Master of Research

Does physical fatigue affect performance on the King-Devick Test?

Candidate
Francesco Fronzoni: M.Chiro, PGDip (Sports Physiotherapy), BPhty, ICCSP, MRCC

Supervisor
Dr. Jennifer Batchelor: PhD

Macquarie University
Department of Psychology
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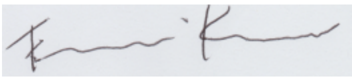
Statement of Originality

I hereby confirm that all material contained in this project are my original authorship and ideas, except where the work of others has been acknowledged or referenced. I also confirm that the work has not been submitted for a higher degree to any other university or institution. The research project was approved by the Macquarie University Human Research Ethics Committee (Approval No. 5201600732).

(Signed)  Date: 5/10/2017

Francesco Fronzoni

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Table of contents

List of Tables

List of Figures

Index of Abbreviations

As is convention in this area, diagnostic terms and radiological techniques are abbreviated throughout this paper. The following index is included to facilitate reading of the assignment.

AWPTAS: Abbreviated Westmead Post-Traumatic Amnesia Scale
BESS: Balance Error Scoring System
CT: Computerised Tomography
GCS: Glasgow Coma Scale
GPS: Global Positioning System
ICC: Interclass Correlation Coefficient
ICD-10: International Classification of Diseases, 10th revision
ImPACT: Immediate Post-Concussion Assessment and Cognitive Test
LOC: Loss of consciousness
MRI: Magnetic Resonance Imaging
TBI: Traumatic Brain Injury
PCS: Post-concsusion Syndrome
PCSS: Post-Concussion Symptoms scale
Pocket CRT: Pocket Concussion Recognition Tool
PTA: Post-traumatic Amnesia
RPE: Rate of Perceived Exertion
SAC: Standardized Assessment of Concussion
SCAT5: Sports Concussion Assessment Tool-Fifth Edition
SRC: Sport related concussion
VO2: Oxygen Consumption

Abstract

Objectives: Sports related concussions have gained increasing awareness over recent years. The diagnosis of sports related concussion is primarily made on the basis of clinical signs and symptoms and can be extremely challenging especially during sporting events when athletes need to be assessed quickly and effectively. There are a number of psychological tests used in the on-field diagnosis of concussion one of which is the King-Devick test. The potentially confounding effect of physical fatigue on the diagnosis of sports related concussion remains poorly understood. The aim of the present study was to assess the effects of physical fatigue on performance on the King-Devick test.

Methods: This study included 140 participants equally divided into two groups: a fatigue group and a control group. The fatigue group comprised 40 males and 30 females with a mean age of 34.24 years ± 12.58 years. The control group included 46 males and 24 females with a mean age of 32.01 years ± 11.38 years. Both groups were assessed on the King-Devick test at baseline and then at a reassessment which was conducted 15 minutes later. Subjects in the fatigue group ran on a treadmill for the 15 minutes intervening the baseline and reassessment conditions. To achieve significant and uniform levels of exertion, subjects in the fatigue group were instructed to run at a rate of perceived exertion of 7/10 for the first 12 minutes and 9/10 for the final 3 minutes. Subjects in the control group rested from physical activity for the 15 minutes separating the baseline and reassessment conditions.

Results: Comparison of baseline and reassessment scores, revealed that the control group demonstrated significantly greater improvement between baseline and reassessment than the fatigue group. A significantly greater number of subjects from the fatigue group (31.4%) scored a slower time at reassessment compared to baseline than did subjects from the control group (14.3%). Finally, five subjects in the fatigue group (7.1%) worsened their score by more than 3 seconds at reassessment relative to baseline, whereas no subject in the control group demonstrated a decrement at reassessment compared to baseline of 3 seconds or more. A significantly greater number of subjects from the fatigue group (n = 25) met criteria for concussion at reassessment than did the control subjects (n = 11).

Conclusion: The results of the current study contrasted previous findings and indicted that physical fatigue had a significant and negative effect on performance on the King-Devick test. Indeed, a significant number of subjects in the fatigue group “failed” the test and met criteria for a diagnosis of concussion. Future studies are required to validate the effects on physical fatigue on the King-Devick test and other concussion assessment instruments.

Chapter 1

Introduction

Sports related concussion (SRC) has become one of the most researched topics in sports medicine (Marshall, 2012). Concussion is defined as a traumatic brain injury caused by a direct blow to the head, face, neck, or elsewhere on the body with forces transmitted to the head (McCrory et al., 2017). The brain is situated inside the skull and surrounded by cerebrospinal fluid, which acts as a cushion and protects the brain from minor mechanical movements. During more major trauma, the brain because of its inertia moves at a different rate to the skull, causing it to impact against the inside of the skull and the meningeal coverings and resulting in contusions and lacerations (Choe, 2016). In addition, different parts of the brain (being of different densities) move relative to one another, causing widespread stretching and shearing of white matter (Meaney and Smith, 2011). These shearing strains represent the mechanical basis of concussion (Meaney and Smith, 2011). In addition, during concussion the balance of ions and chemicals is altered, impairing nerve cell function and potentially causing loss of consciousness (LOC) (Choe, 2016). Both mechanisms can be present together or in isolation (Choe, 2016, Meaney and Smith, 2011). An overproduction of free radicals, inflammation and impaired transport of molecules within nerve cells may also occur (Signoretti et al., 2011). Lastly, blood flow to injured areas is reduced, decreasing the amount of oxygen and nutrients available for recovery (Choe, 2016).

1.1 Definition of Concussion

Traumatic brain injury (TBI) is caused by the sudden application of external forces to the head which causes brain pathology or alteration of brain function, and represents one of the leading causes of death and disability in adults and children (Menon et al., 2010, Singh et al., 2016). TBI is typically classified along a spectrum of severity with concussion traditionally being viewed as representing a relatively minor form of injury. Often confusion arises between a mild TBI and a concussion and the terms are frequently used interchangeably to describe a relatively minor injury to the brain (see Figure 1).

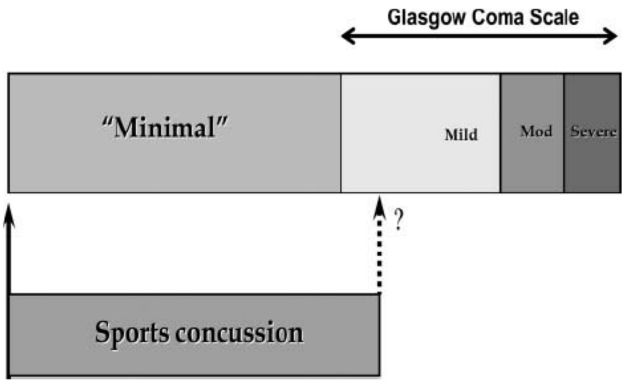

Figure 1: Conceptual understanding of sports related concussion (McCrory et al., 2013).

Currently, there is no agreement as to how concussion and mild TBI should be distinguished (Giza and Hovda, 2001).

TBIs are often the result of more traumatic impacts than those causing concussion (Haslam et al., 1994) and are frequently caused by work related accidents (Sears et al. 2013), motor vehicle accidents (Ruffolo et al., 1999) or domestic violence (Colantonio et al., 2010). Sports related concussions, as the name suggests, represent injuries sustained while playing sports and often occur in athletes including elite athletes (McCrory et al., 2017).

Concussion has been described as an impairment of functional status which is not necessarily related to a pathological injury (McCrory et al., 2013), whereas mild TBI is defined as involving pathophysiological changes to the brain following head trauma (Menon et al., 2010). Thus, the criteria for defining mild TBI are stricter than those used to define concussion and require objective evidence of neurological injury (Ruff et al., 2009, Carroll et al., 2004) such as scores on measures of consciousness and post-traumatic amnesia (PTA).

Two constructs are traditionally referred to in order to measure TBI severity (Alexander, 1995). The Glasgow Coma Scale (GCS), is a validated and reliable objective measure of level of consciousness (Reith et al., 2016). Scores on the GCS range from 3/15, indicating that the individual is deeply unconscious and unresponsive, to 15/15 indicating that the individual is alert and fully responsive as measured by motor, eye and verbal functioning. Post-traumatic amnesia (PTA) is a temporary amnesia that results from diffuse axonal injury (Marshman et al., 2013). There is a large body of literature indicating that the duration of post-traumatic amnesia is the best measure of the severity of TBI and the most accurate predictor of the likelihood of residual cognitive and behavioural sequelae (Haslam et al., 1994). While a number of objective tools have been developed to measure the duration of PTA, in Australia the instrument that is most commonly used is the Westmead Post-Traumatic Amnesia Scale (Shores et al., 2008). A modified version of the scale known as the Abbreviated Westmead Post-Traumatic Amnesia Scale (AWPTAS) has been developed (Meares et al., 2011) and validated (Hayter et al., 2017) for use in cases of mild TBI.

The World Health Organisation (WHO) Collaborating Task Force (Carroll et al., 2004) defines mild TBI as an acute brain injury that results from mechanical energy to the head imposed by external forces and i) one or more of the following: confusion or disorientation, loss of consciousness for 30 minutes or less, PTA for less than 24 hours and/or other transient neurological abnormalities such as focal signs or seizure and intracranial lesion not requiring surgery and ii) GCS score of 13 to 15 after 30 minutes of trauma or on presentation to healthcare. Thus, mild TBI must represent the result of pathophysiological changes to the brain following head trauma. The diagnostic criteria for classifying TBI severity are shown in Table 1 (McDonald et al., 1994, Carroll et al., 2004).

Table 1: Diagnostic criteria for the classifying of traumatic brain injury severity (McDonald et al., 1994, Carrol et al., 2004).

	GCS	LOC	PTA duration
Mild TBI	13-15	<30 minutes	<24 hours
Moderate TBI	9-12	<6 hours	>1 hour < 24 hours
Severe TBI	≤8	>6 hours	>1 day

GSC: Glasgow Coma Scale, LOC: Loss of consciousness, PTA: Post traumatic amnesia

The neuropathology resulting from TBI can be subdivided into primary and secondary damage. Primary neural changes resulting from TBI are caused by the brain displacement inside the skull during the initial impact whereas secondary TBIs consist of further brain damage caused by ongoing cellular events (Prins et al., 2013). Several pathophysiological changes such as impaired neurotransmission, abnormal regulation of ion channels, ionic imbalance, deregulated cellular energy metabolism, and decreased cerebral blood flow are commonly seen after a TBI (Iverson, 2005).

On the other hand, concussion is a complex neuropathophysiological process, consisting of short-term neurologic impairment such as headache and loss of memory, with rapid onset and which may or may not involve loss of consciousness (McCrory et al., 2013). Traditionally, the neurological deficits resulting from concussion have been thought to be largely temporary and to resolve spontaneously with the subject returning to normal brain function on a cellular level and on a functional level (McCrory et al., 2013). However, it is widely accepted that repeated concussions can cause long-term neurological damage and cognitive impairments (Rabadi and Jordan, 2001) and in some cases, chronic traumatic encephalopathy (Baugh et al., 2012, Gavett et al., 2011) which has been defined as a progressive neurodegenerative disease caused by repetitive head trauma (Thurman et al., 1998). Symptoms of chronic traumatic encephalopathy generally appear eight to ten years after an athlete experiences repeated mild TBIs (McKee et al. 2009). Common symptoms include but are not limited to attentional deficits, confusion, disorientation, amnesia or memory loss, dementia, and depression (McKee et al., 2009).

Athletes and relatives of participants in contact and collision sports are becoming increasingly concerned regarding the possible long-term negative effects of concussion on brain function (Plassman et al., 2000). Indeed, it has been reported that concussions may lead to Alzheimer’s disease as shown in a retrospective study on 2552 retired professional football players conducted by Guskiewicz et al. (2005). The study found that the subjects who reported a history of having sustained three or more concussions had a fivefold prevalence of mild cognitive impairment and a threefold prevalence of reported significant memory problems compared with subjects who had not sustained a concussion.

However, the paper by Guskiewicz et al. (2005) has some limitations, Firstly, the study relied on two self-reported questionnaires. In addition, all the participants played football before World War II when the diagnosis of concussion was unknown to many medical staffs. Indeed, and as discussed further in the following sections of this introduction, only in the last decade has awareness of SRC become widespread (Broglio et al., 2011). Therefore, the real estimate of SRCs is likely to have been underreported in the retrospective study conducted by Guskiewicz et al. (2005). However, because the participants suffered from memory problems, recall bias may have affected the results.

In addition, following a concussion individuals may develop post-concussion syndrome (PCS). The WHO's International Classification of Diseases, 10th revision (ICD-10), defines PCS as a syndrome that occurs following head trauma presenting with several symptoms such as headache, dizziness, fatigue, irritability, difficulty in concentration and performing mental tasks, impairment of memory, insomnia, and reduced tolerance to stress, emotional excitement or alcohol (Schneider, 2016). Common features of PCS are depression, nervousness, sleep disturbances, generalised anxiety, panic attacks, travel phobia, and post-traumatic stress (Moore et al., 2006). Indeed, the diagnosis of PCS is made when at least three symptoms are present at three months post injury (APA, 1994). However, it can be challenging to diagnose PCS because all the symptoms are subjective and necessitate reliance on self-report (McCrory et al., 2013).

Furthermore, an undiagnosed concussive episode can have very serious consequences if a second head trauma occurs before symptoms of the initial concussion have completely resolved. This may result in the so-called "second impact syndrome" consisting of cerebral oedema followed by brain herniation, which can be fatal (Bey and Ostick, 2009). The brain is vulnerable to a second impact syndrome in the first seven to ten days after the initial concussion because of the increased extracellular potassium concentration which impairs the ability of the brain to auto regulate intracranial and cerebral perfusion pressures (Fisher and Vaca, 2004). This testifies to the importance of accurately diagnosing and managing a concussive injury.

The mechanisms of concussion described in the literature are many, the most common of which is SRC (Giza and Kutcher, 2014). In addition, concussions can be caused by falls (Voss et al., 2015), military injuries (Mac Donald et al., 2011), playground injuries (Norton et al., 2004), motor vehicle accidents (Anderson, 2004), domestic violence (Valera and Kucyi, 2016) and work related injuries such as being struck by or against an object (Colantonio et al., 2010).

1.2 Concussions in sports

The incidence of concussive injuries while playing sport has gained increasing awareness over recent years (Giza and Kutcher, 2014). This topic gained further popularity when Dr Bennet Omalu, a forensic pathologist and neuropathologist, demonstrated that American football athletes were at risk of CTE after repetitive head traumas. This story was made into a film called "Concussion".

Concussion is difficult to diagnose, due to the lack of radiological abnormalities on magnetic resonance imaging (MRI) and computed tomography (CT) imaging and the impracticality of conducting other radiological investigations. Therefore, the diagnosis is primarily made on the basis of clinical signs and symptoms (Shenton et al., 2012, Iverson et al., 2000). During sporting events, there is a necessity to assess athletes quickly and effectively, especially in professional sports. The time to assess an athlete is usually limited. For instance, a new rule in rugby union allows only 10 minutes to assess the player (IRB, 2017) within which time medical staff are required to make a decision as to whether the athlete is healthy and ready to return to play or is concussed and needs to be removed from the field. It is acknowledged that under such conditions, accurate diagnosis can be extremely challenging (Committee on Sports-Related Concussions in et al., 2014). Rule changes have been enforced in several sports to reduce the incidence of concussions. For instance, World Rugby (2017) stated that a tackled athlete needed to be safely accompanied to the ground, without lifting his/her legs above parallel to the ground, to reduce the risk of head and neck injuries. In addition, rugby league does not allow "shoulder charge" tackling. Interestingly, however, the number of concussive episodes occurring across sports has been increasing (Llewellyn et al., 2014). This may be explained by the fact that there is a greater awareness of concussion, better diagnostic tools and a reduction in the number of individuals who choose to under report symptomatology (Llewellyn et al., 2014)

The literature indicates that the incidence of concussion in sports is between 0.01 and 2.15% (Clay et al., 2013), however, it has been hypothesised that those figures significantly underestimate the actual number of concussive episodes that occur (Meehan et al., 2013).

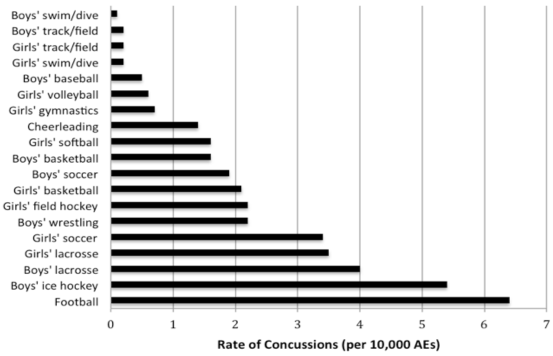

Figure 2: Rate of concussions among United State high school athletes

In addition, Marar et al. (2012) reported the rate of concussion per 10,000 hours of athlete exposure (Figure 2) among United States high school athletes in 20 sports which revealed that football had a rate of 6.4.

Indeed, it has been estimated that in the Unites States alone, four million athletes sustain a concussive injury annually (Plassman et al., 2000). It has been reported that concussion may be underreported by players and by team personnel (Kroshus et al., 2015, Williamson and Goodman, 2006, Anderson et al., 2013). This is often because of internal (Anderson et al., 2013) and external pressures (from coaches, media etc.) to go back on the field and resume play (Kroshus et al., 2015). It has been reported in the news that several athletes had cheated on their baseline concussion tests to return to the field faster (Marvez, 2011). However, the number of unreported concussion episodes has dramatically decreased from 50 to 75%

previously reported in high school athletes (McCrea et al., 2004) to 11.8% described more recently in collegiate athletes (Llewellyn et al., 2014). This change has been attributed to better awareness of the signs and symptoms of concussion, increased understanding of the possible complications associated with concussion, and increased media attention (Llewellyn et al., 2014).

1.3 Using Psychological Tests to Diagnose Concussion

Tests of cognition are frequently used in the diagnosis of concussion, with the selection of measures being determined by their sensitivity to the specific aspects of cognition that have been demonstrated to be particularly susceptible to disruption following TBI. That testing can help specify the severity of acquired brain injury and assist in the creation of specific treatment plans (Harvey and Close, 2012).

There are a number of psychological assessment tools that are currently available to diagnose concussion, many of which have been shown to be reliable. Measures that have been demonstrated to have adequate reliability include the Immediate Post-Concussion Assessment and Cognitive Test (ImPACT) (Covassin et al., 2009), the AWPTAS (Meares et al., 2011), the Sports Concussion Assessment Tool-Fifth Edition (Scat5) (McCrory et al., 2017), the Standardized Assessment of Concussion (SAC) (McCrea, 2001) and the King-Devick Test (Galetta et al., 2011b).

The ImPACT is a computerised test and comprises measures of visual and verbal memory, reaction time and processing speed. It is designed for use with individuals between the ages of 12 and 59 years and takes approximately 25 minutes to administer (Covassin et al., 2009). Given the lengthy administration time, the test is difficult to implement during the sideline assessments of cognition which are conducted during the course of a sporting event. In a study evaluating the diagnostic accuracy of the ImpACT, Schatz et al. (2006) assessed 138 high school athletes, 72 of whom were tested within 72 hours of sustaining a concussion and 66 of whom were non-concussed. They reported that the sensitivity of the test was 81.9% and the specificity was 89.4%. Sensitivity is the ability of a test to correctly identify concussed individuals whereas specificity is the ability of the test to correctly identify those who are non-concussed. However, in the absence of information regarding positive predictive power, defined as the probability that subjects with a positive screening test truly have the disease, figures regarding sensitivity and specificity cannot be applied clinically (Lange and Lippa, 2017). That is because basing decisions regarding the clinical utility of a test or a measure simply on specificity and sensitivity, can lead to erroneous conclusions (Lange and Lippa, 2017). Indeed, Lange and Lippa (2017) highlight the importance of also considering positive predictive power (which is the percentage of subjects with a positive test who actually are concussed) and negative predictive power (which is the percentage of subjects with a negative test who are not concussed) before evaluating the strength of a test and before making a clinical decision.

An additional study by Resch et al. (2013) conducted on 91 subjects divided into two groups, found that the ImPACT test had a high reliability when assessing visual motor speed and reaction time but lower reliability when assessing verbal and visual memory. Moreover, although the test has been reported to have adequate reliability in terms of the measurement of reaction time (Interclass Correlation Coefficient (ICC) 0.26 to 0.88), when accuracy is also evaluated the reliability is considerably lower (ICC .15 to .39) (Resch et al., 2013, Broglio et al., 2007). Low test-retest reliability renders an instrument of limited use for repeated assessments as it implies that there is considerable variability in the scores returned by a single individual when tested on the same instrument, under the same conditions and over a relatively short time interval (Oberlander et al., 2017).

The Scat 3 measures eight different areas of functioning and includes assessment of balance using a modified version of the Balance Error Scoring System (BESS) (McCrory et al., 2013). The BESS has been reported to have high specificity (91%) but low sensitivity (34%) for concussion (Rahn et al., 2015, Riemann et al., 1999, McCrea et al., 2005). Low sensitivity means that many individuals with the condition will not be detected by the test. (Riemann et al., 1999) assessed 111 athletes comparing a force plate and observational assessment. This study demonstrated that the BESS is reliable assessment of postural stability. However, several factors have been found to affect results on the test including fatigue (Fox et al., 2008, Lepers et al., 1997) and pre-existing issues with poor balance (Guskiewicz et al., 2001, Nardone et al., 1997). A literature review conducted by Yengo-Kahn et al. (2016) revealed that no studies have investigated the sensitivity and specificity of the SCAT3. Only one prospective study assessing the sensitivity and specificity of an earlier version of the test (the SCAT2) is available which reported those figures as 96% and 81% respectively (Putukian et al., 2015) in 263 athletes participating in different sports. Again, positive and negative predictive power were not reported.

Following the 5th International Conference on Concussion in Sports held in Berlin in 2016, McCrory et al. (2017) created an upgraded version of the Scat3 named the Scat5. Several modifications have been included in the Scat5. Firstly, McCrory et al. (2017) reported that the Scat5 takes 10 minutes to be correctly completed. Therefore, if using that measure to assist diagnosis, athletes with suspected concussion, even if symptom free, would not be allowed to return to the field for a minimum period of 10 minutes. This new rule has been created to make sure that the athlete is properly assessed and not rushed back onto the field. In addition, in many cases players will have already memorised the 5 words combination used in the Scat3, therefore to minimise the ceiling effects the SAC immediate and delayed word recall, which is part of Scat5, included both five and 10 words. Moreover, a rapid Neurological Screen has been included which consists of evaluation of the cervical spine, the athlete's speech, reading ability, balance, gait, visual tracking and finger to nose coordination. This rapid Neurological Screen is not meant to replace the full assessment but rather, to provide the medical team member an indication on the athlete's neurological condition (Echemendia et al., 2017). Given the length of time required to administer the full Scat5, it is considered an unrealistic assessment tool for clubs and players at an amateur level (Guskiewicz et al., 2013, Dziemianowicz et al., 2012).

An adaptation of the Scat5 that has been designed for use by non-medically trained people, is the Pocket Concussion Recognition Tool (Pocket CRT) which contains the Maddocks Questions and the Post-Concussion Symptoms scale (PCSS) (McCrory et al., 2013). The Maddocks questions are used to assess recent memory and orientation in sport (Maddocks et al., 1995) and have been validated on only a small sample of 28 players. In assessing symptoms of concussion, attention has been given to recording the subjective effects of concussion and monitoring the recovery of those symptoms to determine readiness to return to play (Iverson et al., 2011). Maddocks' questionnaire has been shown to have a specificity between 86 and 100% and a sensitivity between 32 and 75% (McCrory et al., 2013). The PCSS is a self-report inventory and has been shown to be reliable and sensitive to sports concussion (McLeod and Leach, 2012, Lovell et al., 2006, Alla et al., 2009). However, the PCSS has several limitations. Firstly, being a self-report questionnaire, the measure lacks objectivity. Subjective measures can lead to underreporting of symptoms and concussive episodes due the athlete's desire to continue to play (Fazio et al., 2007, Bailey et al., 2006). Secondly, the PCSS has been demonstrated to have poor sensitivity, especially during the recovery phase when athletes who reported resolution of their symptoms were found to have ongoing cognitive deficits on more objective measures (Fazio et al., 2007, McCrea et al., 2005). In addition, the specificity of the PCSS is also poor (Binder et al., 1997) because multiple symptoms included in the test have been reported to be common in healthy samples (Shehata et al., 2009, Lovell et al., 2006, Iverson and Lange, 2003). The test is therefore not the instrument of choice in terms of a concussion diagnostic tool given its poor sensitivity and low specificity.

The SAC is included in the Scat5 assessment. The SAC contains several measures designed to assess orientation, immediate memory (the recall of 5 words over 3 separate trials), loss of consciousness (occurrence, duration), amnesia (either retrograde or anterograde), sensation, coordination, strength, concentration, exertional manoeuvres (jumping jacks, sit-ups) and delayed recall (of 5 words) (McCrea, 2001). The sensitivity of the SAC was initially reported at 95% and the specificity at 76% (McCrea, 2001) but may be lower than that as previous studies (Barr and McCrea, 2001, McCrea et al., 2005) were based on earlier definitions of concussion, which included post-traumatic amnesia, loss of consciousness and alteration of the mental status (McCrea, 2001). That definition may have biased subject selection so as to include players with more severe symptoms and potentially lead examiners to miss concussions presenting with other symptoms such as balance deficit. The positive and negative predictive power of the test have not been examined.

Tjarks et al. (2013) reported that both the King-Devick test and the AWPTAS are reliable measures of concussion. The AWPTAS is a measure of orientation and memory designed to screen for post-traumatic amnesia following mild TBI (Shores et al., 2008). Meares et al. (2011) confirmed the validity of the AWPTAS in 82 concussed patients compared to 88 control subjects. In contrast to the Scat5, the AWPTAS takes only several minutes to administer, which is preferable during a sport side-line assessment. Indeed, a concussion assessment which takes a long time to be administered is not suitable for sporting events which have a set duration that cannot be altered. The use of the AWPTAS has been recommended for emergency departments (Reed, 2011, Meares et al., 2015) and in sports (Hayter et al., 2017). However, to date, the AWPTAS has not been widely used in sports where the Scat5 remains the most frequently used concussion assessment tool (McCrory et al., 2017).

The King-Devick test measures the speed of rapid number naming and has been reported to be sensitive to suboptimal neurological functioning (Galetta et al., 2011b). Galetta et al. (2011b) reported that concussed athletes increased the time taken to complete the King-Devick test by an average of 5.9 seconds compared to baseline times. However, only 10 subjects included in that study were concussed, rendering it at most preliminary evidence of the test's utility. Tjarks et al. (2013) provided evidence of the validity of the King-Devick, demonstrating that all correlations between ImPACT and King-Devick scores were significant, with *P* values less than 0.0001. Indeed, in that study it was found that as ImPACT composite scores improved and symptoms resolved, subjects had faster completion times on the King-Devick test. However, the sample used in the study comprised only 35 participants. Further information about the King-Devick test is detailed in a subsequent section of this review (Hasanaj et al., 2018, Howitt et al., 2016, Subotic et al., 2017).

An additional concussion assessment tools used in sport is the Cogstate which is a computerised test including several tests designed to measure specific areas of cognition such as processing speed, attention, learning and working memory (Ellemberg et al., 2009). The Cogstate test has been shown to a reliable indicator of fitness to return to play following SRC after being tested on 240 Australian Football League athletes (Collie et al., 2003). However, it is an expensive tool which renders it is impractical at junior and amateur levels. Lastly, a Vestibular/Ocular Motor Screening measure has been used for the diagnosis of concussion and has been demonstrated to have good reliability (Yorke et al., 2017)

1.4 Treatment & Recovery

The vast majority of concussions tend to resolve between five and seven days of injury, although more protracted recovery curves have been reported for some individuals (Williams et al., 2015). Common symptoms reported after concussion include headache (McCrory et al. 2012), neck pain (Benson et al., 2011), dizziness and balance disorders (Wasserman et al., 2016), visual disorders (Master et al., 2016), difficulties with exertion (Leddy et al., 2015), cognitive difficulties, mental health disorders, fatigue and sleep difficulties (McCrory et al., 2013) (see Figure 3).

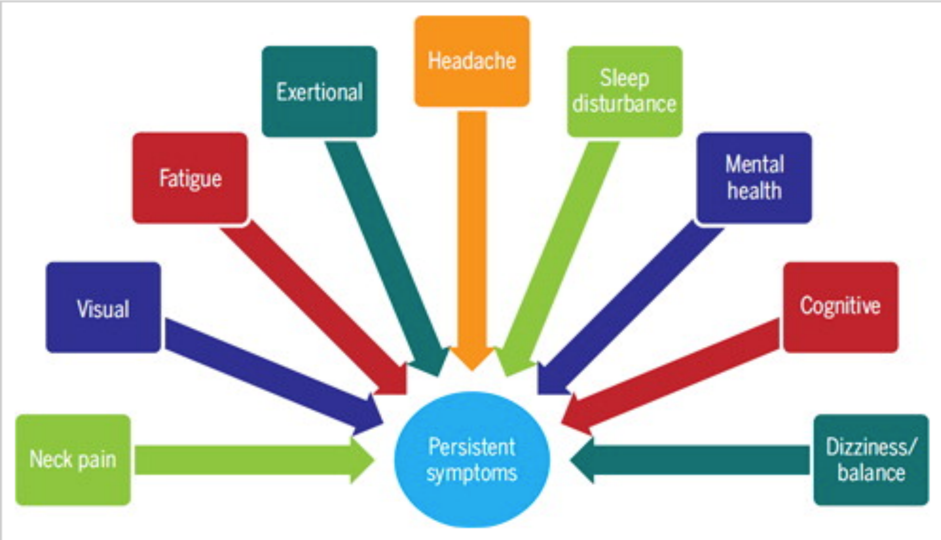

Figure 3: Common symptoms reported after a concussion (Schneider, 2016)

1.5 Management of concussion

The "graduated return-to-sport strategy" is the protocol widely adopted in managing SRC and consists of 6 levels, from a complete rest, followed by return to light activities that do not provoke symptoms to full resumption of normal game play (Fig. 4). Once assessed as being in stage 1 to 5, the athlete must wait at least 24 hours before progressing to the next level. In addition, if the athlete experiences any worsening or reoccurrence of symptoms he/she must return to the previous level (McCrory et al., 2017).

Stage	Aim	Activity	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, eg, 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 sport	Normal game play	

Figure 4: Graduated return-to-sport strategy protocol (McCrory et al., 2013)

The initial management following a concussion is an early period of cognitive and physical rest. This is implemented because exertion can aggravate cognitive and physical symptoms (Majerske et al., 2008). However, it has been shown that prolonged rest is not beneficial (Leddy et al., 2012). In athletes, it causes deconditioning (Willer and Leddy, 2006), creates metabolic disturbances (Hamilton et al., 2004), and can induce fatigue and depression (Berlin et al., 2006). To be able to return to play an athlete must follow the return to play protocol symptom free, be cleared by a medical doctor and according to the guidelines adopted by some sport organizations such as the Scottish Rugby Union, pass an objective assessment such as Cogstate (Ellemberg et al., 2009).

1.6 The King-Devick Test

The King-Devick test assesses eye movement (saccades, convergence and accommodation), attention and language function using a timed number naming task. The King-Devick test is not specific to concussion indeed, it is also used to assess reading performances and as an indicator of neurological function and may include false positives in a sample of fatigued athletes (Galetta et al., 2016).

The King-Devick test has been reported to assess functions that are subserved by the brainstem, cerebellum and cerebral cortex (Galetta et al., 2016). Visual information travels from the eye to the visual cortex via the lateral geniculate nucleus. The visual cortex is located in the occipital lobe and has extended connections with the frontal lobe (including the frontal eye fields and the dorsolateral prefrontal cortex), the parietal lobe (posterior parietal cortex) and the temporal lobe (middle temporal area) (Heitger et al., 2009, White and Fielding, 2012). These areas are involved in planning, initiation and coordination including the coordination of saccadic eye movements (Sparks and Mays, 1990, Heitger et al., 2002). Therefore, a temporary impairment of brain function - such as occurs in a concussive episode - could cause disturbances of eye movement and result in a positive finding (impaired performance) on the King-Devick test (Heitger et al., 2002). Figure 5 shows the cortical areas that control eye movements and visual processing.

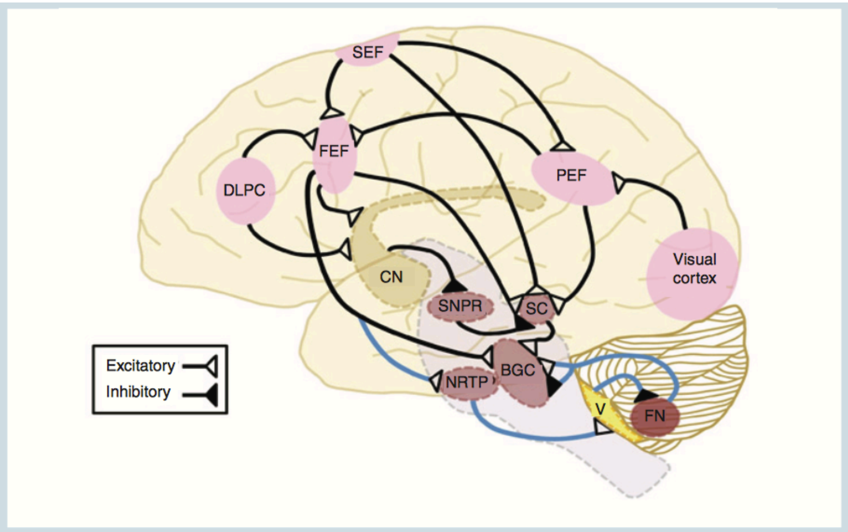

Figure 5: Cortical areas that control eye movements and visual processing (Galetta et al., 2016). BGC: Brainstem gaze centers; CN: Caudate; DLPC: Dorsolateral prefrontal cortex; FEF: Frontal eye eld; FN: Fastigial nucleus; NRTP: Nucleus reticularis tegmenti pontis; PEF: Parietal eye elds; SC: Superior colliculus; SEF: Supplementary eye eld; SNPR: Substantia nigra pars reticulata; V: Vermis.

The instructions for completion of the King-Devick test are standardised and the subject is required to read aloud a series of single-digit numbers from left to right as quickly as possible without making errors. The King-Devick test includes one demonstration card and three test cards, as shown in Figure 6. The test takes less than two minutes to administer.

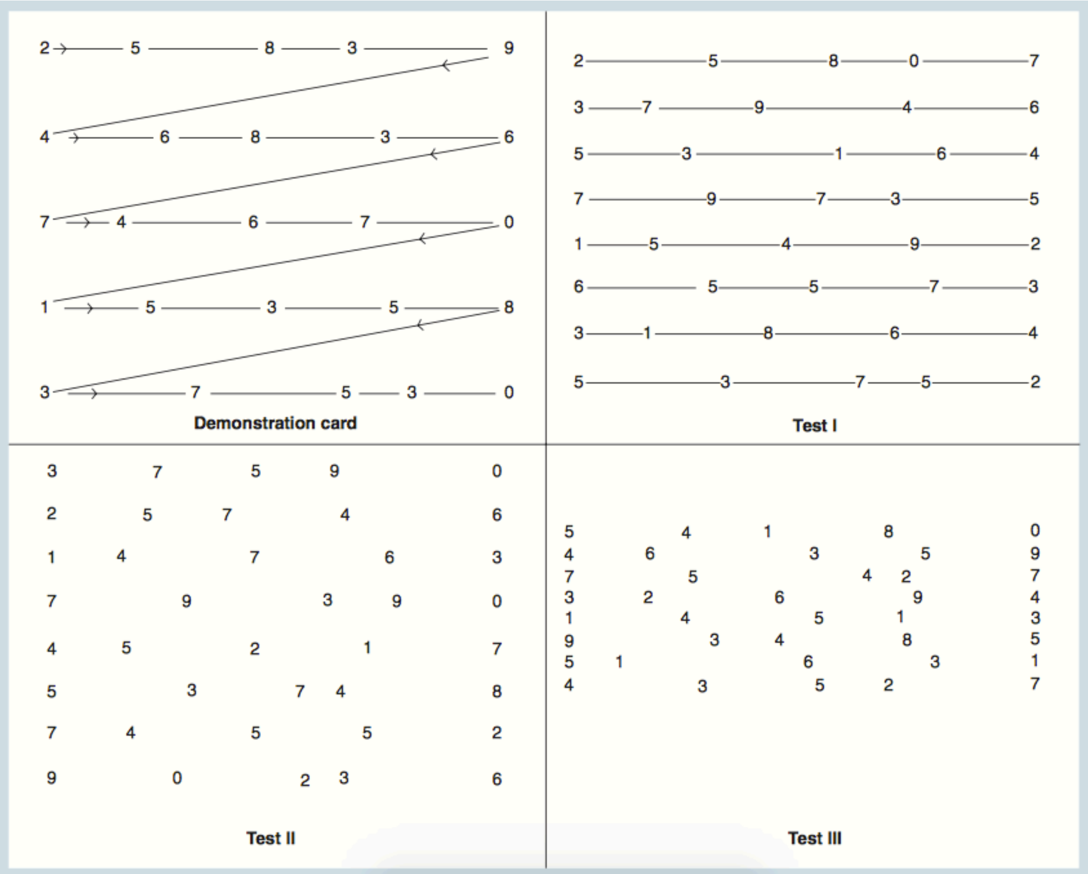

Figure 6: King-Devick test (Galetta et al., 2011)

The time taken to complete the task is recorded using a stopwatch and is formed by the sum of the three cards. The test is repeated twice and the fastest score, without errors, is used as a baseline measure. The number of errors is also recorded. It has been shown that worsening of time and/or an increase in the number of errors committed while completing the King-Devick test are indicative of concussion (Galetta et al., 2011b). Galetta et al. (2011b) conducted a longitudinal study of 219 athletes from different sporting disciplines including soccer, basketball and sprint football. Concussed athletes (n = 10) were reported to take a significantly longer time to complete the test than they did at baseline (obtaining a median score of 46.9 seconds post-concussion compared to 37.0 seconds at baseline) as determined by a Wilcoxon signed-rank test. This marked worsening of the score could be explained by the fact that the concussed athletes were assessed on the side-line immediately after the concussion.

A number of authors have suggested that an increase in the time taken to complete the King-Devick test of more than 3 to 5 seconds can be considered the threshold for a positive assessment of concussion and indicative that the athlete should not be allowed to return to play (Galetta et al., 2015, King et al., 2015, King et al., 2013, King et al., 2012). Galetta et al. (2015) in their prospective study assessed 243 children (mean age 11 ± 3 years, range 5 to 17 years) and 89 collegiate athletes (age 20 ± 1 years, range 18 to 23 years) and found that on average the concussed athletes (n = 12) worsened their score by 5.2 seconds and non-concussed athletes (n = 14) improved their score by 6.4 seconds between baseline and repeat assessment. One of the limitations of that study was the fact that it included both children under the age of 18 years and adults. Indeed, Galetta et al. (2016) reported that children under the age of 18 have significant lower baseline scores compared to adults. Low subject numbers in both the concussed and non-concussed groups at the time of the repeat assessment also limit the generalisability of the results.

The meta-analysis and systematic review conducted by Galetta et al. (2016) included analysis of 15 articles with the determination of study eligibility being conducted by two independent reviewers. Inclusion criteria were that articles that had been published since 2010 and included assessment of athletes or SRC with baseline or post-injury measurements on the King-Devick test and accepted for publication in a peer-reviewed journal. The inclusion and exclusion criteria included in the systematic review were appropriate to the topic of the review. One potential bias was that some of the studies included in the meta-analysis were conducted by Galetta (Galetta et al., 2011a, Galetta et al., 2011b, Galetta et al., 2013, Galetta et al., 2015, King et al., 2014, Marinides et al., 2014). In addition, the systematic review did not include randomised controlled trials. Therefore, according to the NHMRC guidelines this systematic review would be considered level III-2 evidence. The study had a strong consistency because all papers included reached the same conclusion. In addition, the literature review demonstrated that the King-Devick test had a substantial clinical impact because it is low cost tool, with high reliability and high sensitivity and specificity. The level of generalisability is high because the literature review included children, adolescents and adults. In addition, Galetta et at. (2016) included in their study both males and females. The level of applicability of this study is satisfactory, the King-Devick test being suitable to asses the majority of the population. The only individuals for whom that is not true are a small sector of those from a non-English speaking background who are not familiar with English pronunciations of numbers. Galetta et al. (2016) found that the measure was reliable. They reported that among 112 concussed players (form the 15 studies assesses in the meta-analysis), with an age range between 13.3 years (95% CI [12.8, 13.8]) and 27.2 years (95% CI [24.2, 30.1]), the score worsened from baseline by 4.8 seconds, whereas the score for the non-concussed athletes tested on a second occasion improved by 1.9 seconds due to possible learning effects. The King-Devick test has also been reported to have high test-retest reliability for both young athletes aged between 6 and 17 years

(Smolyansky et al., 2016) and adults (Audycki et al., 2015). High levels of reliability have been reported in the absence of concussion with intraclass correlation coefficients ranging from 0.90 (95% CI [0.85-0.95]) to 0.97 (95% CI: 0.90, 1.0) in studies of mixed martial arts fighters (Galetta et al., 2011a), collegiate athletes (Leong et al., 2014) and Elite Junior Olympic Athletes (Smolyansky et al., 2016). Galetta et al. (2016) reported that preseason baseline scores were consistent across all published studies. However, it is possible that the consistency in baseline results reflected the fact that the majority of studies included in the systematic review by Galetta et al. (2016) were conducted by the authors of that review and therefore adopted a similar methodology. In addition, it was found that the King-Devick test had high degrees of sensitivity (86%) and specificity (90%). Moreover, it was found that physical activity does not negatively affect the King-Devick score. Indeed, the authors found and association between physical activity and mild learning effects. Finally, the authors recommended use of the King-Devick test in side-line assessments of concussion.

Using the King-Devick test, Smolyansky et al. (2016) assessed 54 athletes participating in the 2014 Amateur Athletic Union Junior Olympic Games. To assess test-retest reliability, the athletes completed two King-Devick baseline tests, with the second test performed 30 minutes after the first one (Smolyansky et al., 2016). The test-retest showed high reliability between baseline and retest (ICC = 0.93, 95% CI (0.89-0.96)). In addition, it has also been shown that the test-retest reliability is high when administered by non-medically trained personnel, such as athletes' parents (Leong et al., 2014) and this may be useful in situations where qualified medical personnel are not present. In the study by Leong et al. (2014), six non-medically trained parents assessed 34 amateur boxers who competed in three rounds (9 minutes) of sparring boxing. The authors reported that the ICC of the first and second pre-fight King-Devick test was reliable (ICC = 0.90 (95% CI (0.84-0.97)); Spearman rank correlation 0.94, $p < .001$). Moreover, the same authors reported that in non-concussed amateur boxers the King-Devick test was reliable (ICC 0.96 (95% CI 0.93-0.99). Only one fighter committed an error on the King-Devick score and interestingly, he was the same fighter that was diagnosed as concussed by a ring side physician. None of the other non-concussed athletes scored a slower time (worsening performance) after the sparring session (with test completion times of 40.9 ± 8.6 seconds at baseline versus 39.3 ± 9.1 seconds post fight).

Galetta et al. (2011b) described a learning effect on the King-Devick test in 219 football players who scored a lower time (i.e., improved their score) in a second pre-season test session (median

36.1 seconds versus 40.2 seconds) and when tested post season compared to their first pre-season assessment (35.1 seconds versus 37.9 seconds). In addition, learning effects were also noted between the two baseline measurements in 36 sprint football players (38.6 seconds versus 36.1 seconds).

A small study conducted on nine participants, investigated the effect of a noisy environment on performance on the King-Devick test and revealed no significant differences in scores returned when tested in a noisy relative to a quiet environment (Galetta et al., 2011b). This provides preliminary evidence to suggest that the instrument may be suitable for assessing concussion in a sporting/field environment. However, the study had low power due to the small sample size and therefore, it is not possible to draw definitive conclusions.

Galetta et al. (2016) found that for subjects between the ages of 5 and 18 years there was a direct association between increasing age and faster completion times on the King-Devick test, possibly reflecting the effects of brain maturation (Luna et al., 2008). Completion times have been reported to be stable across the second and third decades of life, with a minor worsening of scores for participants in their forth decade (Galetta et al., 2016).

Zuckerman et al. (2015) reported that, in gender-comparable sports, female athletes have an overall higher rate of concussion compared to males. It has been hypothesised that this gender difference could be caused by intrinsic factors such as females having a weaker neck musculature, which has been associated with increased risk of concussion (Zuckerman et al., 2015, Gessel et al., 2007). In addition, females are more likely to report symptoms compared to males (Brown et al., 2015). Lastly, some of the symptoms of premenstrual syndrome, such as headache, difficulty concentrating and emotional symptoms (Freeman et al., 2011), are also common in concussion and therefore could increase the report of concussive episodes (Wunderle et al., 2014). No studies have been conducted to examine potential differences between female and males in performance on the King-Devick test at baseline.

1.7 Effect of physical fatigue on brain function

Phillips (2015) described fatigue as a suboptimal psychophysiological condition caused by exertion. Although an athlete can report fatigue subjectively, the symptoms are poorly defined.

In the literature, the terms physical activity and physical fatigue are often used interchangeably to describe exercise. The World Health Organisation (2017) defines physical activity as body movement produced by muscle activation that requires energy expenditure. On the other hand, physical fatigue or muscle fatigue, has been defined by Abd-Elfattah et al. (2015) as a transitory physical incapacity of a muscle to respond to stimuli and perform functionally and optimally. Therefore, physical fatigue is a common consequence of physical activity and it has been reported by Ament and Verkerke (2009) that physical fatigue is essential to preserve our physical integrity. Indeed, the physiological role of fatigue is protection from the deleterious effects of prolonged and exhausting exercise such as cardiovascular dysfunction, injuries and overtraining syndrome (O'Keefe et al., 2012). Ament and Verkerke (2009) reported that the symptoms of fatigue serve to reduce or stop physical activity, confirming the protective aspect of fatigue.

Fatigue can also be assessed objectively in the form of impaired physical or mental performance (Sharpe and Wilks, 2002). The results of studies on the effects of physical fatigue on brain function have been inconsistent (Abd-Elfattah et al., 2015). Scores on tests of cognitive functioning after exercise have been reported to improve (Hancock and McNaughton, 1986, Weuve et al., 2004), to remain unchanged (Cote et al., 1992) or to decline (Cian et al., 2001, Covassin et al., 2007). However, it appears that the intensity and duration of the exercise may play a major role on the effect of fatigue on brain function (Kamijo et al., 2007, Tomporowski, 2003). Indeed, sub-maximal intensity exercises (heart rate of 110 to 130 beats per minute) of 20 to 40 minutes have been reported to increase cognitive function as measured by tests of verbal memory, category fluency, and attention (Weuve et al., 2004). The latter study, however, included only American women aged between 70 and 81 years of age. On the other hand, longer sub-maximal exercise (Cian et al., 2001) or strenuous exercise, defined as any activity that expends 7 metabolic equivalents per minute or more (Physical Activity Guidelines for Adults issued by the Department of Health and Human Services, 2008), has been demonstrated to decrease brain function as measured by psychological tests administered 30 minutes after the dehydration phase (up to 2.8% of weight loss). However, Cian et al. (2001) tested only seven subjects. Covassin et al. (2007) tested 102 participants between 18 and 24 years old divided into two groups with 54 subjects in a fatigue group and 48 in a control group. The fatigue group was asked to perform a maximal treadmill exercise test to assess maximal oxygen uptake (VO_2 max) whereas the control group was asked to rest for 15 minutes. Both groups were assessed on the ImPACT prior and immediately subsequent to the 15 minute interval. The results revealed that verbal memory scores decreased significantly more in the fatigue group from baseline to reassessment compared to the control group. On the other hand, there were no significant differences in the change demonstrated by each of the two groups on measures of visual memory, motor processing speed or reaction time.

Any improvement in test scores following exercise could be due to either repeated practice on the one test instrument (Bartels et al., 2010) or stimulation of brain function (Winneke et al., 2012), whereas deterioration could be caused by dehydration (Cian et al., 2001) or changes in cortical activity in the brain (Brummer et al., 2011). This latter explanation is detailed by Dietrich (2006) and by Ekkekakis et al. (2005) who hypothesised that because brain resources are limited, during intensive exercise the brain will redistribute its activities. This consist of a shift of brain use towards the of regions of the sensory and motor cortices which are involved in the planning and execution of motor commands. To the best of the author's knowledge, there is no research indicating that fatigue and concussion are correlated either positively or negatively.

1.8 Previous studies on the effects of fatigue on the King-Devick test

Currently in the United States, 0.05% of the National Collegiate Athletic Association teams routinely use the King-Devick test (Kerr et al., 2015). To the best of the author's knowledge, there is no other evidence as to the extent to which the test is presently being used in the assessment of SRC. That is perhaps surprising, given the high reliability, sensitivity and specificity of the test as reported in the literature (Galetta et al., 2011b, Galetta et al., 2016, King et al., 2013, Leong et al., 2014). For any measure of concussion, it is critical to assess whether other determinants, such as physical fatigue and the effects of repeated practice on the one assessment instrument, could impact the results on the test. Indeed, other concussions tests such as BESS and SAC have been shown to be affected by physical activity and learning effects both of which have been found to result in an improvement in scores (faster completion times) (Burk et al., 2013, McCrea et al., 1998). Burk et al. (2013) tested 85 females. They selected only females because it has been shown that there are gender differences in BESS performance (Erkmen et al., 2009). The results showed a significant improvement ($p = .003$) between preseason (9.00 ± 2.97 errors) and end of season (7.92 ± 2.78 errors) BESS performance. It had previously been reported that practice effects on the measure lasted up to 60 days (Guskiewicz, 2011). However, Erkmen et al. (2009) conducted the second test 90 days after baseline to avoid the practice effects reported in the literature.

Several studies have investigated the effect of physical exercise on performance on the King-Devick test. In those studies, physical activity was referred to as fatigue, however, fatigue and how it related to physical activity was not defined. These studies assessed the following sports: basketball (Leong et al., 2015, Galetta et al., 2011b) rugby (King et al., 2013) and hockey (Dhawan et al., 2014). Galetta et al. (2016) in their meta-analysis and systematic review of the literature concluded that physical fatigue does not impact scores on the King-Devick test, however, these studies were based on a small number of participants ranging between 18 and 51 volunteers (Galetta et al., 2011b, Leong et al., 2015, Dhawan et al., 2014) or the number of the participants was not clearly specified (King et al., 2013). In addition, only one study used a specific, standardized and reproducible method to assess the level of physical activity (King et al., 2013). The physical activity consisted of a repeat high intensity endurance test which involved six 70 metre sprints in a 20-metre grid with each sprint departing on a 30 second cycle conducted on an artificial grass turf indoor floor. Players would sprint to a five-metre mark, turn, sprint to the start line, turn, sprint to the ten metre mark, turn, sprint to start line, turn, sprint to the 20 metre mark, turn and sprint to the start line. A 5 seconds warning and verbal feedback ware given to allow the player to be ready to commence the sprint when commanded. The players were asked to indicate their rate of perceived physical exertion and complete the King-Devick test on an IPad2 two minutes after completing the exercise.

All these studies reported that the King-Devick score post exercise, improved by between 1.2 and 3.6 seconds. Indeed, King et al. (2013) reported that performance on the King-Devick test at reassessment post-exercise was on average 1.2 seconds faster (0.1 s to 3.9 s) than at baseline. It has been hypothesized that the scores may improve because of mild learning effects (Galetta et al., 2016). No studies have assessed gender differences in the effect of physical fatigue on the King-Devick test.

Most importantly, none of these studies included a control group during their evaluation of the effect of physical fatigue on the King-Devick test. Therefore, it is not possible to conclude that physical activity may improve the King-Devick test score. It is important to include a control group to ensure that any changes in performance following exercise are not due to the effects of repeated practice on the one test instrument alone. The control group should have the same characteristics as the experimental group except for a predetermined variable, which enables the study of that variable while controlling for the effects of other variables that could potentially result in misleading interpretations of causality (Kinser and Robins, 2013). The use of control groups can be challenging in areas such as concussion assessment for obvious ethical restrictions and because during games it is not possible to pull non-concussed players off the field to be tested. On the other hand, in other disciplines, such as pharmaceutical research, the use of the control group is more common and easier to implement (Tsuyuki, 2014).

1.9 Rate of Perceived Exertion

The physical workload can be measured externally using global positioning system (GPS) tracking or internally. Internal measurement can be achieved objectively, using a heart rate monitor or subjectively, using ratings of perceived physical exertion (RPE) (Foster et al., 2001).

GPS calculates the distance and speed reached during physical activity and its reliability depends on several variables and is reduced by movement velocity, and change of direction during jumping, kicking and tackling actions (Aughey, 2011). Other studies have suggested the use of heart rate monitors or heart rate palpation to assess exercise intensity (Dong, 2016). However, there are several disadvantages to using these methods. Dishman (1994) reports that using the maximal heart rate predictor based on age can create an error of ± 11 heartbeats per minute compared to the desired exercise intensity. Other factors that may affect the heart rate monitor are air temperature, humidity, psychological stress, caffeine and medications (Noble and Robertson, 1996). The heart rate monitor results can vary up to 6.5% for submaximal intensity exercises (Bagger et al., 2003). Furthermore, its usefulness might be limited in intermittent sports such as rugby and football, where the athletes repeatedly stop and restart their activities (Joyce and Lewindon, 2016).

On the other hand, within session recordings of RPE have been reported to represent a valid and reliable method to assess training load and fatigue (Perandini et al., 2012, Coutts et al., 2003, Eston, 2012, Halson, 2014). However, these studies are based on a small number of subjects ranging between 11 (Perandini et al., 2012) and 28 (Eston, 2012). Developed by Borg (Foster, 1998), the modified Borg dyspnoea scale measures RPE which is a method of measuring intensity level during physical activity. RPE gives an indication, based on a scale from 0 (nothing at all) to 10 (maximal) of how hard the athlete feels the body is working. In addition, some studies use the 6-20 RPE scale were 6 represents nothing at all and 20 is maximal exertion. This scale was initially developed to correlate with exercise heart rates (e.g., RPE 15 would approximate a HR of 150 bpm) (Borg, 1982). Both RPE scales are used clinically and currently there are no recommendations regarding use of one scale in preference to another (Irving et al., 2006).

The RPE has been validated in several aerobic studies (Eston and Williams, 1988, Dunbar et al., 1992, Kang et al., 2003, Kang et al., 2009, Robertson et al., 2002). In these papers, the RPE data was compared with heart rate and VO2. Eston and Williams (1988) found the correlation between RPE and VO2 max was true for Borg 6-20 scale above 12. In particular, at RPE 17 the subjects perform 89% VO2 max for running and 81% VO2 max for cycling. Dunbar et al. (1992) tested 17 subjects and found a correlation between RPE and 50 to 70% of VO2 max. Robertson et al. (2002) assessed 36 children between the age of 8 and 12 years and found no differences in estimation and production values between VO2 and RPE of 2 (0.63 versus 0.66 L x min(-1)) and 6 (1.27 vs 1.21 L x min(-1)) after intermittent cycle ergometer exercise. In addition, no difference in estimation and production values were found when comparing heart rate monitor and RPE when the subjects performed the exercise at RPE of 2 (104.1 vs 102.6 beats x min(-1) and 6 (153.7 vs 154.5 beats x min(-1)).

Even though, the numbers of subjects tested was small, varying from 16 (Eston and Williams, 1988) to 48 (Kang et al., 2003), a measure referred to as session-RPE, defined as RPE multiplied by the duration of the activity, is easy used and has been shown to be valid and reliable for team sports (Coutts et al., 2003), endurance sports (Foster et al., 2001) and resistance training (Sweet et al., 2004, Day et al., 2004).

Coutts et al. (2003) assessed 18 Australian semi-professional rugby league players (age 23.3 ± 3.3 years) for 7-weeks recording 306 field training sessions and found that there was a statistically significant correlation ($r = 0.41 - 0.96$). between the session-RPE and heart rate based assessment. Foster et al. (2001) compared the session-RPE with heart rate to quantify aerobic exercise. Subjects were divided into three groups: i) interval aerobic exercises, ii) cycle ergometer, and iii) a basketball practice session group. Even though session-RPE recorded a numerically higher score than the heart rate monitor, there was consistency among the different exercise bouts. It was therefore concluded by Foster et al. (2001) that both methods can be used successfully to quantify training intensities of different types of aerobic exercise. Day et al. (2003) assessed 20 subjects, using session-RPE, who were randomly allocated to three groups of interval training. They found that the ICC was 0.88 with the 95% confidence interval of 0.70 to 0.96 and the coefficient of variation was 14.5%. Sweet et al. (2004) tested 10 men and 10 women and found that RPE and session-RPE were reliable when assessing resistance training at 50%, 70% and 90% of one repetition maximum. Although each of these studies included only a limited number of participants, their results are consistent and provide evidence to indicate that the RPE is a reliable measure of fatigue.

RPE is commonly used as part of an individualized exercise prescription to self-regulate exercise intensity because it is simple, cost-free and reliable (Noble and Robertson, 1996). Dunbar et al. (1994), Kang et al. (2003) and Kang et al. (2009) reported RPE intensity can be reached and maintained during various aerobic exercises of 3 to 40 minutes duration. RPE has been shown to be reliable at lower intensity (Schafer et al. 2013) at moderate intensity (Bayles et al., 1990) and at higher intensity (Smutok et al., 1980, Eston et al., 1987) for exercises of maximum 20 minutes duration.

One study on the effects of physical activity on the King-Devick test score, conducted by King et al. (2013) recorded players RPE (based on 6-20 Borg scale) (Foster et al., 2001) to assess levels of fatigue. Players reported a RPE of 16.6 ± 3.3 units post exercise with the King-Devick test lowered from baseline by a mean of 1.2 seconds (0.1 seconds to 3.9 seconds).

1.10 Research aim and hypotheses

The King-Devick was selected to test subjects in this study for a number of reasons. Firstly, the test has robust psychometric properties, having been demonstrated to posses both construct validity, and high test-retest reliability (90% [181 out of 202 controls had no worsening on the King-Devick test's score; 95% CI: 85%, 93%]). The test has also been reported to have high sensitivity of 86%. Galetta et al., reported that of 112 concussed athletes, 96 demonstrated a worsening of scores on the King-Devick test (95% CI: 78% - 92%). Moreover, specificity was found to be 90%, with 181 of 202 controls demonstrating no worsening of scores on repeat assessment (95% CI: 85%, 93%). To date, the positive and negative predictive power of the test have not been investigated. Finally, the King-Devick test has been shown to be easy to use even among non-medically trained people and quick to administer which are two aspects that are of critical importance for a side-line concussion assessment tool, especially one that is used in amateur sport.

The aim of the current study was to determine the effects of physical fatigue on performance on the King-Devick test.

It was hypothesized that:

1. Physical fatigue would negatively affect scores on the King-Devick test as evidenced by a fatigue group who completed a 15-minute exercise routine demonstrating significantly less improvement in scores between baseline and reassessment than subjects in a control group.

2. The negative effects of fatigue on performance on the King-Devick test would be similar to the effects of concussion, in that significantly more subjects in the fatigue group would demonstrate reduced scores at reassessment relative to baseline than subjects in the control group.

3. The number of mistakes at reassessment relative to baseline would be significantly higher for the fatigue group than the control group

4. The negative effects of physical fatigue on performance on the King-Devick test would be similar to the effects of concussion, in that significantly more subjects in the fatigue group would demonstrate a decrease in scores of three seconds or greater at reassessment relative to baseline than would subjects in the control group.

5. No significant difference in scores on the King-Devick test will be evident at the baseline assessment when comparing gender. In addition, results at baseline would not vary as a function of age or level of education.

6. Both the fatigue and control group would experience some degree of learning effect between baseline and reassessment testing.

7. Using the fastest time of two errorless trials at reassessment will produce a significantly less number of ‘failed’ tests compare to using only the first reassessment test time as per the King-Devick test’s guidelines.

Chapter 2

Methods

Ethics approval for the current study was granted from Macquarie University Ethics Review Committee (Human Research) (Ethics Ref: 5201600732).

2.1 Participants

A total of 140 subjects were recruited from gyms (n = 61), sporting clubs (n = 58), physiotherapy practices (n = 12) and chiropractic clinics (n = 9). The subjects were all volunteers and were recruited using newsletters, email, flyers and word of mouth. Inclusion criteria were that the participants were aged between 18 and 70 years and were fluent in English. The latter criterion was adopted as participation required completion of a test measuring time taken to perform rapid number naming. In addition, the participants from the fatigue group were active people who needed to be able to run on the treadmill for 15 minutes. Most the subjects from the fatigue groups (n = 61) were members of one of two gyms in the Northern Beaches of Sydney. Their level of fitness was not assessed. Thus, fitness could have potentially skewed the results in that different level of fitness might have effected the speed and level of recoverability (Hunter, 2017).

The first author collected the data from the fatigue group. Once he collected data from the participants in the fatigue group, he relocated overseas and therefore the control group data were recruited from a different population, mainly players and staff of the Glasgow Warriors rugby team. The allocation of the subjects into the two groups was not random but was dictated by people’s willingness to run on the treadmill.

The participants were divided into two groups, one of which completed a 15-minute exercise routine (subsequently referred as the fatigue group) and one of which rested between the baseline and the 15-minute follow-up assessment tasks (the control group). Each of the two groups comprised 70 subjects. The fatigue group included 40 males and 30 females. The mean age of the subjects in that group was 34.24 years (SD=12.58 years, range=18 to 69 years). In terms of the highest level of education completed, 30 subjects in the fatigue group reported having completed high school (12 years education), 28 as having completed a Bachelor degree

(16 years education) and 12 as having completed a Master degree (18 years education), resulting in a mean number of years of education of 14.63 (SD = 2.40, Median = 16, IQRs = 4). In terms of neuropsychological risk factors, 19 subjects had sustained at least one head trauma, defined as a damage to the scalp and skull without sustaining a concussion, and 15 subjects had been diagnosed as suffering a concussion on at least one occasion, concussion being defined as a rapid onset of transitory impairment of neurological function that resolves spontaneously caused by a direct blow to the head or by impulsive forces on other parts of the body transmitted to the head (McCrory et al., 2017). No subject responded in the affirmative when asked whether they had any other history of neurological damage. The instructions for administering the King-Devick test indicate that note should be made of whether an individual typically wears glasses or uses contact lenses and whether they were doing so at the time of testing. A total of 27 participants in the fatigue group reported wearing glasses or contact lenses during their daily activities and 16 subjects reported using either glasses or contact lenses during the testing session. Additional inclusion criteria for subjects in the fatigue group were that they were members of a gym or had access to a treadmill and were able to run on that apparatus, uninterrupted, for a period of 15 minutes.

The control group comprised 46 males and 24 females. The mean age of the subjects in the control group was 32.01 years (SD = 11.38 years, range = 20 to 68 years). The highest level of education completed for the control group was identical to the fatigue group ($p > .05$) as shown in Table 2. A total of 29 control subjects reported having sustained at least one head trauma and 33 as being diagnosed with concussion on at least one occasion. One subject reported a previously neurological condition, that being a c4-5 lesion of the spinal cord. Twenty-nine of the control subjects reported wearing glasses or contact lenses during their daily activities and 19 reported using either during the assessment.

Finally, medications and occupation were recorded for both groups. No subject reported being on medications that have documented side-effects that impact cognition as detailed in MIMS Online (MIMS, 2017).

2.2 Measures

The instruments used in this study were: a treadmill, an IPhone 5SE stopwatch, a paper form of the King-Devick test and a RPE scale. The King-Devick test requires the individual to complete a practice trial in which they have to name numbers printed as digits at irregular points on a page as quickly as possible. The subject is then required to read the three cards comprising the test as quickly as possible without making a mistake. If the subject makes a mistake, the trial is discontinued and the test is repeated. The testing procedure is completed twice during baseline testing. The baseline time represents the fastest time of the two errorless trials. The test was repeated twice 15 minutes later. If an error was made, the trial was discontinued and the procedure was repeated until two errorless trials had been completed. The reassessment time represented the time taken to complete the first errorless trial. The number of times a trial had to be discontinued was also recorded. As per the instructions for administration of the test, whether or not the subject used glasses or contact lenses for reading and whether they were worn during testing was recorded. Participants' information was collected on paper and subsequently recorded in an Excel file.

A RPE scale was used to monitor participant's fatigue level, on which perceived exertion was indexed from 0 (none at all) to 10 (maximum).

2.3 Procedure

Participants in the fatigue group completed the King-Devick test, ran on a treadmill for 15 minutes and then repeated the King-Devick test. While on the treadmill, a card showing the 0-10 RPE scale was displayed and subjects were instructed to run on the treadmill at an RPE of 7 for the first 12 minutes and at an RPE of 9 for the final 3 minutes to achieve maximal effort and fatigue as described by Norton et al. (2010). In addition, the initial 10 (14.3%) volunteers were tested with a heart rate monitor as a pilot study, conducted to determine the validity of the RPE measure. Specifically, that procedure was adopted to assess whether the RPE matched results on the heart rate monitor. The heart rate monitor showed the percentage of maximal heart rate for each subject. The goal of the first 12 minutes was 70% and for the last 3 minutes was 90%. The subjects scored an average of 72.6% (± 3.31) for the first 12 minute and 91.4% (± 2.72) for the last 3 minutes. This were similar to findings previously reported in the literature (Foster et al., 2001, Coutts et al., 2003).

Subjects in the control group completed the King-Devick test in the same standardised manner as did participants in the fatigue group, rested from physical activity for 15 minutes and then repeated the King-Devick test twice. During the rest time, the participants could complete tasks such as typing, talking and reading, but they were not allowed to complete any physical activity that could potentially raise their hear rate.

2.4 Statistical analysis

Paired sample t-tests were used to analyze the results on the King-Devick test at baseline and reassessment for each individual group. Independent sample t-tests were used to compare the two groups in relation to variables that were normally distributed (age, differences between pre-and post-tests, etc.). Mann-Whitney U tests and Wilcoxon signed-rank tests were used to compare non-parametric data such as between group differences in education, gender, number of concussions, number of head traumas and use of glasses or contact lenses. If any differences between the two groups on any of those variables were found, the intent was to statistically control for those differences by entering the relevant variables as covariates in an analysis of variance. Statistical analyses were performed using SPSS version 24.0 (IBM, 2017). Significance was set at $p < .05$.

Chapter 3

Results

3.1 Demographic

As can be seen in Table 2, there were no significant differences between the fatigue group and the control group in relation to age, gender, education or the use of glasses/contact lenses during testing. The two groups did not significantly differ in terms of the number of head traumas sustained. However, the number of subjects that had sustained at least one concussion was significantly higher ($Z = -3.546$. $p < .001$) in the control group than in the fatigue group. Given that the difference was not in a direction that would confound results in keeping with the hypotheses, no control of that variable was exercised in subsequent analyses.

Table 2: Demographic, neurological and visual characteristics of the Fatigue and Control groups

	Control (n=70)	Fatigue (n=70)	P Value	Median years (IQRs)
Age ± SD	32.01 ± 11.38	34.24 ± 12.58	0.273	
Gender	46 M; 24 F	40 M; 30 F	0.299	
Education	30 HS; 28 BS; 12 MS	30 HS; 28 BS; 12 MS	1	16 (4)
Glasses	19	16	0.560	
Head trauma	29	19	0.076	
Concussion	34	15	0.000**	

BS: Bachelor; F: Female; HS: High School; M: Male; MS: Master; SD: Standard Deviation. **$p < .005$

3.2 Exercise vs rest

Comparison of scores at baseline and reassessment, revealed that the fatigue group demonstrated significantly less improvement over time (1.2 ± 2.90 seconds) than did the control group (2.52 ± 2.37 seconds) ($t = 2.947$, $p = .004$), as shown in both Figure 7 and Table 3.

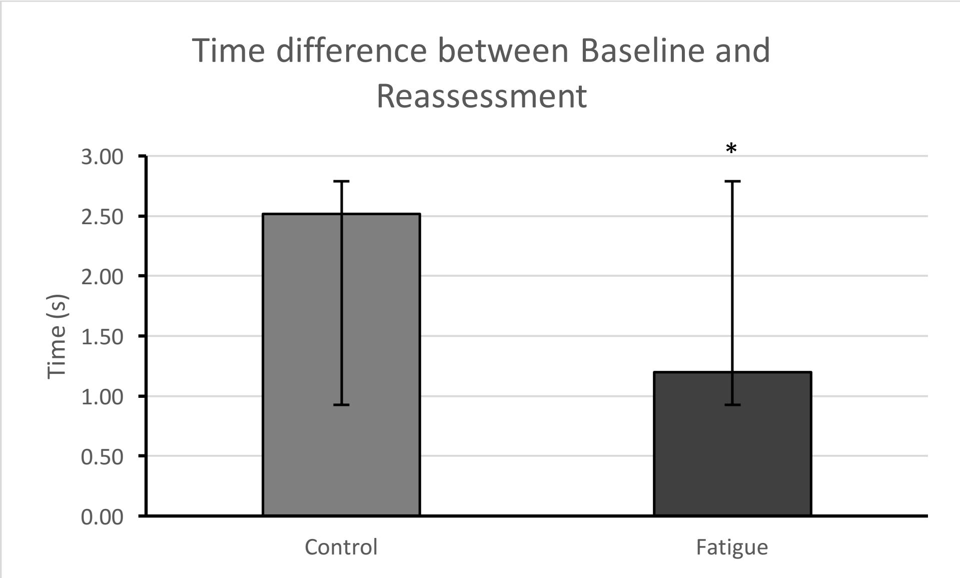

Figure 7: Time difference between Baseline and Reassessment. *p < .05

Table 3: Time difference between Baseline and Reassessment across groups

	Control (SD)	Fatigue (SD)	t-value	df	p-value
Time difference between Baseline and ReAx (sec)	-2.52 (2.37)	-1.2 (2.90)	2.947	138	0.004**

ReAx: Reassessment, SD: Standard Deviation. **p<0.005

A significantly higher number of subjects in the fatigue group (n = 22, 31.4%) scored a slower time at reassessment relative to baseline than did subjects in the control group (n = 10, 14.3%) (Z = -2.407, p = .016) (see Figure 8 and Table 5).

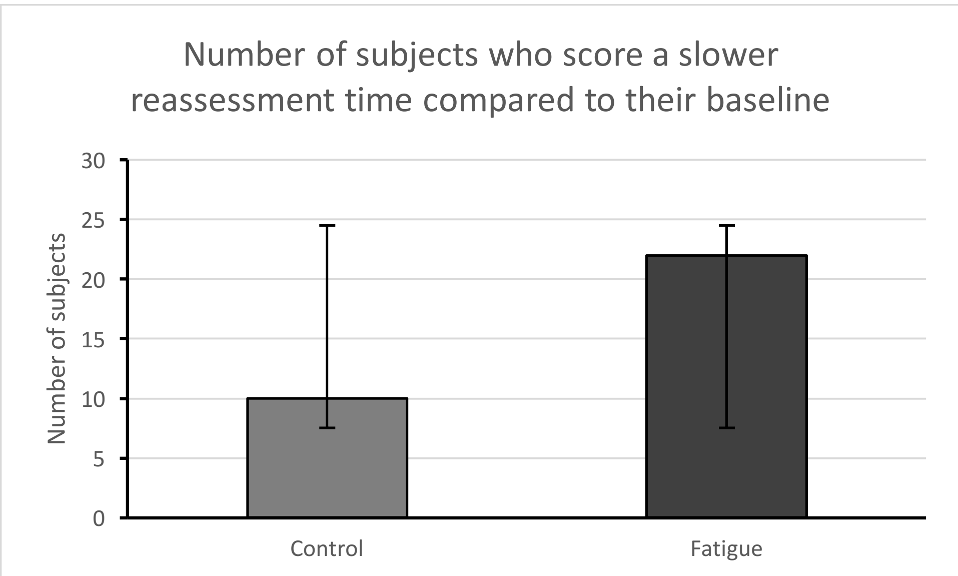

Figure 8: Number of subjects who score a slower reassessment time compared to their baseline

The number of errors at reassessment was calculated for both groups. No subject made more than one error at reassessment. A significantly higher number of subjects in the fatigue group (n = 9, 12.9%) made an error at reassessment than did subjects in the control group (n = 1, 1.4%) (Z = -2.404, p = .016).

The number of subjects who failed the King-Devick test at reassessment when defined as i) committing an error at reassessment and / or ii) returning a slower score at reassessment than at baseline, was 25 subjects (35.7%) in the fatigue group and 11 subjects (15.7%) in the control group. That difference was significant (Z = -2.698, p = .007). Those results are shown in Figure 9.

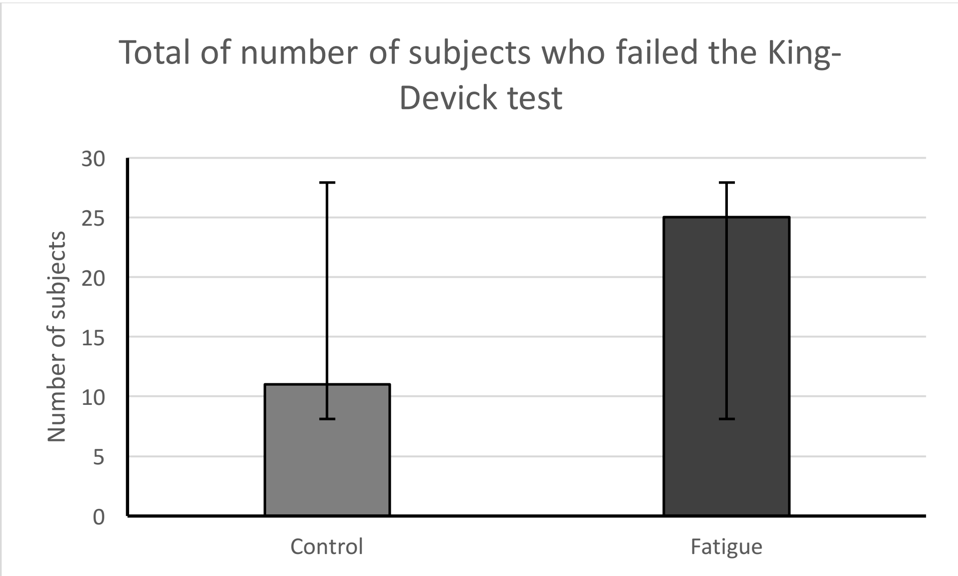

Figure 9: Total of number of subjects who failed the King-Devick test.

Whereas no subject from the control group had a reassessment time that was 3 or more seconds slower than their baseline time, five subjects (7.1%) in the fatigue group worsened their score by 3 or more seconds at reassessment (Z= -2.269, p = .023,) (see Table 4).

Table 4: Failed King-Devick test

	Subjects failed K-D test - Control	Subjects failed K-D test - Fatigue	p-value
Total	10 (14.3%)	22 (31.4%)	0.016*
>3 sec worsening	0	5 (7.1%)	0.023*

K-D: King-Devick. *p < .05

3.3 Gender, age and education

No significant differences were noted between male and female participants across groups at either baseline or reassessment as reported in Table 5. Baseline and reassessment times were compared across level of education to determine if that variable had a significant influence on scores. There was no significant effect of education on performance on the King-Devick test at baseline [F (2,137) = 2.726, p = .069]. On the other hand, there was a significant effect of education on performance at reassessment [F (2,137) = 3.970, p = .021]. The high school participants scored an average of 39.53 ± 7.44 seconds at reassessment. The participants who completed a bachelor achieved an average score of 36.60 ± 5.94 seconds and the participants who completed a master achieved an average score of 35.77 ± 6.48 seconds.

Table 5: Gender differences

	Female (54) Time (s)	Male (86) Time (s)	t-value	Df	P-value
Baseline	40.22 (6.31)	39.16 (6.83)	0.914	138	0.362
Reassessment	38.20 (6.21)	37.40 (7.24)	0.664	138	0.508

The effect of age on performance on the King-Devick test at baseline was also examined. The median age was 29 years, therefore whether there was any significant difference between participants under the age of 30 (71 subjects) and over the age of 30 (69 subjects) was evaluated. No significant difference was found between the two groups. In addition, any difference between subjects younger and older than the age of 40 (104 and 36 participants respectively) was assessed, in accord with the analysis conducted by Galetta et al., (2016). Even though the average time at baseline was slower in the over 40 years of age participants (40.66 ± 5.98 seconds) compared to the younger participants (39.20 ± 6.84 seconds), no significant differences between the groups were found (t = -1.142, df = 138, p = .255) (see Figure 10).

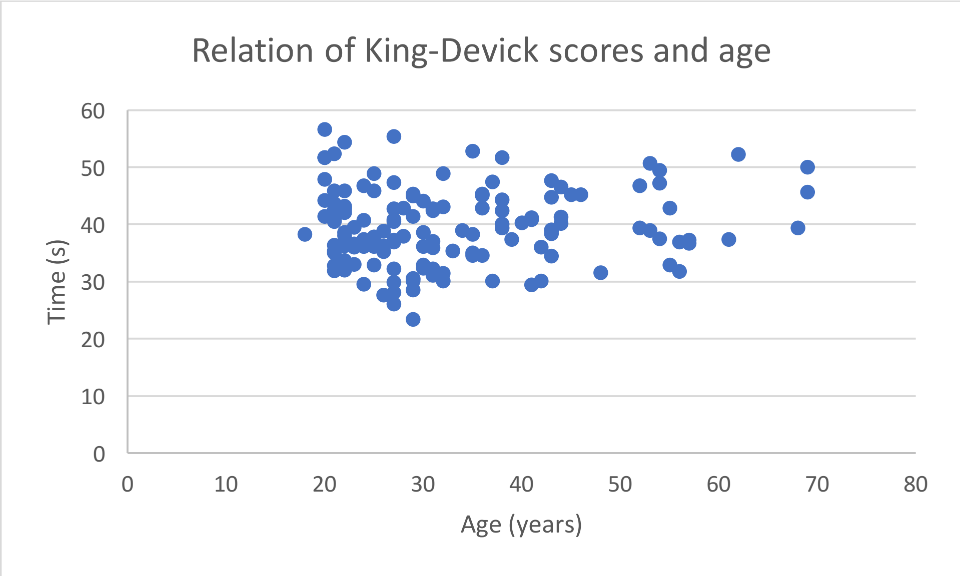

Figure 10: Relation of King-Devick and age

3.4 Learning effects

Finally, the learning effect was calculated by comparing test one with test two performed at baseline and also comparing test one with test two performed at reassessment. Therefore, each group was assessed to analyze possible significant differences between test 1 and 2 baseline. It was noted that in the fatigue group, the second test done at baseline ($t = 2.216$, $df = 69$, $p = .030$) and reassessment ($t = 2.975$, $df = 69$, $p = .004$) was on average significantly quicker than the first test. In addition, the control group was significantly quicker ($t = 3.944$, $df = 69$, $p < .001$) in test 2 at baseline test and significantly slower for test 2 at reassessment ($t = -2.093$, $df = 69$, $p = .04$) (see Table 6).

Table: 6: comparison between test 1 and test 2

	Time 1 (SD)	Time 2 (SD)	t-value	df	p-value
Test 1 and test 2 Baseline - Control	39.36 (8.99)	38.77 (7.36)	3.944	69	0.000***
Test 1 and test 2 Baseline - Fatigue	42.32 (5.98)	41.59 (6.39)	2.216	69	0.030*
Test 1 and test 2 Reassessment - Control	35.86 (6.91)	36.50 (7.14)	-2.093	69	0.04*
Test 1 and test 2 Reassessment - Fatigue	39.57 (6.31)	38.53 (5.81)	2.975	69	0.004**

*p<0.05, **p<0.005, ***p<0.001

As can be seen in Table 7, performance on the King-Devick test at reassessment was significantly faster than performance at baseline for both the control ($t = 8.904$, $p < .001$) and the fatigue group ($t = 3.462$, $p = .001$).

Table 7: Mean scores at Baseline and Reassessment across groups

	Baseline (SD)	ReAx (SD)	t-value	df	p-value
Control Group	38.37 (7.19)	35.86 (6.91)	8.904	69	0.000**
Fatigue Group	40.77 (5.84)	39.57 (6.31)	3.462	69	0.001**

ReAX: Reassessment; SD: Standard Deviation. **p<0.005

3.5 Additional comparisons

Table 8 reports the time taken to complete the King-Devick test at baseline and reassessment for both the fatigue and the control group. It was noted that the control group had a significantly quicker time compared to the fatigue group at baseline (t = -2.17, p = .032) and at reassessment (t = -3.32, p = .001) as shown in Figure 11.

Table 8: Comparison between control and fatigue groups

	Control (SD)	Fatigue (SD)	t-value	df	p-value
Baseline	38.37 (7.19)	40.77 (5.84)	-2.17	138	0.032*
Reassessment	35.85 (6.91)	39.57 (6.31)	-3.32	138	0.001**

SD: Standard Deviation. *p < .05, **p < .005

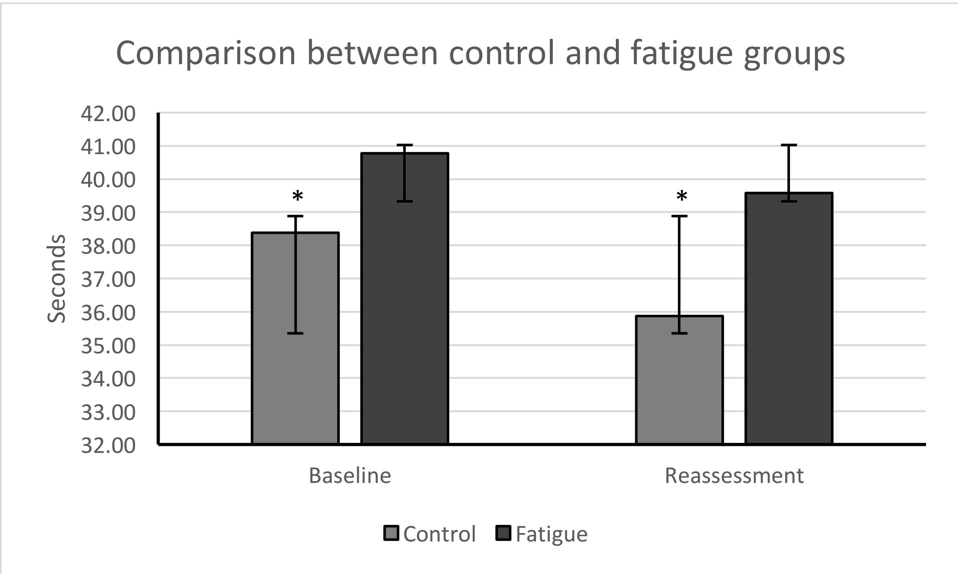

Fig 11: Comparison between control and fatigue groups. * p < .05,

No significant differences were revealed in the scores at baseline between the participants who wore glasses and those who did not (t = 1.092, df = 138, p = .277). In addition, whether there was a significant difference in completion times between subjects who usually wore glasses but did not during the study and those who wore glasses or did not have a prescription was evaluated. No significant differences were noted at baseline (t = -1.678, df = 138, p = .096), at reassessment (trial 1) (t = -1.508, df = 138, p = .134) or in the difference between baseline and reassessment (t = .286, df = 138, p = .776). No significant differences were found between the participants who sustained one or more head trauma and those who had not (t =1.719, df =138, p = .088). Individuals who had sustained at least one concussion in their lifetime had significantly quicker times compared to those who had not (t = 2.309, df = 138, p = .022) (see Figure 12).

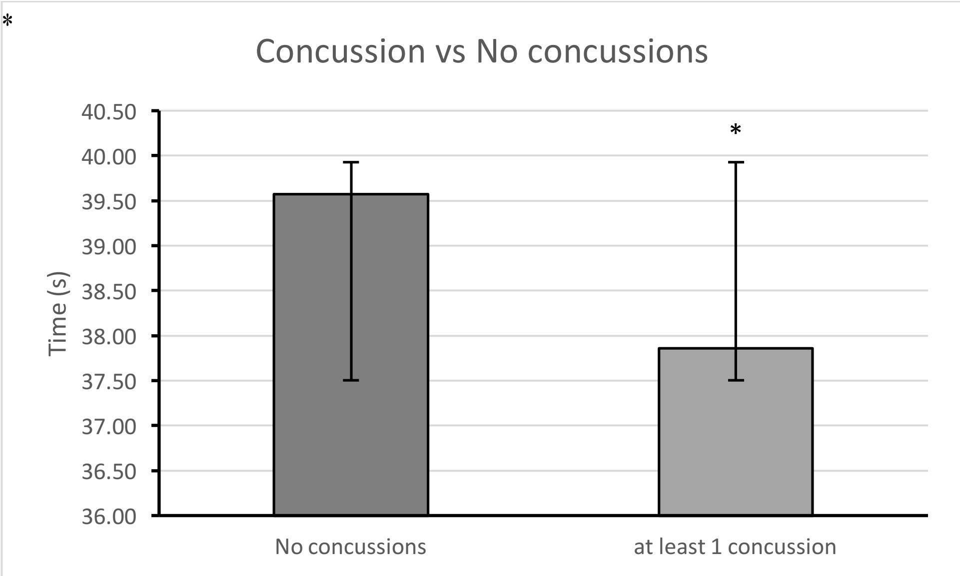

Figure 12: Baseline Concussion vs Non-concussion. *p<0.05

Additionally, whether there were any difference in the number of subjects classified as having failed the King-Devick test on the basis of their score on the first reassessment trial (following the King-Devick guidelines) and their fastest time across the two errorless reassessment trials was evaluated. When using the fastest reassessment time, the number of subjects who failed the test was significantly less for both the fatigue group (n = 12, p < .01) and the control group (n = 6, p = .025) than when the score at the first reassessment time was used. No analysis was post hoc.

Chapter 4

Discussion

4.1 Effects of fatigue on the King-Devick test

The results of the current study provided new evidence revealing how physical fatigue can affect performance on the King-Devick test. In keeping with hypothesis 1, the results revealed that although the average time of both the fatigue and the control groups improved at reassessment relative to baseline, that improvement was significantly greater for the control group than it was for the fatigue group. Whereas the scores of the control group improved, on average, by 2.52 seconds between baseline and reassessment, the scores of the fatigue group improved by only 1.2 seconds. The latter result was similar to that reported by Leong et al. (2015) where there was a significant improvement in the scores of a group of 25 participants following a two and a one-half hour sprint workout. Indeed, the subjects in that study scored 34.5 ± 4.8 seconds at baseline and 31.8 ± 4.9 seconds at reassessment post exercise. However, without the inclusion of a control group it is not possible to determine whether the test score improvement was due learning effects (King et al., 2013, Leong et al., 2015), a possible beneficial effects of physical activity on brain function (Weuve et al., 2004, Hancock and McNaughton, 1986) or even a detrimental effect of exercise on performance that would only become apparent when pre and post exercise scores were compared to the improvement demonstrated by a control group who did not engage in the same exercise. Galetta et al. (2011) tested 18 subjects post exercise. The subjects in that study improved their score by 3.6 seconds (median 38.6 seconds at baseline versus 35.0 seconds at reassessment) after two hours of scrimmage. Even in this instance, the absence of a control group means that the results do not necessarily indicate an improvement of the King-Devick test time that can be attributed to the effects of physical activity. Therefore, a definitive conclusion on the effects of physical activity on the King-Devick score in the absence of a control group cannot be reached. In the current study, there were no significant differences between the fatigue and control groups in relation to the age, education or gender of the participants. The inclusion of a control group enabled the separation of the effects of repeated practice on the one assessment protocol from the effects of physical fatigue. The inclusion of a control group enabled demonstration of lesser improvement at reassessment in the fatigue group compared to the control group and in turn, the negative effect of physical fatigue on performance on the King-Devick test.

In the literature review conducted by Galetta et al. (2016), figures were combined across studies and it was found that in a group of 92 athletes the King-Devick score improved on reassessment by an average of 1.4 seconds (95% CI: -2.1, -0.8) compared to the pre-season baseline. While improvements in scores have been attributed by Del Rossi et al. (2014) to mild practice effects, an important implication of the results of the current study is that following physical exercise at an intensity that subjects rate themselves as 7 to 9 RPE, scores on the King-Devick test will not improve to the same degree as is true of subjects who are not physically fatigued.

Consistent with the second hypothesis, 31.4% of the subjects from the fatigue group returned a slower time at reassessment than they did at baseline, whereas a change in that direction occurred in only 14.3% of the control group. Scoring a slower time at reassessment compared to baseline is considered a "failed" test and indicative of concussion (King et al., 2015). Thus, the results suggest that physical exercise to the point that subjects rate themselves as 7 out of 10 RPE for the first 12 minutes and 9 out of 10 for the final 3 minutes, will potentially confound the evaluation of SRC. To the best of the author's knowledge, this is a novel finding that has not been previously reported in the literature in relation to scores on the King-Devick test.

In keeping with the third hypothesis, nine subjects in the fatigue group (12.9%) committed an error at reassessment compared to only one subject (1.4%) in the control group. Committing an error at reassessment is also considered a "failed" test and indicative of concussion (King et al., 2015). Again, the results provide evidence that physical fatigue has the potential to complicate the assessment of SRC. Again, this represented a novel finding.

Therefore, when considering the total number of subjects who failed the King-Devick test at reassessment, 25 subjects (35.7%) from the fatigue group and 11 (15.7%) from the control group returned results that met criteria for the diagnosis of "concussed". Interestingly, even a significant minority of subjects in the control group scored a slower time on reassessment. The high rate of false positives in the control group differed from what has previously been reported in the literature (Galetta et al., 2016). Firstly, one subject from the control group committed a mistake at reassessment which, according to the criteria of the King-Devick test, would result in a classification of "concussed" which clearly was not the case. Secondly, 14.3% of the control group returned a result at reassessment that was slower than their baseline score, resulting in a classification of "concussed" according to the criteria of the King-Devick test. This resulted in a combined false positive rate of 15.7% which is unacceptably high. The specificity of the King-Devick was reported by Galetta et al. (2016) to be 90% (21 out of 202 controls worsened their score; 95% CI: 85%-93%). The current study had a significant lower specificity of 64% for the fatigue group and 84.3% for the control group. The latter figure could be explained by the possible negative effects of physical activity for the fatigue group.

Previous studies (King et al., 2012, King et al., 2013, King et al., 2015, Galetta et al., 2015) have recommended that an increase in time taken to complete the King-Devick test of 3 to 5 seconds at reassessment relative to baseline be considered to indicate test "failure". Therefore, the number subjects who slowed their time by three seconds or more on reassessment was assessed. In keeping with hypothesis four, a significantly greater number of subjects from the fatigue group (n = 5, 7.1%) worsened their score by 3 or more seconds on reassessment than did subjects from the control group (n = 0).

The results of the current study are inconsistent with those of previous research, which have been reported to indicate that fatigue does not negatively affect performance on the King-Devick test (Galetta et al., 2016). In addition to the failure of past research to include appropriate control groups, there are several other factors that may contribute to the disparities between the results of the current and previous studies. Firstly, previous studies have consistently included small subject numbers, which have ranged from 18 to 51 participants (Galetta et al., 2011, Dhawan et al., 2014, Leong et al., 2015) although in one paper the sample size was not specified (King et al., 2013). As reported by Faber and Fonseca (2014), a small sample size can skew the results and lead the researcher to assume as true a false premise as the study will not sufficient power to detect an effect. Secondly, in no previous study has the extent of the physical activity in which participants engage been quantified. For instance, Leong et al. 2015 reported that their sample engaged in a two and a half hour sprint workout without specifying the type of training in which participants were engaged. Galetta et al. (2011b) reassessed subjects after participating in two hours of scrimmage but the number of repetitions of the sequence of play was not specified. It is important to monitor the level and type of physical activity to know the intensity of the exercise prescribed and to have a standardized and reproducible protocol to utilize for future studies. In addition, in the current study, volunteers were tested between one and two minutes post exercise and therefore, the acute effects of exercises such as dyspnoea (Smoliga et al., 2016) and dehydration (Abd-Elfattah et al., 2015) could have potentially negatively affected the result. Although, this could be argued to have potentially negatively skewed the data, the author's goal was to test the subjects when physically fatigued to mimic a competition game scenario.

The results of the current study provide preliminary evidence to suggest that the King-Devick diagnostic criteria for concussion should be revised. As previously mentioned, the King-Devick criteria for a failed test are either any worsening (increased) time compared to the subject's baseline result or committing an error at reassessment. The author has found that an unacceptably high number of subjects from both the fatigue and the control group scored a higher time at reassessment compared to baseline (31.4% for the fatigue group and 14.3% for the reassessment group). However, none of the control group worsened their score by three seconds or more. Therefore, the results accord with the suggestion that an increase in scores of three or more seconds represents a more appropriate criteria to diagnose concussion. Secondly, the fatigue group failed the King-Devick test (by either scoring a higher reassessment time, or committing an error at reassessment) significantly more times than the control group. Therefore, the author suggests that baseline assessment for the King-Devick test should be performed after physical activity, to simulate "game day" scenario and preserve ecological validity.

4.2 Baseline measurements

In this study, the mean score for the control group was 38.37 seconds and in the fatigue group 40.77 seconds. This is faster that the figures previously reported (Galetta et al., 2016). Indeed, a systematic review by Galetta et al. (2016) found that the King-Devick average baseline score was 43.3 seconds. However, the systematic review showed that the baseline timing varied between 38.5 (Galetta et al., 2011b) and 62.0 seconds (King et al., 2015). The faster average times in the present sample compared to those previously reported in the literature could reflect the age range of the sample. The samples included in the studies by Munce et al. (2014), Duenas et al. (2014) and King et al. (2015) comprised high school athletes. Indeed, as previously mentioned by Galetta et al. (2016), subjects under the age of the 18 years had a significantly slower time compared to adults.

Baseline measurements were assessed to monitor if there were any significant differences between groups. It was found that the control group was significant faster at baseline and reassessment compared to the fatigue group. This the author aimed to compared the reassessment time with the baseline time for each group separately. Therefore, each subject acted as their own control. Thereafter, difference scores from one group were compared to those of the other one to assess if the there was any correlation or significant differences between the fatigue and the control group.

4.3 Gender

In keeping with hypothesis five, the results of the current study revealed no differences in performance on the King-Devick test at baseline between male and females. On the other hand, Covassin et al. (2009) reported that there were significant differences on baseline neuropsychological test performance using the ImPACT test, between males and females. Indeed, females performed significantly better than males on verbal memory scores ($p=0.001$), while males performed significantly better than females on baseline visual memory scores ($p=0.001$). No previous studies have examined gender difference for performance on the King-Devick test.

4.4 Education

In keeping with hypothesis five, the results of the current study revealed that results at baseline did not vary as a function of education. However, a significant effect of education was found at reassessment. Indeed, higher education was associated with faster reassessment times. This could be explained by fact that better educated people have faster processing speeds compared to the less educated ones (Tun and Lachman, 2008), which perhaps become increasingly evident as they become familiar with task requirements. To the best of the author's knowledge, no previous studies have explored the effect of education on scores on the King-Devick test.

4.5 Age

Additionally, baseline measurements were assessed and compared to determine whether performance on the King-Devick test was affected by age. In keeping with hypothesis five, the results of the study revealed no differences at baseline between subjects older and younger than

30 years of age. In addition, no significant differences were found between subjects older and younger than 40 years of age, as previously described by Galetta et. al. (2016).

Indeed, Galetta et al. (2016) found that in children up to the age of 18 years, baseline scores improved exponentially and it was also stated that subjects over the age of 40 had a slower time compared to their younger peers. Slower King-Devick test time in children and adolescents compared to adult can be explained by incomplete development of the brain in children and adolescents (Stiles and Jernigan, 2010) and the more efficient use of the brains as we mature (Brown et al., 2005).

The results from the Galetta et al. (2016) literature review were taken into consideration by the authors of this study when the inclusion and exclusion criteria were established. Indeed, no subjects under the age of 18 years was recruited for this study to reduce the possible negative affect (slower time) of age on the King-Devick test score.

4.6 Learning effects

The current study also assessed the effects of learning on the King-Devick test for both groups. In keeping with hypothesis six, it was found that on average, the second test at baseline was significantly faster compared to the first one. This is similar to what has been previously reported in the literature by Galetta et al. (2015), King et al. (2013) and Leong et al. (2015). Indeed, these authors have previously described the learning effect associated with repeated testing on the King-Devick test in non-concussed subjects as being 2.8 seconds (35.1 versus 37.9 seconds) in the study conducted by Galetta et al. (2015), 0.7 seconds (35.1 ± 5.2 s versus 34.4 ± 5.0 seconds) in the study conducted by Leong et al. (2015) and 2.7 seconds in the study conducted by King et al. (2013).

4.7 Revising Administrative Protocol

As opposed to the King-Devick test instructions, in this study the author adminstered two reassessment trials. In keeping with hypothesis seven, when comparing baseline measure with the best reassessment time, significantly fewer subjects failed the test in both the fatigue group (12 vs 25 subjects) and the control group (6 vs 11 subjects). Having the best of two trials at baseline and only one trail at reassessment may bias the results towards lower scores at reassessment. In terms of the diagnosis of concussion using the King-Devick test, it is therefore recommended that two trials be administered at reassessment and that the fastest reassessment time be compared to the fastest baseline time.

4.8 Strengths and Limitations

Some limitations of this study warrant consideration. Firstly, the study was conducted on a small sample. However, to date, this sample represents the largest group that has been used to assess the effects of fatigue on the King-Devick test and it is the only one in which performance of an experimental group has been compared to the results of a control group. Secondly, the participants were not randomly selected. However, the author included in the study two similar groups with comparable demographic characteristics to increase the statistical strength and yield more accurate measurement by reducing the number of variables that could have skewed the results. Thirdly, the author collected the data and timed the subjects. This could have created a subconscious bias when timing the test. Moreover, the participants could have scored a slower time on the first attempt post exercises because they were short of breath. However, the aim of the study was to test the subjects when they were physically fatigued, reproducing a possible "game-day" scenario. Therefore, the shortness of breath was an important part of preserving the ecological validity of the study.

A potential final limitation of the current study was the fact that it was conducted using a paper form version of the King-Devick test. The King-Devick test is now typically used digitally. The paper version of King-Devick test does not differ from the digital one in terms of the instructions or execution of the test and therefore, the use of the paper version should not have skewed the results. In addition, the authors believe that the use of the digital King-Devick test may reduce uptake of the test for several reasons. Firstly, not all the sports organizations, and particularly junior amateur clubs, can afford a portable electronic device such as an IPad. Secondly, the electronic version has a retail cost of $20 USD which again could be an extra unjustifiable expense for amateur or junior sports teams when other concussion assessments such as the SCAT5 are free of charge (McCrory et al., 2017). An additional limitation was that the level of fitness was not assessed. This could have potentially skewed the results because different level of fitness might have effected recoverability (Hunter, 2017).

One of the strengths of the current study was the inclusion of a control group with similar characteristics to the fatigue group. Indeed, previous studies (Galetta et al., 2011b, Dhawan et al., 2014, King et al., 2013, King et al., 2015), have studied the effects of fatigue on the King-Devick test, without including a control group.

An additional strength of this study was that each subject acted as their own control. Therefore, even though the control group had a significantly faster baseline time, using the participants as their own control meant that baseline differences between groups did not confound interpretation of the results.

Lastly, the authors recorded history of previous head trauma, concussions, other neurological history, medications, and the usual and test wearing of glasses, with a view to controlling for those variables if there were between group differences that would potentially skewed the results in a direction in keeping with any of the hypotheses. No other studies have attempted to exercise such stringent control. Thus, the present study included a level of control of variables that has been absent in any other studies that have been conducted to date.

4.9 Directions for future research

Future studies should aim to validate other concussion assessment tools such as the Scat5 and the AWPTAS immediately after inducing physical fatigue to simulate a game like scenario. In particular, it would be useful to use a similar methodology employed in the present study to examine the effects of physical fatigue on the AWPTAS, given the validity of that measure as reported by Hayter et al. (2017). Every athlete should have concussions baseline assessments both at rest and when physically fatigued to have a more accurate diagnostic tool. In addition, a longitudinal study on concussion assessment tests, such as the 10-word memory test, could assess if athletes decrease performance over time due to repetitive concussions, or if they improve because they are familiar with the test.

Furthermore, larger samples should be recruited when examining the effects of physical activity on the King-Devick test. Additionally, it would be informative to assess whether specific sport populations such as boxers and rugby players differ in performance on the test at baseline and at reassessment. It is possible that there are differences in processing speed times between individuals who practice specific sports. For instance, table tennis players who usually have good reaction times (Bhabhor et al., 2013) may have a faster King-Devick baseline score compared to boxers who frequently have a history of having sustained multiple concussive injuries. On the other hand, reassessment times can be used to determine whether learning effects differ between individuals practising different sports.

Lastly, the administration of other concussion diagnostic tests such as baseline balance assessment should be modified to replicate game like scenarios. For instance, the athletes should use football or rugby boots (with studs) while doing the tandem gait test and the standing balance test, which are both part of the Scat5 assessment (McCrory et al., 2017).

4.10 Conclusion

The diagnosis of concussion can be challenging, especially during sporting competitions when the decision regarding whether an athlete is fit to return to play has to be made quickly, and according to recent guidelines, within 10 minutes of presentation. It is therefore important to use reliable and valid diagnostic tools to ensure that the athletes' health is preserved. Accordingly, it is critical to verify the different variables that could potentially compromise the validity of these diagnostic tools. The present study showed different results compared to those that have previously been reported in the literature. Physical fatigue was found to negatively affect performance on the King-Devick test. Indeed, the subjects in the fatigue group "failed" the test significantly more frequently than did participants in a control group who had not engaged in physical exercise both in terms of returning a slower score at reassessment relative to baseline and committing an error while completing the task. A total of 25 subjects in the fatigue group met diagnostic criteria for concussion versus 11 subjects in the control group.

Similar to the results of previous studies evaluating the psychometric properties of tests such as the AWPTAS, SAC, ImPACT and BESS, the scores obtained by the control subjects included in the current study revealed that the King-Devick test has specificity limitations. Nevertheless, it is important to remember that concussions assessment and diagnosis are also based on clinical judgment. Currently, no single test has been identified as a "gold standard" and consequently used as a stand-alone assessment in the evaluation of concussion. Therefore, during concussion assessment it is important to use a multifaceted assessment battery.

The results of the current assessment provide preliminary evidence to suggest that the criteria to diagnose concussed athletes according to performance on the King-Devick test need to be revised. Specifically, it is suggested that test completion times at reassessment that are three or more seconds slower than performance at baseline be adopted as the new cut off considered suggestive of concussion. In addition, the author suggests that baseline assessment for the King-Devick test should be performed after physical activity, to achieve ecological validity. Lastly, the author suggests repeating the test at reassessment and comparing the fastest time across the two reassessment trials to the fastest baseline time to evaluate the presence of SRC.

It is concluded that the results of the present study emphasise the importance of evaluating the effects on physical fatigue on cognitive measures used to diagnose concussion. In addition, it is recommenced that future studies investigate the possibility of recording athletes' baseline test under conditions of fatigue. Revision of the administrative protocol for the King-Devick test also appears to be indicated.

Chapter 5

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