high prevalence of eye movement deficits in SRC that might outlast the symptoms (Ciuffreda et al. 2007; Hunt et al. 2016), as well as the ability of the eye tracking technology to accurately measure such deficits, eye tracking would be a valid tool to diagnose and monitor SRC. The deficits in self-paced saccades, fixation stability, memory-guided saccades, smooth pursuit, and antisaccades (but not in reflexive saccades) were expected to be most pronounced in the early symptomatic stage, diminish in the recovery stage, and resolve in the post-factum baseline stage.

4. Based on earlier studies that found significant relationship between the concussion symptom scores and several eye tracking variables (Patel et al. 2012; Subramaniam et al. 2018; Taghdiri et al. 2018), a strong positive relationship was expected to exist between the degree of eye movement impairments recorded by the eye tracker with the severity of concussion symptoms. Additionally, since repeat concussions have been associated with more severe and prolonged symptom presentation (Wetjen et al. 2010; Eisenberg et al. 2013; Meehan et al. 2013), a positive relationship was also expected between the degree of eye movement impairments and the number of previous concussions.

1.3.6. Variables

Exposure variable: Presence of a concussion diagnosed by a clinician in accordance with the international consensus criteria (McCrory et al. 2017a).

Response variables were selected based on the findings of the systematic review of the literature on the use of eye tracking technology in sports-related concussion assessment (Snegireva et al. 2018 and Chapter 2). They are summarised in Table 1.1. The variables are grouped by the eye tracking tasks (memory-guided saccades, reflexive saccades & antisaccades, self-paced saccades, fixation stability, and smooth pursuit; see Section 2.2.2 for details) and by the eye tracking metrics (measures of movement, position, count, and latency/distance). Please refer to Section 2.2.3 for detailed explanations.

Table 1.1. Response variables[1].

Tasks → Variables ↓	**Self-paced saccades**	**Fixation stability**	**Memory-guided saccades**	**Smooth pursuit**	**Reflexive saccades**	**Antisaccades**
Movement	Peak Velocity			Peak Velocity	Peak Velocity	Peak Velocity
Position	Blink Duration Average	Blink Duration Average Diversion Duration	Blink Duration Average Positional Errors	Blink Duration Average	Directional Errors	Directional Errors
Count	Saccade Count Blink Rate	Saccade Count Blink Rate	Saccade Count Blink Rate	Intrusive Saccade Count Blink Rate		
Latency				Phase Gain	Latency Gain	Latency Gain

Confounding variables listed below have been identified as potential modifying factors for SRC or for eye tracking performance. Of particular interest are the history (number) of previous concussions, SCAT5 / Child-SCAT5 scores (specifically, the number and severity of self-reported symptoms), and of course age, since these are possible

[1] Pleare refer to Table 4.1. for units of measurement

concussion modifying factors that might affect the duration of recovery (McCrory et al. 2013).

- Age
- Height (measured by the researchers)
- Weight (measured by the researchers)
- Sex
- Self-reported number of previous concussions
- Type of sport
- Number of years spent playing sport
- SCAT5 / Child-SCAT5 symptom severity scores
- Self-reported presence of neurological or oculomotor disorders including ADHD/ADD, headache disorders, epilepsy, autism, nystagmus, amblyopia, alcohol addiction, etc.
- Self-reported use of medication
- Global cognitive function measured with the Montreal Cognitive Assessment (MoCA)
- Depression measured with the Patient Health Questionnaire (PHQ-9)

1.3.7. Assumptions

Several assumptions that might limit the generalisability of the findings were unavoidable for practical reasons of a trial of this nature being conducted in a clinical and pragmatic setting. Firstly, all participants' self-reported data pertaining to the concussive symptom severity, concussion history, current medication, etc. were assumed to be honest, accurate, and transparent. It was also assumed that the participants were compliant with the task instructions and always performed the tests to the best of their abilities. Finally, the concussion diagnosis, as well as application of the return-to-sport guidelines as directed by sports medicine physicians were assumed to be in accordance with the Berlin Consensus statement (McCrory et al. 2017a).

1.3.8. Delimitations

The study was delimited to athletes aged 9-35 years and conducted in a single country (South Africa), with an exception of the sports medicine clinicians' survey which was multinational. The concussions documented in this dissertation were sustained in a sporting-related setting (during games and practice), and the participants had no visual or neurological disorders which would affect responses, nor were the participants ingesting any medication(s) that may affect eye movements. The study only examined the concussions sustained no more than one week before the first testing session.

CHAPTER 2.
LITERATURE REVIEW

2.1. Sports-Related Concussion

2.1.1. Definition

A commonly accepted definition of the sports-related concussion is provided in *The Berlin Consensus Statement on Concussion in Sport* (2017): it is a "traumatic brain injury induced by biomechanical forces" that "typically manifests in the rapid onset of short-term impairment of neurological function" (McCrory et al. 2017a). Even though SRC may lead to neuropathological changes, symptoms and signs usually represent functional disturbance, rather than a structural injury, and are therefore not seen on traditional neuroimaging. Symptoms of a concussion typically appear instantly, although in some cases they may evolve over several minutes or even hours. The symptoms usually resolve sequentially within a week (Henry et al. 2010; Gardner et al. 2015); however, in some cases the symptoms may be prolonged (McCrory et al. 2017a).

In recent research a differentiation can be found between the SRC (as a result of sport trauma) and non-sports-related concussion that could be caused by falls, motor vehicle accidents, or similar (Sojka 2011; McCrory et al. 2017b). While such distinction is mainly driven by the need of the sporting bodies for clear return-to-sport guidelines (McCrory et al. 2017b), there is an important difference between the two. Compared to the general public, athletes (particularly those in contact and collision sports) tend to have a much higher exposure to trauma and hence the probability of sustaining multiple concussions, as well as sub-concussive head impacts that may cause negative consequences in the long term (Shultz et al. 2012; Belanger et al. 2016).

2.1.2. Epidemiology

Around 10% of all contact sport athletes, especially in such high-contact or collision sports as rugby (Tommasone and McLeod 2006; Lincoln et al. 2011; McCrea et al. 2013) experience at least one concussion per year (Satarasinghe et al. 2019), with up to 3.8 million concussions occurring annually in sports and recreational activities in the United States (Langlois et al. 2006). Across all sports and ages, concussion accounts for up to 13% of sports-related injuries (22% in football; 25% in rugby) (Marshall and Spencer 2001; Gessel et al. 2007; Marar et al. 2012; Mc Fie et al. 2014).

Rugby Union (rugby) is a widely-played international sport with over 5 million athletes participating annually (Gardner et al. 2015). The estimated incidence of concussion in rugby ranges from 5 to 15 concussions per 1000 athlete exposures (i.e., one athlete participating in one practice session or game) (Patricios et al. 2010; Mc Fie et al. 2014; Rafferty et al. 2018). There is also evidence that concussion in rugby is more common in youth compared to the adult players (Kirkwood et al. 2015).

Furthermore, football (soccer) is an extremely popular sport with over 265 million active players worldwide (Kunz 2007). Even though the incidence of concussion in football is lower compared to other contact sports, with figures varying from 0.18 to 1.4 per 1000 athletic exposures (Patricios et al. 2010; Maher et al. 2014; Putukian et al. 2019), the risk of concussions caused by falls, head-to-head or head-to-body collisions has been repeatedly emphasised (Barnes et al. 1998; Boden et al. 1998; Fuller et al. 2005; Hubertus et al. 2019). Several studies found that up to 70% of football players experience at least one concussion over the course of their athletic career (80% of whom experience two or more) (Hubertus et al. 2019). Overall, it is estimated that as many as half of concussions in football may be undetected (Harmon et al. 2013), since only 15-20% of the concussed players actually realise that they had sustained a concussion (Delaney et al. 2002, 2007).

2.1.3. Impact on Society

Even when properly diagnosed and managed, concussion may impact both the athlete and society. Concussed athletes sometimes need to refrain from physical activity for a prolonged period or even temporarily abandon their sport. Impaired cognitive functioning is an important symptom and consequence of concussion and may lead to subsequent decreased sporting, academic, and work performance (Wasserman et al. 2015; Russell et al. 2016), although some recent studies seem to refute this hypothesis (Yengo-Kahn et al. 2016a; Reams et al. 2017; Sabesan et al. 2018).

On a macroeconomic level, the annual costs of mild traumatic brain injury (of which concussion is a subset of it) including medical expenses and lost productivity, are estimated to be as high as $60 billion in the United States (850 billion South African

Rand (ZAR)) (Kimbler et al. 2011). For concussions in youth sports, total costs were estimated at $695 million in the first three months after injury, or $1004 per person (14 thousand ZAR) (Graves et al. 2015).

Recently, some institutions, responsible for the player welfare, have been held accountable for holding back information about the consequences of a concussion. In the United States, following concussion lawsuits, the National Football League (NFL) had to establish a program for the retired athletes who suffered from consequences of the repeat concussions or blows to the head with or without concussion symptoms (Yengo-Kahn et al. 2015; Sabesan et al. 2018) and paid $675 million (9,5 bn ZAR) in legal settlements. Also the National Collegiate Athletic Association (NCAA) agreed to pay $75 million in settlements (Sabesan et al. 2018).

It is further worthy of consideration that the excessive precaution and over-diagnosis of concussions may also have detrimental effects. Athletes may needlessly miss out on games and practice, resulting in deconditioning and low spirits, as well as, for professional athletes, in financial loss (Satarasinghe et al. 2019).

2.1.4. Pathophysiology

During a concussive event, the brain undergoes a sequence of events referred to as a neurometabolic cascade caused by the acceleration-deceleration forces on the neural structures including axons, dendrites, and astrocytes (Giza and Hovda 2014; Barkhoudarian et al. 2016).

Axons appear to be particularly vulnerable to the biomechanical stretch typical in a concussion (Giza et al. 2018). The axonal stretching causes excessive potassium efflux into the extracellular space, as well as unregulated sodium and calcium influx (Barkhoudarian et al. 2016; Giza et al. 2018). This process leads to regional depolarisation, unregulated release of glutamate, and ultimately to a widespread suppression of neurons that is associated with a spectrum of symptoms, such as migraines or seizures (Barkhoudarian et al. 2016).

The acute effort to restore ionic and cellular homeostasis increases glycolysis within the first 30 minutes after the injury, which, in combination with the typically reduced cerebral blood flow, leads to a cellular energy crisis (i.e. a mismatch between energy supply and demand) (McCrory et al. 2001; Giza et al. 2018). After six hours, there is an onset of glucose hypometabolism that lasts approximately a week, as was demonstrated in animal studies, and is associated with cognitive impairment (Giza and Hovda 2014; Barkhoudarian et al. 2016). Simultaneously, the mitochondria attempt to balance the calcium overload, resulting in further metabolic irregularity (Giza and Hovda 2014).

It is possible that concussion triggers inflammatory brain changes that further worsen the symptom presentation and duration (Giza et al. 2018; Mc Fie et al. 2018). Microglia become activated, and the glutamate release possibly alters immune receptors, leading to so-called immunoexcitotoxicity (Giza and Hovda 2014).

Neuropsychologic consequences of a concussion include impairments of executive functions, such as memory and planning, the inability to switch mental set, along with reduced attention and speed of information processing (Johnston et al. 2001). These deficits have been attributed to the accumulation of abnormally phosphorylated tau protein in the brain which causes loss in the neuronal network connectivity and cell dysfunction; as well as to white matter tract changes that lead to delayed action potentials (Satarasinghe et al. 2019).

2.1.5. Recovery Time and Modifying Factors

In the large majority of cases, symptoms related to concussion resolve within the early stage (approximately 7-10 days for adult, and up to four weeks for paediatric patients) that corresponds to the neurometabolic cascade (Henry et al. 2010; Gardner et al. 2015). However, the full neurobiological recovery may extend beyond symptom resolution, although this period of physiological recovery is not yet properly defined (Iverson et al. 2017; Pusateri et al. 2018). Concussion symptoms and cognitive dysfunction recover at different rates, with cognitive deficits usually outlasting the other symptoms by two or three days (Makdissi et al. 2010). An earlier comprehensive review concluded that the time for neurobiological recovery (measured with a variety of modalities, such as advanced neuroimaging or blood biomarkers) often exceeded the time for clinical (symptomatic) recovery, adding that physiological disturbance were present for more than 15 days but less than 30 days following the injury (Kamins et al. 2017).

Predicting recovery time remains challenging. Biomechanical studies demonstrate that the magnitude and location of the impact seem to have little effect on the severity of concussion symptoms or neuropsychological function, suggesting a considerable individual difference in the tolerance to head acceleration (Guskiewicz et al. 2007; Rowson et al. 2018). This indicates that similar biomechanical inputs might manifest in different injury presentations and recovery trajectories for different athletes. These individual differences seem to be influenced by a range of factors, including symptom severity, history of prior concussions, age, sex, pre-injury mood disorders, migraines, learning disabilities and ADD/ADHD, as well as energy status and possibly genetic predispositions (Barkhoudarian et al. 2016; Zemek et al. 2016; Zuckerman et al. 2016). However, none of these so-called modifying factors have yet been proven conclusively and may be more useful in designing the recovery protocols than in accurately predicting time to recovery (Pusateri et al. 2018).

Severity of Concussion Symptoms

The overall number and severity of early symptoms following a concussion may correlate with time to recovery (Iverson et al. 2017). In addition, a few specific symptoms have been associated with longer recovery time, namely: prolonged headache, fatigue, dizziness, fogginess, oculomotor impairments and depression symptoms, as well as the presence of greater than three symptoms at initial assessment (Makdissi et al. 2010; Iverson et al. 2017). This suggests that there is a relationship between neurochemical alterations and the severity of clinical symptoms (Johnston et al. 2001; Chamard et al. 2014), and therefore, on one hand, the brain may be vulnerable for a longer period following a more severely manifesting concussion, and, on the other hand, the severity of symptoms may have a certain prognostic significance.

Previous Concussions

Current research suggests that sustaining repeat concussions increases the risk for prolonged and magnified symptoms. A number of studies found that repeat concussions, while the brain was metabolically vulnerable, resulted in prolonged recovery and behavioural impairments ranging from memory loss to cognitive dysfunction lasting weeks or even months (Eisenberg et al. 2013; Kirkwood et al. 2015; Barkhoudarian et al. 2016; Iverson et al. 2017; Kamins et al. 2017).

Age of the Athlete

Age is one of the most frequently named concussion modifying factors (Davis et al. 2017b). Not only are the concussion rates often higher in youth athletes (this term includes young children (6-12 years) and adolescents (13-18 years) (McCrory et al. 2017a)) than in the adult athletes (Purcell 2005; McCrory et al. 2017a), but the adolescent years might represent the greatest period of susceptibility to longer recovery times and more pronounced symptoms (Baillargeon et al. 2012; Rivara and Graham 2014; DeMatteo et al. 2015; Lynch et al. 2015; Iverson et al. 2017). It should be noted, however, that young children, lacking the experience and vocabulary of adolescents and adults, are often unable to correctly identify and describe the symptoms they are experiencing, or to recognise their importance. This may mean that in young children the symptoms may be more pronounced, but simply not as well verbalised.

Studies have found that unmyelinated axons are more susceptible to injury than myelinated axons (Giza and Hovda 2014). Since myelination is one of the maturational processes of the brain (Giza and Hovda 2014), this finding supports the presumption that youth athletes are more prone to demonstrate more severe symptoms and require longer recovery times. In addition, they might be more exposed to the social and psychological effects of having sustained a sports-related concussion or be less compliant, which might prolong the recovery period (Iverson et al. 2017).

Additional Factors

There is a number of additional factors that are gaining recognition as predictors for concussion recovery, such as patient's pre-existing, coexisting and/or resulting mental health and psychosocial status. Thus, for example, pre-existing mental health problems haven been associated with symptom persistence (Iverson et al. 2017). In the current dissertation, these factors, where possible, were controlled for as part of the exclusion criteria.

2.1.6. Assessment Tools in Use or Under Validation for Sports-Related Concussion

A broad body of systematic literature reviews exists covering the available tools (Broglio and Puetz 2008; Dziemianowicz et al. 2012; Marshall 2012; King et al. 2014;

Murray et al. 2014b; Okonkwo et al. 2014; Papa et al. 2015; Valovich McLeod and Hale 2015; Yengo-Kahn et al. 2016b). In preparation for the Fifth International Conference on Concussion in Sport held in 2016 in Berlin, over 60 thousand articles were screened (McCrory et al. 2017a; Pusateri et al. 2018) and twelve systematic reviews were produced covering, among other things, the domains that need to be assessed after a SRC and possible assessment modalities (Patricios et al. 2018).

Along with an overview of all available tools, their relative strengths and weakness, two important trends have crystallised in current literature: Firstly, due to a growing understanding that full physiological recovery may extend beyond symptom resolution, there is increased interest in developing more sensitive tools for assessing and monitoring concussion in the recovery stage (McCrea et al. 2017). Secondly, there is a consensus that it is crucial to utilise a multidimensional, multimodal and multi-timeframe assessment toolbox capable of evaluating the broad range of domains affected by the injury, including somatic, cognitive, behavioural, and vestibular-ocular (Jacquin et al. 2018). Eye tracking technology might be a valuable, accurate, and sensitive addition to the diagnostics toolbox.

Below is a brief overview of the established and emerging SRC assessment tools currently in use.

The Sports Concussion Assessment Tool (SCAT)

The Sport Concussion Assessment Tool (SCAT) and its version for children under the age of 12, Child-SCAT, is the most established tool in SRC diagnostics (Patricios et al. 2017). The latest version, SCAT5 (Appendix 5), was issued in 2017 as a result of the Berlin meeting of the Concussion in Sport Group. It consists of a 22-item symptom checklist, cognitive and physical examination, the Glasgow Coma Scale, Maddocks questions, a modified Balance Error Scoring System (BESS) and Sideline Assessment of Concussion (SAC).

The SCAT has been named the most validated, “rigorously developed and regularly updated” concussion diagnostic instrument that is useful immediately after injury (Samadani et al. 2016; McCrory et al. 2017a). The SCAT is easy to conduct, fast and highly valuable. However, it has two main limitations: first, as the developers of the tool admit, the diagnostic utility of all components of SCAT5 except for the symptom checklist appears to decrease significantly after three to five days post-injury (Echemendia et al. 2017; McCrory et al. 2017a), and the symptom checklist is subjective. This means that SCAT5 is a less appropriate tool for monitoring concussions in the recovery period.

Neurocognitive Tests

Neurocognitive tests measure various domains of an individual's cognitive function, including memory, attention, concentration, learning, and verbal fluency (Peterson et al. 2003). There are pencil-and-paper based and computerised neurocognitive tests; both forms have been useful in contributing towards the assessment of SRC over the past 20 years and have been validated in the early stages following concussion (Johnson et al. 2011; Feddermann-Demont et al. 2017; Howell et al. 2018a). The computerised tests have a number of advantages compared to the pencil-and-paper ones: they are scalable, i.e. many athletes can be tested simultaneously, they measure the reaction times with higher accuracy and reduce inter-rater variability issues; while their main disadvantage is the fact that the clinician is often unable to directly observe the patient taking the test (Johnson et al. 2011). The most common computerised neurocognitive tests include the Immediate Post-Concussion Assessment and Cognitive Test (ImPACT) (Covassin et al. 2009), CogState Sport / Axon Sport and Headminder (Resch et al. 2018). The sensitivity of computerised neuropsychological tests used in combination with self-reporting and brief traditional neuropsychological test battery has been shown to exceed 90% (Johnson et al. 2011). Neurocognitive testing is able to recognise potential deficits extending beyond symptom inventories and may even be effective in distinguishing asymptomatic concussed athletes from uninjured controls (Johnson et al. 2011; Howell et al. 2018a).

Despite the established value, a few concerns exist that the promotion of computerised neurocognitive tests has outpaced their clinical evidence (Howell et al. 2018a). Firstly, the test–retest reliability of these tests has been disputed due to the large number of possible confounding factors, such as test conditions, motivation of the participant, or quality of the test instructions (Feddermann-Demont et al. 2017). In addition, similar to SCAT5, while the sensitivity of neurocognitive tests is reasonable within the first days after the injury, it drops dramatically by eight days post-injury (Howell et al. 2018a) rendering these tests unsuitable for accurate monitoring of the recovery stage.

Therefore, researchers agree that neurocognitive testing should be used not in isolation but as one component of a more comprehensive multidimensional and individualised assessment (Johnson et al. 2011; Feddermann-Demont et al. 2017; Howell et al. 2018a).

Neuroimaging

The research on the neuroimaging and electrophysiological measures has mainly focused on characterising the pathophysiology of SRC using these markers, rather than demonstrating their clinical diagnostic potential (McCrea et al. 2017). It has successfully identified a range of metabolic and physiological changes that take place in the brain following a concussion and correlate with the symptoms (Section 2.1.4).

It is generally agreed that the neurological symptoms caused by a concussion most likely reflect functional or microstructural changes, rather than a visible macroscopic structural injury. Functional injury refers to impaired cellular or physiological function including neurotransmission, ionic shifts, or metabolic changes. Microstructural injury refers to physical changes that may be detected using such techniques as diffusion tensor imaging (DTI). Functional and microstructural injuries are thus not seen on commonly utilised structural magnetic resonance imaging (MRI) or computerised tomography (CT) (Henry et al. 2010; Giza and Hovda 2014; McCrory et al. 2017a).

Diffusion tensor imaging is one of the recent advances in modern imaging, and it shows promise as a sensitive and powerful measure of concussion effects (Barkhoudarian et al. 2016). The latest studies with concussed athletes demonstrated the changes in a range of parameters even after the symptoms reported by the patients resolved (Churchill et al. 2016; Lancaster et al. 2016; Meier et al. 2016; Kamins et al. 2017). The majority of scientific work reported a decrease of fractional anisotropy (a measure of connectivity in the brain (Grieve et al. 2007)) that can happen after axonal disconnection or swelling seen in concussion (Barkhoudarian et al. 2016; Jacquin et al. 2018). Such lowered brain connectivity in concussed patients has been associated with impaired motor speed, executive function, and behavioural ratings (Barkhoudarian et al. 2016). However, an opposite pattern (increase of fractional anisotropy and thus of brain connectivity) as well as null results in concussed patients have also been reported (McCrea et al. 2017), this calling for further investigation.

Also the functional magnetic resonance imaging (fMRI) studies conducted in concussed patients have contrasting findings. Researchers report both increased and decreased activity in task-related networks, possibly due to variability in such factors as time since injury, experimental design, and different symptom presentation (McCrea et al. 2017). Interestingly, some fMRI changes seem to only appear months after the injury, after improvement or even resolution of symptoms (Henry et al. 2010; Kamins et al. 2017), and extensive further research is required to properly understand this phenomenon.

Preliminary studies with positron emission tomography (PET) in concussion suggest metabolic abnormalities in frontotemporal regions (Johnston et al. 2001; Henry et al. 2010). Research using magnetic resonance spectroscopy also provides some early evidence of its ability to detect metabolic abnormalities in white matter up to 30 days after the injury or even more chronically (Kamins et al. 2017; McCrea et al. 2017).

A significant limitation of these advanced, functional imaging modalities is their accessibility and affordability. They remain largely research tools rather than pragmatic clinical entities.

Vestibular and Oculomotor Assessments

Athletes who sustain a concussion frequently report symptoms associated with impairment of the oculomotor and vestibular systems, such as blurred vision, difficulty reading, poor postural control, or dizziness (Anzalone et al. 2017; Kontos et al. 2017). It comes as no surprise, therefore, that *The Berlin Consensus Statement on Concussion in Sport* (2017) stated that it might be beneficial to add further modalities to the assessment of concussion, such as gait and balance assessment, oculomotor screening, or clinical reaction time (McCrory et al. 2017a). Also the position statement issued by the National Athletic Trainers' Association named eye examinations including smooth pursuit, nystagmus and pupillary reflex among the suggested domains of concussion recovery assessment, since they evaluate the function of multiple cranial nerves: II, III (pupillary reflex), III, IV, VI (smooth pursuit), and VIII (nystagmus) (Broglio et al. 2014).

Several tools exist to assess these functions. Thus, the BESS requires the patient to perform three static stances on two different surfaces (Sussman et al. 2016; Kontos et al. 2017). For assessing dynamic balance, the timed tandem gait test is typically used, in which the patient is asked to walk heel-to-toe along a straight line (Sussman et al. 2016). A modified version of both BESS and tandem gait tests is included into the SCAT5 test. Balance is a valid and objective measure of sensorimotor function, however, the BESS scores can often be influenced by multiple confounding factors, such as fatigue, lower limb injuries or age; in addition, significant inter-rater variability in known to exist (Sussman et al. 2016). A systematic review found that balance assessments have a good specificity but a lower sensitivity, and the overall validity of evidence is low (Patricios et al. 2017). Moreover, since most athletes regain normal balance within 3-5 days after a concussion, a different modality is needed for the longer term monitoring (Mucha et al. 2014).

Assessment of oculomotor function in SRC (apart from the computer-interfaced eye tracking technology that is reviewed separately in Section 2.3) include the King-Devick (K-D) test and Vestibular/Ocular-Motor Screening (VOMS). The K-D Test requires a participant to quickly read out loud three cards of irregularly spaced numbers. It evaluates saccadic eye movement as well as language and concentration (Yorke et al. 2017) and has shown great promise in identifying SRC even in the absence of pronounced symptoms (Kontos et al. 2017), especially when used together with further assessments, such as BESS (Sussman et al. 2016; Ventura et al. 2016). A systematic review found a relatively good sensitivity and specificity of the K-D test, which, however, needs to be confirmed in high-quality studies (Patricios et al. 2017). At the same time, the King-Devick test has shown high susceptibility to a learning effect (Kontos et al. 2017), and is therefore not suitable as a monitoring tool.

The VOMS test evaluates smooth-pursuit and saccadic eye movements, vestibular ocular reflex, convergence, and visual motion sensitivity via symptom provocation (Anzalone et al. 2017; Kontos et al. 2017; Yorke et al. 2017). Specifically designed to invoke subtle symptoms that may be overlooked by the BESS or King-Devick tests, VOMS has demonstrated strong internal consistency and significant correlation with the Post-Concussion Symptom Scale (Kontos et al. 2017). However, it is predominantly symptom-based and is thus susceptible to underreporting, and possibly unable to assess the full neurobiological recovery (Mucha et al. 2014; Yorke et al. 2017).

Overall, there is compelling, albeit preliminary, evidence for the use of oculomotor tests for concussion assessment (Hunt et al. 2016), as well as other clinical and technological assessments of oculomotor and VOR function (which are out of scope of the current dissertation, since they cannot be conducted with the utilized eye tracker). These tests have a number of advantages: they are objective, deliver quantifiable results and are less dependent on symptom reporting; compared to neuroimaging, the technology is more affordable, easy-to-learn, and portable. The underlying neurobiology of the oculomotor impairments in SRC, as well as the instrumented tests conducted using an eye tracker, a saccadometer, or similar, are reviewed later in Sections 2.2.4 and 2.3 of the dissertation.

Other measurements

Some electrophysiological changes following a SRC in both symptomatic and asymptomatic athletes compared to baseline values have been detected using event-related potentials (ERP), novel electroencephalography (EEG) algorithms, and transcranial magnetic stimulation (TMS), and have been associated with concussion symptom severity (Henry et al. 2010; Kamins et al. 2017; McCrea et al. 2017). In particular, concussed patients demonstrated decreased latency and amplitude changes in the P300 wave that sometimes persisted for months after the last incident, and changes in phase synchrony and connectivity of the EEG between regions and between neural networks (Henry et al. 2010; Kamins et al. 2017; Jacquin et al. 2018). This reflects a disruption in neural transmission between brain regions (Jacquin et al. 2018). In addition, a correlation was found between increased intracortical inhibition and the number of past concussions, suggesting possible cumulative effects (Henry et al. 2010; Kamins et al. 2017). While promising, EEG has a range of limitations: for example, the EEG signal may vary significantly both between individuals and depending on a situation (e.g. fatigue) and in order to be a sensitive SRC diagnostic tool it would require multiple pre- as well as post-concussion measurements (Conley et al. 2019).

Mounting evidence suggests that fluid biomarkers (especially blood) may assist not only in diagnosing concussion, but also in predicting its outcomes and monitoring recovery; however, research is in its very early stages, and the utility and validity of fluid biomarkers still needs to be proven (Strathmann et al. 2014; Kamins et al. 2017; McCrea et al. 2017; O'Connell et al. 2018).

Overall, advanced neuroimaging, fluid and genetic biomarkers are currently useful as research tools in investigating the neurobiological changes underlying a concussion; however, the level of evidence to justify their utility as diagnostic and prognostic markers of injury and recovery is low (McCrea et al. 2017) due to contradicting research finding, as well as to the high invasiveness, time intensity, and cost of the equipment.

2.2. Eye Movements and the Brain

2.2.1. Visual System

The visual system is multifaceted and complex; it includes the eyes, the connections between the retinal and brain regions, known as visual pathways, and multiple other parts of the brain briefly reviewed below (Figure 2.1, (Gray 1918)).

The image enters the eye through the cornea and the pupil, passes through the lens and the humours (transparent mass that comprises most of the eye's interior) and gets projected onto the photoreceptors on the retina at the back of the eyeball. The greatest density of photoreceptors is found on the fovea, a small section of the retina with a diameter of 1.5mm and covering less than 2° of the visual field (approximately equivalent to the size of the thumb nail at arm's distance) (Holmqvist et al. 2011; Ramamurthy and Lakshminarayanan 2015). Thus, in order to see a sharp, coloured image, the eye must move so that the light falls directly onto the fovea (Liversedge et al. 2011). In addition, the information coming into the cortex from the fovea is prioritised over the information from the rest of retina: about 25% of visual cortex processes just the central 2.5° of the visual scene (Holmqvist et al. 2011).

The information from the retina gets transported through the optic nerve first to three subcortical regions: the pretectum, the superior colliculus, and the lateral geniculate nucleus. The latter mainly serves as a router sending 90% of the information to the primary visual cortex (V1), which in turn projects information to the medial superior temporal visual area and the middle temporal visual area (V5) (Lencer and Trillenberg 2008; Ramamurthy and Lakshminarayanan 2015).

The eye movements are controlled by three antagonist pairs of extraocular muscles that allow rotations with three degrees of freedom: right or left, up or down, and clockwise or counter-clockwise. These six muscles are innervated by neurons in the nuclei of three cranial nerves located in the brainstem: the III (oculomotor), IV (trochlear), and IV (abducens). Cerebellum, basal ganglia, thalamus, posterior parietal cortex, and frontal cortex also contribute to eye movements (Liversedge et al. 2011).

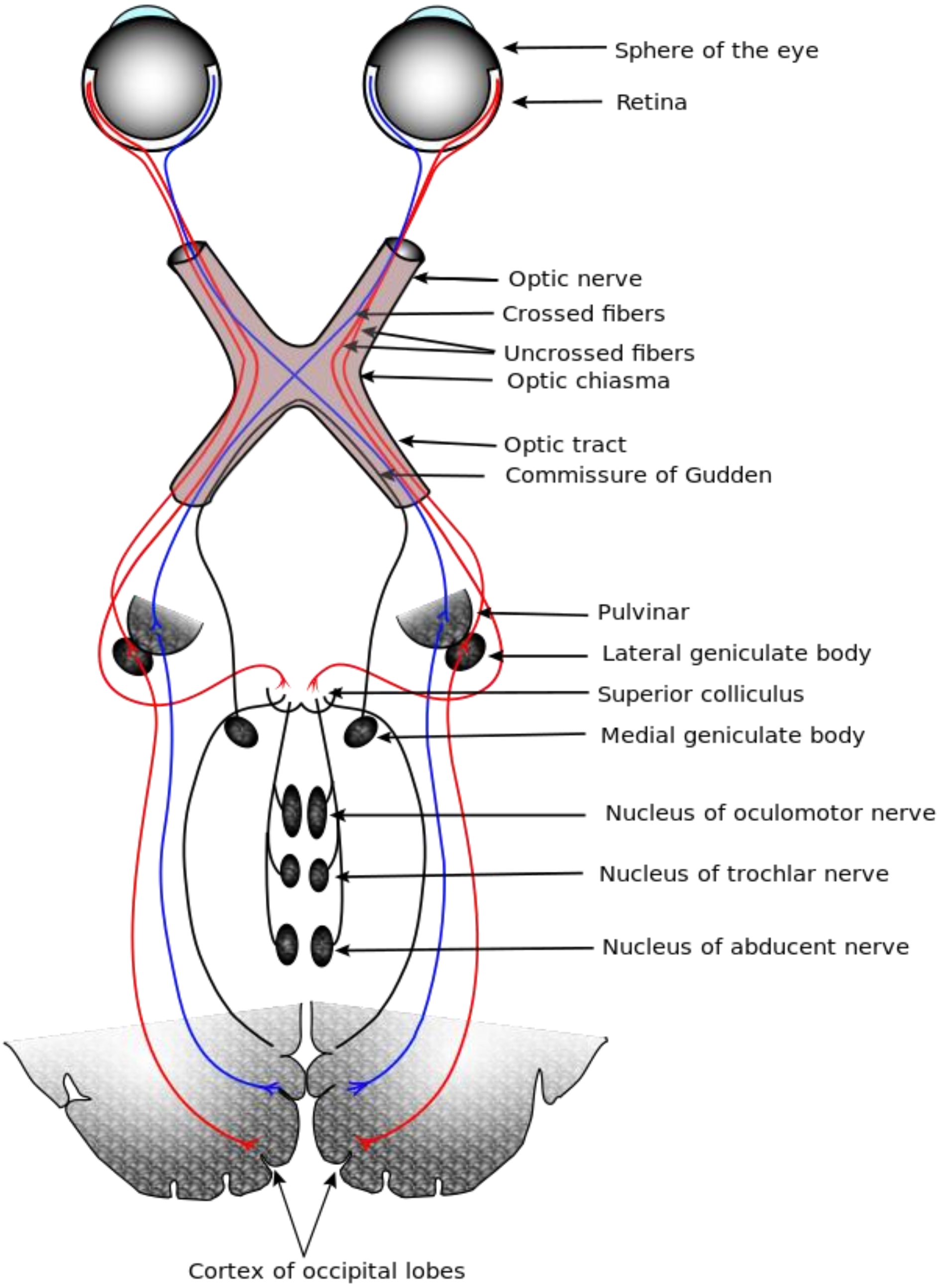


Figure 2.1. Visual system. © Gray 1918.

2.2.2. Types and Functions of Eye Movements

A major purpose of the eye movements is to reposition and stabilise a visual image in the fovea for prioritised processing. There are several types of such positional eye movements. The periods when the eye is held still are called fixations. The eye movements that shift gaze and thus redirect gaze to a certain object in the visual field include saccades, smooth pursuit, and vergence. The eye movements that are responsible for holding the images steadily in focus by compensating for head movements include the vestibulo-ocular reflex and the optokinetic reflex (Liversedge et al. 2011; Leigh and Zee 2015). While the vestibulo-ocular reflex and optokinetic reflex movements are three-dimensional, saccades and smooth pursuit eye movements are restricted to two dimensions and are therefore readily measurable with a computer-interfaced eye tracking device (Liversedge et al. 2011). Non-positional eye movements include vergence and accommodation, and serve the purpose of adapting to different distances and refocusing of the lens (Robinson et al. 1986; Duchowski 2003).

Fixations

A fixation is the state of the eye when the fovea is held still and stable over a stationary object of interest. While a fixation is technically not an eye movement, it requires active neural control – for example, pause neurons located in the pons fire steadily during a fixation in order to inhibit saccades (David 2012; Sussman et al. 2016). Moreover, fixations are typically characterised by miniature eye movements: tremor, drift, and microsaccades that aim to prevent the neural adaptation and thus the fading of the image (Duchowski 2003; Liversedge et al. 2011). During a fixation, the object of interest is cognitively processed by the participant (Holmqvist et al. 2011). In parallel, information obtained from the peripheral vision is compared to the top-down decision-making processes in order to determine the next fixation location (Liversedge et al. 2011). Importantly, the position of the eye during a fixation is controlled by the activity in such brain structures as superior colliculi and medio-posterior cerebellum, and their dysfunction would result in decreased fixation stability (i.e. the ability to maintain a steady gaze and inhibit unwanted saccades (Krauzlis et al. 2017)). Thus, poorer fixation stability has been associated with a range of neurological disorders and lowered attention control, whereas elite athletes demonstrate a better ability to maintain a steady gaze compared to the general population (Unsworth et al. 2019).

Saccades

A saccade is the fast movement of the eyes from one fixation to the next (a video showing an example of a saccade can be found at this link, Wikipedia Creative Commons licence BY-SA 4.0). The purpose of the saccade is to reposition the fovea on the object of interest (Leigh and Kennard 2004). Saccades are the most common eye movements and the fastest movement the body can produce (Liversedge et al. 2011). Saccades can have the duration between 30-100 ms, are fast (up to 500°/s), and usually have an amplitude of less than 20°; humans typically make around three saccades each second (Duchowski 2003; Ramat et al. 2006; Hutton 2008; Liversedge et al. 2011). Saccades with an amplitude of over 10° often undershoot the target and are therefore followed by a corrective saccade (Ramat et al. 2006).

During most of the saccade the visual processing is actively suppressed, otherwise the distortion of the eye's lens caused by the high velocity of the eyes would lead to very blurred vision (Hutton 2008; Liversedge et al. 2011).

Initially saccadic movements were deemed ballistic, implying that the destinations are pre-programmed and cannot be altered once the saccade to the next location has been launched. However, this theory has been replaced by the internal feedback model that assumes that the eye position during the saccade is continuously controlled and compared to an internal copy of the head, eye, and target position (Duchowski 2003; David 2012).

Several distinct neural regions contribute to saccades. The contributions of the cerebellum and brainstem are well understood. The cerebellum is responsible for steering and stopping the saccades, and the brainstem is responsible for generating saccades; in particular, the pons generates the horizontal component of saccades, the midbrain appears to control vertical and torsional components, and the superior colliculus seems responsible for selecting a target for foveation, initiating the movement and contributing to its speed (Ramat et al. 2006; David 2012).

A wide cortical network consisting of the parietal cortex, frontal and supplementary eye fields, visual cortex, and dorsolateral prefrontal cortex, seems to influence the top-down processes reflecting the goals and intentions of the observer and thus the decision whether a saccade should be made (Hutton 2008). This decision-making process may explain why the typical latency of a reflexive saccade is around 200 ms, whereas only 60 ms are required for the superior colliculus to receive the signal from retina and to generate a saccade to a specific location (Hutton 2008).

Saccades are often named according to their role in specific experimental designs; thus, one can differentiate between the pro-saccadic and antisaccadic tasks. The stimuli are often similar, but the instruction for the participants differs: In the pro-saccadic task, the participants are asked to look at the target, while in the antisaccades task, the participants are asked to look away from the target, at a mirrored location (Holmqvist et al. 2011).

Prosaccades can be further subdivided into voluntary and reflexive. Examples of voluntary saccadic paradigms are memory-guided saccades (i.e. eye movements directed towards remembered locations of objects without the presence of a visual stimulus (Kori et al. 1998)) or self-paced saccades that are usually made as fast as possible between two stationary targets in a fixed amount of time. The reflexive saccades occur in response to a sudden appearance of an object of interest. In the reflexive pro-saccadic and in the antisaccadic tasks usually two stimuli are employed: an initial fixation stimulus, and a target stimulus toward which the saccade should be made. These tasks can have three temporal conditions: Step (disappearance of the fixation stimulus is simultaneous with the appearance of the target stimulus), gap (there is a temporal interval between the disappearance of the initial fixation stimulus and the appearance of the target stimulus), and overlap (the fixation stimulus remains visible after the appearance of the target) (Reingold and Stampe 2002; Hutton 2008).

Antisaccades are voluntary saccades made in the direction opposite to the stimulus. An antisaccadic task tests the ability to suppress reflexive saccades to a novel visual target (this inhibitory function is controlled by the dorsolateral prefrontal cortex), and at the same time to initiate a correct antisaccade (controlled by the frontal eye field) (Pierrot-Deseilligny et al. 2004). An established way to assess antisaccades is described in the Internationally Standardised Antisaccades Protocol (Antoniades et al. 2013).

Smooth Pursuit Eye Movements

A type of eye movement where the eye follows an object moving smoothly across a stationary visual background, for example an airplane in the sky, by matching the eye velocity to the velocity of the object. Its purpose is to keep the image of the object in the fovea while it is moving, but not to statically fixate it (Robinson et al. 1986; Lencer and Trillenberg 2008; Larner 2011; Liversedge et al. 2011; Leigh and Zee 2015). Interestingly, it is also possible to pursue non-visible targets, for example a hidden part of an incomplete figure, or own finger in complete darkness (Barnes 2008; Lencer and Trillenberg 2008)

The initiation of the smooth pursuit is driven by visual feedback, while the maintenance relies on the internal feedback mechanism. Once the target starts moving, the eye does not immediately start to follow it. Instead, the first 100-150 ms constitute a pursuit initiation phase (also called open loop) where the eye executes a direct command to go to the new position, typically by initiating a saccade. After that a pursuit maintenance phase starts (also called closed loop) which is controlled by a combination of visual feedback about performance quality and the internal mechanisms that predict the target velocity (Lencer and Trillenberg 2008; Holmqvist et al. 2011; Liversedge et al. 2011). The position errors identified by the visual feedback are usually corrected with catch-up or anticipatory saccades (Lencer and Trillenberg 2008). The predictive mechanism allows to compensate for the delays in motion processing by storing velocity and timing information in short-term memory and calculating the anticipated position of the target (Robinson et al. 1986; Liversedge et al. 2011).

Several cortical regions contribute to the smooth pursuit eye movements. Middle temporal visual area (V5) is a core structure for smooth pursuit control. The frontal eye field transforms predictive signals into motor commands. The dorsolateral prefrontal cortex and the parietal eye field are responsible for monitoring and response selection, especially with non-predictable target movement. Beside cortical structures, the eye movement and visual information is processed in pontine nuclei and then sent to the cerebellum which regulates the initiation and maintenance of smooth pursuit (Lencer and Trillenberg 2008). The brainstem regions associated with suppression of saccades are also involved in smooth pursuit (Barnes 2008; Lencer and Trillenberg 2008).

Blinks

Normal spontaneous blink rate lies within the range of 0.1-0.8 blinks per second (4-48 blinks per minute), with an average of 0.2-0.3 blinks per second (Abusharha 2017; Groen et al. 2017) and a typical blink duration of 100-400 ms (Stern et al. 1984; Ousler et al. 2014). This is not only highly variable, but also much more frequent than would be necessary in order to simply fulfil the function of moisturising the eye (Groen et al. 2017). Researchers therefore believe that the eye blink rate and duration are influenced by a range of factors. First, blinks are linked to central dopamine activity. Longer blink durations and reduced blink rates have been consistently observed in Parkinson's disease (which is associated with the progressive reduction of dopamine activity in the striatum), whereas increased blink rates are characteristic for schizophrenia (which is linked to excessive dopamine activity in the striatum) (Karson et al. 1984; Peddireddy et al. 2006; Jongkees and Colzato 2016; Abusharha 2017). In addition, in a heathy population, blink duration and rates were found to be related to age (e.g. both increase from infancy to adulthood) and influenced by attentional demands and cognitive workload (Doughty 2001). Thus, longer blink durations have been associated with worse performance on the inhibitory control tasks (Colzato et al. 2009), fatigue and decreased vigilance (Ousler et al. 2014; Marandi et al. 2018). Finally, a relationship was found between blinks and inhibitory control, suggesting that saccadic suppression and blink suppression might have a common mechanism (Colzato et al. 2009).

Vestibular-Ocular Reflex (VOR) and Optokinetic Reflex (OKR)

The VOR allows the eyes to remain stable and compensate for head and body movement by moving the eyes in the direction opposite to the motion of the head. The OKR serves to stabilise the moving image when the head remains relatively stationary (Liversedge et al. 2011). There are several clinical and technological measures of the VOR and OKR functions, however, since these eye movements are not readily measurable with the utilised computer-interfaced eye tracker, their detailed analysis is omitted, although data from an eye tracker may complement VOR and OKR measurements.

Vergence and Accommodation

Vergence is the rotation of the eyes in opposite directions (usually towards or away from the nose) in order to fixate on the targets at different distances (Liversedge et al.

2011). Accommodation is the changing of the pupil size that allows focus on an object when its distance changes (Hunt et al. 2016). Since these eye movements are not readily measurable with the utilised computer-interfaced eye tracker, their detailed analysis is omitted.

2.2.3. Eye Tracking: Definition and Metrics

Definition

Eye tracking is the process of determining where someone is looking and analysing the characteristics of their eye movements (Mele and Federici 2012; Bojko 2013). Eye tracking evaluation can be un-instrumented (e.g. a clinician asking the patient to follow their finger) or instrumented, i.e. performed with a device such as an eye tracker, also referred to as camera-based eye tracking technology. Most commercial eye trackers work by emitting near-infrared light into the eye to create reflection patterns on the pupil and cornea (Figure 2.2). The camera of the eye tracker captures these patterns, and the underlying image processing software determines the relative positions of the pupil centre and of the centre of corneal reflection. When the eye moves in its orbit, the position of the corneal reflection stays the same relative to the eye tracker, whereas the position of the pupil changes. This allows precise calculation of how fast and to which positions the eye moves. The remarkable improvements in the development of eye tracking systems in the past decade allow researchers and clinicians to obtain accurate measurements with portable, nonintrusive devices that permit a certain freedom of head movement and do not require any programming skills (Mele and Federici 2012; Ting et al. 2014).

The eye tracker recording frequency, i.e. how many eye images are captured per second, vary from 30 Hertz (Hz) (usually sufficient to generally determine *what* was looked at) to 2000 Hz (used in fundamental vision science to measure, for example, microsaccades). The sampling frequency of 250 Hz has been identified as optimal for the current study, considering that eye trackers with a sampling frequency of 60 Hz or lower cannot reliably measure saccade peak accelerations, decelerations, or peak velocities for saccades smaller than 5° (Wierts et al. 2008). On the other hand, the sampling error rates (important for establishing reliability) seem to equalize at frequencies of 200 Hz, and the sampling frequency of 250 Hz was found to be almost identical to 1250 Hz in terms of detecting fixation and saccade durations (Shic et al. 2010).

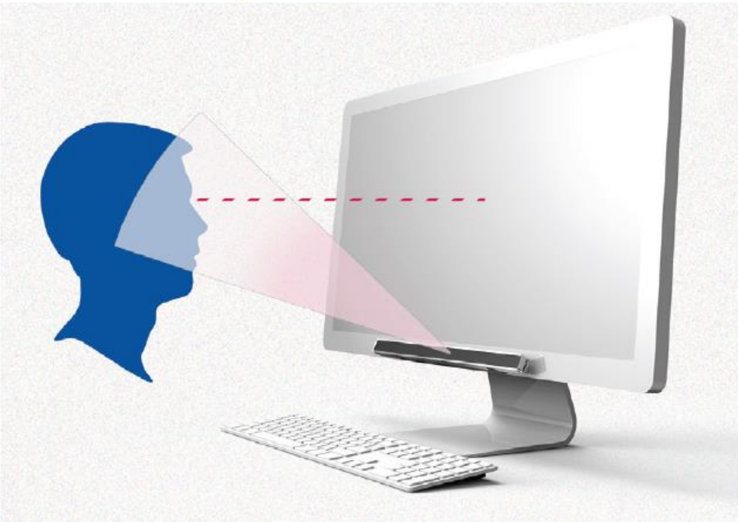


Figure 2.2. *Eye tracker attached to a monitor © SensoMotoric Instruments.*

Metrics

The eye tracking data are very rich in both spatial and temporal information, with over 120 measures that can be grouped into four main classes: movement, position, count, and latency (Figure 2.3 provides some examples of measures within each class) (Holmqvist et al. 2011).

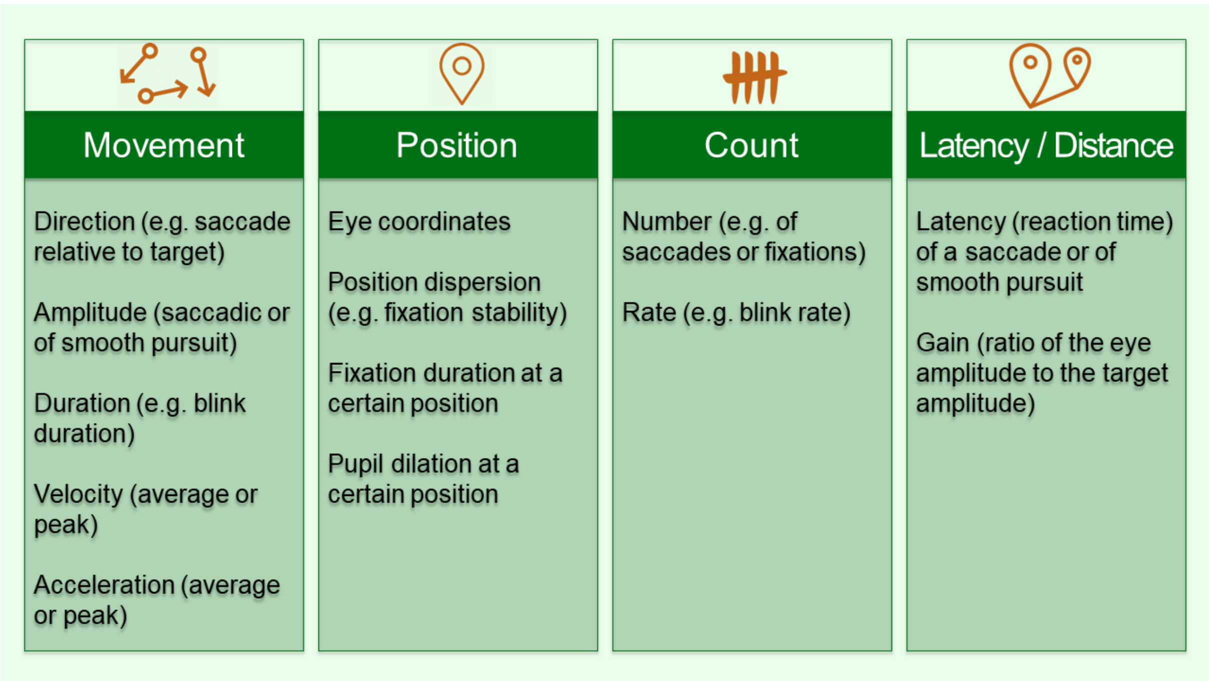


Figure 2.3. *Examples of eye movement metrics by class © Nadja Snegireva*

The measures of movement include amplitude, direction, duration, velocity, and acceleration (Holmqvist et al. 2011). Interestingly, a strong linear relationship exists between the saccadic amplitude and peak velocity, as well as between the amplitude and the duration of a saccade. This relationship is called *the main sequence*, and possibly is a representation of an optimal trade-off between the duration and the accuracy (Ramat et al. 2006; Liversedge et al. 2011). Saccadic velocity involves burst neurones in the brainstem, whereas saccadic amplitude depends on the basal ganglia and cerebellar circuits (Larner 2011).

The measures of position, apart from the basic eye coordinates, include the dispersion of the gaze data (which characterises the gaze stability and can be measured as the perimeter within which the gaze moves while it is supposed to stay steady), duration of fixations at a certain position, pupil dilation at a certain position, and often a comparison between two groups of positions (for example, fixations at sad versus happy faces in depression research) (Holmqvist et al. 2011).

The measures of count, such as the number of saccades or of fixations, can be expressed in absolute numbers or as a rate over time (for example, blink rate is the number of blinks per second) (Holmqvist et al. 2011).

Finally, measures of latency and distance measure certain eye tracking events in relation to other events. For example, saccadic latency is the time required for the participant to initiate a saccade after a target has appeared. Latency is highly variable, ranging from 100 ms to 1000 ms, most likely due to a combination of three factors: time to process the visual stimulus, accumulation of a decision process, and the final motor execution (Liversedge et al. 2011). Saccadic latency involves cortical and basal ganglia circuits (Larner 2011). Another typical measure is the gain, i.e. the ratio of the eye amplitude to the target amplitude. In smooth pursuit eye movements, whenever the gain falls substantially below the normal range of 0.9-1.0, a catch-up saccade is typically made to realign the target on the fovea (Barnes 2008; Lencer and Trillenberg 2008). In eye tracking studies, the latency (i.e. temporal distance, such as the delay between the stimulus and the response), and spatial distance (e.g. between the positions of the target and of the eye) are tightly coupled and therefore grouped together (Holmqvist et al. 2011).

2.2.4. Oculomotor Impairments Associated with Sports-Related Concussion

Vision involves approximately half of all human neural networks, including cortical, subcortical, cerebellar, and brainstem, that are strongly interconnected (Sussman et al. 2016; Ventura et al. 2016). Unsurprisingly therefore, there is a close relationship between impaired eye movements and organic dysfunction in the midbrain, cerebellum, pons, as well as various areas of the cerebral cortex (Ting et al. 2014; Yorke et al. 2017). A concussion can disrupt the function of both afferent (i.e. directed from the sensory system towards the brain) and efferent (i.e. directed from the brain towards the sensory/muscular system) neural pathways. Damage to the afferent system (which includes the optic nerve, white matter tracts, and the cortex) results in impaired acuity or visual processing functions that include visual attention, working visual memory, or visual discrimination (Cripps and Livingston 2015; Sussman et al. 2016; Yorke et al. 2017). The efferent system includes cranial nerves associated with eye movements and vestibular function, and its damage can manifest in smooth pursuit and saccades dysfunction (Sussman et al. 2016).

Several reviews provide insight into the eye movement dysfunctions associated with a concussion (both SRC and non-sports-related), as well as modalities for their assessment (Greenwald et al. 2012; Ting et al. 2014; Ventura et al. 2015b; Hunt et al. 2016; Kontos et al. 2017; Snegireva et al. 2018). Several further articles not following the format of a systematic literature review are also available (Thiagarajan et al. 2011; Singman 2013; Ciuffreda et al. 2014; Ventura et al. 2015a, 2016; Sussman et al. 2016). The main findings are summarised below.

Fixations

Concussion may manifest in a range of fixational dysfunctions, including increased fixational drift, saccadic intrusions, and nystagmus (Han et al. 2004; Kapoor et al. 2004; Ciuffreda et al. 2009). Concussed individuals may also be less accurate while fixating on a target between the saccades (DiCesare et al. 2017). Conversely, no differences in fixations between the concussed and control groups were found in another study (Gitchel et al. 2014).

Saccades and Antisaccades

Diffuse axonal injury caused by a concussion likely causes deficits in volitional saccades such as memory-guided saccades, self-paced saccades, and antisaccades, while likely leaving reflexive saccades unimpaired (Heitger et al. 2002, 2004, 2005). Patients with a concussion demonstrate directional errors in memory-guided and antisaccade tasks, as well as lower self-paced saccade count (Ciuffreda et al. 2009; Taghdiri et al. 2018; Hunfalvay et al. 2019).

A characteristic symptom of concussion is the inability of the patient to sustain uninterrupted attention (Pontifex et al. 2012), which, in turn, was found to correlate with response inhibition tasks, such as antisaccades (Unsworth et al. 2010). Increased antisaccadic latencies and errors have been reported in concussed adults (Heitger et al. 2006; Ettenhofer and Barry 2016), however a study conducted in youth population did not reveal any reduction in performance on saccadic tasks in the concussed group compared to the controls (Phillipou et al. 2013).

Smooth Pursuit

Both youth and adult athletes who sustained a concussion demonstrated range of impairments related to smooth pursuit: increased eye position error and worsened gain resulting in higher frequency of catch-up saccades, as well as variability of eye position (Suh et al. 2006; Caeyenberghs et al. 2009; Ciuffreda et al. 2009; Gitchel et al. 2014).

Pupil Dilation and Constriction

Inspection of the pupil and its reactions is an essential part of the standard neurological examination (Bremner and Smith 2001). The pupil light reflex is the dilation and constriction of the pupil that occurs involuntarily in response to changes in lighting. Pupillary responsiveness has been found to correlate with an increase in the intracranial pressure above normal levels (Taylor et al. 2003; Chen et al. 2011), one of the more severe consequences of concussion (Kelly and Rosenberg 1997; Killu and Coba 2014).

Blinks

Existing evidence suggests that concussion might reduce striatal dopamine levels (Chen et al. 2017; Jenkins et al. 2018), which, in turn, are associated with alterations in the spontaneous blink duration or rate (Jongkees and Colzato 2016; Groen et al.

2017). Despite this connection, as well as indications that brain injury may be associated with a reduced blink rate (Konrad et al. 2003; Brody 2014), with the exception of one study that found an increase in the blink rate of concussed youth athletes (without previously checking for this metric’s reliability) (Hecimovich et al. 2018), there seems to be no literature connecting eye blink duration or rate to SRC.

2.3. Eye Tracking Technology in Sports-Related Concussion

This chapter comprises the following published article:

Snegireva, N., Derman, W., Patricios, J., & Welman, K. E. (2018). Eye tracking technology in sports-related concussion: a systematic review and meta-analysis. Physiological measurement, 39(12), 12TR01.

2.3.1. Introduction

Concussion is a potentially serious and frequently occurring sports injury that has even been called a silent epidemic (Carroll and Rosner 2011; Marar et al. 2012). The incidence of concussion in sport has been estimated at 0.1 to 21.5 per 1000 athlete exposures, depending on the type of sport and methods of reporting (Clay et al. 2013). A widely cited report by the Centres for Disease Control and Prevention estimates that 1.6 to 3.8 million concussions occur in sports and recreational activities annually in the United States of America (Langlois et al. 2006). Due to no available objective assessment tool (to diagnose and monitor) for concussion, many sports-related concussions go undiagnosed and untreated, and subsequently may result in life-threatening conditions (Brewin 2017).

In recent years, research has differentiated between sports-related and non-sports-related concussions (Sojka 2011). In particular, sporting cohorts tend to have a higher probability of sustaining multiple concussions during their athletic careers, as well as the number of sub-concussive impacts (defined as the blows to the head that are below the symptom and force threshold and thus do not meet the criteria for clinical diagnosis of concussion, but possibly have an adverse long-term effect in some athletes (Shultz et al. 2012; Belanger et al. 2016)). Sports-related concussion research has also predominantly focused on determining when it is appropriate to return to play, as well as developing instruments for sideline assessment. Finally, with the sport population, it is possible (albeit not always feasible) to collect baseline data. Considering these specifics, it is reasonable to focus this review on the sports-related concussion rather than on concussion overall.

Even though the awareness of sports-related concussion has increased and management of this injury has evolved significantly, there is still no universally accepted tool to detect concussion and determine when it is safe to return to sport (Lynall et al. 2013; Kenzie et al. 2017). This is further aggravated by the fact that the athletes are often young, motivated individuals who sometimes tend to under-report symptoms and deliberately underperform in the baseline tests (Register-Mihalik et al. 2013; Kroshus et al. 2015; Scolaro Moser and Schatz 2017; Wallace et al. 2017). In 2016, the Berlin Consensus Statement (McCrory et al. 2017a) declared that there is a need for more objective indicators such as diagnostic biomarkers to assess the presence and severity of sports-related concussion in athletes.

The prevalence of eye movement deficits, specifically oculomotor, in acquired brain injury (concussion is a subset thereof) ranges from 40% to as high as 90% (Kapoor et al. 2004; Ciuffreda et al. 2007; Hunt et al. 2016). Unsurprisingly, therefore, eye tracking, a technology for detecting eye movements and analysing visual information processing (Mele and Federici 2012), has been increasingly gaining attention as a possible assessment and monitoring tool.

Ocular motion is controlled by only three sets of oculomotor muscles, but the computation and generation of eye movements involves several neural pathways including the cerebrum, brainstem, and cerebellum, and damage to any of these areas would affect certain types of eye movements (Wilcockson 2018). Moreover, each region of the cortical network that regulates the eye movements has anatomical connections to other brain regions (Ting et al. 2014). Therefore, a close relationship exists between eye movement generation and dysfunction in the brain (Ting et al. 2014). A concussed patient may suffer from several visuo-motor processing impairments that include components of visual attention, working visual memory, visual discrimination, and selective attention (Cripps and Livingston 2015). All this potentially makes eye tracking technology a viable concussion assessment tool.

This review specifically focused on the eye tracking technology-supported assessments, thus excluding other tools such as the King-Devick test (Galetta et al. 2011), as well as EEG or MRI-based measurements. The underlying reason is practical: camera-based eye tracking technology is accurate, objective and un-intrusive (Duchowski 2003; Mele and Federici 2012; Ting et al. 2014); in addition, recent hardware and software developments suggest that the device-embedded cameras are becoming capable of providing data of sufficient quality for reliable and valid eye tracking assessments (Bott et al. 2018; Semmelmann and Weigelt 2018). This implies that high precision eye tracking tests may soon be possible without any additional hardware other than a computer, or even a smartphone, thus making them feasible in many practices.

Several literature reviews covering sports-related concussion diagnostic tools are available (Broglio and Puetz 2008; Dziemianowicz et al. 2012; Marshall 2012; King et al. 2014; Maher et al. 2014; Murray et al. 2014b; Okonkwo et al. 2014; Papa et al. 2015; Valovich McLeod and Hale 2015; Yengo-Kahn et al. 2015, 2016b), however, none has yet specifically focused on eye movement assessments or eye tracking technology. At the same time, to the authors' knowledge, there are several recent reviews that cover oculomotor based concussion assessments (Greenwald et al. 2012; Ting et al. 2014; Ventura et al. 2015b; Hunt et al. 2016; Taghdiri et al. 2017; Mani et al. 2018), however, the clinical setting of all of them is far broader than that of the current study both in terms of mechanism of injury (i.e. the study populations included not only sports-related concussions but also car accidents, domestic falls, military and blast-induced injuries), and in terms of research instrumentation (not only eye tracking technology-supported assessments, but also such tests as King-Devick, or an evaluation by an optometrist). None of these reviews attempted a meta-analysis. There also are several articles providing an overview of concussion-related oculomotor dysfunction and measurements thereof, which do not follow the formal structure of a systematic literature review (Thiagarajan et al. 2011; Singman 2013; Ciuffreda et al. 2014; Ventura et al. 2015a, 2016; Sussman et al. 2016). Consequently, this review set out to appraise the existing literature on eye tracking as an assessment and monitoring tool for sports-related concussion.

2.3.2. Methods

Objectives

This is a systematic review with a primary focus on identifying key variables, measures and analysis methodology utilised by researchers to date. Research outcomes and their practical application constitute a secondary focus of the review. The purpose of the study is to provide a systematic synopsis of all empirical evidence related to sports-related concussion diagnostics and eye tracking, as well as to highlight the limitations and viability of eye tracking technology for concussion assessment.

Protocol

The review as a whole is organised methodologically, while the findings are grouped by concepts (Randolph 2009). Two independent reviewers (NS and KW) used the 'Preferred Reporting Items for Systematic Reviews and Meta-Analyses' (PRISMA) (Moher et al. 2015) guidelines for systematic reviews and 'Meta-analysis of Observational Studies in Epidemiology' (MOOSE) (Stroup 2000). These checklists include the specifications for the conduct and review of the included studies.

An exhaustive search of literature using Google Scholar, Microsoft Academic and PubMed was conducted in an effort to identify all relevant studies, which included keyword searches in the database, and further the ancestry and descendancy approach.

Eligibility criteria

Publications that corresponded to all inclusion and exclusion criteria summarised in Table 2.1 were included in the review.

Table 2.1. Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
Articles in peer-reviewed journals, conference presentations or indexed dissertations, provided the availability of full texts or sufficient information	Non-empirical studies, i.e. literature reviews, retrospective records analyses, qualitative study designs
Research included measurement of eye movements (such as saccades, fixations or smooth pursuit) or of the pupil size using an eye tracking device (e.g. video-based infrared system, saccadometer)	Studies where the eye movements were assessed with a King-Devick test, or a visual examination by an optometrist, as well as attention tests and event-related potentials (ERP) measurements
Published in the period between January 1980 and May 2018	
Available in English language	
At least 50% of the research participants were athletes	
Participants included individuals with a diagnosis of concussion or mild traumatic brain injury (mTBI)	

Search and selection

As a first step, Google Scholar, Microsoft Academic and PubMed were searched for articles containing combinations of relevant keywords (Table 2.2) and published between January 1980 and May 2018. A cut-off year of 1980 was selected because the technological improvements that took place around this time allowed for more accurate and non-intrusive eye tracking measurements. This led to the so-called third era of eye tracking research that focused on using eye movements to infer cognitive processes (Rayner 1998).

The keywords were grouped into three sets: concussion-related, eye tracking-related, and sports-related, and search for articles containing one or more words from each set was executed. The search yielded a total of 10103 articles. The electronic database search was followed by examination of titles and meta-data of the articles, and, in cases of uncertainty, of abstracts, whereby the articles that did not meet the inclusion and exclusion criteria were eliminated. The remaining results underwent a full-text scrutiny. In cases where not all necessary information (such as mechanism of injury, in order to identify the proportion of sports-related concussions) was reported in the text, the corresponding authors were contacted for clarification. In accordance with the ancestry approach, the reference lists of all relevant articles then underwent the same examination of titles and abstracts. Lastly, in accordance with the descendancy approach, references to the selected articles were entered into Google Scholar, and the "cited by" function was used in order to identify later studies referencing this work. The newly found articles were added to the list and were subjected to a full-text inspection, where the articles that did not meet the in- and exclusion criteria were eliminated from the review.

The meta-analysis included only the studies that contained sufficient data to determine the effect sizes or, if these data were subsequently provided by the authors, via correspondence. The variables that were reported in two or more independent studies were included in the meta-analysis. The variables that were reported in less than two studies, as well as the studies with insufficient data for the meta-analysis, were included in the narrative part of this systematic review.

Table 2.2. Search keywords.

Eye tracking-related	Concussion-related	Sports-related
eye movement	closed head injury	athlete
eye tracker	concussion	baseball
eye tracking	mild traumatic brain injury	basketball
gaze tracker	mTBI	boxing
gaze tracking		football
oculomotor		hockey
pupil dilation		lacrosse
pupil size		rugby
pupillometer		soccer
pupillometry		sport
saccade		volleyball
saccadometer		wrestling
saccadometry		
smooth pursuit		
visuomotor		

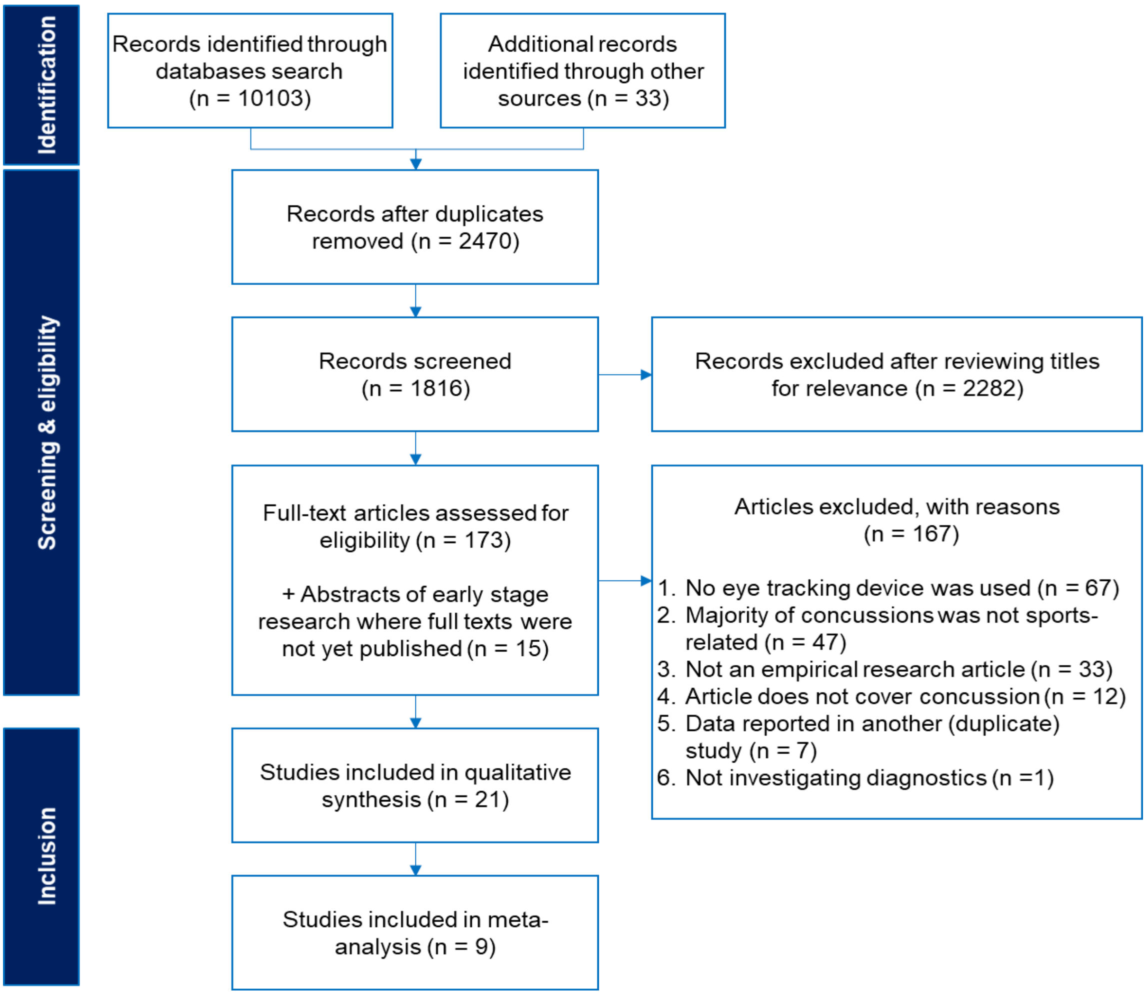


Figure 2.4. PRISMA flow chart describing the selection and exclusion of articles.

The flow diagram in accordance with the PRISMA guidelines (Moher et al. 2015) is presented in Figure 2.4, including the reasons for exclusion at the full-text scrutiny stage.

Data extraction

Data extraction was performed independently by two authors (NS and KW) with differences of opinion resolved by discussion or by consulting the other authors (JP or WD). The data extraction forms were developed using the *checklist of items that should* be included in reports of case-control studies contained in the 'Strengthening the Reporting of Observational Studies in Epidemiology' (STROBE) guidelines (Elm et al. 2007; Vandenbroucke et al. 2007). When data of interest were not reported in the text of the articles, respective corresponding authors were contacted.

Effect sizes for the meta-analysis were calculated using the Review Manager (RevMan, version 5.3) program endorsed by the Cochrane Collaboration (Higgins et al. 2011). RevMan's standardised mean difference (SMD, which is known in social science as Hedges' adjusted *g* (Cochrane 2014)), 95% confidence intervals (CI), and the fixed effects model were used. The statistical significance level was set at $p < 0.05$.

Assessing the quality of studies and risk of bias

Evaluation of the quality of all included articles was performed using the NIH Quality Assessment Tool of Case-Control Studies (National Heart Blood and Lung Institute 2005). The risk of bias was assessed with a relatively new Risk of Bias Assessment Tool for Nonrandomised Studies (RoBANS) (Kim et al. 2013), which is harmonised with the Cochrane's Risk of Bias tool. It does not allow computing a score; however, it is particularly useful when examining observational, non-randomised studies, such as those included in the current review. Two authors (NS and KW) independently assessed the studies using the judging criteria adapted from the Cochrane Handbook for Systematic Reviews of Interventions (Higgins et al. 2011). The results were then compared, and differences resolved in a discussion or in consultation with the other authors (JP or WD).

2.3.3. Results

This systematic review integrated 21 publications on sports-related concussion and eye tracking technology. Of them, nine articles with total 437 participants (concussed n = 160, controls n = 277) qualified for the meta-analysis.

Details of included studies

Seventeen studies used a case-control study design, and four compared the concussed participants' values to their own baseline (Pearson et al. 2007; Brewin 2017; Kelly 2017; Taghdiri et al. 2018). With the exception of Pearson et al (2007) who tested the boxers directly after a boxing bout, there was no sideline testing, and all tests were conducted in laboratory or similar settings. That was likely for practical research reasons, participant recruitment procedures, as well as the fact that the eye tracking technology uses infrared light to precisely identify the position of the eye pupils and may therefore be affected by the strong sunlight if used outside.

The time that passed after a concussion at the moment of testing varied considerably – from 24 hours to over 30 years (Table 2.3). Therefore, in this analysis, the studies were divided into two groups: acute concussion (testing took place on average up to one month after the injury, n = 11 studies) and latent concussion (testing took place on average five months and more after the injury, n = 7 studies). None of the studies fell in the mid-range (testing at more than one and less than five months after the injury on average). Three studies did not report how much time had elapsed since the injury at the moment of testing.

Four studies conducted more than one testing session: Pearson et al. (2007) tested participants right before and right after a boxing bout, and again "days after" the bout, Drew et al. (2007) ran four testing sessions at the following intervals: 2 days, 1 week, 2 weeks, and 1 month after the injury; Johnson et al. (2015) conducted the first test within 7 days after the injury and a second one at 30 days post-injury; finally, Webb (2017) tested the concussed participants at 2-6 days post-injury and repeated at 14-20 days for those cleared to return to play.

The sampling frequency of the eye tracking devices used in the analysed studies varied from 60 Hz to 500 Hz (Table 2.3) and no relationship was found between the significance of findings and sampling frequency. It has been shown previously that eye trackers with a sampling frequency of 50/60 Hz cannot obtain saccade peak accelerations and decelerations, or measure peak saccade velocities for saccades smaller than 5° (Wierts et al. 2008). In addition, a study by Andersson et al. (2010) has established that the sampling frequency of 250 Hz is almost identical to 1250Hz in terms of detecting fixation and saccade durations, while at 50Hz the measures diverge (Andersson et al. 2010). Finally, at 200 Hz or above, there is little marginal benefit of higher sampling frequencies with regard to reducing sampling errors (which are important for correct measurement of saccadic latencies) (Andersson et al. 2010).

Table 2.3. Details of studies included in the systematic review and meta-analysis.

Study ID	Subjects, n (% of athletes)	Mean age of CP	Time after concussion	Device & sampling frequency
Brewin 2017	n/a CP (100%) own baseline	n/a	n/a	n/a
D'Amico 2016#	10 CP (100%) 10 HC (100%)	18.9 ± 0.9	1-2 days (AC)	ASL 7, 240 Hz
Danna-Dos-Santos 2018#	36 CP (56%) 36 HC (n/a)	26.6±9.2	43.1±52.5 months (LC)	VEST, 100 Hz
DiCesare 2015#	17 CP (100%) 17 HC (n/a)	16.8±1.2	7.7±4.7 days (AC)	Tobii X2, 60 Hz
Diwakar 2015#	25 CP (52%) 25 HC (n/a)	32.7±11.2	31.8±18.3 years (range 3-65) (LC)	EyeLink 1000 (MEG), 500Hz
Drew 2007	20 CP (100%) 20 HC (100%)	21.0±1.7	37.0±11.5 hours; follow-up 1 week, 2 weeks, 1 month (AC)	Iris Skalar, 200 Hz
Evans 2016	26 CP (100%) 100 HC (n/a)	17.6±4.8	32.9±37.2 days (AC)	n/a
Heitger 2002#	30 CP (50%) 30 HC (n/a)	22.2±7.1 (15-37)	4.2±1.8 days (range 2-9) (AC)	Iris Skalar, 200 Hz
Johnson 2015#	9 CP (100%) 9 HC (n/a)	18-21	within 7 days; follow-up 30 days (AC)	Arrington (MRI), 60 Hz
Katrahmani 2018	12 CP (83%) 12 HC (n/a)	16-18	n/a	Tobii Pro Glasses 2
Kelly 2017	98 CP (100%) 2736 HC (100%)	n/a	n/a	EyeGuide Focus, 60Hz

Table 2.3 (continued)

Study ID	Subjects, n (% of athletes)	Mean age of CP	Time after concussion	Device & sampling frequency
Ledwidge 2017#	21 CP (100%) 24 HC (100%)	20.2±1.6	4.1±3.9 years (0.8-12.5) (LC)	ICS Chartr 200, 250 Hz
Maruta 2014#	13 CP (70%) 127 HC (n/a)	19.6 (13-41)	within 2 weeks (AC)	EyeLink CL, 500 Hz
Mullen 2016#	23 CP (100%) 23 HC (100%)	college age	n/a (LC)	EyeLink
Murray 2014#	9 CP (100%) 9 HC (100%)	16.0±3.1	48–72 hours (AC)	ASL H6, 120 Hz
Pearson 2007	1 CP (100%) 12 HC (100%)	n/a	minutes before and after match (AC)	OBER saccadometer
Poltavski 2014	17 CP (100%) 25 HC (100%)	20.5 (18-23)	12+ month (LC)	Visagraph
Richard 2009	21 CP (100%) 15 HC (n/a)	20.0±2.1 AC, 22.2 ±2.9 LC	5.3±1.2 days (AC); 1.7±0.7 years (LC)	EyeLink CL, 500 Hz
Samadani 2017	56 CP (50%) 83 HC (n/a)	13 (range 4-21)	22 weeks (LC)	EyeLink 1000, 500 Hz
Taghdiri 2018#	59 CP (86%) 0 HC	33.37±13.9	25.9±63.6 months (LC)	VAST, EL-MAR Inc
Webb 2018#	15 CP (100%) 15 HC (n/a)	range 21-26	2-6 days; follow-up 14-20 days for those cleared to RTP (AC)	ASL Eye-Trac6, 460 Hz

Notes: #: the study was included in the meta-analysis; AC: acute concussion; CP: concussed participants; HC: healthy controls; LC: latent concussion; n: sample size; n/a: not available; RTP: return-to-play

The experimental designs of the reviewed articles included six types of eye tracking tests: smooth pursuit (10 studies), self-paced saccades (5 studies), reflexive saccades (8 studies), memory-guided saccades (2 studies), antisaccades (4 studies), and fixations (4 studies) (Tables 2.4 and 2.5)). Some researchers opted to analyse only one type of eye movement: smooth pursuit (Maruta et al. 2014; Diwakar et al. 2015; Evans et al. 2016; Kelly 2017; Katrahmani and Romoser 2018), self-paced saccades (Brewin 2017; Taghdiri et al. 2018), reflexive saccades (Drew et al. 2007; Pearson et al. 2007), or memory-guided saccades (Heitger et al. 2002). Other researchers used a combination of two or more eye tracking tests (Richard et al. 2009; Johnson et al. 2015a; Mullen et al. 2016; DiCesare et al. 2017; Ledwidge et al. 2017; Danna-Dos-Santos et al. 2018; Webb et al. 2018). While a search was also conducted for the technology-supported pupillometry in concussed athletes, no such studies were found.

Smooth pursuit eye movements hold the image of a moving target (or of a static target during self-motion) in focus (Larner 2011). In the analysed studies, the smooth pursuit eye movements were tracked in a variety of conditions: based on the trajectory (circular trajectory vs. horizontal (or in one case vertical) sinusoidal pattern), the target velocity (ranging from 30°/s up to 360°/s, kept steady or changing randomly), and the visibility of the target (always visible in the continuous condition or disappearing at specified or random intervals in the gap condition).

Saccades are often named for their role in specific eye movement paradigms, such as self-paced saccades, reflexive saccades (also referred to as prosaccades), antisaccades, or memory-guided saccades (Holmqvist et al. 2011). The saccades can be performed either voluntarily (e.g. when a participant is asked to look to the left without moving the head) or reflexively (e.g. when an object suddenly appears in the visual field attracting the participant's attention) (Larner 2011). The term reflexive saccades is commonly used in the eye tracking literature to differentiate this type of eye movement from the voluntary eye movements towards e.g. a remembered or imagined location (Leigh and Zee 2015).A range of saccadic tracking paradigms was used in the reviewed studies. The highest number of articles (n = 8) reported using a reflexive saccade paradigm either in the "step" condition, where the target was shown at one position for a certain (sometimes randomised) period of time, and then stepped to a new position, or in the "gap" condition where a temporal interval was introduced between the disappearance of the first and appearance of the next stimulus. In all studies, the position changes occurred only horizontally. Significant differences between the concussed and control group participants in the reflexive saccade latency were found by DiCesare et al. (2015), Drew et al. (2007), Pearson et al. (2007), Danna-Dos-Santos et al. (2018), and to some extent by Webb (2018). In addition, two studies found that the concussed participants made more positional (DiCesare et al. 2017) or directional (Webb et al. 2018) errors.

A self-paced saccade paradigm was utilised in five studies, in all of which the participants were asked to look as quickly as possible back and forth between two targets displayed at a predefined distance (e.g. 10°) from each other on a horizontal plane. The findings varied: while two studies (Johnson et al. 2015a; Brewin 2017) saw significantly lower number of saccades made by the concussed participants, the other three studies (Richard et al. 2009; DiCesare et al. 2017; Taghdiri et al. 2018) reported that the difference in the number of saccades was not significant.

Only two studies used the memory-guided saccades paradigm, where the targets moved to a predefined successive horizontal position, and the participants were asked to reproduce the sequences from memory by looking at the corresponding positions on the blank screen. Both of these studies found statistically significant differences between the concussed and control participants in most metrics (Heitger et al. 2002; Johnson et al. 2015a).

In the current review, the antisaccades were assessed in four studies which can be split into two heterogeneous groups: One research team ran two separate studies assessing only the fixation stability, i.e. an ability of the participants to maintain their eye gaze fixated on a central target while performing a set of balance tasks (playing a Wii game) (Murray et al. 2014a; D'Amico 2016). In both studies the concussed group made significantly more directional errors. The second group encompasses two classical antisaccades studies where the participants were asked to fixate on the mirrored positions of the target presented at a random distance from centre on a horizontal plane. These studies found that the concussed group performed worse on several metrics, including saccadic latency and the number of position errors (Johnson et al. 2015a; Webb et al. 2018).

The literature analysed in the current review reported statistically significant findings for variables in each of the four classes of eye tracking measurements (i.e. measures of movement, position, count, and latency) as suggested by Holmqvist and colleagues (2011) (Table 2.6). However, despite such considerable overlap in the reported measurements, the eye tracking paradigms used for experimental design varied, thus making a meta-comparison possible only in a handful of cases.

Table 2.4. Experimental design and results reported in the included studies.

Study ID	Eye tracking task description	Eye tracking results
Brewin 2017	n/a	Greater number of multi-saccade gaze shifts in CP (p n/a)
D'Amico 2016#	Fixate centre of the screen while performing a dynamic balance task (practice trial & 2 experimental trials á 1 min)	Greater number ($p < 0.001$), duration & average duration ($p = 0.003$ for both) of gaze deviations from centre in CP
Danna-Dos-Santos 2018#	SP: Follow a target moving in a horizontal sinusoidal pattern; velocity 0.1Hz, magnitude of 20° (−10° to 10°). RS: 29 targets presented horizontally at 2°-35° in right and left directions for 3s	SP: CP less accurate in following the target ($p = 0.029$), larger presence of intrusive saccades ($p < 0.0001$). RS: lower accuracy in the initial phase of the saccadic movement ($p < 0.05$) in CP. Longer time to initiate the saccadic movement (Reaction Time Saccade) in CP ($p < 0.05$). No asymmetries between right and left eyes were found within any of the groups ($p > 0.05$)
DiCesare 2015#	SP: Follow a target moving in a horizontal sinusoidal pattern, velocity 90°/s, 180°/s or 360°/s or randomly changing. RS: Look at the target changing horizontal position (magnitude 4°-10°, displayed for 1-2s), 2 trials á 30s. SPS: Look back and forth at 2 static targets (8° apart), 2 trials á 30s.	Higher fixation and initial fixation errors for RS ($p = 0.006$ and $p = 0.022$, respectively) and SPS ($p = 0.002$ and $p < 0.001$, respectively) in CP. Higher saccade latency for RS ($p = 0.003$) in CP. SP: increased phase lag times of the 180°/s, 360°/s ($p < 0.001$ for both) and random pursuit conditions ($p = 0.013$) in CP. Lower tracking angular velocity for the 180°/s condition ($p = 0.013$) in CP
Diwakar 2015#	Follow a target moving in a circular clockwise pattern (radius 10° at 0.4 Hz), in two conditions: continuous (target always visible) and gap (target visible for a random interval of 1250-3250ms, then disappears for 30°, 45° or 60°). Each condition á 10 trials (=revolutions of the target; 2.5s per trial), repeated 3 times	No significant differences between CP and HC in the continuous tracking condition. In the gap condition, higher average radius during the pre-gap ($p = 0.01$) and the within-gap ($p = 0.02$) time windows for CP. Greater negative average phase during the post-gap 1 ($p = 0.05$) and post-gap 2 ($p = 0.02$) time windows in CP. Fewer months post-injury correlated with a larger within-gap average radius ($p < 0.05$). In the 30° and 45° gap conditions, longer time to synchronise with the target after its re-appearance ($p < 0.05$ for both) in CP

Table 2.4 (continued)

Study ID	Eye tracking task description	Eye tracking results
Drew 2007	Fixate central target for 400-1600ms, then look at the new target appearing at 5° or 10° to the left or right from centre. Two conditions: gap (temporal interval (50, 100, 150, 200, 250, or 300 ms) inserted between the disappearance of central and appearance of lateral target) & no-gap. 10 practice trials & 8 blocks of 29 lateral targets	During the first visit, CP overall slower than HC ($p < 0.0001$). Significant gap effect for both CP and HC ($p = 0.011$) due to faster reaction times during trials with 150 and 200 ms gaps compared to 0 and 50 ms gaps. Reaction times slower in CP for the shortest gap durations (0–100 ms), but similar between CP and HC at the longer gap durations (150–300 ms)
Evans 2016	Follow a target moving on a 180° arc trajectory. 10 trials of 4 conditions including combinations of target speed and visibility. During the invisible condition the target disappeared after 60° of arc and the participant predicted when the target would arrive at the optical goal	Increased mean error during the visible-fast ($p < 0.01$) and invisible-fast ($p < 0.05$) conditions in CP. No detectable performance differences for slow targets
Heitger 2002#	Target appeared in the centre of the screen, then jumped to 2/3 successive pseudo-random positions 5° or 15° to the left or right from centre, then returned to centre. 6 sequences á 3/5 times, after that subject repeated the sequence in darkness	More directional errors in the 3-step sequences (10.4% vs. 2.6%, $p = 0.003$) but not for 2-step sequence in CP. Poorer spatial accuracy on final eye position in both 2- and 3-step sequence as measured by position error ($p = 0.001$ and $p = 0.006$, respectively) in CP. Comparison of individual steps showed larger position and amplitude errors on all steps for 10°, 15°, and 20° amplitudes ($p < 0.05$) in CP. Increased position errors were matched by abnormally large final saccade gains (2-step: $p = 0.02$, 3-step: $p = 0.019$). The difference between CP and HC was more pronounced for smaller target amplitudes

Table 2.4 (continued)

Study ID	Eye tracking task description	Eye tracking results
Johnson 2015#	SP: Track stimulus moving for 40s in a predictable sinusoidal pattern with peak velocity 40°/s; circular pattern with 12° visual arc as radius and 30°/s tangential velocity; random horizontal pattern with peak velocity 60°/s. Fixation task: look at the target for 30s. RS: Follow quickly and accurately 44 targets presented randomly at 0°, 5°, 10°, 15° from centre. AS: Look to the mirrored position of 32 targets presented randomly at 5° and 10° from centre (avoid looking at targets). MGS: Repeat a sequence on blank screen (6 sequences á 3 steps á 5 times). SPS: Look back and forth at 2 static targets (±15° from centre) for 30s	AS: LC cohort of CP showed improvement from their previous lag of 40 ms in the AC phase (p = 0.04), but no significant difference to HC. More directional and position errors (p = 0.001 and p = 0.02, respectively) in CP; reduced from AC to LC (p = 0.03 for both). Same trend for primary and final eye gain (LC vs HC p = 0.01 and p = 0.05, respectively; AC vs LC p = 0.05 and p = 0.2). Increased mean number of SPS for CP in LC phase (p = 0.03) despite still being lower than HC (p = 0.01). MGS: reduction in directional and position errors in LC compared to AC (p = 0.002, and p = 0.02, respectively), but still significantly higher than HC (p = 0.03 for both). No significant differences were seen for the other 4 tasks tested
Katrahmani 2018	Follow a moving target; trace the outline of an object	Difficulties in acquiring and following objects as well as with tracing the outlines of objects with their eyes in CP (p-value n/a)
Kelly 2017	Follow the target moving in a circular pattern through one cycle of a "lazy 8" path for 10s	Baseline scores lower than in CP (p = 0.001)
Ledwidge 2017#	SP: Follow a target moving in a sinusoidal pattern with a max subtended arc of 30° with frequency sweeps 0.2-0.7 Hz, 3 trials á 50s. RS: Look at the target presented at random horizontal positions at a distance 5°-30° at intervals 1.5-2s for a total of 80s (total 60 targets).	CP and HC did not significantly differ on all measures (p > 0.05)

Table 2.4 (continued)

Study ID	Eye tracking task description	Eye tracking results
Maruta 2014#	Follow a target moving in a circular clockwise pattern (radius 10° at 0.4 Hz in a continuous condition (target always visible); 2 runs á 15s)	More radial errors, higher standard deviation of tangential errors, higher horizontal gain, higher vertical gain ($p < 0.001$ for each), higher mean radius and mean phase ($p = 0.003$ for each) in CP. Increased gaze position error variability, reduced radius of gaze trajectory, phase leading, and reduced smooth pursuit velocity in CP. Although statistically significant, the decrease in mean radius was only by 2% and did not explain the larger decrease in velocity gains. Within 8 adolescent CP, none of the visual tracking indices showed a significant linear dependence on age ($0.10 < p < 0.64$)
Mullen 2016#	RS: Fixate a central target while a peripheral target flashed briefly. After a short time, look to the location of the flashed target	Slight differences in saccadic accuracy for high impact vs. low impact CP, with high impact having increased hypometria
Murray 2014#	Fixate centre of the screen while performing a dynamic balance task (practice trial & 3 experimental trials á 3 min)	Greater number of gaze deviations from centre ($p < 0.001$) in CP
Pearson 2007	Follow the central target that, after a random delay of 0.5-1.5 s, jumped randomly 10˚ to the left or right. 240 targets, total duration approximately 8 min	9 boxers showed a latency distribution alteration after their bout ($p < 0.05$); in 6 boxers the median latency was increased ($p < 0.05$); in 4 boxers with greatest post-fight latency increases seemed to have experienced more head, one being deemed concussed at the time (34 ms, $p < 0.01$). In these 4 boxers, the shift was transient and reversible, with recovery over a few days to a median latency not significantly different from pre-fight values
Poltavski 2014	Reading task	Longer fixation duration ($p = 0.02$) in CP

Table 2.4 (continued)

Study ID	Eye tracking task description	Eye tracking results
Richard 2009	SP: Follow a target moving in a circular or a horizontal sinusoidal pattern. SPS: look back and forth between two targets displayed at 5° and 10°.	SPS: in the 10° condition, longer fixations ($p < 0.05$) in AC compared to HC. In the 5° condition, greater saccadic amplitude in AC compared to HC ($p < 0.05$). SP: larger saccadic amplitude in the fast horizontal and the slow clockwise task ($p < 0.05$ for both) for AC compared to HC
Samadani 2017	Watch a 220-s video as it rotated clockwise around the periphery of a monitor	12 metrics significantly different between Cp and HC (details n/a). A model built on a balanced sub-sample to classify concussion based on eye tracking achieved an AUC of 0.854 (sensitivity 71.9%; specificity 84.4%)
Taghdiri 2018#	Look back and forth at two static targets (±10° off-centre in the horizontal dimension) as many times as possible in 40s	No significant relationship between the number of saccades with the self-reported number of concussions ($p = 1.00$). However, a negative correlation existed between the number of saccades with the total number of symptoms ($p = 0.026$)
Webb 2018#	Look at the central fixation point, then at the target (RS) or to the mirrored position (AS) presented for 50ms at horizontal eccentric positions (4 trials á 10 targets for prosaccades, same for antisaccades)	Longer latency of AS for HC at the initial assessment ($p < 0.001$), but not at the follow-up. The coefficient of variation of latency values for both types of saccades at the initial assessment were larger for CP than for HC ($p < 0.001$), whereas at follow-up values were smaller for CP than for HC ($p < 0.001$). More RS and AS directional errors in CP at initial and follow-up assessment ($p < 0.05$ for each). Lower AS gains for CP ($p < 0.001$)

Notes: #: the study was included in the meta-analysis; AC: acute concussion; AS: antisaccades; CP: concussed participants; ID: identification; HC: healthy controls; LC: latent concussion; MGS: memory-guided saccades; ms: milliseconds; n: sample size; n/a: not available, RS: reflexive saccades; SP: smooth pursuit; SPS: Self-paced saccades

Table 2.5. Variables reported in the included studies.

Study ID	Smooth Pursuit	Self-Paced Saccades	Reflexive Saccades	Memory-Guided Saccades	Antisaccades	Fixations
Brewin 2017		Multi-saccade gaze shifts (n)*				
D'Amico 2016#					directional errors (n)*	duration (s)*, mean duration (s)*
Danna-Dos-Santos 2018#	accuracy*, intrusive saccades (%)*		reaction time*, accuracy initial phase*, overall accuracy			
DiCesare 2015#	gaze velocity (°/s)*; phase lag (°)*	n, velocity (°/s), error (cm)*; initial error (cm)	latency (ms)*, velocity (°/s), error (cm)*; initial error (cm)*			
Diwakar 2015#	radial error (°), mean radius (°)*, tangential error (°), mean phase (°)*, saccade frequency					
Drew 2007			latency (ms)*			
Evans 2016	mean error (°)*					

Table 2.5 (continued)

Study ID	Smooth Pursuit	Self-Paced Saccades	Reflexive Saccades	Memory-Guided Saccades	Antisaccades	Fixations
Heitger 2002#				directional errors (%)*, saccades per step (n), primary saccade gain*, gain of final eye position*, mean position error (%)*, amplitude error (%)*		
Johnson 2015#	Peak gaze velocity (°/s; data n/a), tracking lag (ms)	n*, gain of final eye position, position error (%)	Latency (ms, data n/a), velocity (°/s, data n/a), mean absolute position error (%)	Directional errors (%)*, primary saccade gain*, gain of final eye position, position error (%)*	Latency (ms)*, directional errors (%)*, primary saccade gain*, gain of final eye position*, position error (%)*	Position errors (n, data n/a)
Katrahmani 2018	n/a					
Kelly 2017	Phase (score, data n/a)*					
Ledwidge 2017#	Gain		Gain			
Maruta 2014#	Radial error (°)*, standard deviation of tangential errors (°)*, mean radius (°)*, mean phase (°)*, horizontal gain*, vertical gain*					

Table 2.5 (continued)

Study ID	Smooth Pursuit	Self-Paced Saccades	Reflexive Saccades	Memory-Guided Saccades	Antisaccades	Fixations
Mullen 2016#			Gain, latency (ms)			
Murray 2014#					Directional errors (n)*	% time on centre
Pearson 2007			Latency (ms)*			
Poltavski 2014						n, duration (s)*
Richard 2009	Saccades (n), fixations (n), fixation duration, saccade amplitude*	Saccades (n), fixations (n), fixation duration*, saccade amplitude*				
Samadani 2017						
Taghdiri 2018#		n				
Webb 2018#			Latency (data n/a), coefficient of variation of latency*, directional errors (%)*, horizontal amplitude gain		Reaction time (data n/a)*, coefficient of variation of latency*, directional errors (%)*, horizontal amplitude gain*	

*Notes: #: the study was included in the meta-analysis; *: a significant difference between concussed and control participants was found for at least one stimulus condition; °/s: degrees per second; n: number; n/a: not available*

Table 2.6. Variables and classes of eye tracking measurement with significant findings.

Class	Variable	Studies that found significant differences between concussed and control participants
Movement	Saccadic amplitude	Richard, Johnson, and Ellemberg 2009
	Proportion of the directional errors	Heitger, Anderson, and Jones 2002; Johnson, Hallett, and Slobounov 2015; Webb 2018
	Eye movement radius	Maruta et al. 2014; Diwakar et al. 2015
	Gaze velocity	Dicesare et al. 2015
Position	Proportion of position errors	Dicesare et al. 2015; Evans et al. 2016; Heitger, Anderson, and Jones 2002; Johnson, Hallett, and Slobounov 2015; Maruta et al. 2014
	Duration of fixations	D'Amico 2016; Richard, Johnson, and Ellemberg 2009; Poltavski and Biberdorf 2014
Count	Number of saccades	Johnson, Hallett, and Slobounov 2015; Danna-Dos-Santos et al. 2018; Brewin 2017; D'Amico 2016; Murray, Ambati, et al. 2014
Latency	Latency	Dicesare et al. 2015; Drew et al. 2007; Johnson, Hallett, and Slobounov 2015; Pearson et al. 2007; Webb 2018; Danna-Dos-Santos et al. 2018
	Phase (mean and initial)	Maruta et al. 2014; Danna-Dos-Santos et al. 2018; Diwakar et al. 2015; Kelly 2017
	Gain (vertical, horizontal, of the primary saccade, and of the final eye position)	Heitger, Anderson, and Jones 2002; Johnson, Hallett, and Slobounov 2015; Maruta et al. 2014; Webb 2018; Danna-Dos-Santos et al. 2018

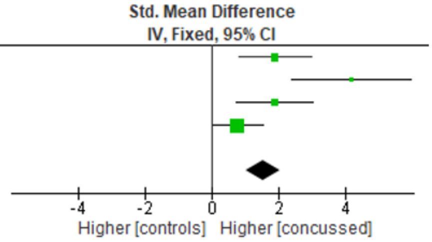
Effect size quantification

The meta-analysis was run on seven variables for acute concussions. The concussed group performed significantly worse than the control group participants for all of these variables: Number of self-paced saccades ($p = 0.003$), proportion or number of the directional errors in the antisaccade task ($p < 0.001$), phase lag of the smooth pursuit ($p = 0.02$), and four variables for the memory-guided saccades task: proportion of the position errors ($p < 0.001$), proportion of the directional errors ($p < 0.001$), primary saccade gain ($p = 0.007$), and gain of the final eye position ($p = 0.01$) (Figures 2.5-2.8). One variable, gain of the smooth pursuit, was analysed for the latent concussions, however, it did not yield a significant difference between the concussed and the control groups (Figure 2.9).

Antisaccades: Directional errors (n or %)

Study or Subgroup	Concussed Mean	Concussed SD	Concussed Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
D'Amico 2016	11.85	6.89	10	2	1.67	10	22.7%	1.88 [0.79, 2.97]
Johnson 2015	15	4	9	2.6	0.33	9	8.4%	4.16 [2.37, 5.96]
Murray 2014	46.5	13.58	9	24.1	8.82	9	20.3%	1.86 [0.71, 3.02]
Webb 2017	20	11	15	13	6	15	48.6%	0.77 [0.02, 1.51]
Total (95% CI)			**43**			**43**	**100.0%**	**1.53 [1.01, 2.05]**

Heterogeneity: Chi² = 12.99, df = 3 (P = 0.005); I² = 77%
Test for overall effect: Z = 5.76 (P < 0.00001)



Memory-guided saccades: Directional errors (%)

Study or Subgroup	Concussed Mean	Concussed SD	Concussed Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Heitger 2002	10.4	11.5	30	2.6	5.2	30	88.0%	0.86 [0.33, 1.39]
Johnson 2015	7.1	2.44	9	1.5	0.65	9	12.0%	2.99 [1.55, 4.43]
Total (95% CI)			**39**			**39**	**100.0%**	**1.12 [0.62, 1.61]**

Heterogeneity: Chi² = 7.36, df = 1 (P = 0.007); I² = 86%
Test for overall effect: Z = 4.40 (P < 0.0001)

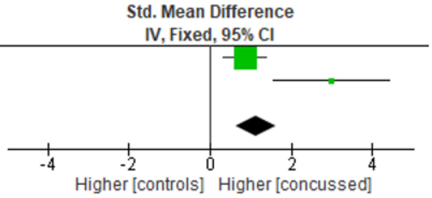
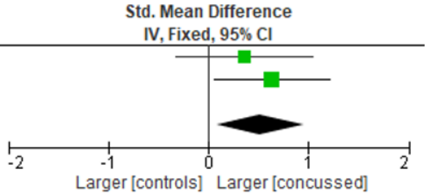


Figure 2.5. Acute concussions: Forest plots for the measures of movement.

Phase lag of the smooth pursuit (°)

Study or Subgroup	Concussed Mean	Concussed SD	Concussed Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
DiCesare 2015	15.84	13.67	17	11.57	9.24	17	41.9%	0.36 [-0.32, 1.04]
Maruta 2014	1.35	6.15	13	-0.63	2.64	127	58.1%	0.63 [0.06, 1.21]
Total (95% CI)			**30**			**144**	**100.0%**	**0.52 [0.08, 0.96]**

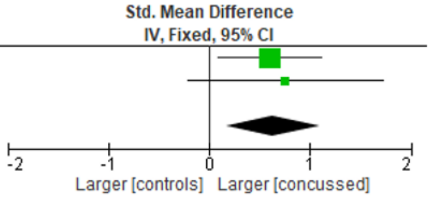
Heterogeneity: Chi² = 0.37, df = 1 (P = 0.54); I² = 0%
Test for overall effect: Z = 2.31 (P = 0.02)



Memory-guided saccades: Primary saccade gain

Study or Subgroup	Concussed Mean	Concussed SD	Concussed Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Heitger 2002	1.11	0.3	30	0.96	0.18	30	77.6%	0.60 [0.08, 1.12]
Johnson 2015	1.25	0.39	9	1.01	0.18	9	22.4%	0.75 [-0.21, 1.72]
Total (95% CI)			**39**			**39**	**100.0%**	**0.63 [0.18, 1.09]**

Heterogeneity: Chi² = 0.08, df = 1 (P = 0.78); I² = 0%
Test for overall effect: Z = 2.72 (P = 0.007)



Memory-guided saccades: Gain of the final eye position

Study or Subgroup	Concussed Mean	Concussed SD	Concussed Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Heitger 2002	1.35	0.42	30	1.13	0.2	30	76.1%	0.66 [0.14, 1.18]
Johnson 2015	1.2	0.39	9	1.11	0.2	9	23.9%	0.28 [-0.65, 1.21]
Total (95% CI)			**39**			**39**	**100.0%**	**0.57 [0.11, 1.02]**

Heterogeneity: Chi² = 0.50, df = 1 (P = 0.48); I² = 0%
Test for overall effect: Z = 2.45 (P = 0.01)

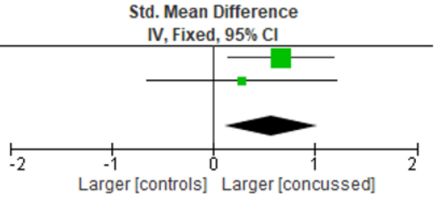


Figure 2.6. Acute concussions: Forest plots for the measures of latency.

Smooth pursuit gain

Study or Subgroup	Concussed Mean	Concussed SD	Concussed Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Danna-Dos-Santos 2018	1.05	0.21	36	1.01	0.06	36	61.4%	0.26 [-0.21, 0.72]
Ledwidge 2017	0.93	0.07	21	0.96	0.9	24	38.6%	-0.04 [-0.63, 0.54]
Total (95% CI)			**57**			**60**	**100.0%**	**0.14 [-0.22, 0.50]**

Heterogeneity: Chi² = 0.62, df = 1 (P = 0.43); I² = 0%
Test for overall effect: Z = 0.76 (P = 0.45)

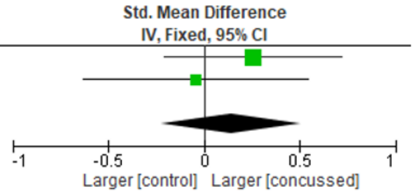


Figure 2.7. Latent concussions: Forest plot for the measure of latency.

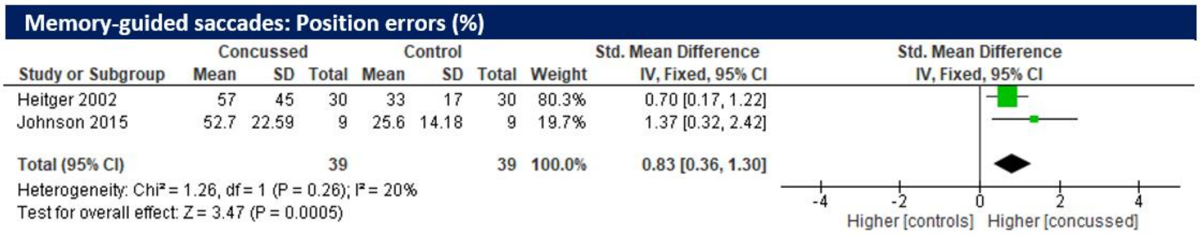


Figure 2.8. Acute concussions: Forest plot for the measure of position.

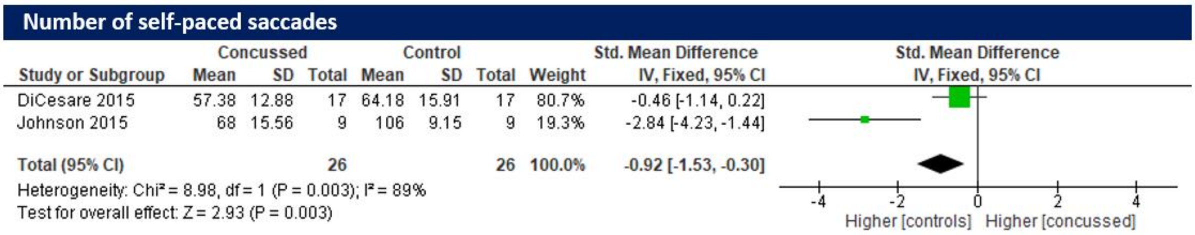


Figure 2.9. Acute concussions: Forest plot for the measure of count.

Risk of bias and study quality

Only the limitations relevant to the eye tracking assessments were considered in this review. Thus, we excluded from analysis the limitations pertaining to other tests that were sometimes conducted along with the eye tracking assessments, such as fMRI or balance.

Overall, the reviewed literature showed a number of limitations. Some of them are inherent in the studies of concussion in general, such as the vagueness of the distinction between the terms concussion and mTBI, sometimes used synonymously. Thus, different authors use different criteria to define the cases of concussion, which makes the body of research susceptible to the information bias, or misclassification. In addition, observational studies generally may be prone to higher and greater bias due to the lack of randomization and concealment of allocation (Eden et al. 2011). The number of participants in the concussed group of the 21 analysed studies ranged between one and 98, with a mean of 25 and a standard deviation of 23, thus making the studies disposed to a sample bias. A large variation in how much time passed after concussion when the eye tracking measurements were taken represents another risk of bias across the studies.

It is worth separately noting the selection bias caused by the inadequate selection of participants or inadequate confirmation and consideration of confounding variables. Only twelve studies report that the control group was matched to the concussed group by both age and sex (including the studies where the values for the concussed participants were compared to own baseline) (Heitger et al. 2002; Drew et al. 2007; Maruta et al. 2014; Murray et al. 2014a; Diwakar et al. 2015; Johnson et al. 2015a; D'Amico 2016; DiCesare et al. 2017; Kelly 2017; Danna-Dos-Santos et al. 2018; Taghdiri et al. 2018; Webb et al. 2018), further three studies matched the groups only by age (Richard et al. 2009; Poltavski and Biberdorf 2014; Ledwidge et al. 2017). None of the studies provided stratification by either sex or age. The remaining six studies did not provide adequate information on these factors (Pearson et al. 2007; Evans et al. 2016; Mullen et al. 2016; Brewin 2017; Samadani et al. 2017; Katrahmani and Romoser 2018). As previous research has shown, sex and age may have influence on both the concussion symptoms and eye movements (Munoz et al. 1998; Contreras et al. 2008; Baillargeon et al. 2012; Li et al. 2012; Graham et al. 2014; DeMatteo et al. 2015; Lynch et al. 2015; Ono et al. 2016), thus indicating that the reviewed studies are all susceptible to the selection of participants bias. In addition, whereas the majority or all participants of the concussed groups were athletes, only nine studies report that the majority of the control groups participants were also athletes (Drew et al. 2007; Pearson et al. 2007; Murray et al. 2014a; Poltavski and Biberdorf 2014; D'Amico 2016; Mullen et al. 2016; Brewin 2017; Kelly 2017; Ledwidge et al. 2017), one study did not use any control group (Taghdiri et al. 2018), and the remaining ten did not provide such information at all.

Further, presence of an ADHD/ADD diagnosis has been reported in only three cases as a confounding or an exclusion criterion (Poltavski and Biberdorf 2014; Diwakar et al. 2015; D'Amico 2016). ADHD has been shown to affect the saccadic and pursuit eye movements (Karatekin 2007), therefore failure to control for this variable represents another risk of selection bias.

None of the reviewed studies reported blinding of outcome assessors, however, due to the objective nature of assessments and of the analysis, the results of the studies are unlikely to be affected by this potential bias. The reason for this lies in the combination of the highly automated experimental design and quantitative nature of data. The summary of the bias evaluation including the support arguments for judgement in accordance with the RoBANS tool, as well as the quality of the individual studies are presented in Appendix 8.

2.3.4. Discussion

This is the first systematic review and meta-analysis that specifically evaluate the use of oculomotor assessments with eye tracking technology in sports-related concussions. The primary aim of this review was to identify key variables, measures and analysis methodology reported in the relevant literature. The main findings suggest that a variety of eye tracking tests were implemented at various time points (< 30 or > 152 days post-concussion); the most often reported was the smooth pursuit test, followed by reflexive saccades, while the least reported was the memory-guided saccades test. Overall, the studies predominantly included smooth pursuit and/or saccadic eye movements for analysis. These two eye movements have different functional areas but also share common brain regions, i.e. brain areas involved in attention and executive functions.

Due to the heterogeneity of the studies, statistical analyses to quantitatively summarise the pooled effect of eye movement variables were only possible on a select few outcome variables. This meta-analysis studied an overall sample of 160 athletes diagnosed with a concussion and 277 controls, but total sample size varied between respective eye measurement analyses. Significant findings were found only for acute phase concussion assessments (< 30 days post-concussion).

The next four subsections look at the specific findings of this meta-analysis for the oculomotor assessments.

Eye Tracking Variables

Measures of Movement

The measures of movement refer to the properties of eye movement events during a finite period of time that include direction, amplitude, duration, velocity, and acceleration (Holmqvist et al. 2011). The systematic review found that saccadic amplitude, proportion of the directional errors (for the reflective and memory-guided saccades, as well as for the antisaccades), and those tasks related to smooth pursuit tasks (i.e. eye movement radius and gaze velocity) were contrasting in concussed participants compared to non-concussed measures. Where concussed athletes performed poorer in all of these respective metrics. However, the number of the directional errors in the antisaccades and memory-guided saccades tasks were the only homogenous metrics to be included in the meta-analysis.

Within 30 days following a concussion, participants showed significantly more directional errors during antisaccade and memory-guided saccades tasks. Conversely, both variables showed high heterogeneity (I^2 statistic > 50% and Chi^2 significant), suggesting that other factors than mere chance influenced the results and that the effect was not consistent across studies. This may be attributed to difference in populations, sporting codes, gender and age ranges between the small samples of included studies.

Previous fMRI studies on acute phase sports-related concussions have also found that antisaccades and memory-guided saccades are impaired (Johnson et al. 2015a, 2015b). This type of saccade gives an indication of the brain functions and cortical structures that are affected (see Ventura et al. (2016) for review). Antisaccades involve higher cognitive functioning, like executive functioning. Executive functions allow a person to make decisions, adapt to situations and pay attention to relevant information. This is important in everyday life, but in particular for athletes in dynamic environments or team sports (Vestberg et al. 2012). The antisaccades tasks require the participant to inhibit reflexive saccades towards the target stimulus, and produce volitional saccades to the opposite direction (Johnson et al. 2015b; Ventura et al. 2016). In other words, antisaccades are important during inhibitory control (Johnson et al. 2015b). The memory-guided saccades task also involves a higher cognitive load, since it relies on the participant's memory to recall the target stimulus location and to guide the eyes toward the remembered location when there is no visual stimulus (Massendari et al. 2018).

Measures of Position

The position measures can be divided into five groups: basic measures (where did the participant look), dispersion of the gaze data, similarity of the positions of two groups of gaze data, duration, and pupil dilation at the certain position (Holmqvist et al. 2011). Based on the findings of the review, the concussed participants made more positional errors (during either smooth pursuit and/or self-paced, reflective, and memory-guided saccades as well as antisaccades tasks) and/or their fixation duration (for example, in a reading task) was longer. In conjunction with the findings of Johnson et al. (2015), results obtained from the meta-analysis suggest that changes in the proportion of the position errors for memory-guided saccades is a sensitive enough variable to potentially distinguish between those who are suspected of a sports-related concussion from those who have not been concussed. This specific eye measurement relies on the brain areas such as the hippocampus and cerebellum (Johnson et al. 2015b). Johnson et al. (2015) found that more challenging tasks, like memory-guided saccades, compared to basic saccade or smooth pursuit eye measures often show underperformance (i.e. more position errors) in concussed athletes during the acute phase. Again, this may be attributed to the high cognitive load and neuronal effort exerted by the memory-guided saccades when encoding and retrieving information. Additionally, position information from saccades stored in memory is provided by the perceptual mechanisms in the ventral pathway (Massendari et al. 2018). This implies that athletes who make more positional errors during these tasks may also be more affected by perceptual illusion. Finally, the variability between studies can probably be attributed to chance, as the heterogeneity was low.

Measures of Count

Measures of count refer to the numbers of eye movement events either in absolute numbers, in proportion to the total number of events, or as a rate over time (Holmqvist et al. 2011). The number of saccades in a self-paced saccades task tends to be higher in participants who do not have a concussion compared to those with concussions. The meta-analysis is inconclusive, even though significantly more self-paced saccades were found in the control condition as indicated by the pooled estimate. The larger of the two studies included in the meta-analysis, by Dicesare et al. (2015), contains the null value in its 95% confidence interval. Along with a large amount of variability between the two studies, suggesting that co-founding variables or methodological differences may have contributed to the differences during this volitional eye movement task. MRI studies have shown that self-paced saccades are associated with lesions of various brain areas, such as the frontal eye field or the connections between this area or dorsolateral prefrontal cortex and superior colliculus (Heitger et al. 2002; Johnson et al. 2015b). The wide-spread nature of the ocular network may contribute to the variability in findings as well. More homogenous research is needed to report a conclusive finding.

Measures of Latency and Distance

Measures of latency (i.e. the temporal distance, a measure of time delay between the on- or offset of two events) and distance (this term refers to the spatial distance, e.g. between the positions of the target and of the eye gaze) pertain to the unitary eye tracking events in relation to other events. In eye tracking studies, the temporal and spatial distances are tightly coupled and therefore often used interchangeably (Holmqvist et al. 2011). In general, concussed participants underperformed compared to non-concussed controls in latency, phase (mean and initial) and gain (vertical, horizontal, of the primary saccade, and of the final eye position) metrics. The only variables that were homogenous enough (in the acute phase) to complete the meta-analysis were phase lag of the smooth pursuit, as well as primary saccade gain and final eye position gain, specifically for memory-guided saccades. While only the smooth pursuit gain for the latent phase was sufficiently homogenous to be included into the meta-analysis, the results were not significant. For all three acute measures of latency, the point estimate of the pooled studies showed significantly poorer performances in the concussed group, when comparing homogeneous studies. Even though all the larger study samples favoured this outcome, for each of these measures there was one of the two studies (included in the meta-analysis) that contained the null value in 95% confidence interval. These factors make confirmation of the findings difficult and are indicative that more studies are needed, with larger samples over various time points.

As the complexity of memory-guided saccades has been discussed in the previous sections, smooth pursuit metrics should be considered. The gaze stabilizing function of the smooth pursuit is reliant on the vestibulo-ocular and visually mediated reflexes (Larner 2011). Predictive visual tracking involves input from the retina, cerebellum and higher cortical input (Barnes 2008; Fukushima et al. 2013). The nature of the task influences the results, as tasks that require more predictive tracking, place more challenges on the individual’s oculomotor system as well as the attentional, anticipatory and working memory capacity (Johnson et al. 2015b). Consequently, the nature of the task and the level of cognitive dysfunction of participants may add to the variability in data. And even though larger study samples are needed to draw conclusive inferences, due to the logistical nature of concussion research, more stringent exclusion criteria necessary to reduce possible confounding factors may result in even smaller sample sizes.

Binocular disparity, i.e. the distance between the gaze positions of the left and the right eye, has been proven to occur in a range of neurological conditions, such as dyslexia or multiple sclerosis (Holmqvist et al. 2011). However, in sports concussion studies it is common to consider the movement of both eyes as conjugate. The two exceptions in the current review are the line of research pursued by Samadani et al. (2017) who previously investigated the movement of the right and left eyes separately and found that the concussed population was less capable of generating coordinated eye movement (Samadani 2015; Samadani et al. 2015), and the study by Danna-dos-Santos et al. (2018) who measured both eyes separately and found no asymmetries between right and left eyes.

Sex Differences

There had been a reported higher concussion incidence among female compared to male sportspersons (Ono et al. 2016; Black et al. 2017), suggesting an intrinsic difference in the abilities of men and women to withstand head impacts (Covassin et al. 2003; Dick 2009; Patricios et al. 2010; Harmon et al. 2013; Benedict et al. 2015). Furthermore, sex has been found to have influence on saccadic and antisaccadic performance, although the reasons for it remain unclear (Oohira et al. 1983; Müri et al. 1991; Li et al. 2012). It is therefore possible that the recovery time and eye movement data for concussed and recovering patients may differ between sexes. While most of the reviewed studies controlled for the participants' gender, regrettably, none attempted a separate comparison between male and female participants.

Age Differences

Concussions are often more frequent in childhood (6-12 years) and adolescent athletes (13-18 years) compared to the adult athletes (Purcell 2005; McCrory et al. 2013). In addition, it has been found that adolescents are the most susceptible to the consequences of concussion, as well as most prone to prolonged recovery patterns and post-concussion syndrome, compared to children and adults (Baillargeon et al. 2012; Graham et al. 2014; DeMatteo et al. 2015; Lynch et al. 2015). Even though seven of the reviewed papers included participants under the age of 18, only one (Maruta et al. 2014) stratified the participants by age. In addition, the study populations of DiCesare et al. (2015) and Murray et al. (2014) consisted predominantly of adolescents (mean age 16.8 ± 1 years, and 16 ± 3 years, respectively). All three studies found that the eye movement deficits in adolescents were consistent with the research on adults and thus possibly not dependent on age. In addition, Samadani et al. (2017) conducted a study with the youth population (mean age of 13), however, due to the early stage of the research, the detailed data are not yet available.

Duration of Recovery

There has only been limited longitudinal research on eye movements in sports-related concussion with highly variable findings between studies. On the one hand, two studies reported no long-lasting effects of concussion in the reflexive saccade task performance (Drew et al. 2007) or in the antisaccade task performance (Webb et al. 2018) of the study population monitored over a period of 2-4 weeks. On the other hand, failures in sustained attentional vigilance that are a characteristic symptom of concussion (Pontifex et al. 2012), had been previously found to correlate with response inhibition tasks, such as antisaccades, for as long as six months post-concussion (Unsworth et al. 2010; Johnson et al. 2015a). Two studies in the current review concur: Johnson et al. (2015) reported that there were still significant differences in some of the metrics at 30 days post-injury, despite an improvement in test results compared to 7 days post-injury that seemed to be on a trajectory to normal. Webb (2018) discovered that the concussed participants made more errors in the reflexive saccades test both at the initial test and at the subsequent test, after being cleared to return to play by a medical professional (i.e. when deemed healthy).

2.3.5. Limitations

This review should be interpreted in light of its limitations. First, as of now there is a suboptimal amount of research on using eye tracking for sports-related concussion assessment. The studies that do exist and contain sufficient quantitative data, used a broad range of metrics across various eye tracking paradigms with little overlap, making the comparison between them, especially a meta-analysis, very difficult. Thus, the quality of this review is limited by both quantity and quality of the included studies. We attempted to mitigate the publication bias and associated dissemination biases by using all available sources of obtaining full texts and data tables of the selected publications, including contacting the authors, and by including all relevant studies regardless of their outcomes or statistical significance of findings. In addition, not only the peer-reviewed publications but also conference abstracts and dissertations were included.

2.3.6. Conclusions and Practical Implications

Most saccadic and pursuit deficits may be missed during clinical examination, and therefore eye tracking technology, due to its quick and objective nature, may be a useful and sensitive diagnostic and monitoring tool for sports-related concussions. Even though there is no consensus regarding the time frame within which these eye movements would remain affected, some have suggested up to 6 months post-concussion (Johnson et al. 2015b; Ventura et al. 2016); our meta-analysis however, was only able to confirm that these metrics are affected in the acute phase (< 30 days post-concussion).

The cognitive deficits caused by concussion or even by sub-concussive head impacts (List et al. 2015; Koerte et al. 2017) manifest in a variety of symptoms and indicators which include poorer performance on the neurocognitive tests, balance and oculomotor impairments, and other symptoms. Eye tracking is one of several possible concussion diagnostic tools and, due to the complexity of this injury, the best strategy might be to use a battery of several assessment tools to obtain the full picture. Additionally, using challenging tasks that are closely related to brain areas involved in executive functions (such as memory-based saccade or antisaccade tasks) may improve the reliability of the eye tracking tests for concussion diagnostics. In particular, assessing memory-guided position errors, within 30 days after a sports-related concussion, may show differences between athletes who have a concussion compared to those who do not.

Overall, the inconsistencies between the employed eye tracking metrics and methodology currently make inferences challenging. Therefore, more research is needed to draw reliable conclusions on the validity and utility of eye tracking for sports concussion assessment and to establish best practices.

Acknowledgements

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Conflict of interest

The authors declare that they have no conflict of interest.

2.4. Knowledge-to-action Framework

This dissertation relied on the knowledge-to-action framework (Graham et al. 2006; Field et al. 2014) that was designed to help health professionals and researchers integrate knowledge creation and knowledge application. Since it suggests that scientific research should be complemented with targeted information dissemination activities among relevant professionals (Provvidenza et al. 2013), this project focused not only on evaluating eye movements in concussed athletes, but also on expanding concussion knowledge among all stakeholders. This was achieved by interacting with concussed and healthy individuals, informing them of the latest concussion guidelines, conducting workshops for students, encouraging athletes with a suspected concussion to see a doctor, as well as further educational efforts. Thus, the clinicians survey presented in the next chapter, was designed with knowledge-to-action framework in mind.

CHAPTER 3.

AWARENESS AND PERCEIVED VALUE OF EYE TRACKING TECHNOLOGY FOR CONCUSSION ASSESSMENT AMONG SPORTS MEDICINE CLINICIANS

This chapter comprises the following published article:

Snegireva, N., Patricios, J., Derman, W., and Welman, K. (2019) Awareness and Perceived Value of Eye Tracking Technology for Concussion Assessment among Sports Medicine Clinicians: A Multinational Study. The Physician and Sportsmedicine. DOI:10.1080/00913847.2019.1645577

3.1. Introduction

Concussion is a serious and frequently occurring sports injury that has even been called a silent epidemic (Carroll and Rosner 2011; Marar et al. 2012). The incidence of concussion in sport has been estimated at 0.1 to 21.5 per 1000 athlete exposures, depending on the type of sport and methods of reporting (Clay et al. 2013). A widely cited report by the Centre for Disease Control and Prevention estimates that 1.6 to 3.8 million concussions occur in sports and recreational activities annually in the United States of America (Langlois et al. 2006).

Even though the awareness of concussion has increased and management of this injury has evolved significantly, there is still no universally effective tool to detect concussion and determine when it is safe to return to sport (Lynall et al. 2013; Kenzie et al. 2017). This is further aggravated by the fact that the athletes are often young, motivated individuals who sometimes tend to under-report symptoms and deliberately under-perform in the baseline tests (Register-Mihalik et al. 2013; Kroshus et al. 2015; Scolaro Moser and Schatz 2017; Wallace et al. 2017). The 2016 Berlin Consensus Statement (McCrory et al. 2017a) declares that there is a need for more objective ways to assess the presence and severity of sports-related concussion in athletes.

Eye movements may be one of these objective measures, since the generation of eye movements involves several neural pathways including the cerebrum, brainstem, and cerebellum. Consequently, damage to any of these areas would affect certain types of eye movements (Wilcockson 2018). Research has already established that eye movement evaluation may be indicative of a range of neurological disorders, such as schizophrenia (Subramaniam et al. 2018), Huntington's (Patel et al. 2012), or Parkinson's (Kitagawa et al. 1994) diseases. Eye movements can be assessed with the use of the eye tracking technology, i.e. the equipment for detecting eye movements and analysing visual information processing (Mele and Federici 2012), and/or without (for example, by asking a patient to follow the doctor's finger, or a paper-based King-Devick test) (Wilcockson 2018).

Indeed, eye tracking has been consistently gaining attention of both researchers and sports medical professionals (i.e. sports physicians, physiotherapists, athletic trainers and clinical exercise therapists) as a possible concussion diagnostic and screening tool. Technical improvements in eye tracking systems allow for more accurate measurement of the eye movements with non-intrusive technologies (Mele and Federici 2012; Ting et al. 2014). Recent systematic reviews concluded that portable eye trackers hold promise in assisting concussion detection and monitoring recovery, but require further investigation (Ventura et al. 2016; Snegireva et al. 2017).

In the current article, the term sports medicine clinician is used in reference to all professionals involved in the clinical practice of sports medicine including sports physicians, physiotherapists, clinical exercise therapists and athletic trainers, as well as the general practitioners (GPs) who are interested in sports medicine (Dijkstra et al. 2014). The latter were included in the cohort because they often are a primary point of contact for the injured athletes (Anderson 2009; Baarveld et al. 2011). Sports medicine clinicians often direct the assessment and/or management of concussion and take responsibility for decisions regarding an athlete's readiness to return to play. They should therefore be aware and have access to the best evidence-based practice for injured athletes (Ferrara et al. 2001; McGrann and Keating 2012). Previous surveys conducted with medical professionals (including allied health professionals and athletic trainers) concentrated on general knowledge, attitudes and beliefs in the recognition and treatment of concussions (Zonfrillo et al. 2012; Lebrun et al. 2013, 2017; White et al. 2014; Moreau et al. 2015; Yorke et al. 2016; Salisbury et al. 2017). These studies found that while the respondents demonstrated solid knowledge about concussion, gaps still existed between the latest guidelines and practice. A large body of literature specifically examined the implementation of rules and best practice guidelines in sports medicine (Ferrara et al. 2001; Esquivel et al. 2013; Lynall et al. 2013; Stoller et al. 2014; Baugh et al. 2015; Stern et al. 2017). Some studies focused on the knowledge of concussion among paediatricians (Zonfrillo et al. 2012; Gordon et al. 2014; White et al. 2014), finding that only 25% of coaches and sports trainers recognised that younger athletes take longer than adults to recover after sustaining a concussion, and over 40% were uncertain about it (White et al. 2014). Overall, a significant variability in concussion care practices was found (Stern et al. 2017), and the effective implementation generally lagged behind the development of guidelines and latest research (Lebrun et al. 2013, 2017; Stoller et al. 2014; Baugh et al. 2015). Sadly, according to some studies, a large proportion of respondents were unaware that concussion was usually associated with normal neuroimaging (Yorke et al. 2016) or failed to recognise vestibular disorders or abnormal eye tracking as phenomena related to concussion (Zonfrillo et al. 2012). On the positive side, contemporary use of concussion guidelines seems to be improving (Gordon et al. 2014).

To the authors’ knowledge, no survey to date has investigated the awareness and perceived value of utilizing of eye tracking technology, either in concussion assessment, or in any other medical or non-medical field. Thus, the current study was motivated by the previous surveys and the consensus statements calling for further research regarding the knowledge and adherence of the sports medicine clinicians to the innovative assessment tools that can assist in concussion diagnostics and return-to-play decisions (Ferrara et al. 2001; Zonfrillo et al. 2012; McCrory et al. 2013, 2017a; Yorke et al. 2016). The authors hypothesised that while clinicians may be aware that utilizing the eye tracking technology in concussion diagnostics can be beneficial, it is possible that due to the novelty of the technology and limited access or exposure only a few actually use it in their practice. The objectives of this study were to assess the awareness of eye movement deficits associated with concussion amongst a group of sports medicine clinicians, and to determine the utilization, in addition to perceptions of the value, of eye tracking technology for concussion diagnosis and screening compared to current tools.

3.2. Materials and Methods

This was a cross-sectional survey based on the knowledge-to-action framework (Graham et al. 2006; Field et al. 2014). Ethical clearance was provided by the institutional health research committee (HREC Approval #S16/07/129). The survey was designed and conducted in English using Google Forms (Google LLC, Mountain

View, CA, USA) and distributed online between January and December 2017 directly (via email to the members of the Sports Medicine Associations of South Africa, Turkey, Croatia, Greece, as well as British Association of Sport and Exercise Sciences,) and indirectly (using LinkedIn groups and Twitter posts as well as communication channels of the 2017's Annual Meeting of the European Federation of Sports Medicine Associations). Repeat emails and reminders were sent throughout the survey period, while retaining full anonymity of the recipients. While the research team attempted to contact all member associations under the umbrellas of the International and European Federations of Sports Medicine (FIMS and EFSMA), it is impossible to estimate how many physicians in fact received and read the email with the survey invitation, thus making it difficult to determine the response rate.

The survey (Appendix 7) consisted of eighteen open-ended, forced selection, or multiple choice questions that were structured as follows: items 1-2 assessed the respondents' demographics; items 3-5 aimed to determine the level of awareness and exposure of the respondents to eye tracking; items 6-12 evaluated the current concussion assessment practices of the respondents, including the frequency and duration of the assessments, currently used diagnostic tools and their limitations; finally, items 13-18 focused on the observed eye movement deficits and perception of potential benefit of eye tracking in concussion diagnostics. The content validity of the survey was determined by two independent sports medicine experts, and concussion methodologists, prior to implementation.

Eligible participants included medical personnel such as sports physicians, neuropsychiatrists, and general practitioners, as well as allied health professionals such as physiotherapists, athletic trainers and clinical exercise therapists. Consent was implied by completion of the survey. The exposure variables included the current usage of the sport concussion diagnostics tools and their perceived limitations, presence of abnormal eye movements in concussed athletes, experience working with eye tracking, familiarity with eye movement assessment tools. The outcome variables were the level of awareness of the sports medicine clinicians about the eye tracking technology, and perceived benefit of this technology for concussion assessment.

The data were analysed using Statistica 13 (Dell Inc, Tulsa, OK, USA) and Excel (Microsoft® Corporation, Redmond, WA, USA). Descriptive statistics for categorical variables were used; averages and standard deviations together with 95% confidence intervals (CI) (where applicable), are reported for quantitative data. In addition, cross-tabulation with chi-squared test was applied. The significance level was set at $p \leq 0.05$.

3.3. Results

3.3.1. Respondents' Demographics

The survey yielded a total of 171 responses. Similar to other surveys (Baugh et al. 2015; Salisbury et al. 2017), the majority of participants were sport physicians (46%, Figure 3.1). The respondents also included such professions as neurosurgeons and orthopaedic surgeons who, due to low numbers, were grouped under category "other medical practitioners.

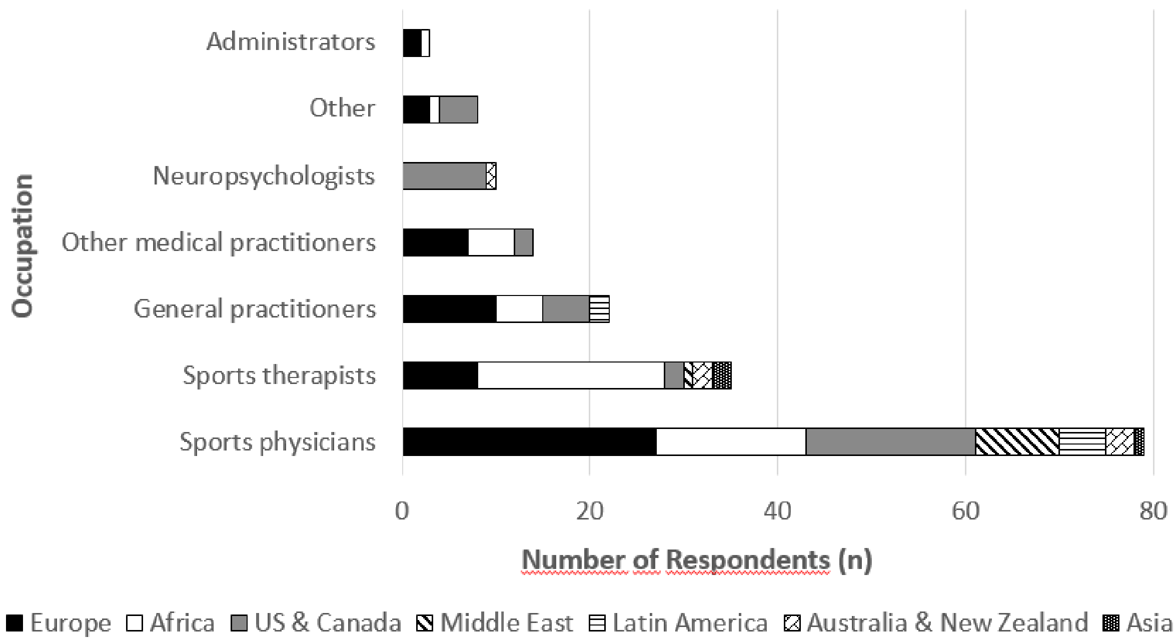

Figure 3.1. Respondents' occupations and regions of residence.

The research team was located in South Africa, where most of survey dissemination effort took place, which explains that 26% of all respondents were from this country. Nevertheless, due to support provided by a number of associations, such as European Federation of Sports Medicine Associations (EFSMA), as well as to communication activities on social media, which are borderless by nature, other regions, specifically Europe and North America (33% and 23% of all respondents, respectively), were also well presented in the survey.

3.3.2. Current Concussion Assessment Practices

Most often the survey participants evaluated each concussed patient at least three times (n = 76, 51% of the total 148 respondents who provided a definite answer to this question), followed by 53 (36%) who reported seeing each patient twice – to diagnose and to clear; only 19 (13%) evaluated each patient on average only once – to diagnose. In diagnosing concussed patients, 93% (n = 159) of the respondents reported that they used at least one established tool (Table 3.1), and 62% (n = 106) used a combination of two or more tools.

A quantifiable answer regarding typical duration of recovery for concussed patients was provided by 139 respondents, 91% of who (n=126) stated that this period equalled to or exceeded one week. Notably, there was high divergence in responses regarding the average duration of recovery from concussion – they ranged from 1-2 days to 6 months (21.2 ± 30.9 days; median 14; 95% CI 15.9-26.4), with a frequent comment that this time varied from patient to patient. Five respondents specified that this time significantly depended on age (longer for young patients), and eight participants named severity and previous history of concussion as factors affecting the duration of recovery. No further confounding factors were named.

The fact that, with the current diagnostic tools, players can under-report or exaggerate their symptoms was pointed out by 47 respondents (31% of total 152 who provided an answer to this question). Other reported limitations included: too time-consuming: 18% of the respondents, low accuracy (sensitivity, specificity): 14%, no tools exist, only clinical diagnosis: 9%, lack of baseline or normative data (7% and 2%, respectively), low predictive power: 6%, no gold standard: 6%, lack of awareness & training: 5%, do not assess fine neurological deficits: 5%, reliability: 5%, conflicting evidence: 4%, cost: 4%, individual variability: 3%, not suitable for children: 1% and not suitable for or para-athletes:1%.

Table 3.1. Current concussion diagnostics tools.

Which concussion diagnostic tests do you use, and what is your primary tool?	**Used by: No. of responses (*f*)**	**Used by: % of resp. (n = 161)**	**Primary tool: No. of responses (*f*)**	**Primary tool: % of resp. (n = 155)**
Sports Concussion Assessment Test (SCAT), versions 3 and 5	128	80%	95	61%
Balance Error Scoring System (BESS)	60	37%	1	1%
Immediate Post-concussion Assessment and Cognitive Testing (ImPACT)	40	25%	11	7%
Post-Concussion Symptom Scale (PCSS)	39	24%	5	3%
Standardised Assessment of Concussion (SAC)	39	24%	4	3%
CogState Sport / Axon	38	24%	4	3%
Cranial Computerised Tomography (CT)	19	12%	1	1%
Magnetic Resonance Imaging (MRI)	5	3%		0%
Vestibular-Ocular Motor Screen (VOMS)	5	3%	4	3%
Drop Test	4	2%		
Neuropsychological Test Battery	4	2%	4	3%
Physical Examination and/or Clinical History	3	2%	36	23%
Vestibular Testing	2	1%	2	1%
King-Devick Test	1	1%	1	1%
RightEye (Eye Tracking Device)	1	1%	1	1%
Saccadometer	1	1%		
Other	12	7%	11	7%

Abbreviations: ƒ: frequency, resp.: respondents

3.3.3. Level of Awareness and Exposure to Eye Tracking Technology

Only 11% of the respondents had experience working with eye tracking (n = 18), further 66% (n = 113) had heard of it but had never worked with it, while 23% of the respondents (n=40) were not familiar with the eye tracking technology at all.

Understandably, an overwhelming majority (88%, n = 150) of the survey participants did not use eye tracking in their practice. Seventy-four percent (n = 127) named one or more reason for not using the eye tracker for concussion diagnostics (Table 3.2), of which being not familiar with it and not having access to the equipment ranked the highest. Only four respondents showed knowledge of sampling frequency of an eye tracker device to be used for concussion diagnosis.

Table 3.2. Reasons for not using eye tracking technology.

Reason for not using ETT	**No. of responses (ƒ; multiple possible)**	**% of respondents (n = 127)**
Not familiar with it	41	32%
Don't have access to equipment	40	31%
Have no training / experience	19	15%
Cost	13	10%
Lack of evidence	13	10%
Not an established tool	13	10%
No need	9	7%
Don't work with concussed athletes	8	6%
Lack of good product on the market	1	1%

Abbreviations: ETT: Eye tracking technology; ƒ: frequency

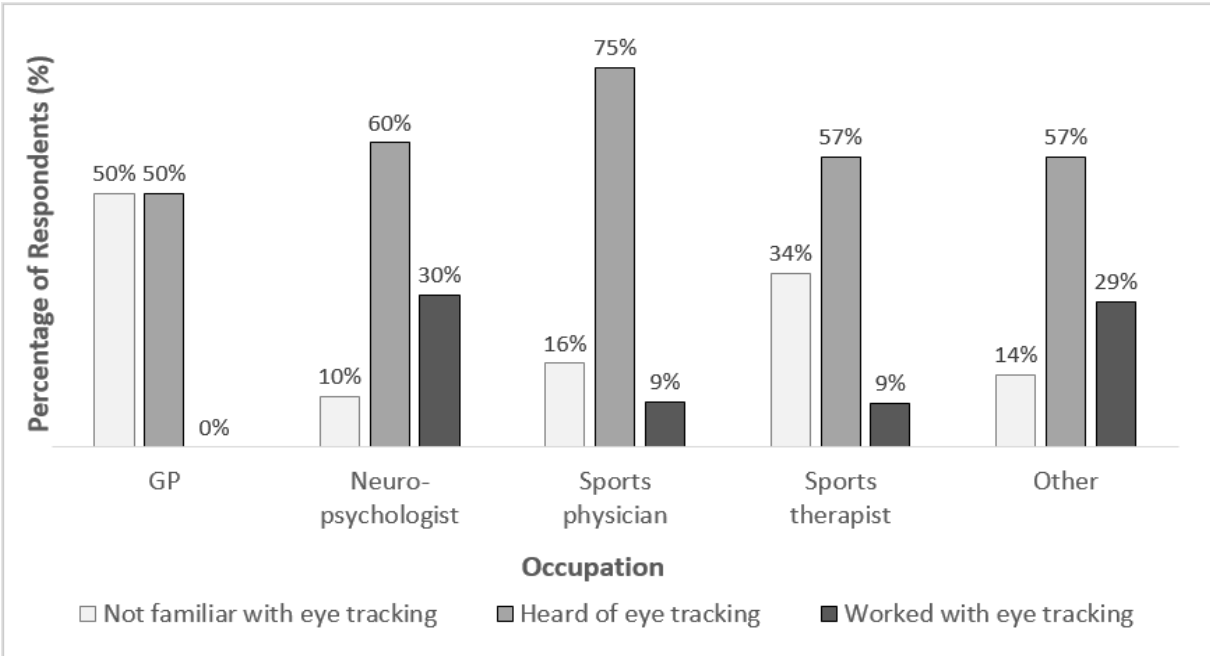

Figure 3.2. Occupation and familiarity with eye tracking.

There was a relationship (χ^2(df=8) = 22.6, p = 0.004) between the profession of the respondents and their familiarity with the eye tracking (Figure 3.2). The GPs showed the lowest level of exposure to the technology, and neuropsychologists the highest.

3.3.4. Observed Eye Movement Deficits

Seventy-seven percent of the respondents (n = 132) did not use any eye movement assessment tools other than own clinical assessment to diagnose concussion. A relatively small proportion named the King-Devick test or a pupillometer (9% and 5%, respectively), and only 5% (n = 8) used an eye tracking device or a saccadometer.

The survey inquired whether and how often various eye movement deficits were observed in concussion patients (Figure 3.3). With the exception of the abnormal pupil light reflex, which was checked by 68% of the respondents, each of the eye movement deficits was inspected by less than half of the respondents (46.3 ± 12.0%), and 20% selected “I do not check for it” for all of the deficits. The respondents who reported looking at the eye movements in the concussed patients, observed at least one deficit in 29.9 ± 23.3% of patients (Table 3.3).

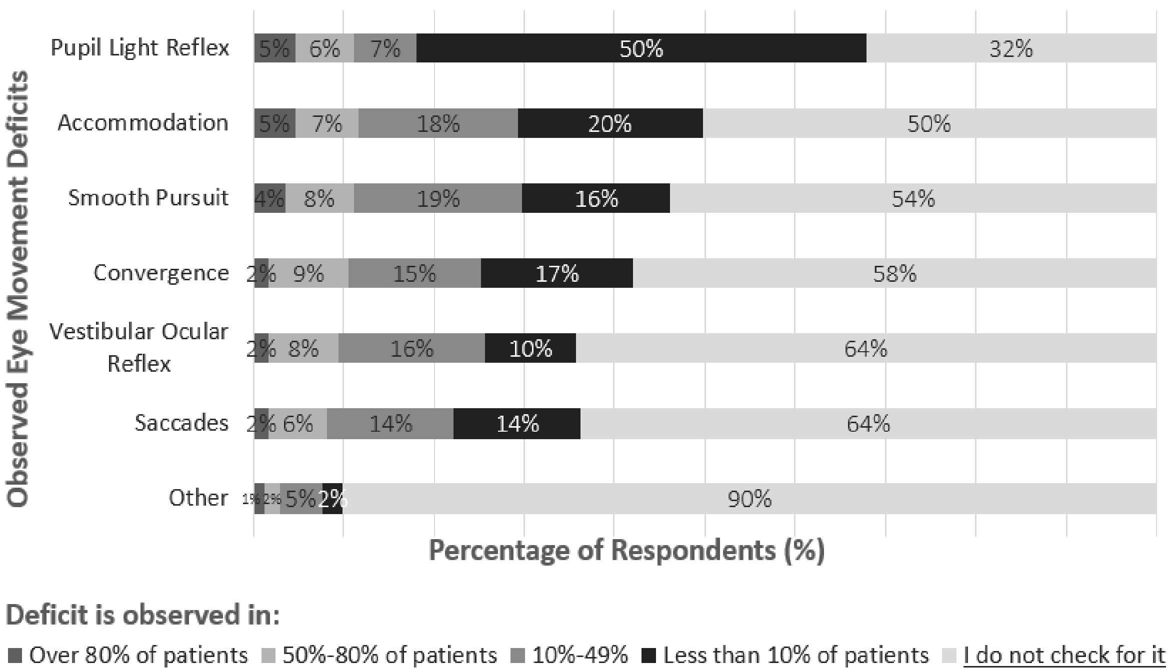

Figure 3.3. Observed eye movement deficits in patients with concussions.

Table 3.3 shows that the most commonly observed eye movement deficits in patients were the impairments of the vestibular ocular reflex followed by the abnormal smooth pursuit; whereas the pupil light reflex impairments were observed in the least number of patients.

A quarter of all respondents (n = 42) named smooth pursuit among eye tracker measured data that they would use to support concussion diagnostics, and 22% (n= 37) named saccades and/or antisaccades.

Table 3.3. Proportion of patients (%) with concussions showing eye movement deficits.

Observed Eye Movement Deficits	**No. of responses (ƒ; excl. "I do not check for it" answers)**	**$\bar{x}$ patients (%)**	**SD patients (%)**	**95% CI**
Pupil Light Reflex	116	22.1	22.9	17.9 - 26.3
Accommodation	85	31.4	24.0	26.3 - 36.5
Smooth Pursuit	79	32.5	23.1	27.4 - 37.6
Convergence	72	31.3	22.9	26.0 - 36.6
Saccades	62	30.9	22.4	25.3 - 36.5
Vestibular Ocular Reflex	61	34.3	22.0	28.8 - 39.8
Other	17	37.4	24.2	26.0 - 49.0

Abbreviations: Excl.: excluding; SD: standard deviation; $\bar{x}$: mean, CI: confidence interval

3.3.5. Perception of Potential Benefits of Eye Tracking

The percentages of respondents who stated that they did see potential benefit of eye tracking technology in concussion diagnostics and of those who were unsure about perceived benefit were nearly equally split (49% and 48%, respectively). When asked specifically to name the benefits of eye tracking, 61% (n = 104) of the respondents provided at least one benefit (Table 3.4), 9% (n = 15) explicitly stated that they did not see any benefit, and 30% (n = 52) said that they were unsure or did not provide any answer.

At the same time, a relationship (χ^2(df=4) = 12.29, p = 0.015) existed between the experience of using eye tracking and the perceived benefit of the eye tracking technology (Figure 3.4).

Table 3.4. Perceived benefits of eye tracking technology.

What are the main benefits of using an eye tracking device?	**No. of responses (*f*; multiple possible)**	**% of respondents (n = 104)**
Objectivity of assessment	71	68%
Ease of use for the clinician	49	47%
Replicability	44	42%
Results are quantified	36	35%
Requires little effort from the patient	35	34%
Reliability of assessment	34	33%
Speed of use	32	31%
High sensitivity	24	23%
High specificity	15	14%
I do not see any benefit	15	14%
Unsure / No answer	52	50%

Abbreviations: f: frequency

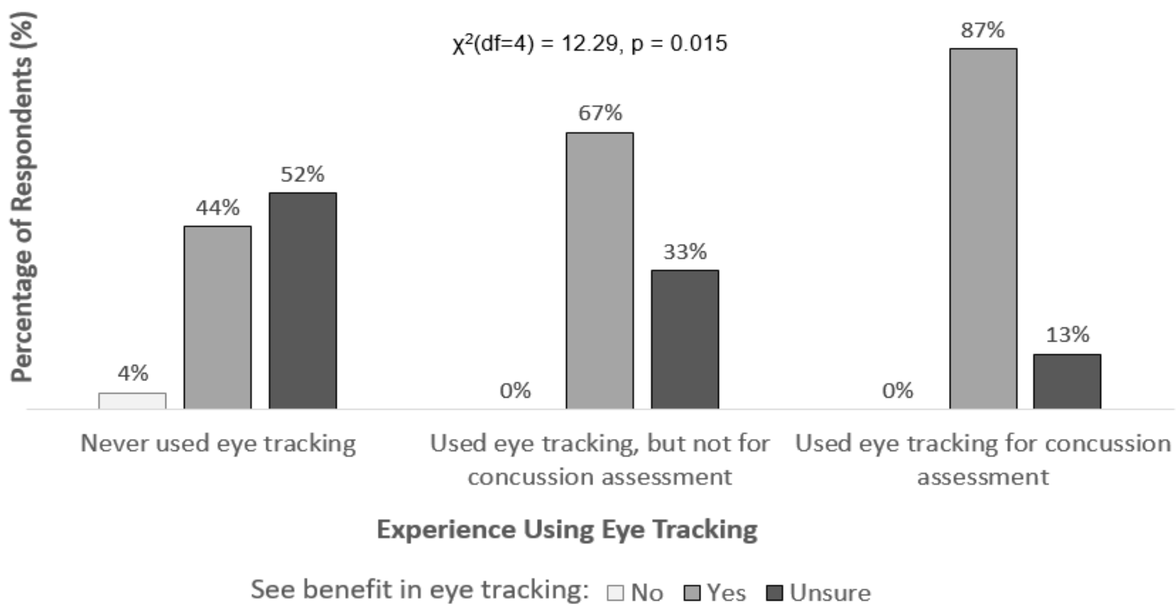

Figure 3.4. Relationship between experience in using eye tracking and its perceived benefit.

3.4. Discussion

This study is the first to assess the link between awareness and perceived value of eye tracking in concussion assessment among sports medicine clinicians from different geographical locations.

Despite a significant amount of concussion research that has increased significantly in the last decade, diagnosing and assessing concussion continues to be challenging (Yorke et al. 2016). Consistent with previous studies (Gordon et al. 2014; Yorke et al. 2016; Salisbury et al. 2017), there was high variability in the answers pertaining to the usual duration of assessment, and the time it took the patients to recover. Currently the diagnostic process includes the reporting of symptoms, neurocognitive examination, and balance, vestibular, or exertional testing. In line with past surveys in the chiropractor community (Moreau et al. 2015), the current study demonstrates that the SCAT remains the most commonly used tool in concussion diagnostics. This test has been named the most validated and well-established, rigorously developed and regularly updated concussion diagnostic instrument (Samadani et al. 2016; McCrory et al. 2017a). The SCAT is a comprehensive yet fast and easy to conduct test, and its value in assisting the sports medicine clinicians in early stage concussion diagnostics is undisputed. However, still today it remains largely subjective and thus may be prone to manipulation by some ambitious athletes (Smith et al. 2017). Moreover, as the developers of the test themselves admit, the diagnostic utility of all components of SCAT5 except the symptom checklist appears to decrease significantly after 3-5 days post-injury (Echemendia et al. 2017; McCrory et al. 2017a). As indicated by the survey respondents, typical duration of recovery for concussed patients equals to or exceeds one week; moreover, the research has shown that the full neurobiological recovery may outlast the symptom resolution (Iverson et al. 2017) – which is unlikely to be identified by the SCAT. Indeed, the major limitations of the existing tools named by the respondents were subjectivity and low accuracy – which both lead to a degree of uncertainty in concussion assessment. A practical implication thereof is that, even after the concussed patients become asymptomatic, sports medicine clinicians often prefer to wait at least one week or even longer before initiating the return to play protocol (Gordon et al. 2014; Salisbury et al. 2017). Thus, there is both an objective and a perceived need for a better solution.

Recent research shows that adding eye tracking to the concussion assessment toolbox might help confine these limitations (Diwakar et al. 2015; Samadani et al. 2016; Snegireva et al. 2017). As the survey participants pointed out, the main potential benefits of eye tracking were objectivity of assessment, ease of use (both for the clinician and the patient), replicability of the tests, and the fact that the results can be quantified. However, despite the promise that eye tracking holds, sports medicine clinicians seem reluctant to implement this technology in their practice, and only 49% of the survey respondents explicitly stated that they considered utilizing eye tracking technology for concussion diagnostics beneficial. A large number of respondents stated that the reasons for such reluctance were not being familiar with the technology at all, as well as lack of access to the equipment or experience and training. Certainly, the eye tracking technology itself also has limitations: there is insufficient research validating the metrics, the variability of features and algorithms in different products is high, and the cost of equipment, while declining steadily, is often perceived as prohibitive. In addition, eye tracking devices have only recently started getting approvals for concussion diagnostics in clinical settings (for example, in the US by the Food and Drug Administration (FDA)) (Oculogica 2019; RightEye LLC 2019).

The current survey also indicates that even in populations such as sports medicine clinicians who regularly diagnose and manage patients with concussion, there is insufficient awareness that concussion can lead to abnormal eye tracking behaviour. Indeed, contrary to previously estimated prevalence of oculomotor deficits in traumatic brain injury (concussion being a subset thereof) ranging from 40% to as high as 90% (Kapoor et al. 2004; Ciuffreda et al. 2007; Hunt et al. 2016), participants of the current study reported observing eye movement deficits on average only in 30% of the concussion patients. Moreover, 20% of the survey participants admitted that they were not checking for any of the eye movement deficits at all. This reflects findings of an earlier survey that found that some medical practitioners did not believe that abnormal eye tracking was related to concussion (Zonfrillo et al. 2012). A possible reason for the relatively low observed frequency of eye movement deficits may be that, even though measuring the eye movements without the equipment is possible (e.g. asking a patient to look side to side) (Wilcockson 2018), it is not as accurate. Thus, even though some eye movements might be indicative of a concussion, lack of equipment for their assessment limits the clinicians in using this indicator. In addition, the survey revealed a significant relationship between the experience of using eye tracking and the perceived benefit of the eye tracking technology. This may demonstrate that the level of exposure to novel diagnostics tools and their acceptance go hand in hand.

There are some limitations associated with this study. Similar to other recent surveys distributed electronically through various channels (White et al. 2014; Yorke et al. 2016; Salisbury et al. 2017), it was virtually impossible to obtain the denominator of the number of questionnaires distributed and thus the response rate. This means that the non-response bias could not be determined; restricting the inferences made on the reliability and validity of the survey findings. Similar to most survey studies, there is a risk for response bias. There was no systematic way to determine characteristics of those who took the survey compared with those who declined, and it is possible that these characteristics differed from each other. It is assumed that the population that responded represented a relatively small portion of sports medicine clinicians. Online surveys are typically criticised for not having a standardised sampling frame and may result in selection bias (Ekman et al. 2006). The sample in this study was restricted towards those who have internet access, and who would have been skilled in online tools. The self-reporting format of the survey also had some limitations. Respondents may have given exaggerated answers, as they may have tried to answer questions based on what they considered as the most favourable or helpful answer, and this social desirability bias may have affected the results (Larson 2018).The differences in geographic and occupational background make it unlikely that the respondents had a similar training in sports concussion, although most would have been exposed to the same international consensus guidelines. Even though the responses are similarly distributed between South Africa, North America and Europe, due to the small sample the authors are unable to make cross-regional comparisons and generalise findings on geographical sites.

3.5. Conclusion

Increasing educational and training opportunities along with practical experience of sports medicine clinicians regarding concussion evaluation, including the use of potential innovative technology (such as eye tracking), is strongly advocated. Better interaction between researchers and sports medicine clinicians regarding the use of eye tracking technology for concussion assessment is also suggested. It could lead to its higher adoption rate, which in turn might enable the evaluation of currently neglected eye movement deficits caused by concussion and ultimately more accurate evaluation of concussion resolution over days to weeks. Therefore, scientific research should be complemented with targeted information dissemination activities among relevant professionals in accordance with the knowledge-to-action framework suggestions (Provvidenza et al. 2013). The survey revealed that GPs had the lowest, and the neuropsychologists the highest level of exposure to the technology, thus providing guidance for the direction of such dissemination efforts.

Further research in this area should be performed to determine if there are measurable differences in the levels of knowledge and acceptance of medical professionals pertaining new relevant technological developments, as well as whether a relationship between them exists. Should it be the case, one might conclude that broader educational efforts for new validated assessment tools might facilitate their acceptance rate. Finally, as lack of evidence regarding the validity of eye tracking and the fact that eye tracking is not an established tool were among the reasons for not using eye tracking technology in concussion assessment process, further empirical validation of this tool is called for.

Acknowledgements

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CHAPTER 4.
RELIABILITY AND VALIDITY OF EYE TRACKING FOR SPORTS-RELATED CONCUSSION ASSESSMENT IN YOUTH AND ADULT ATHLETES

This chapter comprises the following submitted article:

Snegireva, N., Patricios, J., Derman, W., and Welman, K. (n.d) Blink duration is increased in concussed children: a reliability and validity study using eye tracking in male youth and adult athletes of selected sports.

Disclaimer: At the time of submission this article was not accepted by a journal. Therefore, the dissertation manuscript may differ from the published article (in the event that a journal accepts it).

4.1. Introduction

Awareness and management of sports-related concussion (SRC) have evolved significantly, however the most recent Consensus Statement on Concussion in Sport emphasises that it remains challenging to identify, assess and manage (McCrory et al. 2017a). In most cases, with proper and timely treatment, concussed athletes will recover fully; however, if unrecognised, there may be significant health implications. Not only can the immediate concussive symptoms be debilitating, but there is also an elevated risk of subsequent concussive and musculoskeletal injuries in the period following a concussion, and a spectrum of further possible long-term sequelae (Dashnaw et al. 2012; Hubertus et al. 2019). The diagnostic challenge is largely attributed to the absence of a universal objective tool to detect SRC and to determine when it is safe to return to sport (Lynall et al. 2013; Kenzie et al. 2017), leading to a heavy reliance on the athlete's self-reporting of symptoms.

Importantly, SRC or even sub-concussive head impacts (List et al. 2015; Koerte et al. 2017) manifest in a variety of symptoms, including worsened performance on neurocognitive tests, balance impairment and abnormal eye movements. The prevalence of eye movement deficits following a concussion is estimated at 40% to 90% (Kapoor et al. 2004; Ciuffreda et al. 2007; Hunt et al. 2016). Unsurprisingly, camera-based eye tracking technology has increasingly been gaining attention as a possible diagnostic and monitoring tool for SRC as demonstrated by empirical studies (Diwakar et al. 2015; DiCesare et al. 2017; Bin Zahid et al. 2018; Danna-Dos-Santos et al. 2018; Webb et al. 2018) and literature reviews (Greenwald et al. 2012; Ting et al. 2014; Hunt et al. 2016; Ventura et al. 2016; Kontos et al. 2017; Snegireva et al. 2018). Thus, studies in concussed individuals have found worsened gaze stability (Murray et al. 2014a), lower number of self-paced saccades (Taghdiri et al. 2018), increased saccadic latencies, increased position errors in saccadic and smooth pursuit tasks (Ventura et al. 2016), and lower saccadic velocity to accuracy ratio (Hunfalvay et al. 2019).

However, a number of factors make inferences challenging. These include inconsistencies between eye movement metrics and experimental designs, high variability in the time elapsed after the injury at the moment of testing, and lack of uniformity in participant selection. For these reasons, recent studies and commentaries have called for research using a more comprehensive battery of eye tracking measures (Taghdiri et al. 2018). Moreover, research involving youth athletes (i.e. ≤ 18 years as stipulated in the Berlin Consensus Statement (McCrory et al. 2017a)) and subjects aged specifically 18 to 26 years is needed in order to clarify whether there is any age effect on SRC-related eye tracking measures (Samadani et al. 2017; Bin Zahid et al. 2018). Thus, this study investigated whether selected eye tracking variables measured across established tasks would constitute a reliable and valid tool to diagnose and monitor SRC in adult and youth participants in such contact sports as Rugby Union (rugby) and football (soccer). It was hypothesized that differences would exist between the concussed and control groups in self-paced saccades (SPS), fixation stability, memory-guided saccades (MGS), smooth pursuit (SP), and antisaccades (AS), but not in reflexive saccades (RS). These differences were expected to be most pronounced in the early symptomatic stage of a concussion (up to one week post-injury, the period of the neurometabolic cascade within which the concussion symptoms are present but gradually resolve (Henry et al. 2010; Gardner et al. 2015)), diminish in the recovery stage (two to four weeks post-injury, usually sufficient for a full neurobiological recovery to take place (Iverson et al. 2017; Pusateri et al. 2018)), and not be detectable in the post-factum baseline stage (approximately three months post-injury, subject to subject to being cleared to return to sport by a clinician).

4.2. Material and Methods

This prospective cohort study was approved by the health research ethics committee of Stellenbosch University (S16/07/129, Appendix 3). During the first session, after a brief introduction of the study, all participants and their parents if under the age of 18, provided informed consent and/or assent prior to participation (Appendix 4). The study adhered to the guidelines provided by the Declaration of Helsinki.

4.2.1. Participants

According to the a priori power analysis ($1 - \beta = 0.80$; $\alpha = 0.05$; $d = 0.50$) conducted using G*Power 3.1.9.3 for Windows software (Faul et al. 2007), a target of 51 participants per age group was set. The athletes were recruited from football and rugby clubs and clinics in the Western Cape region, South Africa and via the Sports Concussion South Africa Schools' Programme in Johannesburg, South Africa. The inclusion criteria for all participants were active participation in a sport like rugby and football, age between 9 and 35 years, and attending or having attended school. Additionally, for the concussed group an inclusion criterion was the presence of a recent concussion (not older than one week), whereas for the control group the criteria included the absence of concussions in the past two years, as well as being age- and sex-matched to the concussed group. Confirmation of a recent concussion was based on a diagnosis by sports and exercise medicine physicians using the clinical criteria defined at the 5th International Consensus Conference on Concussion in Sport (McCrory et al. 2017a), and verification of a history of previous concussion(s) was based on the participants' and parents reported data. The exclusion criteria for all participants were: major depression (score of ≥10 on the Patient Health Questionnaire (PHQ-9) (Richardson et al. 2010; Manea et al. 2012; Suzuki et al. 2015)), poor global cognition (score of ≤ 26 on the Montréal Cognitive Assessment (MoCA) (Pike et al. 2017; Carson et al. 2018)), self-reported diagnoses of ADD/ADHD, psychiatric, neurological and/or neurodevelopment disorders, vision disorders or vision not corrected-to-normal, consumption of alcohol or drugs in the past 24 hours, antipsychotic, anticonvulsant, or antidepressant medication (Leigh and Zee 2015), orthopaedic injuries or inability to follow the instructions. In addition, the testing was aborted, and concussed participants were excluded if the tests provoked worsening of concussive symptoms (e.g. headache or sensitivity to light).

4.2.2. Apparatus

Eye movements were recorded using an infrared eye tracker SMI RED250mobile (SensoMotoric Instrument GmbH, Teltow, Germany) sampling at 250 Hz (Figure 4.1). Stimuli were generated using SMI Experiment Center software and presented on a Lenovo ThinkPad laptop monitor (Lenovo Group Ltd, Quarry Bay, Hong Kong) with a resolution of 1920x1080 pixels.

The utilized eye tracker, SMI RED250mobile, is considered to be among the most precise devices with a gaze position accuracy of 0.4° and spatial resolution of 0.03° measured with human eye (Conklin et al. 2018). According to the manufacturer, it has a high tolerance for head movements and is able to reliably track the eyes within the head box (i.e. the space within which the head should be able to move freely without compromising the data quality) of 32 x 21 cm at 60 cm distance (SensoMotoric Instruments 2015; Conklin et al. 2018).

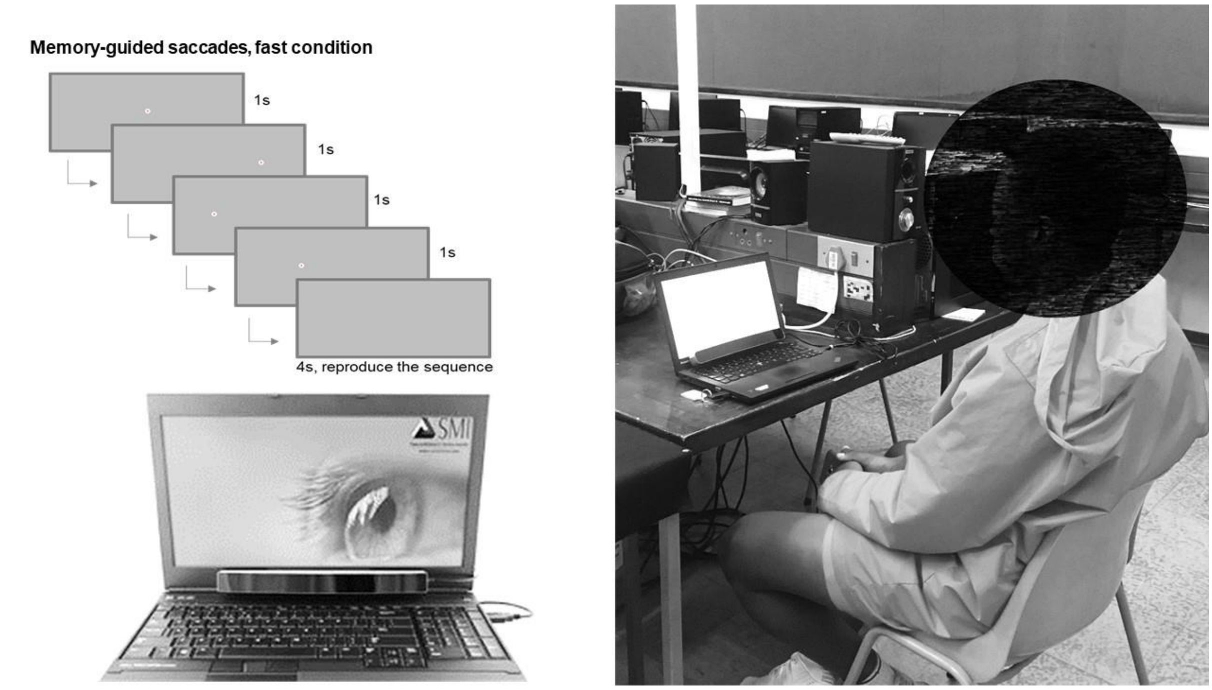

Figure 4.1. Experimental setup © Nadja Snegireva.

4.2.3. Procedure

The concussed participants attended three testing sessions: in the early stage as soon as possible after the injury (a maximum of one week, hereafter referred to as session

1), in the recovery stage at 2-4 weeks post-injury (session 2), and finally at post-factum baseline stage approximately 3 months post-injury, subject to being symptom free at rest and exercise, having completed a graded return-to-play programme and received clearance for return to sport by a sports physician (session 3). The participants in the control group completed two testing sessions separated by one week in order to approximate the time between sessions 1 and 2 of the concussed group. Identical procedures were used for the concussed and control group participants by the same trained assessor. During each session, all participants completed a computer-based eye tracking test. In addition, at session 1 researchers implemented the Sport Concussion Assessment Tool 5 (SCAT5, or Child-SCAT5 for athletes younger than 12 years of age) (Echemendia et al. 2017) with all participants and conducted a structured interview to obtain demographic information and medical history. At the final session the researchers additionally conducted the Montréal Cognitive Assessment (MoCA) (sections which are not covered by the SCAT5), followed by the self-administered Patient Health Questionnaire (PHQ-9) for depressive mood screening.

4.2.4. Eye Tracking Tasks

Participants were seated comfortably at a distance of approximately 70 cm from the computer monitor (Figure 4.1). All instructions were presented automatically as a video to minimize the influence by the operator. A five-point calibration was performed by the operator at the beginning of the session, and re-calibration was performed three more times throughout the experiment to account for a possible shift in the head or body position. The duration of the eye tracking tasks was 19 minutes, and the total duration of the eye tracking experiment including video instructions, breaks and calibration was approximately 45 minutes. In order to minimise the effects of fatigue, covert attention, or mind wandering known to happen in eye tracking experiments (Hvelplund 2014), the duration of most tasks was kept under a minute, and after each task the participants were given an opportunity to take a break. The instructional videos were made in an engaging manner in order to keep participants motivated.

For all tasks, participants used their eyes to track a white circular target (diameter 0.5°) with red contour and a red dot in the middle. The test battery consisted of six tasks: (1) two SPS tasks, (2) a single fixation stability task, (3) two groups of MGS tasks, (4) three

SP tasks, (5) two RS tasks, and (6) three AS tasks. A description of each task is provided below.

1. For each of the **self-paced saccade tasks,** the participants were shown two targets for 30s at a distance of 10° (task 1) / 20° (task 2) and instructed to look back and forth between them as fast as possible. This experimental design has been previously used in several concussion studies (Heitger et al. 2009; Johnson et al. 2015b; DiCesare et al. 2017). Self-paced saccades are defined as a type of voluntary saccade usually made as fast as possible between two stationary targets in a fixed amount of time; the decision when to start a saccade and where to move the eyes next is intentional and planned (McDowell et al. 2008; Berchicci et al. 2012). This task is aimed to determine the ability of the participant to initiate the saccades without verbal commands, as well as disengage the fixations and maintain the motivation in order to trigger repeated saccades (Taghdiri et al. 2018).

2. In the **fixation stability task,** the participants were shown a 90-second video of balls moving rapidly towards them and an overlaid central fixation cross. They were instructed to head the balls by slightly moving their head while keeping the eyes steadily focused on the central fixation cross. This task was designed in approximation to the methodology of Murray et al. (2017a) and tests the individual's ability to maintain a steady gaze and inhibit unwanted saccades (Krauzlis et al. 2017).

3. In each of the **memory-guided saccade tasks**, the participants were shown a target that jumped three times in a sequence. In accordance to the methodology described in relevant studies (Heitger et al. 2009; Johnson et al. 2015b), the sequence was repeated five times, after which the participants were asked to reproduce the sequence with their eyes on a blank screen. A total of five tasks were grouped into two conditions: slow (duration of each target position was 2s, two tasks), and fast (target duration 1s, three tasks, Figure 4.1). MGS are defined as the eye movements directed towards remembered locations of objects without the presence of a visual stimulus (Kori et al. 1998). This task is used to assess both the executive function (encode and memorize the target locations) and

oculomotor function (plan and execute a sequence of voluntary saccades) (Pierrot-Deseilligny et al. 1991).

4. The **smooth pursuit tasks,** also designed according to the methodology provided by relevant studies (DiCesare et al. 2017; Danna-Dos-Santos et al. 2018), required the participants to follow the moving target with their eyes. Three conditions were employed: sinusoidal (target moved in a horizontal sinusoidal pattern for 30s at the amplitude of 20° with an average velocity of 14°/s and peak velocity of 21.6°/s; this task was repeated three times), diagonal (target moved in a diagonal sinusoidal pattern for 30s at the amplitude of 20° along the x-axis and 10° along the y-axis with an average velocity of 14°/s and peak velocity of 22°/s), and sawtooth (target moved in a horizontal sawtooth pattern for 30s at the amplitude of 20° with an average velocity of 14°/s). Smooth pursuit eye movements allow to track moving objects across a stationary background, such as an airplane in the sky (Robinson et al. 1986). The purpose of this task is to test the ability to keep the fovea steadily focused on the object by utilizing reactive mechanisms of the oculomotor system, predictive compensation for the change in direction, gain control, as well as the working memory component (Fukushima et al. 2013).

5. The **reflexive saccade and antisaccade tasks** were designed in accordance with the internationally standardized AS protocol (Antoniades et al. 2013): the participants were shown a fixation cross followed by the target positioned pseudo-randomly at 4°, 5° or 10° to the left or to the right from centre, and asked to look either at the target (RS) or at the exact opposite (mirrored) location (AS) as fast and as accurately as possible. Each RS task consisted of 60 targets and each AS task consisted of 40 targets. All targets were balanced between left and right. Reflexive saccades are defined as eye movements that occur in response to a sudden appearance of an object of interest (Hutton 2008), whereas AS are voluntary saccades made in the direction opposite to the stimulus (Pierrot-Deseilligny et al. 2004). These tasks are used to assess the sensorimotor transformation (i.e. the process of converting sensory stimuli into motor commands) (Pouget and Snyder 2000) and the ability to sustain attention; AS additionally provide insight into the complex executive functions like spatial memory and inhibition (McDowell et al. 2008).

The first task, SPS, was preceded by a practice trial in order to allow participants to familiarise themselves with the environment. Additionally, preliminary tests demonstrated that the MGS task often came unexpected despite the detailed instructions; therefore, a practice trial was added for it as well. All other tasks were well understood and didn’t require practice trials.

4.2.5. Eye Tracking Data Analysis

The eye tracking data processing was performed by SMI BeGaze software (SensoMotoric Instruments GmbH, Teltow, Germany), the event detection parameters were as follows: minimum saccade duration 22 ms, peak saccadic velocity threshold 40°/s, minimum fixation duration 50 ms. The gaze and target positions were converted from pixels into the degrees of visual angle or back using OpenSesame code (Mathôt 2012; Mathôt et al. 2012).

The eye tracking variables for the analysis were pre-specified in the experimental design phase based on the systematic review of the literature covering the use of eye tracking technology in sports-related concussion assessment (Snegireva et al. 2018) and further extensive analyses of literature on eye movement impairments associated with brain traumas. Table 4.1 provides an overview of the variables structured according to four classes of eye tracking measurements (i.e. movement, position, count, latency) (Holmqvist et al. 2011), as well as according to six types of task used in the current study (i.e. SPS, fixation stability, MGS, SP, RS and AS). Across all measures and stimulus conditions, in total there were 47 variables. The latency of RS and AS was calculated only for the saccades that were made in the correct direction and had a duration of ≥ 50ms (Antoniades et al. 2013). Peak velocity of the SP was calculated upon excluding saccades.

Table 4.1. Experimental design and response variables.

Tasks → Variables ↓	**Self-paced saccades**	**Fixation stability**	**Memory-guided saccades**	**Smooth pursuit**	**Reflexive saccades**	**Antisaccades**
Instruction	*"You will see two dots that do not move. Look between these two dots back and forth, back and forth as quickly as you can, and as accurately as you can."*	*"You will see balls flying at you. Don't look at them – look at the middle of the screen and try to hit each ball by slightly moving your head towards it. Keep your eyes focused on the centre of the screen."*	*"A dot will jump 3 times in a sequence from one position to the next, and to the next. Remember this sequence! It will be repeated to you 5 times. After that you will see an empty screen. Repeat the sequence you saw from your memory."*	*"You will see a dot that is moving, like this. Follow it with your eyes until it disappears."*	*"A dot will appear to the left or to the right from centre. As soon as it appears, look at it as fast as you can."*	*"A dot will appear to the left or to the right from centre. As soon as it appears, look at the exact opposite (mirrored) location as fast and as accurately as you can."*
Conditions	*Two conditions: 10° and 20° (distance between targets)*		*Two conditions: slow and fast*	*Three conditions: Sinusoidal, diagonal, saw tooth*		
Movement	Peak Velocity [°/s]			Peak Velocity [°/s]	Peak Velocity [°/s]	Peak Velocity [°/s]
Position	Blink Duration Average [ms]	Blink Duration Average [ms] Diversion Duration [ms]	Blink Duration Average [ms] Positional Errors [%]	Blink Duration Average [ms]	Directional Errors [%]	Directional Errors [%]
Count	Saccade Count [n] Blink Rate [n/s]	Saccade Count [n] Blink Rate [n/s]	Saccade Count [n] Blink Rate [n/s]	Intrusive Saccades Count [n] Blink Rate [n/s]		
Latency				Phase horizontal [%] Gain horizontal [%]	Latency [ms] Gain [%]	Latency [ms] Gain [%]

Abbreviations: s: second; ms: millisecond; °/s: degrees per second; n: number; n/s: number per second; %: percentage

4.2.6. Statistical Analysis

Statistical analyses were performed separately for adult and youth groups using TIBCO Statistica® (TIBCO Software Inc., Palo Alto, CA, USA) software, version 13 and Excel (Microsoft® Corporation, Redmond, WA, USA). A priori and post-hoc power analyses were done using G*power 3.1.9.3 for Windows software (Faul et al. 2007) with power set at 0.80 and alpha set at 0.05.

First, the normality of the distribution of each selected variable was examined using the Shapiro–Wilk test and visually (i.e. skewness and kurtosis). As expected, the majority of variables were not normally distributed, even following a log-transformation (mostly due to the outliers, which are common in eye tracking data (Holmqvist et al. 2011)). The descriptive statistics are presented according to the normalcy of distribution: means ($\bar{x}$), standard deviations (± SD) and 95% confidence intervals (CI) are provided for the normally distributed variables, and medians (MED) with interquartile ranges (IQR) are provided for the non-normally distributed variables.

Further, in accordance with the literature (de Vet et al. 2006; Koo and Li 2016), the sessions 1 and 2 of the control group were compared in order to assess the reliability of the eye tracking protocol. Four measures were employed: the intraclass correlation coefficient (ICC) measures (specifically, $ICC_{agreement}$ (de Vet et al. 2006)), standard error measures (SEM, specifically, $SEM_{agreement}$ (de Vet et al. 2006)), smallest real difference (SRD), and the percentage mean (% mean). Minimum norm quadratic unbiased estimator method was used to estimate the variance components used for ICC calculation, since it does not require normality assumptions (Rao 1971). The ICC was calculated by dividing the variance in persons by total variance, where the total variance consisted of variance in persons, systematic variance between testing sessions, and residual variance. The SEM was calculated as a square root of the error measurement, the latter consisting of a sum of systematic variance between testing sessions and residual variance. Since ICC scores are lowered if the variance in persons is low (as is evident from the formula), SRD is also presented, calculated as $1.96 \times \sqrt{2} \times \sigma \times \sqrt{(1\text{-}ICC)}$ (Beckerman et al. 2001; Schuck and Zwingmann 2003), and the percentage mean metric calculated by dividing the SRD of each variable by the mean value of this variable between testing sessions 1 and 2 of the concussed group (Cochrane et al. 2019).

An ICC score of above 0.90 indicates excellent reliability, $0.75 < ICC \leq 0.90$ indicates good reliability, $0.50 < ICC \leq 0.75$ indicates moderate reliability, and ICC score below 0.50 indicates poor reliability (Cicchetti 1994; Koo and Li 2016; Post 2016; Murray et al. 2017b). Therefore, all variables that presented $ICC > 0.75$ were selected for further analyses. While the authors are aware of the criticism regarding accepting the ICC scores below 0.75 (Post 2016), in order to minimize the type II error, the variables with the moderate reliability score ($0.50 < ICC \leq 0.75$) that demonstrated the percentage mean of below 30% were also included in subsequent analyses. The same method was used by Cochrane et al. (2019) who investigated oculomotor function in SRC.

Subsequently, the differences between the concussed and control groups at session 1, as well as the changes across the testing sessions 1, 2 and 3 within the concussed group were analysed using a series of independent samples Mann–Whitney U tests and Wilcoxon signed ranks tests (for non-normally distributed variables) or repeated measures ANOVA (for normally distributed variables). Post-hoc tests were performed on the variables with significant effects identified by the ANOVA. For these comparisons, the alpha level was set at 0.01 following a Bonferroni correction. For all other comparisons (e.g. demographic information) the alpha level was set at 0.05.

The effect sizes (eta-squared; η^2) were calculated based on the Z-score in accordance with the recommendations for non-parametric tests (Fritz et al. 2012; Grissom and Kim 2012). The resulting effect size values range from 0 to 1 and indicate the proportion of variance in the dependent variable that can be explained by the independent variable (Tomczak and Tomczak 2014). The effect sizes can be considered small ($\eta^2 \geq 0.01$), medium ($\eta^2 \geq 0.06$) or large ($\eta^2 \geq 0.14$) (Lakens 2013).

Finally, a series of Spearman correlation (Spearman rho (ρ)) analyses were carried out for the results of session 1 to determine whether there was an association between the eye tracking metrics and (1) the severity of the concussive symptoms measured with the SCAT5, as well as (2) self-reported number of previous concussions. Correlation was considered strong ($\rho \geq 0.60$), moderate ($0.40 < \rho < 0.60$), weak ($0.2 \leq \rho \leq 0.40$), or negligible ($\rho < 0.2$) (Portney and Watkins 2009; Akoglu 2018).

4.3. Results

4.3.1. Demographic Information

Seventy male athletes (34 adult athletes, age ranging from 19-34, and 36 youth athletes, age ranging from 10-18 years) with a recent concussion and 92 male age-matched healthy controls (33 adult and 59 youth athletes) were enrolled in the study and completed session 1. Due to attrition, the participant numbers at subsequent sessions were lower: session 2 was completed by 56 concussed (28 adult and 28 youth athletes) and 70 controls (27 adult and 43 youth athletes), and session 3 was completed by 20 concussed participants (18 adult and 2 youth athletes). One-third of participants were cleared by a medical specialist to return to sport by session 2, and all participants were cleared by session 3. Concussed participants completed session 1 at 3.0 [2.0-4.0] days post-injury, session 2 at 10.5 [9.0-12.5] days and session 3 at 40.5 [33.0-70.5] days post-injury. Time that elapsed between sessions 1 and 2 of the control group was 7.0±3.9 days. The demographic information is summarised in Table 4.2. There were no differences between the control and concussed groups in any of the characteristics except the number of past concussions.

4.3.2. Post-hoc Power Analysis of Sample Sizes

Post-hoc power analysis (Table 4.4) in the adult cohort revealed that the difference in the SPS saccade count had a power of 0.73 between sessions 1 and 2, and 0.98 between sessions 1 and 3. In the youth cohort, the differences between sessions 1 and 2 had the following power: 0.99 for the average blink duration of the sinusoidal SP, 0.90 for the average blink duration of the fast MGS, 0.80 for the directional errors of AS, and 0.18 for the gain of the diagonal SP.

4.3.3. Reliability

The response variables that were considered reliable differed between adult and youth groups; consequently, age group comparisons were not possible. Overall, the reliability of most variables was low: only 6 variables for adult and 11 for youth groups achieved the ICC of above 0.50 (Table 4.3).

Table 4.2. Demographic information of participants reported as $\overline{x}$ ± SD [95% CI].

	Adult			Youth		
Variables	**Concussed**	**Control**	**p-value**	**Concussed**	**Control**	**p-value**
Age (y)	*22.5 ± 3.6 [2.9 - 4.9]*	*22.2 ± 2.9 [2.3 - 3.8]*	*0.74*	*14.8 ± 2 [1.7 - 2.7]*	*15.4 ± 2.2 [1.8 - 2.7]*	*0.23*
Height (cm)	*179.8 ± 9.3 [7.3 - 12.8]*	*177.1 ± 6.7 [5.4 - 8.9]*	*0.20*	*167.9 ± 10.8 [8.6 - 14.5]*	*172.4 ± 13.3 [11.2 - 16.2]*	*0.12*
Weight (kg)	*89.2 ± 16 [12.6 - 21.9]*	*85.3 ± 12.2 [9.8 - 16.2]*	*0.29*	*62.8 ± 16.4 [13.1 - 22.1]*	*64 ± 15.3 [12.9 - 18.7]*	*0.74*
Sport participation (y)	*13.7 ± 4.1 [3.2 - 5.6]*	*11.9 ± 4.2 [3.4 - 5.6]*	*0.10*	*5.8 ± 2 [1.6 - 2.8]*	*6.6 ± 2.7 [2.3 - 3.3]*	*0.20*
Education (y)	*13.4 ± 1.9 [1.5 - 2.6]*	*13.6 ± 2 [1.6 - 2.7]*	*0.73*	*11.1 ± 1.9 [1.6 - 2.5]*	*10.9 ± 2.1 [1.8 - 2.6]*	*0.69*
Past concussions (*f*)	*1.3 ± 1.5 [1.2 - 2.1]*	*0.2 ± 0.4 [0.3 - 0.5]*	*<0.01*	*0.8 ± 0.8 [0.7 - 1.1]*	*0 ± 0.2 [0.2 - 0.2]*	*<0.01*
Days since injury (session 1)	*2.7 ± 1.1 [0.9 - 1.5]*			*3.3 ± 1.6 [1.3 - 2.1]*		
MoCA score (last session)	*16.6 ± 1.4 [1 - 2.1]*	*16.6 ± 1.3 [1 - 1.7]*	*0.99*	*16.7 ± 0.8 [0.5 - 2]*	*16.6 ± 1.3 [1.1 - 1.6]*	*0.10*
PHQ-9 score (last session)	*2.4 ± 3.3 [2.5 - 5]*	*3 ± 2.4 [1.9 - 3.2]*	*0.53*	*7.2 ± 1.9 [1.2 - 4.8]*	*3.5 ± 3 [2.5 - 3.6]*	*0.01*

Abbreviations: y: years; f: frequency; $\overline{x}$: mean, SD: standard deviation; CI: confidence interval; MoCA: Montreal Cognitive Assessment; PHQ-9: Patient Health Questionnaire

Table 4.3. Eye movement variables demonstrating ICC scores [95% CI] > 0.50 with standard error measures, smallest real difference, and percentage mean.

Stimulus, condition	Variable	Unit	ICC [95% CI]	SEM	SRD	% mean
			Adult			
SPS, 10°	Saccade count	n	0.86 [0.77 - 0.91]	21.12	146.57	119%
AS	Directional errors	%	0.68 [0.51 - 0.79]	17.02	30.25	47%
SPS, 20°	Saccade count	n	0.60 [0.41 - 0.74]	38.46	166.20	118%
Fixation stability	Blink rate	n/s	0.57 [0.37 - 0.72]	0.35	1.03	200%
SPS, 10°	Blink rate	n/s	0.56 [0.35 - 0.71]	0.09	0.37	113%
SP, saw tooth	Blink duration average	ms	0.53 [0.27 - 0.71]	97.81	399.04	134%
			Youth			
MGS, fast	Blink duration average	ms	0.99 [0.98 - 0.99]	21.76	59.44	19%
AS	Directional Errors	%	0.78 [0.69 - 0.85]	9.38	25.33	49%
SP, diagonal	Gain	%	0.77 [0.68 - 0.84]	145.99	395.10	166%
SP, sinusoidal	Blink Duration Average	ms	0.63 [0.49 - 0.74]	63.95	173.49	23%
SP, diagonal	Blink rate	n/s	0.62 [0.48 - 0.73]	0.37	1.01	276%
SP, sinusoidal	Gain	%	0.59 [0.45 - 0.7]	144.38	408.07	187%
SP, sinusoidal	Blink rate	n/s	0.55 [0.4 - 0.67]	0.32	0.91	300%
SP, saw tooth	Gain	%	0.54 [0.39 - 0.66]	299.54	818.00	377%
Fixation stability	Fixation dispersion average	px	0.52 [0.36 - 0.65]	62.79	167.33	149%
MGS, slow	Saccade count per step	n	0.52 [0.36 - 0.65]	1.88	5.25	136%
AS	Latency	ms	0.51 [0.35 - 0.64]	32.38	91.93	52%

Abbreviations: ms: millisecond; °/s: degrees per second; n: number; n/s: number per second; %: percentage; px: pixels; SEM: standard error measures; SRD: smallest real difference; AS: antisaccades; MGS: memory-guided saccades; SP: smooth pursuit; SPS: self-paced saccades

4.3.4. Validity

Comparison of the concussed and control groups at session 1

Five variables were selected for further analysis: one for the adult group, and four for the youth group (Table 4.4).

Table 4.4. Between-group differences at session 1 for concussed and control groups in adult and youth participants reported either as $\bar{x}$ [95% CI] or MED {IQR}.

Adult

Stimulus, condition	**Variable**	**Concussed**	**Control**	**p-value**	**η^2**	**Power (1-β)**
Self-paced saccades 10°	Saccade count	*110.4 [44.5 - 76.6]*	*137.3 [44.6 - 73.3]*	*0.383*	*0.06^M*	*0.45*
Youth						
Memory-guided saccades, fast	Blink duration average	*281.9 {236.7 - 442.1}*	*209 {183.1 - 246.1}*	*0.001**	*0.17^L*	*0.53*
Smooth pursuit, sinusoidal	Blink duration average	*265.7 {229.6 - 359.6}*	*229.1 {188.9 - 290.6}*	*0.016*	*0.06^M*	*0.52*
Smooth pursuit, diagonal	Gain	*171.3 {154 - 219.9}*	*164.2 {146.1 - 227.4}*	*0.399*	*0.01^S*	*0.08*
Antisaccades	Directional errors	*45.9 [17.5 - 28.2]*	*52.4 [15.1 - 22]*	*0.056*	*0.02^S*	*0.33*

*Abbreviations: ^{S}: small effect size ($\eta^2 \geq 0.01$); ^{M}: medium effect size ($\eta^2 \geq 0.06$), ^{L}: large effect size ($\eta^2 \geq 0.14$); CI: confidence interval; IQR: interquartile range; $\bar{x}$: mean, MED: median; η^2: effect size; β:beta (probability of type II error); *: statistically significant ($p \leq 0.01$)*

Comparisons of the sessions 1, 2 and 3 within the concussed group

The concussed adult group demonstrated a gradual increase in the number of saccades (Figure 4.2) with the largest difference between session 1 and session 3 (p = 0.02).

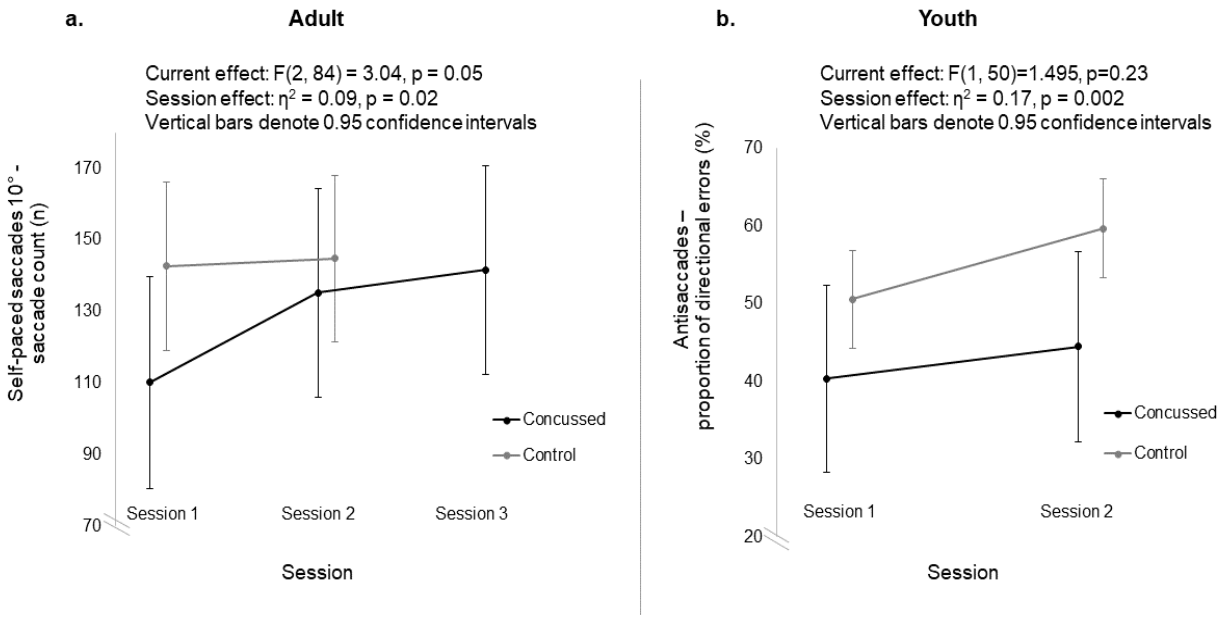

Figure 4.2. a. Number of SPS over the sessions for concussed vs. control adult groups; b. Proportion of directional errors for AS over the sessions for concussed vs. control youth groups.

Due to high attrition, only comparisons between the sessions 1 and 2 were possible for the youth group. The concussed participants had significantly lower error rates in the AS task (Figure 4.2). Post-hoc analysis revealed a significant increase in the proportion of errors in the control group from session 1 to session 2 (p = 0.002).

Although not statistically significant, the average blink duration in the concussed group decreased from session 1 to session 2 (MGS: MED and IQR 281.9 [236.7 - 442.1] for session 1 and 232.9 [173.2 – 325.1] for session 2, p= 0.35; diagonal SP: MED and IQR 265.7 [229.6 - 359.6] for session 1 and 237.3 [193.7 – 279.1] for session 2, p = 0.48).

Relationship between the eye tracking performance and symptom severity and number of past concussions

Several eye tracking variables showed weak correlations in the expected direction with the SCAT symptom severity score at session 1 and the number of past concussions (Table 4.5).

Table 4.5. The relationship between eye tracking variables and SCAT5 symptom severity score as well as number of past concussions.

Stimulus, condition	Variable	Symptom severity		Past concussions	
		ρ	p-value	ρ	p-value
Adult					
SPS, 10°	Saccade count	-0.36*	< 0.01	0.17	0.19
Youth					
MGS, fast	Blink duration average	0.12	0.36	0.24	0.06
SP, diagonal	Gain	0.26*	0.01	0.25*	0.02
SP, sinusoidal	Blink duration average	0.08	0.45	0.08	0.48
AS	Directional errors	-0.24*	0.02	-0.03	0.80

*Abbreviations: ρ: Spearman rho; AS: antisaccades; MGS: memory-guided saccades; SP: smooth pursuit; SPS: self-paced saccades; *: p < 0.05*

4.4. Discussion

There were three main findings of the study. First, the overall reliability of eye tracking variables assessed in athletes participating in contact sports was relatively low for most eye measurements. Second, reduced number of self-paced saccades might be a reliable indicator of a concussion in adult athletes. Finally, concussed youth athletes exhibited longer blink durations for MGS and diagonal SP compared to the healthy controls that improved over time. The findings are discussed in detail below.

4.4.1. Reliability

This is the first comprehensive longitudinal study that systematically assessed the reliability and validity of eye tracking metrics across several paradigms in heathy and concussed adult and youth athletes participating in such contact sports as rugby and football. Establishing the level of reliability is crucial for eye tracking to be considered for clinical application; therefore, researchers should not assume that a variable is reliable in the context of their experimental design and participant cohort. A recognized method of quantifying reliability is the intraclass correlation coefficient (ICC) which is the ratio of the between-subject component of the variance to the total variance (Beckerman et al. 2001; Schuck and Zwingmann 2003). The higher the ratio, the better the reproducibility. Since the ICC is focused on the between-subject variability, while the within-subject variability over time is left out of scope (Beckerman et al. 2001), the smallest real difference (SRD) was also calculated. It establishes the boundaries of a difference that can reliably be detected by the tool. The SRD is expressed in the same units as the measurement tool and is therefore easier for clinical interpretation. The absolute difference between any two future measurements is expected to not exceed the value of the SRD, and if it does, this indicates the presence of real differences between patients and healthy controls or a real change over time (de Vet et al. 2006; Vaz et al. 2013; Nij Bijvank et al. 2018). To give the SRD scores a perspective, the percentage means that provide the ratio of the SRD to the mean score of the concussed participants. It should be noted, however, that the percentage mean does not give any indication of whether the utilised protocol is actually able to measure the minimal clinically relevant change, which is the amount of minimal change that clinicians and researchers (subjectively) consider important (Beckerman et al. 2001).

Most of the variables in the current study failed to demonstrate the satisfactory levels of reliability. There are several possible reasons for this. First, the ICC is directly affected by between-subject variability in healthy people; thus, in a homogeneous population, such as athletes, with low between-subject variance (e.g. in reaction times or accuracy) the ICC is lower. For example, similar to another recent study (Nij Bijvank et al. 2018), the ICC scores in the fixation stability task were low, because all participants generally were able to maintain a similarly steady fixation. Additionally, another study found that healthy athletes demonstrated lower variability in the saccadic reaction times compared to non-athletes (Lange et al. 2018), possibly due to regular exposure to the environment fostering visual skills, whereas the concussed cohorts tend to have higher variability compared to healthy controls (Dockree et al. 2006; Ghajar and Ivry 2008; Lange et al. 2018).

Second, since the control group consisted of athletes participating predominantly in contact or even collision sports, such as rugby, and the absence of concussions in the past two years was only confirmed by their self-reports, it is quite possible that the performance of the control group was affected by undetected recent concussions and by the effects of sub-concussive head impacts. This is in line with an earlier comparison of the AS error rates of healthy controls in two concussion studies, one conducted in a general population (Balaban et al. 2016), and the other with athletes (Cochrane et al. 2019), with athletes performing markedly worse than the general population. Correspondingly, the previous studies that found high reliability in eye tracking metrics were conducted in a general population (Bargary et al. 2017), whereas the reliability measurements found in the athletic cohorts were much lower (Howell et al. 2018b; Cochrane et al. 2019). Taken together, this invites dedicated research to further investigate eye tracking metrics reliability specifically in athletes. Moreover, since age might also affect variability (for example, working memory capacities might be lower in paediatric populations compared to the adults (Gathercole 1998)), it is recommended to further investigate the reliability of eye tracking metrics particularly in paediatric athletes.

Third, the accuracy and precision of any eye tracking experiment can deteriorate due to head movements or change in operating distance (Blignaut and Wium 2014). Similar to other studies that found rather low ICC scores (Lange et al. 2018; Cochrane et al. 2019), and opposite to earlier studies where the scores were higher (Ettinger et al. 2003; Maruta et al. 2013), the head position of the participants was not fixated. A recent study established that the eye tracking data quality generally deteriorates when the participant's head is not in an optimal position in front of the eye tracker (Niehorster et al. 2018). Therefore, even though the SMI eye tracker has a high tolerance for head movements (SensoMotoric Instruments 2015; Conklin et al. 2018), all participants were made sure to be positioned optimally, and recalibration was performed regularly, some reduction of data accuracy caused by shifts in the position and movement of the head is possible. Ethnicity (different shapes of the eyes) has been shown in one study to worsen results but only in Asian participants, with no difference between the African and Caucasian participants (Blignaut and Wium 2014) and therefore would in all likelihood not have impacted the current study.

Finally, it is known that the eye movements are affected by a myriad of confounding factors, such as mental disorders (ADHD, autism, schizophrenia, depression) (Karatekin 2007; O'Driscoll and Callahan 2008), lighting conditions, and also tiredness (Stern et al. 1994; Di Stasi et al. 2012), caffeine intake (Smith et al. 2003), or emotional status (Beckerman et al. 2001). Thus, the peak velocity of the saccades has long been known to present a large intra-individual variability in a healthy population (Bollen et al. 1993). Generally, in neuropsychological studies, it is common for healthy individuals to present high intra-individual variability that can be attributed to a range of situational factors, such as fluctuations in motivation and effort, inattentiveness, fatigue, or minor illness (Binder et al. 2009). Since the testing took place at different times of the day, it is also possible that this factor affected the reliability of some variables, for example, the ability to concentrate is known to be more variable in the morning compared to the afternoon (Roy-Byrne et al. 1995). Even though most of these factors were considered and controlled for with strict in- and exclusion criteria; it is possible that some factors (like fatigue, day-to-day variability, and/or motivation) still reduced the reliability scores.

On the other hand, in order to be practical and useful in assisting the clinicians in concussion diagnostics, a biomarker needs to present a certain level of robustness to situational factors. Therefore, the subsequent comparisons between the concussed and control groups focused only on variables that demonstrated such robustness. Further dedicated studies with large samples are required to verify the reliability of the eye tracking variables.

4.4.2. Validity

This study resulted in several reliable metrics that might be indicative of a recent concussion. In line with the growing appeal for sport and medical researchers to report both statistical and clinical significance (Sullivan and Feinn 2012; Tomczak and Tomczak 2014), the findings are considered in light of the identified p-values, as well as of effect sizes. The effect sizes in the current study are in keeping with acceptable values in clinical sciences which tend to be rather low, since predicting neurological outcomes is an extremely complex undertaking (Hamilton et al. 2015).

Saccades and Antisaccades

Since SRC is more likely to manifest in eye movements involving complex cognitive skills (Mani et al. 2018; Snegireva et al. 2018), the concussed group was expected to underperform in MGS, AS, and SPS tasks, but not in RS task. Since most of the variables did not demonstrate sufficient reliability, only the saccade count in the SPS task in the adult group, and proportion of the directional errors in the AS task for the youth group can be discussed.

The trend observed in the saccade count in the SPS task suggests that this metric might indeed be indicative of a concussion in the adult athletes, since the concussed group presented a gradual increase in the number of saccades from session to session, with the results of the last session approaching the healthy controls. This confirms the findings of an earlier meta-analysis (Snegireva et al. 2018) that demonstrated significantly higher number of saccades in healthy controls. The effect size in the current study was promising, and the level of statistical significance was possibly not reached due to the sample size. The statistical power between the sessions was very high, indicating that a comparison within the same individuals over time is more likely to detect the effect of a SRC than comparison to healthy controls.

Neuroimaging studies demonstrated that SPS were associated with the activity of multiple brain areas: information is processed in the fovea, superior colliculus, supplementary eye fields, and dorsolateral prefrontal cortex; frontal eye fields are responsible for disengaging fixations; brainstem generates a neural command to initiate a saccade; and anterior cingulate cortex maintains the motivation to complete the task) (Gaymard et al. 1998; Heitger et al. 2002; Johnson et al. 2015b; Leigh and Zee 2015; Taghdiri et al. 2018) and are therefore likely to be affected by a concussion regardless of the location of the impact.

Worth discussing is the fact that the proportion of directional errors in the AS task showed good reliability in the youth group, and a moderate level of reliability in the adult group. This finding is in line with an earlier study of reliability of eye tracking measurements (Ettinger et al. 2003) and further strengthens the evidence that this measure can serve as an oculomotor marker for recognising brain disorders or traumas (Subramaniam et al. 2018; Kleineidam et al. 2019). The proportion of errors in the AS task in the current study was higher in the youth control group compared to the youth concussed group (even though statistical significance was not reached); and the performance of the control group significantly worsened (i.e. the proportion of errors increased) at the second session compared to the first. At first sight, this seems counter to expectations, even though an earlier study showed similar reductions in error rate of the control group between two sessions conducted one week apart (Ettinger et al. 2003). However, in the context of the other variables, particularly latency and gain of the primary saccade, it becomes evident that the control group made a speed-accuracy trade-off that is common when decision-making is involved (Gold and Shadlen 2007) and was observed in the prior studies (Wu et al. 2010; Lange et al. 2018). Namely, both latency and gain were the lowest in session 2 of the control group compared to session 1 and to the concussed group. This indicates that the control group in their second session reacted to the target faster but made a trade-off in terms of the number of directional errors they made.

Finally, due to the low reliability of this variable in the adult cohort, the current study did not confirm the findings of a meta-analysis of studies with adult athletes (Snegireva et al. 2018) where the concussed group showed a significantly higher proportion of errors. As Leigh and Zee (2015) point out, the AS tasks is a valuable tool for evaluating the function of the brain, but since it is highly sensitive to artefacts and confounding factors (motivation, fatigue, age, executive functions, reward, target pattern, and many more) it requires careful and standardized approach.

Interestingly, contrary to an earlier study (Irving et al. 2009), adult and youth populations demonstrated similar error rate trends in the RS compared to the AS: all participants in the concussed as well as in the control groups made numerous AS errors and very few RS errors, implying that the latter variable alone is not sufficient for concussion diagnosis.

Smooth Pursuit Eye Movements

Based on previous research, a number of impairments with respect to SP in concussed athletes were expected, including larger gain resulting in higher frequency of catch-up saccades (Suh et al. 2006; Caeyenberghs et al. 2009; Ciuffreda et al. 2009; Gitchel et al. 2014; Samadani et al. 2016). In contrast to the study hypotheses, the results indicated that there was no significant difference in the analysed variable, diagonal SP gain in the youth group, and the effect size was very small.

Since only classic SP paradigms were used, the nature of the task might have influenced the results: the tasks that require more predictive tracking put more challenges on the individual's oculomotor system as well as the attentional, anticipatory and working memory capacity (Johnson et al. 2015b). Consequently, more demanding SP tasks, such as ones employing a gap paradigm or a dual-task paradigm (e.g. adding a working memory component) might demonstrate higher sensitivity to the consequences of a concussion, and further research focusing on such tasks is called for.

Fixation stability

Based on a previous experiment of a similar design (Murray et al. 2017a), the concussed athletes were expected to demonstrate decreased fixation stability manifesting in a higher dispersion of the fixations (i.e. the perimeter within which the gaze moves while it is supposed to stay steady) and higher saccade count. However, since the reliability of these metrics was not sufficient to justify including them into the analysis (often due to low variability within the healthy subjects), it was not possible to confirm or disprove this hypothesis.

Blink variables

This is the first eye tracking study to assess spontaneous blink performance in concussed athletes. Researchers believe that the spontaneous eye blinks are influenced by a range of factors. First, they are linked to central dopamine activity. Longer blink durations and reduced blink rates have been consistently observed in Parkinson's disease (which is associated with the progressive reduction of dopamine activity in the striatum), whereas increased blink rates and shorter durations are characteristic for schizophrenia (which is linked to excessive dopamine activity in the striatum) (Karson et al. 1984; Jongkees and Colzato 2016; Abusharha 2017). In a healthy population, blinks are sensitive to the attentional demands and cognitive workload (Doughty 2001). Thus, longer blink durations have been associated with worse performance on the inhibitory control tasks (Colzato et al. 2009) and fatigue (Marandi et al. 2018). Overall, blink duration lies within a range of 100-400 ms (Stern et al. 1984; Ousler et al. 2014).

The findings of this study demonstrate that the concussed youth athletes tend to exhibit longer blink durations compared to the healthy controls. This can possibly be explained by the potential reduction of striatal dopamine levels associated with a concussion (Chen et al. 2017; Jenkins et al. 2018), which, in turn, may cause the alterations in the spontaneous blinks (Jongkees and Colzato 2016; Groen et al. 2017). The findings were most prominent for the MGS task which also involves working memory and attention (Snegireva et al. 2018). It is therefore possible that impairments in these higher executive functions that are characteristic of a youth concussion (Moore et al. 2016) increased the fatigue of the concussed participants while executing the tasks, which is known to lead to longer blink durations (Stern et al. 1994; Schleicher et al. 2008). In agreement with the systematic review that found MGS impairments only in acute (up to 30 days post-injury) concussions (Snegireva et al. 2018), current results showed a gradual improvement of the eye blink duration from session 1 to session 2:

the blink duration decreased by 24% and 18% for MGS and sinusoidal SP, accordingly, although statistical significance was not reached.

Additionally, in a heathy population, blinks were found to be related to age: thus, blink rate and duration increase from infancy to adulthood and reach adult levels by the age of 20 (Caplan et al. 1996; Liu and Shen 2011; Groen et al. 2017). It is possible, therefore, that blink-related metrics in a youth population show higher sensitivity to a concussion compared to adults. To authors' knowledge there is no literature connecting eye blink duration to SRC, and further research is certainly called for in order to confirm this novel finding. Again, the high power revealed by the post-hoc comparison of sessions 1 and 2 of the concussed group suggests that a comparison within the same individuals over time is more likely to detect the effect of a SRC than comparison to healthy controls.

4.4.3. Relationship between Eye Tracking Performance and Symptom Severity and Number of Past Concussions

In the adult group, there was a weak, albeit approaching moderate, negative correlation between the self-reported severity of concussion symptoms and the number of SPS. This confirms the findings of Taghdiri et al. (2018) and Heitger et al. (2009) that this eye tracking variable might reflect the concussion symptom presentation, since this task involves several white matter tracts and cognitive functions that are also associated with concussion symptoms, such as difficulty to concentrate, or feeling in a fog. In the youth group, only weak correlation was found between two variables (gain of the diagonal smooth pursuit and proportion of antisaccade errors) and the symptom severity. Interestingly, two recent studies (Bin Zahid et al. 2018; Mani et al. 2018) suggested that the eye movement impairments in concussion possibly manifest regardless of the reported symptoms, indicating that that eye tracking could be an objective measure largely independent from symptom reporting. Taken together, it is possible that there is a relationship between eye tracking and cognitive symptoms of a concussion, and eye tracking technology can provide the clinicians with further insights in addition to the subjective symptom reports.

Finally, only gain of the diagonal smooth pursuit demonstrated a weak correlation with the number of past concussions. It is possible that the duration and severity of post-concussion pathophysiology might be affected more by the timing of repeat injuries rather than the previous concussion history alone (Giza and Hovda 2014).

4.4.4. Limitations and Future Research

While this research addressed a number of limitations of the previous studies mentioned in the introduction, it has several limitations of its own. A considerable effort was put in assessing the concussed participants at exact same timeframe after a concussion, however, a certain degree of variability in the time that had elapsed after the injury at the moment of testing was unavoidable and constitutes a pragmatic clinical reality of standard and accepted practice. This might have affected the results, since some participants might have been further into the recovery process than others. Additionally, there was certain attrition of participants, since most of the players were cleared to play well before the third scheduled testing session and had little motivation to return.

There is a possibility that the cognitive or physical activities that place increased demands on the oculomotor system or promote general fatigue (for example, sports training or studying for exams), as well as further situational factors (such as motivation or lighting (Hvelplund 2014)) might have affected the eye tracking performance in both the concussed and control groups. In future research, it is recommended to introduce an even more stringent control for confounding factors by, for example, fixating the head, providing identical lighting and sitting conditions, conducting the testing sessions at the same time of the day (e.g. in the morning before school and sporting sessions), and randomizing the order of the tests to prevent a possible learning effect or effects of a fatigue. While an assumption was made that the participants were honest in reporting the symptoms and providing such information as current medications or concussion history, as well as compliant with the task instructions, this cannot be guaranteed. Apart from the antisaccades protocol (Antoniades et al. 2013) and recently published saccades quantification protocol (Nij Bijvank et al. 2018), research on standardised eye movement assessments in brain disorders is lacking, leading to a reliance on single studies in experimental design and making comparisons between studies challenging. Consequently, the utilized protocols may not be fully suitable for SRC assessment, and the ability to reproduce the results of this study needs further investigation. Additionally, due to the general susceptibility of eye tracking technology to the artefacts from analysis algorithms (Shaikh and Zee 2018) and variability of features across different devices, generalizability of findings across devices needs to be confirmed.

Selection bias towards concussed athletes with a higher symptom burden or longer recovery, or control group participants with higher interest in the topic (possibly caused, for instance, by an earlier incident of a subconcussive head impact) might have affected the results of the study, as is common in concussion research (Kristman et al. 2014). Since this study specifically targeted athletes located in South Africa, the findings might not be representative of non-sporting cohorts or other regions. Also, a gender bias is present, since both concussed and control groups consisted of male athletes; therefore, extrapolation to female athletes may be limited. However, studies have established that, when controlled for age, sex does not affect the saccadic or SP performance (Hutton 2008; Sufrinko et al. 2017). Additionally, it is possible that the different sample sizes between the adult and youth groups hindered the comparisons between the age groups. Thus, the findings require confirmation in larger studies comprising further geographic regions, other sports, and both sexes. Further research should also consider investigating in more detail the reliability of eye tracking metrics specifically in sporting cohorts, as well as differentiating according to age in order to see whether younger or older age is associated with higher reliability of eye tracking data.

Finally, using challenging tasks that are closely related to the brain areas involved in executive functions or incorporating a dual-task element may improve the reliability and validity of the eye tracking tests for concussion diagnostics, and further research in this direction is suggested. It is important to recognise that since eye movements are known to be idiosyncratic and related to anatomical (e.g. shape of and length of the eyeball) and personality characteristics (impulsivity, anxiety) (Pearson et al. 2007; Holmqvist et al. 2011; Leigh and Zee 2015), future research should focus on comparing concussed individuals to their own pre-injury or post-recovery baseline values rather than comparing them to healthy controls, yet this research design is not without significant challenge.

4.5. Conclusion

Given the heterogeneity of clinical presentations and outcomes after SRC, sporting and medical experts agree that an individualised and multimodal assessment approach is required that relies on a combination of clinical evaluation, symptom reporting and objective tests (Sherry and Collins 2019). Eye movements have already become an easy-to-measure and easy-to-quantify biomarker for a range of disorders (Shaikh and Zee 2018), however their potential for concussion assessment still needs to be validated. This pragmatic study based in a clinical setting contributes to recent significant advancements in research of the tools available for evaluating SRC.

In conclusion, this study was not able to confirm a large portion of previous research suggesting eye tracking metrics for SRC assessment, primarily due to the fact that the suggested protocols may not be sufficiently reliable for assessing athletes participating in contact sports. A novel finding of this study was that blink duration in MGS and sinusoidal SP was increased in concussed children, and future research should focus on inclusion of this metric to further understand this phenomenon.

While the strengths of this study clearly lie in the very careful selection of variables, unity in the time that elapsed after a concussion at each testing session, and clear stratification by the age group, a broader sample of participants and other combinations of metrics might create models with better reliability and validity.

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CHAPTER 5.
GENERAL DISCUSSION AND CONCLUSION

5.1. Summary of Findings

The overall purpose of this dissertation was to establish whether computer-interfaced eye tracking technology would be a clinically useful, reliable, and valid method to diagnose and monitor youth and adult athletes who have sustained a sports-related concussion (SRC). To summarise the findings, the hypotheses from Chapter 1 are revisited.

Hypothesis 1: Sport medicine clinicians would be aware that in diagnosing a SRC, assessing the eye movements can be useful; however, since the technology is relatively new and needs more extensive validation, only a few clinicians would utilise the ETT in their practice.

The study revealed that even among sports medicine clinicians who regularly diagnose and manage patients with concussion, there is insufficient awareness that concussion can be associated with abnormal eye movements. Indeed, contrary to the literature estimating the prevalence of abnormal eye tracking behaviour in concussion to be in the range of 40% to 90% (Kapoor et al. 2004; Ciuffreda et al. 2007; Hunt et al. 2016), the findings of this study point to a prevalence of only 30% (Snegireva et al. 2019). It is possible that many eye movement deficits are missed if assessments take place without suitable equipment, such as eye tracking technology, since they lack the necessary sensitivity to minor deviations (Wilcockson 2018). Additionally, 20% of the sampled clinicians admitted that they were not inspecting for eye movement dysfunctions in concussed patients at all. This finding suggests that some medical practitioners possibly do not believe that concussion can lead to eye movement dysfunction (Zonfrillo et al. 2012).

The clinicians were indeed aware of several benefits of eye tracking technology: it was described as objective, easy to use, replicable and quantifiable. Nevertheless, the reluctance to implement this technology in practice was high: only 49% of the clinicians explicitly stated that they considered it beneficial to use the eye tracking technology for concussion diagnostics. The main reasons can be summarized as concerns caused by the limited exposure to this (for example that it is too expensive or difficult to learn).

Consequently, a significant relationship was found between the experience of using eye tracking technology and the perception of its benefit: clinicians who were regularly exposed to this technology showed higher acceptance and appreciation of its value.

Thus, the first hypothesis was confirmed only to some degree. There is insufficient awareness in clinical practice that concussion can be associated with abnormal eye movements, since one-fifth of the clinicians did not inspect for any eye movement deficits in the concussed patients. Additionally, only a half of the respondents saw value in using eye tracking technology for more accurate assessment. Since only few clinicians have actually worked with this technology, this lack of exposure and related concerns act as a limiting factor for its broader use.

Hypothesis 2: Due to the ability of ETT to measure eye movements objectively, in quantifiable manner, and with minimal operator influence, thus leading to repeatable results, it was expected to be a reliable tool for assessing SRC in athletic cohorts.

A high level of reliability of eye movement metrics is crucial for clinical application, since it ensures that the results are due to the study and not possible external influences. For the majority of variables in this study, the reliability was low: only 6 variables for adult and 11 for youth groups (out of total 47 for each age group) demonstrated sufficient reliability (i.e. moderate to good). The main possible reasons for this finding are discussed below.

When reliability and validity of a diagnostic test are evaluated, it is important that all research participants are correctly classified as diseased or healthy (Linnet et al. 2012); however the border becomes blurry when the investigation concerns concussion in contact or even collision sports, such as rugby. Multiple studies have demonstrated that sub-concussive impacts caused by falls or head-to head or head-to body collisions (List et al. 2015; Koerte et al. 2017), may have adverse long-term neurocognitive effects even in the athletes who have never been diagnosed with a concussion (Shultz et al. 2012; Belanger et al. 2016). In the current study, the absence of concussions in the past two years in the control group was only confirmed by participants' own self-reports, and therefore, the results might have been affected by undetected recent concussions and by the effects of sub-concussive impacts. This is in line with an earlier comparison of the antisaccadic error rates of healthy controls in two concussion studies, one conducted in a general population (Balaban et al. 2016), and the other with athletes (Cochrane et al. 2019), with athletes performing markedly worse than the general population. Correspondingly, the previous studies that found high reliability of eye tracking metrics were conducted in a general population (Bargary et al. 2017), whereas the reliabilities found in the athletic cohorts were much lower (Howell et al. 2018b; Cochrane et al. 2019). Additionally, healthy athletes may demonstrate lower within-subject variability (which negatively affects the reliability score) in metrics such as saccadic reaction times compared to non-athletes (Lange et al. 2018), possibly due to regular exposure to the environment fostering certain visual skills.

On the other hand, it is also possible that the lower reliability was caused by situational factors or unaccounted for confounding variables, such as data artefacts caused by head movements, posture shifts, fatigue, minor illness, or emotional status (Stern et al. 1994; Beckerman et al. 2001; Di Stasi et al. 2012).

Taken together, it can be concluded that current eye tracking protocols to a large degree failed to present a sufficient level of robustness to situational factors required for a biomarker to be both practical and useful in assisting the clinicians specifically in sports-related concussion diagnostics. Further dedicated studies with large cohorts of healthy athletes are required to verify the reliability of the eye tracking metrics in this population and determine the optimal testing protocols.

Hypothesis 3: Due to a high prevalence of eye movement deficits in SRC that might outlast the symptoms, as well as the ability of the ETT to accurately measure such deficits, eye tracking would be a valid tool to diagnose and monitor SRC. The deficits in self-paced saccades, fixation stability, memory-guided saccades, smooth pursuit, and antisaccades (but not in reflexive saccades) were expected to be most pronounced in the early symptomatic stage, diminish in the recovery stage, and resolve in the post-factum baseline stage.

This study did yield some metrics that demonstrated both sufficient reliability and validity and thus could serve as concussion markers.

In the adult group, the trend observed in the self-paced saccade count suggests that this metric might indeed be indicative of a concussion, since the concussed group presented a gradual increase in the number of saccades from session to session, with the results of the last session approaching those of the healthy controls. As demonstrated by neuroimaging studies, self-paced saccades are associated with the activity of multiple brain areas: information is processed in the fovea, superior colliculus, supplementary eye fields, and dorsolateral prefrontal cortex; frontal eye fields are responsible for disengaging fixations; brainstem generates a neural command to initiate a saccade; and anterior cingulate cortex maintains the motivation to complete the task) (Gaymard et al. 1998; Heitger et al. 2002; Johnson et al. 2015b; Leigh and Zee 2015; Taghdiri et al. 2018). Therefore, self-paced saccades are likely to be affected by a concussion regardless of the location of the impact.

In the youth group, the most insightful finding of this study was that the concussed youth athletes had longer blink durations compared to the healthy youth controls. Researchers believe that spontaneous eye blinks are generally influenced by a range of factors. First, they are linked to central dopamine activity: reduced or increased dopamine activity in the striatum has been associated with lower or higher blink rates and durations, accordingly (Karson et al. 1984; Jongkees and Colzato 2016; Abusharha 2017). Blinks are also sensitive to the attentional demands and cognitive workload of the visual task and their duration tends to increase with the fatigue (Doughty 2001). Finally, blink rate increases steadily from infancy to adulthood and reaches adult levels by the age of 20 (Caplan et al. 1996; Groen et al. 2017). It is possible, therefore, that blink-related metrics in youth population show higher sensitivity to a concussion compared to the adults. Thus, the increased blink duration in the youth concussed group of the present study can possibly be explained by the reduction of striatal dopamine levels caused by a concussion (Chen et al. 2017; Jenkins et al. 2018). It is also possible that impairments in working memory and attention that are characteristic of a youth concussion (Moore et al. 2016) increased the fatigue of the concussed participants while executing the tasks, which is known to lead to longer blink durations (Stern et al. 1994; Schleicher et al. 2008). With the exception of one study that found an increase in the blink rate of concussed youth athletes (without previously checking for this metric's reliability) (Hecimovich et al. 2018), there seems to be no literature connecting eye blink metrics to SRC, and further research is certainly called for in order to confirm this novel finding.

In contrast to the hypothesis, there was no significant difference in the analysed smooth pursuit variable. Since only the classic smooth pursuit paradigms were employed, the nature of the task might have influenced the results. More challenging tasks, such as dual task paradigm (e.g. adding a working memory component), are more demanding both for the oculomotor system and for the executive functions (Johnson et al. 2015b) and might therefore demonstrate higher sensitivity to the consequences of a concussion. Further research focusing on such tasks is recommended.

The statistical power between the sessions was very high, both for the self-paced saccade count in adults and for the blink durations in youth, indicating that a comparison within the same individuals over time is more likely to detect the effect of a SRC than comparison to healthy controls.

Hypothesis 4: Based on earlier studies that found significant relationship between concussion symptom scores and several eye tracking variables, a strong positive relationship was expected to exist between the degree of eye movement impairments recorded by the eye tracker with the severity of concussion symptoms. Additionally, since repeat concussions have been associated with more severe and prolonged symptom presentation, a positive relationship was also expected between the degree of eye movement impairments and the number of previous concussions.

Due to the absence of relevant literature specifically on the relationship between eye tracking technology measures and SRC symptoms at the moment of hypothesis formulation, a starting point was provided by a study that found a significant relationship between convergence insufficiency and symptom scores (Pearce et al. 2015) and a study with post-concussion symptom patients that found an association between the number of self-paced saccades and the symptom burden (Taghdiri et al. 2018), as well as studies with schizophrenia patients (Subramaniam et al. 2018), Huntington's disease patients (Patel et al. 2012) Parkinson's patients (Kitagawa et al. 1994) that found relationships between negative symptoms and antisaccade error rates and latencies.

This hypothesis was confirmed only to a certain extent in the SRC population. In the adult group, there was a weak, albeit approaching moderate, negative correlation between the self-reported severity of concussion symptoms and the number of SPS. This confirms the findings of Taghdiri et al. (2018) and Heitger et al. (2009) that this eye tracking variable might reflect the concussion symptom presentation, since this task involves several white matter tracts and cognitive functions that are also associated with concussion symptoms, such as difficulty to concentrate, or feeling in a fog. In the youth group, only weak correlation was found between two variables (gain of the diagonal smooth pursuit and proportion of antisaccade errors) and the symptom severity. Interestingly, two recent studies (Bin Zahid et al. 2018; Mani et al. 2018) suggested that the eye movement impairments in concussion possibly manifest regardless of the reported symptoms, indicating that that eye tracking could be an objective measure largely independent from symptom reporting. Taken together, it is possible that there is a relationship between eye tracking and cognitive symptoms of a concussion, and eye tracking technology can provide the clinicians with further insights in addition to the subjective symptom reports.

Finally, the number of past concussions was correlated only with one variable, the diagonal smooth pursuit gain, and this correlation was weak. It is possible that the duration and severity of post-concussion pathophysiology might be affected more by the timing of repeat injuries rather than the previous concussion history alone (Giza and Hovda 2014).

5.2. Clinical Applications and Academic Contribution

This study expands the scope of existing research by addressing some of the limitations presented in the introduction and makes the following novel methodological contributions: (1) clear stratification of participants according to their age groups, (2) unity in the time that elapsed after the injury at the moment of testing, (3) very careful selection of variables and usage of established eye tracking protocols whenever available; and (4) control for possible confounding variables, such as history of previous concussions, as well as clinical conditions that affect eye movements (for example, attention deficit disorder) or are similar to the concussion symptom representation (for example, depression). The outcomes of this study at the intersection of sports sciences, sports medicine, and neuroscience, contribute to the establishment of more accurate concussion diagnostics and monitoring practices through better understanding of eye movement impairment following concussion and of methods to assess these impairments.

An important contribution of this study is the finding that the reliability of eye tracking measures in athletic cohorts might be lower compared to the general population. This might be due to undiagnosed concussions and sub-concussive head impacts that provoke adverse long-term neurocognitive effects even in athletes who have never been formally diagnosed with a concussion. Therefore, further scientific and clinical investigations should be directed at fully understanding the phenomenon of sub-concussive impacts, its consequences and possible mitigation strategies. For example, as this study revealed, football professionals working with larger and more active teams tended to be more risk prone, demonstrating the importance of addressing the culture of sport to encourage more awareness of the risks of head impacts.

A novel finding of this study pertains to the blinks in youth cohort that tended to have longer duration in the concussed group, possibly due to the reduction of striatal dopamine levels associated with a concussion. Since eye blinks develop throughout childhood and adolescence, further studies are invited to evaluate this promising and easy-to-quantify metric for SRC assessment in youth population.

Finally, unlike the SCAT5, the diagnostic utility of which is reduced after 3-5 days post-injury, the literature review demonstrated that the eye movements might remain affected by a concussion for up to 30 days and could therefore provide the clinicians with further insights into the extent of neurobiological recovery in addition to subjective symptom reporting.

Ultimately, the goal of this research project was to contribute to the accurate recognition and management of SRC in order for the athletes to receive the timely and effective treatment and thus have longer and safer careers. This study is applied, translational and interdisciplinary, involving medical doctors, allied health professionals, athletic trainers, and athletes. It is part of a set of projects affiliated with the concussion centres in Western Cape and Gauteng, allowing for repeated data collection and re-usage – an important metric of sustainability of research. In the course of the project we collaborated with multiple rugby and football clubs, schools and clinics in order to promote the knowledge about SRC and eye tracking.

5.3. Study Limitations and Future Research

While this research addressed a number of limitations of the previous studies mentioned in the introduction, it has several limitations of its own. Firstly, the quality of the systematic literature review and meta-analysis is limited by both quantity and quality of the included studies, since as of now there is a suboptimal amount of research on using eye tracking for sports-related concussion assessment. Secondly, the conducted survey might have been susceptible to the response (and non-response) bias, since there was no systematic way to determine the response rate and the characteristics of those who completed the survey compared with those who declined. The differences in geographic and occupational background make it unlikely that the respondents had a similar training in sports concussion, although most would have been exposed to the same international consensus guidelines. A broader survey is recommended to enable cross-regional comparisons.

Thirdly, the results of the prospective cohort study might have been influenced by situational factors, such as general fatigue from sports or studying, lighting conditions, or motivation, and stricter control for such factors is recommended for future studies. Additionally, due to the general susceptibility of eye tracking technology to the artefacts from analysis algorithms (Shaikh and Zee 2018) and variability of features across different devices, generalizability of findings across devices needs to be confirmed. Further, a certain degree of variability in the time that has elapsed after the injury at the moment of testing was unavoidable and constitutes a clinical reality of standard and accepted practice. This might have affected the results, since some participants might have been further into the recovery process than others. At the moment of this study only one standardized protocol was available (Antoniades et al. 2013), leading to a reliance on single studies in experimental design. Consequently, the utilized protocols may not be fully suitable for SRC assessment, and the ability to reproduce the results of this study needs further investigation. It is possible that using more demanding tasks that involve executive functions may improve the reliability and validity of the eye tracking tests for concussion diagnostics, and further research in this direction is suggested. Finally, since eye movements are known to be idiosyncratic (Pearson et al. 2007; Holmqvist et al. 2011), future research should focus on comparing concussed individuals to their own pre-injury or post-recovery baseline values rather than comparing them to healthy controls.

Thus, the findings require confirmation in larger studies comprising further geographic regions, both sexes, and suitable eye tracking protocols if these become available. Further research should also consider investigating in more detail the reliability of eye tracking metrics specifically in sporting cohorts.

5.4. Conclusions

Sports-related concussion manifests in a range of symptoms and deficits that include worsened performance on the neurocognitive tests, impaired balance, abnormal eye movements, and many more. Due to the complexity of this injury, sporting and medical experts agree that it requires an individualised and multimodal assessment approach that relies on a comprehensive battery of tools to get the full picture (Sherry and Collins 2019). Eye movements have already become an easy-to-measure and easy-to-quantify biomarker for a range of disorders (Shaikh and Zee 2018), and this study contributes to the understanding of saccadic, smooth pursuit, blink and fixation impairments associated with sports-related concussion, as well as of the ability of eye tracking technology to detect deficits that are missed during un-instrumented clinical examination.

The clinicians survey revealed that even among sports medicine clinicians who regularly diagnose and manage patients with concussion, there is insufficient awareness that concussion can be associated with abnormal eye movements. Additionally, only a half of the respondents saw value in using eye tracking technology for more accurate assessment. Since only few clinicians have actually worked with this technology, this lack of exposure and related concerns act as a limiting factor for its broader use. Therefore, increasing educational and training opportunities along with practical experience of sports medicine clinicians regarding concussion evaluation, including the use of potential innovative technology (such as eye tracking), is strongly advocated. Better interaction between researchers and sports medicine clinicians regarding the use of eye tracking technology for concussion assessment is also suggested. It could lead to its higher adoption rate, which in turn might enable the evaluation of currently neglected eye movement deficits caused by concussion and ultimately more accurate evaluation of concussion resolution over days to weeks.

Overall, this study was not able to confirm a large portion of previous research on suggested eye tracking metrics for sports-related concussion assessment, primarily due to the fact that current eye tracking protocols to a large degree failed to present a sufficient level of robustness to situational factors required for a biomarker to be both practical and useful in assisting the clinicians specifically in sports-related concussion diagnostics. It is possible that the reliability of eye tracking variables assessed in athletes participating in contact sports might be lower compared to a general population, since it is a homogeneous group with lower between-persons variance. Further dedicated studies with large cohorts of healthy athletes are required to verify the reliability of the eye tracking metrics specifically in this population and determine the optimal protocols.

Two metrics, however, did show promise in SRC assessment. Lower self-paced saccade count might be indicative of a concussion among adult athletes, whereas longer blink durations in memory-based saccade or sinusoidal smooth pursuit tasks might indicate a concussion in youth athletes. Additionally, in the adult group, a negative correlation between the self-reported severity of concussion symptoms and the number of self-paced saccades indicates that there may be a relationship between eye tracking and cognitive symptoms of a concussion, and eye tracking technology can provide the clinicians with further insights in addition to the subjective symptom reports.

Lastly, even though there is no consensus regarding the time frame after the injury within which the eye movements would remain affected, the meta-analysis pointed at the presence of the impairments in the acute phase (< 30 days post-concussion). Research contributing to further understanding of this time frame is invited. Facilitating the awareness of objective methods, like eye tracking technology, may help assure the appropriate continuum of identification and treatment for concussed athletes, and this study contributes to recent significant advancements in research of the tools available for evaluating sports-related concussion.

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APPENDICES

1. Turnitin report (cover page)
2. Declaration indicating the nature and extent of the contributions of co-authors
3. Ethics approval letter
4. Informed consent and assent forms (English)
5. SCAT5 and Child-SCAT5
6. General questionnaire + PHQ9 + MoCA forms
7. Sports medicine clinicians survey questions
8. Risk of bias and quality assessment of each study included in the systematic review and meta-analysis

Appendix 1. Turnitin report

Eye tracking as a diagnostic and monitoring tool for sports-related concussion (full dissertation 02.10.2019)

ORIGINALITY REPORT

17%	10%	8%	8%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Nadja Snegireva, Wayne Derman, Jon Patricios, Karen Estelle Welman. "Eye tracking technology in sports-related concussion: a systematic review and meta-analysis", Physiological Measurement, 2018 Publication	2%
2	Nadja Snegireva, Wayne Derman, Jon Patricios, Karen E. Welman. "Awareness and Perceived Value of Eye Tracking Technology for Concussion Assessment among Sports Medicine Clinicians: A Multinational Study", The Physician and Sportsmedicine, 2019 Publication	1%
3	www.tandfonline.com Internet Source	<1%
4	link.springer.com Internet Source	<1%
5	scholar.sun.ac.za Internet Source	<1%

Appendix 2. Declaration

Declaration indicating the nature and extent of the contributions of co-authors

Declaration by the candidate:

With regard to the Section 2.3. *Eye Tracking Technology in Sports-Related Concussion*, pages 33-64 of the dissertation, the nature and scope of my contribution were as follows:

Nature of contribution	Extent of contribution
Study conception, design, funding and instrumentation, subject recruitment, data collection and processing, data analysis and interpretation, literature review, writer, critical review	61%

The following co-authors have contributed to the Section 2.3. *Eye Tracking Technology in Sports-Related Concussion,* pages 33-64 of the dissertation (listed alphabetically by last name):

Name	E-mail address	Nature of contribution	Extent of contribution
Prof Wayne Derman	ewderman@iafrica.com	Supervision, subject recruitment, critical review	9%
Prof Jon Patricios	jpat@mweb.co.za	Supervision, data collection, critical review	11%
Dr Karen Welman	welman@sun.ac.za	Design, supervision, subject recruitment, data analysis and interpretation, critical review	19%

With regard to the Chapter 3. *Awareness and Perceived Value of Eye Tracking Technology for SRC Assessment among Sports Medicine Clinicians*, pages 65-79 of the dissertation, the nature and scope of my contribution were as follows:

Nature of contribution	Extent of contribution
Study conception, design, funding and instrumentation, subject recruitment, data collection and processing, data analysis and interpretation, literature review, writer, critical review	61%

The following co-authors have contributed to the Chapter 3. *Awareness and Perceived Value of Eye Tracking Technology for SRC Assessment among Sports Medicine Clinicians*, pages 65-79 of the dissertation (listed alphabetically by last name):

Name	E-mail address	Nature of contribution	Extent of contribution
Prof Wayne Derman	ewderman@iafrica.com	Supervision, subject recruitment, critical review	9%
Prof Jon Patricios	jpat@mweb.co.za	Supervision, data collection, critical review	11%
Dr Karen Welman	welman@sun.ac.za	Design, supervision, subject recruitment, data analysis and interpretation, critical review	19%

With regard to the Chapter 4. *Reliability and Validity of Eye Tracking for Sports-Related Concussion Assessment in Youth and Adult Athletes*, pages 80-106 of the dissertation, the nature and scope of my contribution were as follows:

Nature of contribution	Extent of contribution
Study conception, design, funding and instrumentation, subject recruitment, data collection and processing, data analysis and interpretation, literature review, writer, critical review	61%

The following co-authors have contributed to the Chapter 4. *Reliability and Validity of Eye Tracking for Sports-Related Concussion Assessment in Youth and Adult Athletes*, pages 80-106 of the dissertation (listed alphabetically by last name):

Name	E-mail address	Nature of contribution	Extent of contribution
Prof Wayne Derman	ewderman@iafrica.com	Supervision, subject recruitment, critical review	9%
Prof Jon Patricios	jpat@mweb.co.za	Supervision, data collection, critical review	11%
Dr Karen Welman	welman@sun.ac.za	Design, supervision, subject recruitment, data analysis and interpretation, critical review	19%

Signature of candidate: ……………………………………………………

Date: 28.09.2019

Declaration by co-authors:

The undersigned hereby confirm that

1. The declaration above accurately reflects the nature and extent of the contributions of the candidate and the co-authors to the Section 2.3 and Chapters 3 and 4 of this dissertation.

2. No other authors contributed to the Section 2.3 and Chapters 3 and 4 of this dissertation besides those specified above, and

3. Potential conflicts of interest have been revealed to all interested parties and that the necessary arrangements have been made to use the material in the Section 2.3 and Chapters 3 and 4 of this dissertation.

Name	**Institutional affiliation**	**Signature**	**Date**
Prof Wayne Derman	Institute of Sport and Exercise Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University, South Africa		28.09.2019
Prof Jon Patricios	Wits Institute for Sport and Health, Faculty of Health Sciences, University of the Witwatersrand, South Africa		28.09.2019
Dr Karen Welman	Movement Laboratory, Department of Sport Science, Faculty of Medicine and Health Sciences, Stellenbosch University, South Africa		28.09.2019

Declaration with signatures in possession of candidate and supervisor

Appendix 3. Ethics approval letter

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jou kennisvennoot • your knowledge partner

Ethics Letter

18-Jan-2017
Snegireva, Nadja N

Ethics Reference #: S16/07/129
Title: Eye tracking as tool for sports concussion diagnostics and monitoring

Dear Ms Nadja Snegireva

Your letter dated 1 December 2016 refers.

We acknowledge your response to stipulations and confirm that it is in order. You may proceed with the research project.

Where to submit any documentation
Kindly submit **ONE HARD COPY** to Elvira Rohland, RDSD, Room 5007, Teaching Building, and **ONE ELECTRONIC COPY** to ethics@sun.ac.za

Please remember to use your **protocol number** **(S16/07/129)** on any documents or correspondence with the HREC concerning your research protocol.

Federal Wide Assurance Number: 00001372
Institutional Review Board (IRB) Number: IRB0005240 for HREC1
Institutional Review Board (IRB) Number: IRB0005239 for HREC2

The Health Research Ethics Committee complies with the SA National Health Act No.61 2003 as it pertains to health research and the United States Code of Federal Regulations Title 45 Part 46. This committee abides by the ethical norms and principles for research, established by the Declaration of Helsinki, the South African Good Clinical Pracices Guidelines as well as the Guidelines for Ethical Research: Principles Structures and Processes 2004 (Department of Health).

Sincerely,
Ashleen Fortuin
REC Coordinator
Health Research Ethics Committee 2

	STELLENBOSCH UNIVERSITY	

PARTICIPANT INFORMATION LEAFLET AND CONSENT FORM

TITLE OF THE RESEARCH PROJECT:
Eye Tracking as Tool for Sports Concussion Diagnostics and Monitoring
REFERENCE NUMBER: S16/07/129
PRINCIPAL INVESTIGATOR: Ms Nadja Snegireva, Department of Sport Science, Stellenbosch University
STUDY SUPERVISORS: Dr Karen Welman, Department of Sport Science, Stellenbosch University;
Prof Wayne Derman, Faculty of Medicine and Health Sciences, Stellenbosch University;
Prof Jon Patricios, Faculty of Health Sciences, University of Witwatersrand
CONTACT NUMBER: +27 (0)72 584 3577

You are invited to take part in a research project. Please read the information presented here, which will explain the details of this project. Feel free to ask the study staff or doctor any questions about any part of this project that you do not fully understand. It is very important that you are fully satisfied that you clearly understand what this research entails and how you could be involved. Also, your participation is **entirely voluntary,** and you are free to decline to participate. If you say no, this will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point, even if you do agree to take part. You have the right to be told any new relevant information that arises during the course of the trial; where appropriate, this consent form will be revised to incorporate this information.

This study has been approved by the **Health Research Ethics Committee at Stellenbosch University** and will be conducted according to the ethical guidelines and principles of the international Declaration of Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research.

What is this research study all about?

- The study will evaluate the validity, reliability, and utility of eye tracking as a sport concussion assessment tool by comparing concussed patients to healthy controls over a period of one month.
- This is a non-sponsored student research for degree purposes at Stellenbosch University. The researchers have no conflict of interest.

Why have you been invited to participate?

- You were selected as a possible participant in this study because you are an athlete aged between 18 and 35; taking part in a contact sport; have no oculomotor, neurological or psychiatric disorders (incl. ADD/ADHD, depression). If you are part of the control group, you also have no history of concussion.

What will your responsibilities be?

- If you had a concussion and volunteer to participate in this study, we will conduct testing sessions at least three times: (1) at 1-3 days after the injury, (2) at 5-7 days and (3) at 30 days; an additional session (4) upon return to sport if the return is longer than 30 days post injury.

- Each testing session will include:
    - Sport Concussion Assessment Tool 5 (SCAT5) or Sport Concussion Assessment Tool 5 for Children (Child SCAT5) [duration 8 min]
    - General participant information form [duration 1 min]
    - Computer-based eye tracking test [duration appr. 45 minutes including breaks]
- In addition, the last testing session will include:
    - Signing the consent & assent forms [explained at first session and signed at the last to ensure that the brain injury did not influence the participant's decision to take part].
    - Montreal Cognitive Assessment (MoCA) or School-Years Screening Test for the Evaluation of Mental Status (SYSTEMS) or similar for assessing the cognitive state [duration 10 min]
    - Patient Health Questionnaire (PHQ-9) for adolescent group

- If you have never had a concussion and volunteer to participate in this study, we will include you in the control group. You will be tested twice, with one-week interval between the testing sessions.
- The first testing session will include:
    - Signing the consent & assent forms
    - SCAT5 / Child SCAT5
    - General participant information form
    - MoCA / SYSTEMS
    - PHQ-9 (for adolescents)
    - Computer-based eye tracking test
- The second testing session will include:
    - Computer-based eye tracking test
- The total duration of each session is maximum one hour.

Will you benefit from taking part in this research?

- There likely will not be any direct benefit to you as a study participant. The main benefit will likely pertain a more effective diagnosis/treatment of concussion in the future. The comparison of the data across age groups and between genders might help better tailor the tests to each of these groups, potentially leading to a more precise diagnostics and monitoring of the recovery.

Are there in risks involved in your taking part in this research?

- This study will not involve any intervention or invasive data recording technology, therefore there are no serious risks that could arise for you from taking part in the tests.
- As some of the tests will take place shortly after the concussion, you may feel dizzy, disoriented, experience headaches or a loss of balance. To mitigate this risk, the tests will be conducted always in a safe environment without any distractions. You will be seating during the majority of tests (questionnaires, eye tracking), and whenever a test (i.e. the balance assessment) requires you to stand, you will have a chair placed next to you for the case of dizziness. During any test, you can take a break or stop whenever you feel like doing so. The assessor will be near you for support at all times.
- The SCAT5 test will be conducted by a trained biokineticist or a sports physio. If a concussion is suspected with the SCAT5 test you will be referred to a physician.

If you do not agree to take part, what alternatives do you have?

- You can choose whether to be in this study or not. If you volunteer to be in this study, you may withdraw at any time without consequences of any kind. You may also refuse to answer any questions you don't want to answer and still remain in the study. The investigator may withdraw you from this research if circumstances arise which warrant doing so.
- Currently sports concussion is diagnosed by medical doctors with the use of such tests as SCAT5, ImPACT, CogState. You can always consult a medical doctor of your choice.
-

Who will have access to your medical records?

- Any information that is obtained in connection with this study and that can be identified with you will remain confidential and will be disclosed only with your permission or as required by law. Confidentiality will be maintained by means of coding your name as, for example, Participant 2016001.
- Furthermore, all data will be stored on a password protected notebook to which only the researcher and project leader will have access to. The hard copies of the questionnaires, personal information, consent forms and variables assessed will be stored in a secure filling cabinet in the Movement Laboratory of the Sport Science Department (Stellenbosch University). All data will be kept for 3 years; after that it will be destroyed.
- In publications or presentations of findings no names will be mentioned, and only average data will be reported. Upon request, you can receive a copy of your data in a report at the end of the study.

What will happen in the unlikely event of some form injury occurring as a direct result of your taking part in this research study?

- The researchers will do everything in their power to prevent injury or risk to you (according to Good Clinical guidelines).
- Should an emergency arise, the researchers will phone the medical services or take you to a doctor.
- In case of a research-related accident, the costs will be covered by the university insurance. If the accident is not research-related, the costs will have to be covered by the affected person themselves. A log of all events will be kept by the principle investigator.

Will you be paid to take part in this study and are there any costs involved?

- You will not be paid to take part in the study, but there will be no costs involved for you, if you do take part. As a compensation for participating in the study, after the last test you will receive a voucher for a balance assessment or functional movement screening or training with a value of R150-250, valid for 6 months.

Is there anything else that you should know or do?

- You can contact study co-supervisor Prof. Jon Patricios, Faculty of Health Sciences, University of Witwatersrand (phone 011 883 9000, email jpat@mweb.co.za) if you have any further queries.
- You can contact the Health Research Ethics Committee at 021-938 9207 if you have any concerns or complaints that have not been adequately addressed by your study doctor.
- You will receive a copy of this information and consent form for your own records.

Declaration by participant

By signing below, I …………………………………..………… agree to take part in a research study entitled *Eye Tracking as Tool for Sports Concussion Diagnostics and Monitoring*.

I declare that:

- I have read or had read to me this information and consent form and it is written in a language with which I am fluent and comfortable.
- I have had a chance to ask questions and all my questions have been adequately answered.
- I understand that taking part in this study is **voluntary** and I have not been pressurised to take part.
- I may choose to leave the study at any time and will not be penalised or prejudiced in any way.
- I may be asked to leave the study before it has finished, if the study doctor or researcher feels it is in my best interests, or if I do not follow the study plan, as agreed to.

Signed at (*place*) ....…........…………….. on (*date*) …………....……….. 20__.

....

Signature of participant **Signature of witness**

Declaration by investigator

I *(name)* ……………………………………………..……… declare that:

- I explained the information in this document to …………………………………..
- I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understands all aspects of the research, as discussed above
- I did/did not use a interpreter. (*If a interpreter is used then the interpreter must sign the declaration below.*

Signed at (*place*) ....…........…………….. on (*date*) …………....……….. 20__.

....

Signature of investigator **Signature of witness**

STELLENBOSCH UNIVERSITY

FACULTY OF HEALTH SCIENCES

PARTICIPANT INFORMATION LEAFLET AND ASSENT FORM

TOPIC OF THE RESEARCH PROJECT:
Using people's eyes to diagnose sport concussion

RESEARCHERS:
Ms Nadja Snegireva, Department of Sport Science, Stellenbosch University
Dr Karen Welman Department of Sport Science, Stellenbosch University;
Prof Wayne Derman, Faculty of Medicine and Health Sciences, Stellenbosch University;
Prof Jon Patricios, Faculty of Health Sciences, University of Witwatersrand

CONTACT NUMBER: +27 (0)72 584 3577

What is RESEARCH?

Research is something we do to find new knowledge about the way things (and people) work. We use research projects or studies to help us find out more about disease or illness. Research also helps us to find better ways of helping or treating children who are sick.

What is this research project all about?

We will do several tests with the athletes to find out if it is possible to use the movements of the eyes to find a serious knock/ bump to the head which can hurt your brain and change the way your brain works for a few days or even weeks (called a concussion) and to see the healing.

Why have I been invited to take part in this research project?

We invited you because you are an athlete who plays a contact sport, and you are between 9 and 12 years old.

Who is doing the research?

Ms. Nadja Snegireva is doing this research as part of her study at the University. She will use the results of this research to publish articles and receive her degree.

What will happen to me in this study?

If you got a concussion, we will ask you to do these tests together with your parent:

- Some questions about you and your health
- Child-SCAT5 = a concussion test
- A computer test with an eye tracker which will record how your eyes move.

You will do these tests as soon as possible after your concussion, and again one week later and one last time one month later.

If you never had a concussion, we will ask you to be part of the "healthy" group. You will do the same tests as the concussed children once, and repeat the eye tracking test once again one week later.

All tests will altogether last maximum one hour.

Can anything bad happen to me?

None of the tests will hurt you. We will not use any dangerous technology, so nothing bad can happen to you from taking part in the tests. Some tests may take place soon after a concussion, that is why you may feel dizzy, or lose your balance, or your head may ache. To make sure that you do not fall or feel bad, you will be sitting on a chair most of the time. During the balance test you have to stand, so during this test we will put a chair near you. During any test, you can take a break or stop whenever you want. One of our research team will stay near you for support all the time. If we suspect a concussion, we will refer you to a doctor.

Can anything good happen to me?

We hope that we can add an eye tracking test to the other tests that doctors use for people with concussion. And that it will make these tests better and they will find even very light concussions. It is important to know exactly who received a concussion, so that the doctors can provide the necessary treatment and help athletes to heal. We will also try to create tests specifically for children and teenagers, as well as specifically for the boys and girls, to make the tests even better.

Will anyone know I am in the study?

No, we will keep all information about you confidential (it means, we will not tell anything about you to anyone), and we will only share information if the law requires it, or if you and your parent / legal guardian allow us. We will use a special code instead of your name (for example, Participant 1). We will protect all computers with a password, and we will always lock the room where we put the papers. If you want, you can ask for a copy of your tests in a report at the end of the study.

Who can I talk to about the study?

If you have any questions or problems, you can talk to Ms. Nadja Snegireva (at any time if day or night, cell phone: 072 584 3577, email nadja.snegireva@gmail.com), or her co-supervisor Prof. Jon Patricios, Faculty of Health Sciences, University of Witwatersrand (phone 011 883 9000, email jpat@mweb.co.za).

What if I do not want to do this?

You can always say no to participating in this study, even if you or your parents agreed to your participation. You can stop being in the study at any time without getting in trouble.

Do you understand this research study and are you willing to take part in it?

YES NO

Has the researcher answered all your questions?

YES NO

Do you understand that you can pull out of the study at any time?

YES NO

_____________________________ _____________________________

Name / Signature of Child Date

Appendix 5. SCAT5 and Child-SCAT5

SCAT5©

SPORT CONCUSSION ASSESSMENT TOOL — 5TH EDITION

DEVELOPED BY THE CONCUSSION IN SPORT GROUP
FOR USE BY MEDICAL PROFESSIONALS ONLY

supported by

FIFA® FEI

Patient details

Name: ______________________________

DOB: ______________________________

Address: ______________________________

ID number: ______________________________

Examiner: ______________________________

Date of Injury: ________________ Time: ________________

WHAT IS THE SCAT5?

The SCAT5 is a standardized tool for evaluating concussions designed for use by physicians and licensed healthcare professionals[1]. The SCAT5 cannot be performed correctly in less than 10 minutes.

If you are not a physician or licensed healthcare professional, please use the Concussion Recognition Tool 5 (CRT5). The SCAT5 is to be used for evaluating athletes aged 13 years and older. For children aged 12 years or younger, please use the Child SCAT5.

Preseason SCAT5 baseline testing can be useful for interpreting post-injury test scores, but is not required for that purpose.Detailed instructions for use of the SCAT5 are provided on page 7. Please read through these instructions carefully before testing the athlete. Brief verbal instructions for each test are given in italics. The only equipment required for the tester is a watch or timer.

This tool may be freely copied in its current form for distribution to individuals, teams, groups and organizations. It should not be altered in any way, re-branded or sold for commercial gain. Any revision, translation or reproduction in a digital form requires specific approval by the Concussion in Sport Group.

Recognise and Remove

A head impact by either a direct blow or indirect transmission of force can be associated with a serious and potentially fatal brain injury. If there are significant concerns, including any of the red flags listed in Box 1, then activation of emergency procedures and urgent transport to the nearest hospital should be arranged.

Key points

- Any athlete with suspected concussion should be REMOVED FROM PLAY, medically assessed and monitored for deterioration. No athlete diagnosed with concussion should be returned to play on the day of injury.
- If an athlete is suspected of having a concussion and medical personnel are not immediately available, the athlete should be referred to a medical facility for urgent assessment.
- Athletes with suspected concussion should not drink alcohol, use recreational drugs and should not drive a motor vehicle until cleared to do so by a medical professional.
- Concussion signs and symptoms evolve over time and it is important to consider repeat evaluation in the assessment of concussion.
- The diagnosis of a concussion is a clinical judgment, made by a medical professional. The SCAT5 should NOT be used by itself to make, or exclude, the diagnosis of concussion. An athlete may have a concussion even if their SCAT5 is "normal".

Remember:

- The basic principles of first aid (danger, response, airway, breathing, circulation) should be followed.
- Do not attempt to move the athlete (other than that required for airway management) unless trained to do so.
- Assessment for a spinal cord injury is a critical part of the initial on-field assessment.
- Do not remove a helmet or any other equipment unless trained to do so safely.

1

IMMEDIATE OR ON-FIELD ASSESSMENT

The following elements should be assessed for all athletes who are suspected of having a concussion prior to proceeding to the neurocognitive assessment and ideally should be done on-field after the first first aid / emergency care priorities are completed.

If any of the "Red Flags" or observable signs are noted after a direct or indirect blow to the head, the athlete should be immediately and safely removed from participation and evaluated by a physician or licensed healthcare professional.

Consideration of transportation to a medical facility should be at the discretion of the physician or licensed healthcare professional.

The GCS is important as a standard measure for all patients and can be done serially if necessary in the event of deterioration in conscious state. The Maddocks questions and cervical spine exam are critical steps of the immediate assessment; however, these do not need to be done serially.

STEP 1: RED FLAGS

RED FLAGS:

- **Neck pain or tenderness**
- **Double vision**
- **Weakness or tingling/ burning in arms or legs**
- **Severe or increasing headache**
- **Seizure or convulsion**
- **Loss of consciousness**
- **Deteriorating conscious state**
- **Vomiting**
- **Increasingly restless, agitated or combative**

STEP 2: OBSERVABLE SIGNS

Witnessed ☐ Observed on Video ☐

Lying motionless on the playing surface	Y	N
Balance / gait difficulties / motor incoordination: stumbling, slow / laboured movements	Y	N
Disorientation or confusion, or an inability to respond appropriately to questions	Y	N
Blank or vacant look	Y	N
Facial injury after head trauma	Y	N

STEP 3: MEMORY ASSESSMENT MADDOCKS QUESTIONS[2]

"I am going to ask you a few questions, please listen carefully and give your best effort. First, tell me what happened?"

____

____

Mark Y for correct answer / N for incorrect

What venue are we at today?	Y	N
Which half is it now?	Y	N
Who scored last in this match?	Y	N
What team did you play last week / game?	Y	N
Did your team win the last game?	Y	N

Note: Appropriate sport-specific questions may be substituted.

Name: ______________________________

DOB: ______________________________

Address: ______________________________

ID number: ______________________________

Examiner: ______________________________

Date: ______________________________

STEP 4: EXAMINATION GLASGOW COMA SCALE (GCS)[3]

Time of assessment			
Date of assessment			
Best eye response (E)			
No eye opening	1	1	1
Eye opening in response to pain	2	2	2
Eye opening to speech	3	3	3
Eyes opening spontaneously	4	4	4
Best verbal response (V)			
No verbal response	1	1	1
Incomprehensible sounds	2	2	2
Inappropriate words	3	3	3
Confused	4	4	4
Oriented	5	5	5
Best motor response (M)			
No motor response	1	1	1
Extension to pain	2	2	2
Abnormal flexion to pain	3	3	3
Flexion / Withdrawal to pain	4	4	4
Localizes to pain	5	5	5
Obeys commands	6	6	6
Glasgow Coma score (E + V + M)			

CERVICAL SPINE ASSESSMENT

Does the athlete report that their neck is pain free at rest?	Y	N
If there is NO neck pain at rest, does the athlete have a full range of ACTIVE pain free movement?	Y	N
Is the limb strength and sensation normal?	Y	N

In a patient who is not lucid or fully conscious, a cervical spine injury should be assumed until proven otherwise.

Echemendia RJ, *et al. Br J Sports Med* 2017;**51**:851–858. doi:10.1136/bjsports-2017-097506SCAT5

OFFICE OR OFF-FIELD ASSESSMENT

Please note that the neurocognitive assessment should be done in a distraction-free environment with the athlete in a resting state.

STEP 1: ATHLETE BACKGROUND

Sport / team / school: ______________________

Date / time of injury: ______________________

Years of education completed: ______________________

Age: ______________________

Gender: M / F / Other

Dominant hand: left / neither / right

How many diagnosed concussions has the athlete had in the past?: ______________________

When was the most recent concussion?: ______________________

How long was the recovery (time to being cleared to play) from the most recent concussion?: ______________ (days)

Has the athlete ever been:

Hospitalized for a head injury?	Yes	No
Diagnosed / treated for headache disorder or migraines?	Yes	No
Diagnosed with a learning disability / dyslexia?	Yes	No
Diagnosed with ADD / ADHD?	Yes	No
Diagnosed with depression, anxiety or other psychiatric disorder?	Yes	No

Current medications? If yes, please list:

____

____

____

____

____

____

Name: ______________________

DOB: ______________________

Address: ______________________

ID number: ______________________

Examiner: ______________________

Date: ______________________

2

STEP 2: SYMPTOM EVALUATION

The athlete should be given the symptom form and asked to read this instruction paragraph out loud then complete the symptom scale. For the baseline assessment, the athlete should rate his/her symptoms based on how he/she typically feels and for the post injury assessment the athlete should rate their symptoms at this point in time.

Please Check: ☐ **Baseline** ☐ **Post-Injury**

Please hand the form to the athlete

	none	mild		moderate		severe	
Headache	0	1	2	3	4	5	6
"Pressure in head"	0	1	2	3	4	5	6
Neck Pain	0	1	2	3	4	5	6
Nausea or vomiting	0	1	2	3	4	5	6
Dizziness	0	1	2	3	4	5	6
Blurred vision	0	1	2	3	4	5	6
Balance problems	0	1	2	3	4	5	6
Sensitivity to light	0	1	2	3	4	5	6
Sensitivity to noise	0	1	2	3	4	5	6
Feeling slowed down	0	1	2	3	4	5	6
Feeling like "in a fog"	0	1	2	3	4	5	6
"Don't feel right"	0	1	2	3	4	5	6
Difficulty concentrating	0	1	2	3	4	5	6
Difficulty remembering	0	1	2	3	4	5	6
Fatigue or low energy	0	1	2	3	4	5	6
Confusion	0	1	2	3	4	5	6
Drowsiness	0	1	2	3	4	5	6
More emotional	0	1	2	3	4	5	6
Irritability	0	1	2	3	4	5	6
Sadness	0	1	2	3	4	5	6
Nervous or Anxious	0	1	2	3	4	5	6
Trouble falling asleep (if applicable)	0	1	2	3	4	5	6

Total number of symptoms:	of 22
Symptom severity score:	of 132
Do your symptoms get worse with physical activity?	Y N
Do your symptoms get worse with mental activity?	Y N
If 100% is feeling perfectly normal, what percent of normal do you feel?	

If not 100%, why?

____

____

____

Please hand form back to examiner

3

STEP 3: COGNITIVE SCREENING

Standardised Assessment of Concussion (SAC)[4]

ORIENTATION

What month is it?	0	1
What is the date today?	0	1
What is the day of the week?	0	1
What year is it?	0	1
What time is it right now? (within 1 hour)	0	1
Orientation score		of 5

IMMEDIATE MEMORY

The Immediate Memory component can be completed using the traditional 5-word per trial list or optionally using 10-words per trial to minimise any ceiling effect. All 3 trials must be administered irrespective of the number correct on the first trial. Administer at the rate of one word per second.

Please choose EITHER the 5 or 10 word list groups and circle the specific word list chosen for this test.

I am going to test your memory. I will read you a list of words and when I am done, repeat back as many words as you can remember, in any order. For Trials 2 & 3: I am going to repeat the same list again. Repeat back as many words as you can remember in any order, even if you said the word before.

List	Alternate 5 word lists					Score (of 5) Trial 1	Trial 2	Trial 3
A	Finger	Penny	Blanket	Lemon	Insect			
B	Candle	Paper	Sugar	Sandwich	Wagon			
C	Baby	Monkey	Perfume	Sunset	Iron			
D	Elbow	Apple	Carpet	Saddle	Bubble			
E	Jacket	Arrow	Pepper	Cotton	Movie			
F	Dollar	Honey	Mirror	Saddle	Anchor			
					Immediate Memory Score			of 15
					Time that last trial was completed			

List	Alternate 10 word lists					Score (of 10) Trial 1	Trial 2	Trial 3
G	Finger Candle	Penny Paper	Blanket Sugar	Lemon Sandwich	Insect Wagon			
H	Baby Elbow	Monkey Apple	Perfume Carpet	Sunset Saddle	Iron Bubble			
I	Jacket Dollar	Arrow Honey	Pepper Mirror	Cotton Saddle	Movie Anchor			
					Immediate Memory Score			of 30
					Time that last trial was completed			

Name: ______________________

DOB: ______________________

Address: ______________________

ID number: ______________________

Examiner: ______________________

Date: ______________________

CONCENTRATION

DIGITS BACKWARDS

Please circle the Digit list chosen (A, B, C, D, E, F). Administer at the rate of one digit per second reading DOWN the selected column.

I am going to read a string of numbers and when I am done, you repeat them back to me in reverse order of how I read them to you. For example, if I say 7-1-9, you would say 9-1-7.

Concentration Number Lists (circle one)					
List A	List B	List C			
4-9-3	5-2-6	1-4-2	Y	N	0
6-2-9	4-1-5	6-5-8	Y	N	1
3-8-1-4	1-7-9-5	6-8-3-1	Y	N	0
3-2-7-9	4-9-6-8	3-4-8-1	Y	N	1
6-2-9-7-1	4-8-5-2-7	4-9-1-5-3	Y	N	0
1-5-2-8-6	6-1-8-4-3	6-8-2-5-1	Y	N	1
7-1-8-4-6-2	8-3-1-9-6-4	3-7-6-5-1-9	Y	N	0
5-3-9-1-4-8	7-2-4-8-5-6	9-2-6-5-1-4	Y	N	1
List D	List E	List F			
7-8-2	3-8-2	2-7-1	Y	N	0
9-2-6	5-1-8	4-7-9	Y	N	1
4-1-8-3	2-7-9-3	1-6-8-3	Y	N	0
9-7-2-3	2-1-6-9	3-9-2-4	Y	N	1
1-7-9-2-6	4-1-8-6-9	2-4-7-5-8	Y	N	0
4-1-7-5-2	9-4-1-7-5	8-3-9-6-4	Y	N	1
2-6-4-8-1-7	6-9-7-3-8-2	5-8-6-2-4-9	Y	N	0
8-4-1-9-3-5	4-2-7-9-3-8	3-1-7-8-2-6	Y	N	1
		Digits Score:			of 4

MONTHS IN REVERSE ORDER

Now tell me the months of the year in reverse order. Start with the last month and go backward. So you'll say December, November. Go ahead.

Dec - Nov - Oct - Sept - Aug - Jul - Jun - May - Apr - Mar - Feb - Jan	0 1
Months Score	of 1
Concentration Total Score (Digits + Months)	of 5

4

STEP 4: NEUROLOGICAL SCREEN

See the instruction sheet (page 7) for details of test administration and scoring of the tests.

Can the patient read aloud (e.g. symptom check-list) and follow instructions without difficulty?	Y	N
Does the patient have a full range of pain-free PASSIVE cervical spine movement?	Y	N
Without moving their head or neck, can the patient look side-to-side and up-and-down without double vision?	Y	N
Can the patient perform the finger nose coordination test normally?	Y	N
Can the patient perform tandem gait normally?	Y	N

BALANCE EXAMINATION

Modified Balance Error Scoring System (mBESS) testing[5]

Which foot was tested (i.e. which is the non-dominant foot) ☐ Left ☐ Right

Testing surface (hard floor, field, etc.) ____________________

Footwear (shoes, barefoot, braces, tape, etc.) ____________________

Condition	Errors
Double leg stance	of 10
Single leg stance (non-dominant foot)	of 10
Tandem stance (non-dominant foot at the back)	of 10
Total Errors	of 30

Name: ____________________

DOB: ____________________

Address: ____________________

ID number: ____________________

Examiner: ____________________

Date: ____________________

5

STEP 5: DELAYED RECALL:

The delayed recall should be performed after 5 minutes have elapsed since the end of the Immediate Recall section. Score 1 pt. for each correct response.

Do you remember that list of words I read a few times earlier? Tell me as many words from the list as you can remember in any order.

Time Started ____________________

Please record each word correctly recalled. Total score equals number of words recalled.

____

____

____

Total number of words recalled accurately: of 5 or of 10

6

STEP 6: DECISION

Domain	Date & time of assessment:		
Symptom number (of 22)			
Symptom severity score (of 132)			
Orientation (of 5)			
Immediate memory	of 15 of 30	of 15 of 30	of 15 of 30
Concentration (of 5)			
Neuro exam	Normal Abnormal	Normal Abnormal	Normal Abnormal
Balance errors (of 30)			
Delayed Recall	of 5 of 10	of 5 of 10	of 5 of 10

Date and time of injury: ____________________

If the athlete is known to you prior to their injury, are they different from their usual self?

☐ **Yes** ☐ **No** ☐ **Unsure** ☐ **Not Applicable**

(If different, describe why in the clinical notes section)

Concussion Diagnosed?

☐ **Yes** ☐ **No** ☐ **Unsure** ☐ **Not Applicable**

If re-testing, has the athlete improved?

☐ **Yes** ☐ **No** ☐ **Unsure** ☐ **Not Applicable**

I am a physician or licensed healthcare professional and I have personally administered or supervised the administration of this SCAT5.

Signature: ____________________

Name: ____________________

Title: ____________________

Registration number (if applicable): ____________________

Date: ____________________

SCORING ON THE SCAT5 SHOULD NOT BE USED AS A STAND-ALONE METHOD TO DIAGNOSE CONCUSSION, MEASURE RECOVERY OR MAKE DECISIONS ABOUT AN ATHLETE'S READINESS TO RETURN TO COMPETITION AFTER CONCUSSION.

CLINICAL NOTES:

Name:

DOB:

Address:

ID number:

Examiner:

Date:

CONCUSSION INJURY ADVICE

(To be given to the person monitoring the concussed athlete)

This patient has received an injury to the head. A careful medical examination has been carried out and no sign of any serious complications has been found. Recovery time is variable across individuals and the patient will need monitoring for a further period by a responsible adult. Your treating physician will provide guidance as to this timeframe.

If you notice any change in behaviour, vomiting, worsening headache, double vision or excessive drowsiness, please telephone your doctor or the nearest hospital emergency department immediately.

Other important points:

Initial rest: Limit physical activity to routine daily activities (avoid exercise, training, sports) and limit activities such as school, work, and screen time to a level that does not worsen symptoms.

1) Avoid alcohol

2) Avoid prescription or non-prescription drugs without medical supervision. Specifically:

a) Avoid sleeping tablets

b) Do not use aspirin, anti-inflammatory medication or stronger pain medications such as narcotics

3) Do not drive until cleared by a healthcare professional.

4) Return to play/sport requires clearance by a healthcare professional.

Clinic phone number:

Patient's name:

Date / time of injury:

Date / time of medical review:

Healthcare Provider:

Contact details or stamp

Echemendia RJ, *et al. Br J Sports Med* 2017;**51**:851–858. doi:10.1136/bjsports-2017-097506SCAT5

INSTRUCTIONS

Words in *Italics* throughout the SCAT5 are the instructions given to the athlete by the clinician

Symptom Scale

The time frame for symptoms should be based on the type of test being administered. At baseline it is advantageous to assess how an athlete "typically" feels whereas during the acute/post-acute stage it is best to ask how the athlete feels at the time of testing.

The symptom scale should be completed by the athlete, not by the examiner. In situations where the symptom scale is being completed after exercise, it should be done in a resting state, generally by approximating his/her resting heart rate.

For total number of symptoms, maximum possible is 22 except immediately post injury, if sleep item is omitted, which then creates a maximum of 21.

For Symptom severity score, add all scores in table, maximum possible is 22 x 6 = 132, except immediately post injury if sleep item is omitted, which then creates a maximum of 21x6=126.

Immediate Memory

The Immediate Memory component can be completed using the traditional 5-word per trial list or, optionally, using 10-words per trial. The literature suggests that the Immediate Memory has a notable ceiling effect when a 5-word list is used. In settings where this ceiling is prominent, the examiner may wish to make the task more difficult by incorporating two 5–word groups for a total of 10 words per trial. In this case, the maximum score per trial is 10 with a total trial maximum of 30.

Choose one of the word lists (either 5 or 10). Then perform 3 trials of immediate memory using this list.

Complete all 3 trials regardless of score on previous trials.

"I am going to test your memory. I will read you a list of words and when I am done, repeat back as many words as you can remember, in any order." The words must be read at a rate of one word per second.

Trials 2 & 3 MUST be completed regardless of score on trial 1 & 2.

Trials 2 & 3:

"I am going to repeat the same list again. Repeat back as many words as you can remember in any order, even if you said the word before."

Score 1 pt. for each correct response. Total score equals sum across all 3 trials. Do NOT inform the athlete that delayed recall will be tested.

Concentration

Digits backward

Choose one column of digits from lists A, B, C, D, E or F and administer those digits as follows:

Say: *"I am going to read a string of numbers and when I am done, you repeat them back to me in reverse order of how I read them to you. For example, if I say 7-1-9, you would say 9-1-7."*

Begin with first 3 digit string.

If correct, circle "Y" for correct and go to next string length. If incorrect, circle "N" for the first string length and read trial 2 in the same string length. One point possible for each string length. Stop after incorrect on both trials (2 N's) in a string length. The digits should be read at the rate of one per second.

Months in reverse order

"Now tell me the months of the year in reverse order. Start with the last month and go backward. So you'll say December, November ... Go ahead"

1 pt. for entire sequence correct

Delayed Recall

The delayed recall should be performed after 5 minutes have elapsed since the end of the Immediate Recall section.

"Do you remember that list of words I read a few times earlier? Tell me as many words from the list as you can remember in any order."

Score 1 pt. for each correct response

Modified Balance Error Scoring System (mBESS)[5] testing

This balance testing is based on a modified version of the Balance Error Scoring System (BESS)[5]. A timing device is required for this testing.

Each of 20-second trial/stance is scored by counting the number of errors. The examiner will begin counting errors only after the athlete has assumed the proper start position. The modified BESS is calculated by adding one error point for each error during the three 20-second tests. The maximum number of errors for any single condition is 10. If the athlete commits multiple errors simultaneously, only one error is recorded but the athlete should quickly return to the testing position, and counting should resume once the athlete is set. Athletes that are unable to maintain the testing procedure for a minimum of five seconds at the start are assigned the highest possible score, ten, for that testing condition.

OPTION: For further assessment, the same 3 stances can be performed on a surface of medium density foam (e.g., approximately 50cm x 40cm x 6cm).

Balance testing – types of errors

1. Hands lifted off iliac crest
2. Opening eyes
3. Step, stumble, or fall
4. Moving hip into > 30 degrees abduction
5. Lifting forefoot or heel
6. Remaining out of test position > 5 sec

"I am now going to test your balance. Please take your shoes off (if applicable), roll up your pant legs above ankle (if applicable), and remove any ankle taping (if applicable). This test will consist of three twenty second tests with different stances."

(a) Double leg stance:

"The first stance is standing with your feet together with your hands on your hips and with your eyes closed. You should try to maintain stability in that position for 20 seconds. I will be counting the number of times you move out of this position. I will start timing when you are set and have closed your eyes."

(b) Single leg stance:

"If you were to kick a ball, which foot would you use? [This will be the dominant foot] *Now stand on your non-dominant foot. The dominant leg should be held in approximately 30 degrees of hip flexion and 45 degrees of knee flexion. Again, you should try to maintain stability for 20 seconds with your hands on your hips and your eyes closed. I will be counting the number of times you move out of this position. If you stumble out of this position, open your eyes and return to the start position and continue balancing. I will start timing when you are set and have closed your eyes."*

(c) Tandem stance:

"Now stand heel-to-toe with your non-dominant foot in back. Your weight should be evenly distributed across both feet. Again, you should try to maintain stability for 20 seconds with your hands on your hips and your eyes closed. I will be counting the number of times you move out of this position. If you stumble out of this position, open your eyes and return to the start position and continue balancing. I will start timing when you are set and have closed your eyes."

Tandem Gait

Participants are instructed to stand with their feet together behind a starting line (the test is best done with footwear removed). Then, they walk in a forward direction as quickly and as accurately as possible along a 38mm wide (sports tape), 3 metre line with an alternate foot heel-to-toe gait ensuring that they approximate their heel and toe on each step. Once they cross the end of the 3m line, they turn 180 degrees and return to the starting point using the same gait. Athletes fail the test if they step off the line, have a separation between their heel and toe, or if they touch or grab the examiner or an object.

Finger to Nose

"I am going to test your coordination now. Please sit comfortably on the chair with your eyes open and your arm (either right or left) outstretched (shoulder flexed to 90 degrees and elbow and fingers extended), pointing in front of you. When I give a start signal, I would like you to perform five successive finger to nose repetitions using your index finger to touch the tip of the nose, and then return to the starting position, as quickly and as accurately as possible."

References

1. McCrory et al. Consensus Statement On Concussion In Sport – The 5th International Conference On Concussion In Sport Held In Berlin, October 2016. British Journal of Sports Medicine 2017 (available at www.bjsm.bmj.com)
2. Maddocks, DL; Dicker, GD; Saling, MM. The assessment of orientation following concussion in athletes. Clinical Journal of Sport Medicine 1995; 5: 32-33
3. Jennett, B., Bond, M. Assessment of outcome after severe brain damage: a practical scale. Lancet 1975; i: 480-484
4. McCrea M. Standardized mental status testing of acute concussion. Clinical Journal of Sport Medicine. 2001; 11: 176-181
5. Guskiewicz KM. Assessment of postural stability following sport-related concussion. Current Sports Medicine Reports. 2003; 2: 24-30

CONCUSSION INFORMATION

Any athlete suspected of having a concussion should be removed from play and seek medical evaluation.

Signs to watch for

Problems could arise over the first 24-48 hours. The athlete should not be left alone and must go to a hospital at once if they experience:

- Worsening headache
- Drowsiness or inability to be awakened
- Inability to recognize people or places
- Repeated vomiting
- Unusual behaviour or confusion or irritable
- Seizures (arms and legs jerk uncontrollably)
- Weakness or numbness in arms or legs
- Unsteadiness on their feet.
- Slurred speech

Consult your physician or licensed healthcare professional after a suspected concussion. Remember, it is better to be safe.

Rest & Rehabilitation

After a concussion, the athlete should have physical rest and relative cognitive rest for a few days to allow their symptoms to improve. In most cases, after no more than a few days of rest, the athlete should gradually increase their daily activity level as long as their symptoms do not worsen. Once the athlete is able to complete their usual daily activities without concussion-related symptoms, the second step of the return to play/sport progression can be started. The athlete should not return to play/sport until their concussion-related symptoms have resolved and the athlete has successfully returned to full school/learning activities.

When returning to play/sport, the athlete should follow a stepwise, **medically managed exercise progression, with increasing amounts of exercise.** For example:

Graduated Return to Sport Strategy

Exercise step	Functional exercise at each step	Goal of each step
1. Symptom-limited activity	Daily activities that do not provoke symptoms.	Gradual reintroduction of work/school activities.
2. Light aerobic exercise	Walking or stationary cycling at slow to medium pace. No resistance training.	Increase heart rate.
3. Sport-specific exercise	Running or skating drills. No head impact activities.	Add movement.
4. Non-contact training drills	Harder training drills, e.g., passing drills. May start progressive resistance training.	Exercise, coordination, and increased thinking.
5. Full contact practice	Following medical clearance, participate in normal training activities.	Restore confidence and assess functional skills by coaching staff.
6. Return to play/sport	Normal game play.	

In this example, it would be typical to have 24 hours (or longer) for each step of the progression. If any symptoms worsen while exercising, the athlete should go back to the previous step. Resistance training should be added only in the later stages (Stage 3 or 4 at the earliest).

Written clearance should be provided by a healthcare professional before return to play/sport as directed by local laws and regulations.

Graduated Return to School Strategy

Concussion may affect the ability to learn at school. The athlete may need to miss a few days of school after a concussion. When going back to school, some athletes may need to go back gradually and may need to have some changes made to their schedule so that concussion symptoms do not get worse. If a particular activity makes symptoms worse, then the athlete should stop that activity and rest until symptoms get better. To make sure that the athlete can get back to school without problems, it is important that the healthcare provider, parents, caregivers and teachers talk to each other so that everyone knows what the plan is for the athlete to go back to school.

Note: If mental activity does not cause any symptoms, the athlete may be able to skip step 2 and return to school part-time before doing school activities at home first.

Mental Activity	Activity at each step	Goal of each step
1. Daily activities that do not give the athlete symptoms	Typical activities that the athlete does during the day as long as they do not increase symptoms (e.g. reading, texting, screen time). Start with 5-15 minutes at a time and gradually build up.	Gradual return to typical activities.
2. School activities	Homework, reading or other cognitive activities outside of the classroom.	Increase tolerance to cognitive work.
3. Return to school part-time	Gradual introduction of schoolwork. May need to start with a partial school day or with increased breaks during the day.	Increase academic activities.
4. Return to school full-time	Gradually progress school activities until a full day can be tolerated.	Return to full academic activities and catch up on missed work.

If the athlete continues to have symptoms with mental activity, some other accomodations that can help with return to school may include:

- Starting school later, only going for half days, or going only to certain classes
- More time to finish assignments/tests
- Quiet room to finish assignments/tests
- Not going to noisy areas like the cafeteria, assembly halls, sporting events, music class, shop class, etc.
- Taking lots of breaks during class, homework, tests
- No more than one exam/day
- Shorter assignments
- Repetition/memory cues
- Use of a student helper/tutor
- Reassurance from teachers that the child will be supported while getting better

The athlete should not go back to sports until they are back to school/learning, without symptoms getting significantly worse and no longer needing any changes to their schedule.

Child SCAT5©

SPORT CONCUSSION ASSESSMENT TOOL

FOR CHILDREN AGES 5 TO 12 YEARS

FOR USE BY MEDICAL PROFESSIONALS ONLY

supported by

IIHF FIFA® FEI

Patient details

Name: ______________________

DOB: ______________________

Address: ______________________

ID number: ______________________

Examiner: ______________________

Date of Injury: ______________ Time: ______________

WHAT IS THE CHILD SCAT5?

The Child SCAT5 is a standardized tool for evaluating concussions designed for use by physicians and licensed healthcare professionals[1].

If you are not a physician or licensed healthcare professional, please use the Concussion Recognition Tool 5 (CRT5). The Child SCAT5 is to be used for evaluating Children aged 5 to 12 years. For athletes aged 13 years and older, please use the SCAT5.

Preseason Child SCAT5 baseline testing can be useful for interpreting post-injury test scores, but not required for that purpose. Detailed instructions for use of the Child SCAT5 are provided on page 7. Please read through these instructions carefully before testing the athlete. Brief verbal instructions for each test are given in italics. The only equipment required for the tester is a watch or timer.

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Recognise and Remove

A head impact by either a direct blow or indirect transmission of force can be associated with a serious and potentially fatal brain injury. If there are significant concerns, including any of the red flags listed in Box 1, then activation of emergency procedures and urgent transport to the nearest hospital should be arranged.

Key points

- Any athlete with suspected concussion should be REMOVED FROM PLAY, medically assessed and monitored for deterioration. No athlete diagnosed with concussion should be returned to play on the day of injury.
- If the child is suspected of having a concussion and medical personnel are not immediately available, the child should be referred to a medical facility for urgent assessment.
- Concussion signs and symptoms evolve over time and it is important to consider repeat evaluation in the assessment of concussion.
- The diagnosis of a concussion is a clinical judgment, made by a medical professional. The Child SCAT5 should NOT be used by itself to make, or exclude, the diagnosis of concussion. An athlete may have a a concussion even if their Child SCAT5 is "normal".

Remember:

- The basic principles of first aid (danger, response, airway, breathing, circulation) should be followed.
- Do not attempt to move the athlete (other than that required for airway management) unless trained to do so.
- Assessment for a spinal cord injury is a critical part of the initial on-field assessment.
- Do not remove a helmet or any other equipment unless trained to do so safely.

1

Name:	
DOB:	
Address:	
ID number:	
Examiner:	
Date:	

IMMEDIATE OR ON-FIELD ASSESSMENT

The following elements should be assessed for all athletes who are suspected of having a concussion prior to proceeding to the neurocognitive assessment and ideally should be done on-field after the first first aid / emergency care priorities are completed.

If any of the "Red Flags" or observable signs are noted after a direct or indirect blow to the head, the athlete should be immediately and safely removed from participation and evaluated by a physician or licensed healthcare professional.

Consideration of transportation to a medical facility should be at the discretion of the physician or licensed healthcare professional.

The GCS is important as a standard measure for all patients and can be done serially if necessary in the event of deterioration in conscious state. The cervical spine exam is a critical step of the immediate assessment, however, it does not need to be done serially.

STEP 1: RED FLAGS

RED FLAGS:

- **Neck pain or tenderness**
- **Double vision**
- **Weakness or tingling/ burning in arms or legs**
- **Severe or increasing headache**
- **Seizure or convulsion**
- **Loss of consciousness**
- **Deteriorating conscious state**
- **Vomiting**
- **Increasingly restless, agitated or combative**

STEP 2: OBSERVABLE SIGNS

Witnessed ☐ Observed on Video ☐

Lying motionless on the playing surface	Y	N
Balance / gait difficulties / motor incoordination: stumbling, slow / laboured movements	Y	N
Disorientation or confusion, or an inability to respond appropriately to questions	Y	N
Blank or vacant look	Y	N
Facial injury after head trauma	Y	N

STEP 3: EXAMINATION GLASGOW COMA SCALE (GCS)[2]

Time of assessment			
Date of assessment			
Best eye response (E)			
No eye opening	1	1	1
Eye opening in response to pain	2	2	2
Eye opening to speech	3	3	3
Eyes opening spontaneously	4	4	4
Best verbal response (V)			
No verbal response	1	1	1
Incomprehensible sounds	2	2	2
Inappropriate words	3	3	3
Confused	4	4	4
Oriented	5	5	5
Best motor response (M)			
No motor response	1	1	1
Extension to pain	2	2	2
Abnormal flexion to pain	3	3	3
Flexion / Withdrawal to pain	4	4	4
Localizes to pain	5	5	5
Obeys commands	6	6	6
Glasgow Coma score (E + V + M)			

CERVICAL SPINE ASSESSMENT

Does the athlete report that their neck is pain free at rest?	Y	N
If there is NO neck pain at rest, does the athlete have a full range of ACTIVE pain free movement?	Y	N
Is the limb strength and sensation normal?	Y	N

In a patient who is not lucid or fully conscious, a cervical spine injury should be assumed until proven otherwise.

OFFICE OR OFF-FIELD ASSESSMENT

STEP 1: ATHLETE BACKGROUND

Please note that the neurocognitive assessment should be done in a distraction-free environment with the athlete in a resting state.

Sport / team / school: ______

Date / time of injury: ______

Years of education completed: ______

Age: ______

Gender: M / F / Other

Dominant hand: left / neither / right

How many diagnosed concussions has the athlete had in the past?: ______

When was the most recent concussion?: ______

How long was the recovery (time to being cleared to play) from the most recent concussion?: ______ (days)

Has the athlete ever been:

Hospitalized for a head injury?	Yes	No
Diagnosed / treated for headache disorder or migraines?	Yes	No
Diagnosed with a learning disability / dyslexia?	Yes	No
Diagnosed with ADD / ADHD?	Yes	No
Diagnosed with depression, anxiety or other psychiatric disorder?	Yes	No

Current medications? If yes, please list: ______

STEP 2: SYMPTOM EVALUATION

The athlete should be given the symptom form and asked to read this instruction paragraph out loud then complete the symptom scale. For the baseline assessment, the athlete should rate his/her symptoms based on how he/she typically feels and for the post injury assessment the athlete should rate their symptoms at this point in time.

To be done in a resting state

Please Check: ☐ **Baseline** ☐ **Post-Injury**

Name: ______
DOB: ______
Address: ______
ID number: ______
Examiner: ______
Date: ______

2

Child Report[3]

	Not at all/ Never	A little/ Rarely	Somewhat/ Sometimes	A lot/ Often
I have headaches	0	1	2	3
I feel dizzy	0	1	2	3
I feel like the room is spinning	0	1	2	3
I feel like I'm going to faint	0	1	2	3
Things are blurry when I look at them	0	1	2	3
I see double	0	1	2	3
I feel sick to my stomach	0	1	2	3
My neck hurts	0	1	2	3
I get tired a lot	0	1	2	3
I get tired easily	0	1	2	3
I have trouble paying attention	0	1	2	3
I get distracted easily	0	1	2	3
I have a hard time concentrating	0	1	2	3
I have problems remembering what people tell me	0	1	2	3
I have problems following directions	0	1	2	3
I daydream too much	0	1	2	3
I get confused	0	1	2	3
I forget things	0	1	2	3
I have problems finishing things	0	1	2	3
I have trouble figuring things out	0	1	2	3
It's hard for me to learn new things	0	1	2	3
Total number of symptoms:				of 21
Symptom severity score:				of 63
Do the symptoms get worse with physical activity?			Y	N
Do the symptoms get worse with trying to think?			Y	N

Overall rating for child to answer:

	Very bad	Very good
On a scale of 0 to 10 (where 10 is normal), how do you feel now?	0 1 2 3 4 5 6 7 8 9 10	

If not 10, in what way do you feel different?:

______

Parent Report

The child:	Not at all/ Never	A little/ Rarely	Somewhat/ Sometimes	A lot/ Often
has headaches	0	1	2	3
feels dizzy	0	1	2	3
has a feeling that the room is spinning	0	1	2	3
feels faint	0	1	2	3
has blurred vision	0	1	2	3
has double vision	0	1	2	3
experiences nausea	0	1	2	3
has a sore neck	0	1	2	3
gets tired a lot	0	1	2	3
gets tired easily	0	1	2	3
has trouble sustaining attention	0	1	2	3
is easily distracted	0	1	2	3
has difficulty concentrating	0	1	2	3
has problems remembering what he/she is told	0	1	2	3
has difficulty following directions	0	1	2	3
tends to daydream	0	1	2	3
gets confused	0	1	2	3
is forgetful	0	1	2	3
has difficulty completing tasks	0	1	2	3
has poor problem solving skills	0	1	2	3
has problems learning	0	1	2	3
Total number of symptoms:				of 21
Symptom severity score:				of 63
Do the symptoms get worse with physical activity?			Y	N
Do the symptoms get worse with mental activity?			Y	N

Overall rating for parent/teacher/coach/carer to answer

On a scale of 0 to 100% (where 100% is normal), how would you rate the child now?

______

If not 100%, in what way does the child seem different?

______

3

STEP 3: COGNITIVE SCREENING

Standardized Assessment of Concussion - Child Version (SAC-C)[4]

IMMEDIATE MEMORY

The Immediate Memory component can be completed using the traditional 5-word per trial list or optionally using 10-words per trial to minimise any ceiling effect. All 3 trials must be administered irrespective of the number correct on the first trial. Administer at the rate of one word per second.

Please choose EITHER the 5 or 10 word list groups and circle the specific word list chosen for this test.

I am going to test your memory. I will read you a list of words and when I am done, repeat back as many words as you can remember, in any order. For Trials 2 & 3: I am going to repeat the same list again. Repeat back as many words as you can remember in any order, even if you said the word before.

List	Alternate 5 word lists					Score (of 5) Trial 1	Trial 2	Trial 3
A	Finger	Penny	Blanket	Lemon	Insect			
B	Candle	Paper	Sugar	Sandwich	Wagon			
C	Baby	Monkey	Perfume	Sunset	Iron			
D	Elbow	Apple	Carpet	Saddle	Bubble			
E	Jacket	Arrow	Pepper	Cotton	Movie			
F	Dollar	Honey	Mirror	Saddle	Anchor			
					Immediate Memory Score	of 15		
					Time that last trial was completed			

List	Alternate 10 word lists					Score (of 10) Trial 1	Trial 2	Trial 3
G	Finger	Penny	Blanket	Lemon	Insect			
	Candle	Paper	Sugar	Sandwich	Wagon			
H	Baby	Monkey	Perfume	Sunset	Iron			
	Elbow	Apple	Carpet	Saddle	Bubble			
I	Jacket	Arrow	Pepper	Cotton	Movie			
	Dollar	Honey	Mirror	Saddle	Anchor			
					Immediate Memory Score	of 30		
					Time that last trial was completed			

Name:
DOB:
Address:
ID number:
Examiner:
Date:

CONCENTRATION

DIGITS BACKWARDS

Please circle the Digit list chosen (A, B, C, D, E, F). Administer at the rate of one digit per second reading DOWN the selected column.

I am going to read a string of numbers and when I am done, you repeat them back to me in reverse order of how I read them to you. For example, if I say 7-1-9, you would say 9-1-7.

Concentration Number Lists (circle one)					
List A	List B	List C			
5-2	4-1	4-9	Y	N	0
4-1	9-4	6-2	Y	N	1
4-9-3	5-2-6	1-4-2	Y	N	0
6-2-9	4-1-5	6-5-8	Y	N	1
3-8-1-4	1-7-9-5	6-8-3-1	Y	N	0
3-2-7-9	4-9-6-8	3-4-8-1	Y	N	1
6-2-9-7-1	4-8-5-2-7	4-9-1-5-3	Y	N	0
1-5-2-8-6	6-1-8-4-3	6-8-2-5-1	Y	N	1
7-1-8-4-6-2	8-3-1-9-6-4	3-7-6-5-1-9	Y	N	0
5-3-9-1-4-8	7-2-4-8-5-6	9-2-6-5-1-4	Y	N	1
List D	List E	List F			
2-7	9-2	7-8	Y	N	0
5-9	6-1	5-1	Y	N	1
7-8-2	3-8-2	2-7-1	Y	N	0
9-2-6	5-1-8	4-7-9	Y	N	1
4-1-8-3	2-7-9-3	1-6-8-3	Y	N	0
9-7-2-3	2-1-6-9-	3-9-2-4	Y	N	1
1-7-9-2-6	4-1-8-6-9	2-4-7-5-8	Y	N	0
4-1-7-5-2	9-4-1-7-5	8-3-9-6-4	Y	N	1
2-6-4-8-1-7	6-9-7-3-8-2	5-8-6-2-4-9	Y	N	0
8-4-1-9-3-5	4-2-7-3-9-8	3-1-7-8-2-6	Y	N	1
		Digits Score:			of 5

DAYS IN REVERSE ORDER

Now tell me the days of the week in reverse order. Start with the last day and go backward. So you'll say Sunday, Saturday. Go ahead.

Sunday - Saturday - Friday - Thursday - Wednesday - Tuesday - Monday	0 1
Days Score	of 1
Concentration Total Score (Digits + Days)	of 6

4

STEP 4: NEUROLOGICAL SCREEN

See the instruction sheet (page 7) for details of test administration and scoring of the tests.

Can the patient read aloud (e.g. symptom check-list) and follow instructions without difficulty?	Y	N
Does the patient have a full range of pain-free PASSIVE cervical spine movement?	Y	N
Without moving their head or neck, can the patient look side-to-side and up-and-down without double vision?	Y	N
Can the patient perform the finger nose coordination test normally?	Y	N
Can the patient perform tandem gait normally?	Y	N

BALANCE EXAMINATION

Modified Balance Error Scoring System (BESS) testing[5]

Which foot was tested (i.e. which is the non-dominant foot) ☐ Left ☐ Right

Testing surface (hard floor, field, etc.) ____________

Footwear (shoes, barefoot, braces, tape, etc.) ____________

Condition	Errors	
Double leg stance	of 10	
Single leg stance (non-dominant foot, 10-12 y/o only)	of 10	
Tandem stance (non-dominant foot at back)	of 10	
Total Errors	5-9 y/o of 20	10-12 y/o of 30

Name: ____________

DOB: ____________

Address: ____________

ID number: ____________

Examiner: ____________

Date: ____________

5

STEP 5: DELAYED RECALL:

The delayed recall should be performed after 5 minutes have elapsed since the end of the Immediate Recall section. Score 1 pt. for each correct response.

Do you remember that list of words I read a few times earlier? Tell me as many words from the list as you can remember in any order.

Time Started ____________

Please record each word correctly recalled. Total score equals number of words recalled.

____

____

____

Total number of words recalled accurately: of 5 or of 10

6

STEP 6: DECISION

Domain	Date & time of assessment:		
Symptom number Child report (of 21) Parent report (of 21)			
Symptom severity score Child report (of 63) Parent report (of 63)			
Immediate memory	of 15 of 30	of 15 of 30	of 15 of 30
Concentration (of 6)			
Neuro exam	Normal Abnormal	Normal Abnormal	Normal Abnormal
Balance errors (5-9 y/o of 20) (10-12 y/o of 30)			
Delayed Recall	of 5 of 10	of 5 of 10	of 5 of 10

Date and time of injury: ____________

If the athlete is known to you prior to their injury, are they different from their usual self?

☐ **Yes** ☐ **No** ☐ **Unsure** ☐ **Not Applicable**

(If different, describe why in the clinical notes section)

Concussion Diagnosed?

☐ **Yes** ☐ **No** ☐ **Unsure** ☐ **Not Applicable**

If re-testing, has the athlete improved?

☐ **Yes** ☐ **No** ☐ **Unsure** ☐ **Not Applicable**

I am a physician or licensed healthcare professional and I have personally administered or supervised the administration of this Child SCAT5.

Signature: ____________

Name: ____________

Title: ____________

Registration number (if applicable): ____________

Date: ____________

SCORING ON THE CHILD SCAT5 SHOULD NOT BE USED AS A STAND-ALONE METHOD TO DIAGNOSE CONCUSSION, MEASURE RECOVERY OR MAKE DECISIONS ABOUT AN ATHLETE'S READINESS TO RETURN TO COMPETITION AFTER CONCUSSION.

Davis GA, *et al. Br J Sports Med* 2017;**51**:862–869. doi:10.1136/bjsports-2017-097492childscat5

For the Neurological Screen (page 5), if the child cannot read, ask him/her to describe what they see in this picture.

Name: ______________________
DOB: ______________________
Address: ______________________
ID number: ______________________
Examiner: ______________________
Date: ______________________

CLINICAL NOTES:

____

____

____

____

____

____

Concussion injury advice for the child and parents/carergivers

(To be given to the person monitoring the concussed child)

This child has had an injury to the head and needs to be carefully watched for the next 24 hours by a responsible adult.

If you notice any change in behavior, vomiting, dizziness, worsening headache, double vision or excessive drowsiness, please call an ambulance to take the child to hospital immediately.

Other important points:

Following concussion, the child should rest for at least 24 hours.

- The child should not use a computer, internet or play video games if these activities make symptoms worse.
- The child should not be given any medications, including pain killers, unless prescribed by a medical doctor.
- The child should not go back to school until symptoms are improving.
- The child should not go back to sport or play until a doctor gives permission.

Clinic phone number: ______________________

Patient's name: ______________________

Date / time of injury: ______________________

Date / time of medical review: ______________________

Healthcare Provider: ______________________

Contact details or stamp

INSTRUCTIONS

Words in *Italics* throughout the Child SCAT5 are the instructions given to the athlete by the clinician

Symptom Scale

In situations where the symptom scale is being completed after exercise, it should still be done in a resting state, at least 10 minutes post exercise.

At Baseline

- The child is to complete the Child Report, according to how he/she feels today, and
- The parent/carer is to complete the Parent Report according to how the child has been over the previous week.

On the day of injury

- The child is to complete the Child Report, according to how he/she feels now.
- If the parent is present, and has had time to assess the child on the day of injury, the parent completes the Parent Report according to how the child appears now.

On all subsequent days

- The child is to complete the Child Report, according to how he/she feels today, and
- The parent/carer is to complete the Parent Report according to how the child has been over the previous 24 hours.

For Total number of symptoms, maximum possible is 21

For Symptom severity score, add all scores in table, maximum possible is 21 x 3 = 63

Standardized Assessment of Concussion Child Version (SAC-C)

Immediate Memory

Choose one of the 5-word lists. Then perform 3 trials of immediate memory using this list.

Complete all 3 trials regardless of score on previous trials.

"I am going to test your memory. I will read you a list of words and when I am done, repeat back as many words as you can remember, in any order." The words must be read at a rate of one word per second.

OPTION: The literature suggests that the Immediate Memory has a notable ceiling effect when a 5-word list is used. (In younger children, use the 5-word list). In settings where this ceiling is prominent the examiner may wish to make the task more difficult by incorporating two 5–word groups for a total of 10 words per trial. In this case the maximum score per trial is 10 with a total trial maximum of 30.

Trials 2 & 3 MUST be completed regardless of score on trial 1 & 2.

Trials 2 & 3: *"I am going to repeat the same list again. Repeat back as many words as you can remember in any order, even if you said the word before."*

Score 1 pt. for each correct response. Total score equals sum across all 3 trials. Do NOT inform the athlete that delayed recall will be tested.

Concentration

Digits backward

Choose one column only, from List A, B, C, D, E or F, and administer those digits as follows:

"I am going to read you some numbers and when I am done, you say them back to me backwards, in reverse order of how I read them to you. For example, if I say 7-1, you would say 1-7."

If correct, circle "Y" for correct and go to next string length. If incorrect, circle "N" for the first string length and read trial 2 in the same string length. One point possible for each string length. Stop after incorrect on both trials (2 N's) in a string length. The digits should be read at the rate of one per second.

Days of the week in reverse order

"Now tell me the days of the week in reverse order. Start with Sunday and go backward. So you'll say Sunday, Saturday ... Go ahead"

1 pt. for entire sequence correct

Delayed Recall

The delayed recall should be performed after at least 5 minutes have elapsed since the end of the Immediate Recall section.

"Do you remember that list of words I read a few times earlier? Tell me as many words from the list as you can remember in any order."

Circle each word correctly recalled. Total score equals number of words recalled.

Neurological Screen

Reading

The child is asked to read a paragraph of text from the instructions in the Child SCAT5. For children who can not read, they are asked to describe what they see in a photograph or picture, such as that on page 6 of the Child SCAT5.

Modified Balance Error Scoring System (mBESS)[5] testing

These instructions are to be read by the person administering the Child SCAT5, and each balance task should be demonstrated to the child. The child should then be asked to copy what the examiner demonstrated.

Each of 20-second trial/stance is scored by counting the number of errors. The This balance testing is based on a modified version of the Balance Error Scoring System (BESS)[5].

A stopwatch or watch with a second hand is required for this testing.

"I am now going to test your balance. Please take your shoes off, roll up your pants above your ankle (if applicable), and remove any ankle taping (if applicable). This test will consist of two different parts."

OPTION: For further assessment, the same 3 stances can be performed on a surface of medium density foam (e.g., approximately 50cm x 40cm x 6cm).

(a) Double leg stance:

The first stance is standing with the feet together with hands on hips and with eyes closed. The child should try to maintain stability in that position for 20 seconds. You should inform the child that you will be counting the number of times the child moves out of this position. You should start timing when the child is set and the eyes are closed.

(b) Tandem stance:

Instruct or show the child how to stand heel-to-toe with the non-dominant foot in the back. Weight should be evenly distributed across both feet. Again, the child should try to maintain stability for 20 seconds with hands on hips and eyes closed. You should inform the child that you will be counting the number of times the child moves out of this position. If the child stumbles out of this position, instruct him/her to open the eyes and return to the start position and continue balancing. You should start timing when the child is set and the eyes are closed.

(c) Single leg stance (10-12 year olds only):

"If you were to kick a ball, which foot would you use? [This will be the dominant foot] *Now stand on your other foot. You should bend your other leg and hold it up (show the child). Again, try to stay in that position for 20 seconds with your hands on your hips and your eyes closed. I will be counting the number of times you move out of this position. If you move out of this position, open your eyes and return to the start position and keep balancing. I will start timing when you are set and have closed your eyes."*

Balance testing – types of errors

1. Hands lifted off iliac crest
2. Opening eyes
3. Step, stumble, or fall
4. Moving hip into > 30 degrees abduction
5. Lifting forefoot or heel
6. Remaining out of test position > 5 sec

Each of the 20-second trials is scored by counting the errors, or deviations from the proper stance, accumulated by the child. The examiner will begin counting errors only after the child has assumed the proper start position. The modified BESS is calculated by adding one error point for each error during the 20-second tests. The maximum total number of errors for any single condition is 10. If a child commits multiple errors simultaneously, only one error is recorded but the child should quickly return to the testing position, and counting should resume once subject is set. Children who are unable to maintain the testing procedure for a minimum of five seconds at the start are assigned the highest possible score, ten, for that testing condition.

Tandem Gait

Instruction for the examiner - Demonstrate the following to the child:

The child is instructed to stand with their feet together behind a starting line (the test is best done with footwear removed). Then, they walk in a forward direction as quickly and as accurately as possible along a 38mm wide (sports tape), 3 metre line with an alternate foot heel-to-toe gait ensuring that they approximate their heel and toe on each step. Once they cross the end of the 3m line, they turn 180 degrees and return to the starting point using the same gait. Children fail the test if they step off the line, have a separation between their heel and toe, or if they touch or grab the examiner or an object.

Finger to Nose

The tester should demonstrate it to the child.

"I am going to test your coordination now. Please sit comfortably on the chair with your eyes open and your arm (either right or left) outstretched (shoulder flexed to 90 degrees and elbow and fingers extended). When I give a start signal, I would like you to perform five successive finger to nose repetitions using your index finger to touch the tip of the nose as quickly and as accurately as possible."

Scoring: 5 correct repetitions in < 4 seconds = 1

Note for testers: Children fail the test if they do not touch their nose, do not fully extend their elbow or do not perform five repetitions.

References

1. McCrory et al. Consensus Statement On Concussion In Sport – The 5th International Conference On Concussion In Sport Held In Berlin, October 2016. British Journal of Sports Medicine 2017 (available at www.bjsm.bmj.com)
2. Jennett, B., Bond, M. Assessment of outcome after severe brain damage: a practical scale. Lancet 1975; i: 480-484
3. Ayr, L.K., Yeates, K.O., Taylor, H.G., Brown, M. Dimensions of postconcussive symptoms in children with mild traumatic brain injuries. Journal of the International Neuropsychological Society. 2009; 15:19–30
4. McCrea M. Standardized mental status testing of acute concussion. Clinical Journal of Sports Medicine. 2001; 11: 176-181
5. Guskiewicz KM. Assessment of postural stability following sport-related concussion. Current Sports Medicine Reports. 2003; 2: 24-30

CONCUSSION INFORMATION

If you think you or a teammate has a concussion, tell your coach/trainer/parent right away so that you can be taken out of the game. You or your teammate should be seen by a doctor as soon as possible. YOU OR YOUR TEAMMATE SHOULD NOT GO BACK TO PLAY/SPORT THAT DAY.

Signs to watch for

Problems can happen over the first 24-48 hours. You or your teammate should not be left alone and must go to a hospital right away if any of the following happens:

- New headache, or headache gets worse
- Neck pain that gets worse
- Becomes sleepy/drowsy or can't be woken up
- Cannot recognise people or places
- Feeling sick to your stomach or vomiting
- Acting weird/strange, seems/feels confused, or is irritable
- Has any seizures (arms and/or legs jerk uncontrollably)
- Has weakness, numbness or tingling (arms, legs or face)
- Is unsteady walking or standing
- Talking is slurred
- Cannot understand what someone is saying or directions

Consult your physician or licensed healthcare professional after a suspected concussion. Remember, it is better to be safe.

Graduated Return to Sport Strategy

After a concussion, the child should rest physically and mentally for a few days to allow symptoms to get better. In most cases, after a few days of rest, they can gradually increase their daily activity level as long as symptoms don't get worse. Once they are able to do their usual daily activities without symptoms, the child should gradually increase exercise in steps, guided by the healthcare professional (see below).

The athlete should not return to play/sport the day of injury.

NOTE: An initial period of a few days of both cognitive ("thinking") and physical rest is recommended before beginning the Return to Sport progression.

Exercise step	Functional exercise at each step	Goal of each step
1. Symptom-limited activity	Daily activities that do not provoke symptoms.	Gradual reintroduction of work/school activities.
2. Light aerobic exercise	Walking or stationary cycling at slow to medium pace. No resistance training.	Increase heart rate.
3. Sport-specific exercise	Running or skating drills. No head impact activities.	Add movement.
4. Non-contact training drills	Harder training drills, e.g., passing drills. May start progressive resistance training.	Exercise, coordination, and increased thinking.
5. Full contact practice	Following medical clearance, participate in normal training activities.	Restore confidence and assess functional skills by coaching staff.
6. Return to play/sport	Normal game play.	

There should be at least 24 hours (or longer) for each step of the progression. If any symptoms worsen while exercising, the athlete should go back to the previous step. Resistance training should be added only in the later stages (Stage 3 or 4 at the earliest). The athlete should not return to sport until the concussion symptoms have gone, they have successfully returned to full school/learning activities, and the healthcare professional has given the child written permission to return to sport.

If the child has symptoms for more than a month, they should ask to be referred to a healthcare professional who is an expert in the management of concussion.

Graduated Return to School Strategy

Concussion may affect the ability to learn at school. The child may need to miss a few days of school after a concussion, but the child's doctor should help them get back to school after a few days. When going back to school, some children may need to go back gradually and may need to have some changes made to their schedule so that concussion symptoms don't get a lot worse. If a particular activity makes symptoms a lot worse, then the child should stop that activity and rest until symptoms get better. To make sure that the child can get back to school without problems, it is important that the health care provider, parents/caregivers and teachers talk to each other so that everyone knows what the plan is for the child to go back to school.

Note: If mental activity does not cause any symptoms, the child may be able to return to school part-time without doing school activities at home first.

Mental Activity	Activity at each step	Goal of each step
1. Daily activities that do not give the child symptoms	Typical activities that the child does during the day as long as they do not increase symptoms (e.g. reading, texting, screen time). Start with 5-15 minutes at a time and gradually build up.	Gradual return to typical activities.
2. School activities	Homework, reading or other cognitive activities outside of the classroom.	Increase tolerance to cognitive work.
3. Return to school part-time	Gradual introduction of schoolwork. May need to start with a partial school day or with increased breaks during the day.	Increase academic activities.
4. Return to school full-time	Gradually progress school activities until a full day can be tolerated.	Return to full academic activities and catch up on missed work.

If the child continues to have symptoms with mental activity, some other things that can be done to help with return to school may include:

- Starting school later, only going for half days, or going only to certain classes
- More time to finish assignments/tests
- Quiet room to finish assignments/tests
- Not going to noisy areas like the cafeteria, assembly halls, sporting events, music class, shop class, etc.
- Taking lots of breaks during class, homework, tests
- No more than one exam/day
- Shorter assignments
- Repetition/memory cues
- Use of a student helper/tutor
- Reassurance from teachers that the child will be supported while getting better

The child should not go back to sports until they are back to school/learning, without symptoms getting significantly worse and no longer needing any changes to their schedule.

Appendix 6. General questionnaire + PHQ9 + MoCA forms

Name ______________________________

Phone number ______________________________

Date ____________________ First language ____________________

Weight (kg) ____________ Position on field ____________________

Height (cm) ____________ Years in current sport ____________

Normal vision?	YES	NO
Diagnosed with: Autism	YES	NO
Neurological disorders (e.g. epilepsy)	YES	NO
Vision disorders (e.g. nystagmus, amblyopia)	YES	NO
Drug / alcohol addition	YES	NO
Consumed alcohol or drugs in the past 24 hours?	YES	NO

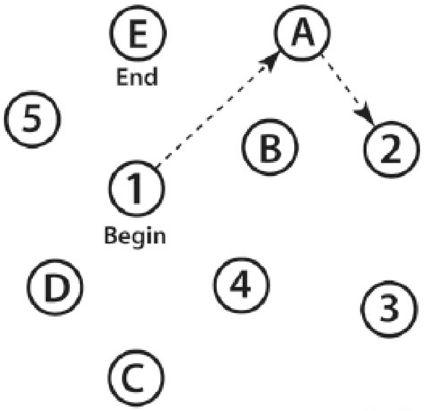
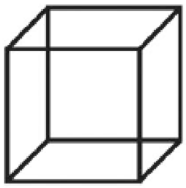
Over the past 2 weeks, how often have you been bothered by any of the following problems?	**Not at all**	**Several days**	**More than half the days**	**Nearly every day**
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed or hopeless	0	1	2	3
3. Trouble falling asleep, staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself – or that you're a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that the other people could have noticed. Or, the opposite – being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

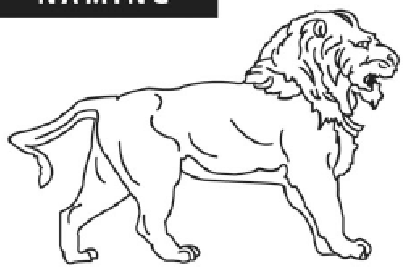
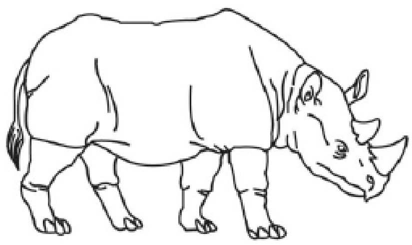
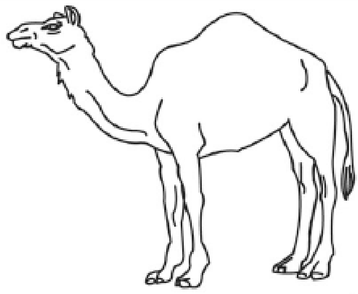
Column totals ________ + ________ + ________

Add totals together ____________________

10. If you checked off any problems, how difficult have those problems made it for you to do your work, take care of things at home, or get along with other people?

☐ Not difficult at all ☐ Somewhat difficult ☐ Very difficult ☐ Extremely difficult

VISUOSPATIAL / EXECUTIVE			POINTS
 [ ]	 Copy cube [ ]	Draw CLOCK (Ten past eleven) (3 points) [ ] Contour [ ] Numbers [ ] Hands	___/5

NAMING			
 [ ]	 [ ]	 [ ]	___/3

ATTENTION	Read list of digits (1 digit/ sec.). Subject has to repeat them in the forward order [ ] 2 1 8 5 4	___/1
	Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors [ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B	___/1
	Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65 4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**	___/3
LANGUAGE	Repeat : I only know that John is the one to help today. [ ] The cat always hid under the couch when dogs were in the room. [ ]	___/2
	Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words)	___/1
ABSTRACTION	Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler	___/2

TOTAL _____/18

Add 1 point if ≤ 12 yr edu

Appendix 7. Sports medicine clinicians survey questions

Concussion and Eye Tracking

We appreciate that you agreed to complete this survey. The data will be averaged and used anonymously in a PhD project "Eye Tracking as a Tool for Concussion Assessment" conducted at Stellenbosch University. Eye tracking is a technology for detecting eye movements and analysing visual information processing.
What is this for? Concussion has been called a "silent epidemic": For example, research found that up to 70% of collegiate soccer players experience concussion symptoms during the playing season, but only 20% realize that they received a concussion. Assessment of concussion is often a challenge, therefore we are investigating the potential benefits of adding eye tracking to the diagnostics toolbox. Please complete the survey even if you have no experience with eye tracking.

*Required

1. **Your name (optional)**

____

2. **Your occupation** *

Mark only one oval.

- ( ) Biokineticist
- ( ) Emergency medical practitioner
- ( ) GP
- ( ) Neurologist
- ( ) Physio
- ( ) Researcher
- ( ) Sports physician
- ( ) Other: ____________________

3. **Current country of residence** *

____

4. **Are you familiar with eye tracking?** *

Mark only one oval.

- ( ) Yes, I have experience working with an eye tracking device
- ( ) Yes, I have heard about it but never worked with it
- ( ) No

5. **Do you currently use eye tracking technology in your medical practice or research?** *

Mark only one oval.

- ( ) Yes, in relation to concussion diagnostics
- ( ) Yes, but not related to concussion
- ( ) No

6. **If you do not use eye tracking technology, what are the reasons for it?**

____

____

____

____

____

7. **How many concussions do you diagnose per month on average?** *

____

8. **How long do your patients usually take to recover from a concussion?** *

9. **In most cases, how many times do you see a concussed patient on average** *
Mark only one oval.
- Only once to diagnose
- Twice – to diagnose and to clear
- Three times or more
- Other: ____________

10. **How long (in minutes) does it take you on average to assess one concussed patient?** *

11. **What limitations do you see in current concussion diagnostic tools?** *

12. **Which concussion diagnostic tests do you use? (please mark all that apply)** *
Tick all that apply.
- [ ] Automated Neuropsychological Assessment Metric (ANAM)
- [ ] Balance Error Scoring System (BESS)
- [ ] CogState Sport / Axon
- [ ] Cranial computerized tomography (CT)
- [ ] Drop Test
- [ ] Immediate Postconcussion Assessment and Cognitive Testing (ImPACT)
- [ ] Post-Concussion Symptom Scale (PCSS)
- [ ] Sport Concussion Assessment Tool (SCAT)
- [ ] Standardized Assessment of Concussion (SAC)
- [ ] Other: ____________

13. **What is your primary concussion diagnostics tool?** *

14. **Which eye movement assessment tools do you use to diagnose concussion? (please mark all that apply)** *

Tick all that apply.

- [ ] Assessment by optometrist
- [ ] Convergence Insufficiency Symptom Survey (CISS)
- [ ] Eye tracking device
- [ ] King-Devick Test
- [ ] Pupillometer
- [ ] Saccadometer
- [ ] None
- [ ] Other: ______________________

15. **Please describe which eye movement deficits you observe in patients with concussion, and how often** *

Mark only one oval per row.

	Over 80% of patients	50%-80% of patients	10%-49%	Less than 10% of patients	I do not check for it
Abnormal pupil light reflex	◯	◯	◯	◯	◯
Accommodative disorders	◯	◯	◯	◯	◯
Convergence insufficiency	◯	◯	◯	◯	◯
Impaired smooth pursuit	◯	◯	◯	◯	◯
Impaired vestibular ocular reflex	◯	◯	◯	◯	◯
Saccadic dysfunction	◯	◯	◯	◯	◯
Other (please specify below)	◯	◯	◯	◯	◯

16. **Please specify which other eye movement deficits you observe in your concussed patients**

____
____
____
____
____

17. **Do you see benefit in using an eye tracking device for concussion diagnostics and management?** *

Mark only one oval.

- Yes
- No
- Unsure

18. **What are the main benefits of using an eye tracking device?** *

Tick all that apply.

- [ ] Ease of use for the practitioner
- [ ] High sensitivity
- [ ] High specificity
- [ ] Objectivity of assessment
- [ ] Reliability of assessment
- [ ] Replicability - tests can always be repeated in exact same way
- [ ] Requires little effort from the patient
- [ ] Results are quantified
- [ ] Speed of use
- [ ] I do not see any benefit
- [ ] Other: ____________________

19. **Which eye tracker-measured data would you use to diagnose concussion?** *

Tick all that apply.

- [ ] Antisaccades
- [ ] Microcaccades
- [ ] Saccades (e.g. memory-guided)
- [ ] Fixations
- [ ] Pupil dilation
- [ ] Vergence
- [ ] Smooth pursuit
- [ ] None
- [ ] Other: ____________________

20. **What minimal sampling frequency should an eye tracker have to be a valid and reliable concussion diagnostics tool?** *

Mark only one oval.

- 60Hz
- 120 Hz
- 240 Hz
- 500 Hz
- 1000Hz
- Unsure

21. **If you have any comments or additional information, please provide them below**

22. **Please leave your email address if you would like to receive information on the results of the survey, and the publication(s) resulting from it**

Appendix 8. Risk of bias and quality assessment of each study included in the systematic review and meta-analysis

Risk of bias and quality assessment of each study included in the systematic review and meta-analysis

Risk of bias assessment

Study ID	Selection of participants: Selection bias caused by the inadequate selection of participants	Confounding variables: Selection bias caused by the inadequate confirmation and consideration of confounding variable	Measurement of exposure: Performance bias caused by the inadequate measurement of exposure	Blinding of outcome assessments: Detection bias caused by the inadequate blinding of outcome assessments	Incomplete outcome data: Attrition bias caused by the inadequate handling of incomplete outcome data	Selective outcome reporting: Reporting bias caused by the selective reporting of outcomes
Brewin 2017	Low	Unclear	Unclear	Low	Unclear	Unclear
	Convenience sample (collegiate soccer players); however, the participants are representative of the target group	Not specified	Not specified	Blinding is not specified, however, the study is unlikely to be affected by blinding, as the experimental design is automated, and the data are of quantitative nature	Not specified	Values for variables not provided in the abstract
D'Amico 2016	Low	Low	Low	Low	Low	Low
	Convenience sample (student-athletes of one university); however, the participants are representative of the target group. In- and exclusion criteria well specified	Previous injuries; sex, age, type of sport; postural assessment	All concussions were confirmed by the head certified Athletic Trainer and/or a medical doctor	The study design did not require blinding. The study is unlikely to be affected by blinding, as the experimental design is automated, and the data are of quantitative nature	No missing outcome data	All pre-specified relevant variables have been reported
Danna-Dos-Santos et al. 2018	Low	Low	Unclear	Low	Low	Low
	In- and exclusion criteria well specified	Number of previous concussions, time since most recent concussion; sex, age, mechanism of injury (sport vs. other; but not type of sport)	Not specified	Blinding is not specified, however, the study is unlikely to be affected by blinding, as the experimental design is automated, and the data are of quantitative nature	No missing outcome data	All pre-specified relevant variables have been reported
DiCesare et al. 2015	Unclear	High	Low	Low	High	Low
	Not specified	Post-Concussion symptoms inventory, sex, age, but not previous injuries, neurological or vision deficits	The concussion was confirmed by a diagnosis and a Post-Concussion Symptoms Inventory	Blinding is not specified, however, the study is unlikely to be affected by blinding, as the experimental design is automated, and the data are of quantitative nature	The data for two participants (of 17) were missing	All pre-specified relevant variables have been reported
Diwakar et al. 2015	Low	Low	Low	Low	Low	Low
	Multiple recruitment channels, in- and exclusion criteria well specified, participants representative of the target group	Age, sex, education level, right vs. left-handedness, ADHD, depression, stress, cognitive functions, previous injuries, time post injury, mechanism of injury, amnesia, loss of consciousness, symptoms	Participants recruited from clinics, referrals from neurologists and other mTBI studies (clinical diagnosis can be assumed)	Blinding is not specified, however, the study is unlikely to be affected by blinding, as the experimental design is automated, and the data are of quantitative nature	No missing outcome data	All pre-specified relevant variables have been reported

Risk of bias assessment (continued)

Study ID	Selection of participants: Selection bias caused by the inadequate selection of participants	Confounding variables: Selection bias caused by the inadequate confirmation and consideration of confounding variable	Measurement of exposure: Performance bias caused by the inadequate measurement of exposure	Blinding of outcome assessments: Detection bias caused by the inadequate blinding of outcome assessments	Incomplete outcome data: Attrition bias caused by the inadequate handling of incomplete outcome data	Selective outcome reporting: Reporting bias caused by the selective reporting of outcomes
Drew et al. 2007	Low Convenience sample (students of one university); however, the participants are representative of the target group. In- and exclusion criteria well specified	Low age, sex, education, time since injury, mechanism of injury. Not controlled for previous injuries	Low The concussed participants were initially identified by certified athletic trainers and/or medical doctors. Each of the participants was categorized as having a Grade 2 concussion	Low Blinding is not specified, however, the study is unlikely to be affected by blinding, as the experimental design is automated, and the data are of quantitative nature	Low No missing outcome data	Low Main variable of interest reported, even though mean and standard deviation values not provided
Evans et al. 2016	Unclear Not specified	Unclear Not specified	Unclear Not specified	Low Blinding is not specified, however, the study is unlikely to be affected by blinding, as the experimental design is automated, and the data are of quantitative nature	Low No missing outcome data	Low All pre-specified relevant variables have been reported
Heitger et al. 2002	Unclear Not specified except for in- and exclusion criteria	Low age, sex, education, time since injury, mechanism of injury, duration of post-traumatic amnesia and loss of consciousness; Glasgow Coma Scale score. Not controlled for previous injuries	Low Inclusion criteria for the concussed group included documented mild closed head injury within the previous 2 days	Low Blinding is not specified, however, the study is unlikely to be affected by blinding, as the experimental design is automated, and the data are of quantitative nature	Low No missing outcome data	Low All pre-specified relevant variables have been reported
Johnson et al. 2015	Low Convenience sample (college student athletes); however, the participants are representative of the target group. In- and exclusion criteria well specified	Low Previous injuries; sex, age	Low The initial diagnosis of concussion was made on the field by certified athletic trainers. All subjects had a Grade 1 concussion	Low Blinding is not specified, however, the study is unlikely to be affected by blinding, as the experimental design is automated, and the data are of quantitative nature	Low No missing outcome data at the first test; two participants lost due to attrition at the second test	High Saccade amplitude data were lost due to a breakdown in proper data backup procedures. Apart from that, all significant results reported fully, insignificant results mentioned (although values are not reported)
Katrahmani et al. 2018	Unclear Not specified	Unclear Not specified	Unclear Not specified	Low Blinding is not specified, however, the study is unlikely to be affected by blinding, as the experimental design is automated, and the data are of quantitative nature	Unclear Not specified	Unclear Values for variables not provided in the abstract

Risk of bias assessment (continued)

Study ID	Selection of participants: Selection bias caused by the inadequate selection of participants	Confounding variables: Selection bias caused by the inadequate confirmation and consideration of confounding variable	Measurement of exposure: Performance bias caused by the inadequate measurement of exposure	Blinding of outcome assessments: Detection bias caused by the inadequate blinding of outcome assessments	Incomplete outcome data: Attrition bias caused by the inadequate handling of incomplete outcome data	Selective outcome reporting: Reporting bias caused by the selective reporting of outcomes
Kelly 2017	Low	High	Low	High	Low	High
	Multiple locations throughout the US; the participants are representative of the target group. However, in- and exclusion criteria not specified	IMPACT scores; age; sex. However, there was no accounting for prescription drug use, lack of sleep, previous mTBI incidence, or other factors that might influence test scoring	Concussions confirmed by physicians	Blinding not specified and unlikely to affect the study. However, the results were not part of a controlled study. Test administrators were not tasked with employing a specific protocol for testing athletes before or after injury	No missing outcome data	Only the custom scores reported; underlying variables not provided
Ledwidge et al. 2017	Low	Low	Low	Low	Low	Low
	Convenience sample (participants recruited from NCAA football and soccer teams); however, the participants are representative of the target group. In- and exclusion criteria well specified	Number of concussions and time since recent concussion, current symptoms, balance, neuropsychological tests, age	Concussion history confirmed through athletic medical records	Blinding is not specified, however, the study is unlikely to be affected by blinding, as the experimental design is automated, and the data are of quantitative nature	No missing outcome data	All pre-specified relevant variables have been reported
Maruta et al. 2014	Low	High	Low	Low	Low	Low
	Participants recruited through referrals from physicians and representative of the target group. In- and exclusion criteria well specified	Age, sex, mechanism of injury (provided by authors via email). Not controlled for number of previous injuries, time since last injury (only "within 2 weeks")	The concussed participants were recruited through referrals from physicians	Blinding is not specified, however, the testing protocol was automated with each step in the experiment preceded with preprogrammed audio and video instructions, whereas interventions by the experimenter were reduced to entering the data file name, optimizing video images of the eyes, initiating the calibration procedure, and ensuring valid calibration. Therefore, the study is unlikely to be affected by blinding	No missing outcome data	Both statistically significant and statistically insignificant results for all tests are reported
Mullen et al. 2016	Unclear	Unclear	Unclear	Low	Low	Low
	Not specified	Not specified	Not specified	Blinding is not specified, however, the study is unlikely to be affected by blinding, as the experimental design is automated, and the data are of quantitative nature	No missing outcome data with an exception: Two subjects showed no adaptation and were removed	Outcome data not reported in the abstract (due to the nature of the publication) but readily provided by the authors upon request

Risk of bias assessment (continued)

Study ID	Selection of participants: Selection bias caused by the inadequate selection of participants	Confounding variables: Selection bias caused by the inadequate confirmation and consideration of confounding variable	Measurement of exposure: Performance bias caused by the inadequate measurement of exposure	Blinding of outcome assessments: Detection bias caused by the inadequate blinding of outcome assessments	Incomplete outcome data: Attrition bias caused by the inadequate handling of incomplete outcome data	Selective outcome reporting: Reporting bias caused by the selective reporting of outcomes
Murray et al. 2014	Low	Low	Low	Low	Low	Low
	Participants recruited from a Concussion Management Clinic and representative of the target group; in-and exclusion criteria well specified	Age, sex, ImPACT test scores, self-reported symptoms, balance. Not controlled for number of previous injuries	Athletes with concussions were diagnosed and referred to the clinic by their physician or athletic trainers. In addition, the researchers reported the IMPACT test results	Blinding is not specified, however, the study is unlikely to be affected by blinding, as the experimental design is automated, and the data are of quantitative nature	No missing outcome data	All pre-specified relevant variables have been reported
Pearson et al. 2007	High	High	High	Low	Low	Low
	Only boxers from Cambridge University Amateur Boxing Club	No confounding variables specified. Not controlled for potential previous concussions which seem likely in the participants group (boxers)	Authors do not report on any methods of assessing concussion; one participant "deemed concussed"	Blinding is not specified, however, the study is unlikely to be affected by blinding, as the experimental design is automated, and the data are of quantitative nature	No missing outcome data	All pre-specified relevant variables have been reported
Poltavski et al. 2014	Low	Low	High	Low	Low	Low
	Convenience sample (student-athletes from NCAA Division male and female Hockey Teams); however, the participants are representative of the target group	ADHD, vision conditions, IMPACT scores, position on field, previous injuries, age but not sex. Not controlled for time after the injury	Concussion diagnosis based on self-reporting	Blinding is not specified, however, the study is unlikely to be affected by blinding, as the experimental design is automated, and the data are of quantitative nature	No missing outcome data	All pre-specified relevant variables have been reported
Richard et al. 2009	Unclear	Low	High	Low	Low	Low
	Not specified	time after the injury, age, symptoms and severity for current and/or prior concussions	Concussion diagnosis based on self-reporting	Blinding is not specified, however, the study is unlikely to be affected by blinding, as the experimental design is automated, and the data are of quantitative nature	No missing outcome data	All pre-specified relevant variables have been reported
Samadani et al. 2017	Low	Unclear	Low	Low	Low	Unclear
	Recruitment through referral centres; the participants are representative of the target group	Acute Concussion Evaluation (ACE) scores and clinical assessments of convergence and accommodation, time since the injury. Not controlled for number of previous injuries. Age and sex not specified	Participants were diagnosed with concussion in a referral centre	Blinding is not specified, however, the study is unlikely to be affected by blinding, as the experimental design is automated, and the data are of quantitative nature	No missing outcome data	Values for variables not provided in the abstract

Risk of bias assessment (continued)

Study ID	Selection of participants: Selection bias caused by the inadequate selection of participants	Confounding variables: Selection bias caused by the inadequate confirmation and consideration of confounding variable	Measurement of exposure: Performance bias caused by the inadequate measurement of exposure	Blinding of outcome assessments: Detection bias caused by the inadequate blinding of outcome assessments	Incomplete outcome data: Attrition bias caused by the inadequate handling of incomplete outcome data	Selective outcome reporting: Reporting bias caused by the selective reporting of outcomes
Taghdiri et al. 2018	Low	Low	Low	Low	Low	Low
	Participants recruited from a Concussion Clinic and representative of the target group; exclusion criteria well specified	Age, sex, education, previous injuries, number of symptoms, time after last injury; neuropsychological tests; mechanism of injury	Diagnosis of a concussion was made by a medical practitioner	Blinding is not specified, however, the study is unlikely to be affected by blinding, as the experimental design is automated, and the data are of quantitative nature	No missing outcome data	All pre-specified relevant variables have been reported
Webb 2017	Low	Low	Low	Low	Low	High
	Participants recruited at a sports concussion clinic and representative of the target group; in-and exclusion criteria well specified	Handedness, age, sex, concussion history, time after the injury	Participants were diagnosed with a concussion via SCAT3 and combined clinical judgments of a sports physician and/or physiotherapist	Blinding is not specified, however, the study is unlikely to be affected by blinding, as the experimental design is automated, and the data are of quantitative nature	No missing outcome data	Missing means and standard deviations for saccadic latency, despite the implied statistical significance of this variable

Notes: ID: identification

Study quality assessment

Study ID	1. Was the research question or objective in this paper clearly stated and appropriate?	2. Was the study population clearly specified and defined?	3. Did the authors include a sample size justification?	4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?	5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	6. Were the cases clearly defined and differentiated from controls?	7. If less than 100% of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?	8. Was there use of concurrent controls?	9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?	11. Were the assessors of exposure/risk blinded to the case or control status of participants?	12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?
Brewin 2017	Yes	No	No	NR	NR	NR	No	NR	Yes	NR	NR	NR
D'Amico 2016	Yes	Yes	No	Yes	Yes	Yes	No	NR	Yes	Yes	No	Yes
Danna-Dos-Santos et al. 2018	Yes	Yes	No	Yes	Yes	Yes	No	NR	Yes	NR	NR	Yes
DiCesare et al. 2015	Yes	Yes	Yes	Yes	NR	Yes	No	NR	Yes	Yes	NR	No
Diwakar et al. 2015	Yes	Yes	No	Yes	Yes	Yes	No	NR	Yes	Yes	NR	Yes
Drew et al. 2007	Yes	Yes	No	Yes	Yes	Yes	No	NR	Yes	Yes	NR	Yes
Evans et al. 2016	Yes	No	No	NR	NR	Yes	No	NR	Yes	NR	NR	NR
Heitger et al. 2002	Yes	Yes	No	Yes	Yes	Yes	No	NR	Yes	Yes	NR	Yes
Johnson et al. 2015	Yes	Yes	No	Yes	Yes	Yes	No	NR	Yes	Yes	NR	Yes

Study quality assessment (continued)

Study ID	1. Was the research question or objective in this paper clearly stated and appropriate?	2. Was the study population clearly specified and defined?	3. Did the authors include a sample size justification?	4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?	5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?	6. Were the cases clearly defined and differentiated from controls?	7. If less than 100% of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?	8. Was there use of concurrent controls?	9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?	10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?	11. Were the assessors of exposure/risk blinded to the case or control status of participants?	12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?
Katrahmani et al. 2018	Yes	No	No	NR	NR	Yes	No	NR	Yes	NR	NR	NR
Kelly 2017	Yes	Yes	No	Yes	No	Yes	No	NR	Yes	Yes	NR	No
Ledwidge et al. 2017	Yes	Yes	No	Yes	Yes	Yes	No	NR	Yes	Yes	NR	Yes
Maruta et al. 2014	Yes	Yes	No	Yes	Yes	Yes	No	NR	Yes	Yes	NR	No
Mullen et al. 2016	Yes	Yes	No	Yes	NR	Yes	No	NR	Yes	NR	NR	NR
Murray et al. 2014	Yes	Yes	No	Yes	Yes	Yes	No	NR	Yes	Yes	NR	Yes
Pearson et al. 2007	Yes	Yes	No	NR	NR	NR	No	NR	No	No	NR	No
Poltavski et al. 2014	Yes	Yes	Yes	Yes	NR	Yes	No	NR	Yes	No	NR	Yes
Richard et al. 2009	Yes	Yes	No	NR	NR	Yes	No	NR	Yes	No	NR	Yes
Samadani et al. 2017	Yes	Yes	No	Yes	NR	Yes	No	NR	Yes	Yes	NR	Yes
Taghdiri et al. 2018	Yes	Yes	No	NR	Yes	Yes	No	NR	Yes	Yes	NR	Yes
Webb 2017	Yes	Yes	No	Yes	Yes	Yes	No	NR	Yes	Yes	NR	Yes

Notes: ID: identification; NR: not reported