Brain Health in Retired Professional Rugby Union Players with a History of Concussion/Head Impact Exposure

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Declaration

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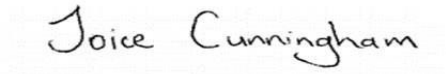

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Summary of Thesis

Rugby has one of the highest incidences of concussion among all full-contact sports. There has been a global increase in rugby participation, now estimated at over eight million people worldwide. With the introduction of professionalism in 1995, an increase in injuries at both amateur and professional level in northern hemisphere international rugby has coincided with increases in average body mass of rugby players by an estimated 25%. Hence, the modern game has larger, stronger players with greater body mass, experiencing larger impact forces, resulting in greater risk of head injury. Alongside increasing concussion incidence among professional rugby players in recent times due to greater awareness and higher rates of head injury reporting, the risks posed by repeated concussion have become a focus of scientific investigation and a major public health concern. Given the elevated risk of concussion in rugby, there is a need to investigate long-term brain health outcomes in this population. There is emerging evidence suggesting associations between concussion and/ or head impact exposure and potential long term neurological impairments and neurodegenerative diseases. In an effort to expand the limited evidence base in this field, the overall aim of this thesis was to explore the influence of a career of professional rugby on brain health in retirement.

In pursuing this aim, two systematic reviews of the existing literature and five original studies were completed. Systematic Review I – the first review of brain health in retired professional rugby players aimed to establish the evidence regarding long-term neurocognitive functioning and mental health status of living retired rugby players. Nine studies met the inclusion criteria; the available evidence suggested some preliminary evidence for decreased cognitive functioning and a high mental health burden among retired rugby players. However, cautious interpretation of findings was needed as methodological biases reduced the overall quality of studies and limited the conclusions that could be drawn. The heterogeneity of outcome measures, participant characteristics and self-reported methods were among the noted study limitations. This review suggested that large gaps remain in the understanding of the cause-and-effect relationships between playing rugby and long-term brain health in retired players.

Given the limited studies found pertaining to retired rugby players specifically in Systematic Review I, a broader scope of the literature was undertaken in Systematic Review 2. The specific aim of the review was to appraise and synthesise the literature on the long-term cognitive health status of retired athletes. Evidence of poorer cognitive health among retired athletes with a history of concussion and head-impact exposure was found to be mixed. The results indicated that retired athletes with a history of sports-related concussion had declined

cognitive performance in domains of memory, executive function and psychomotor function later in life. Retired athletes also appeared to have increased self-reported cognitive difficulties, but the paucity of high-quality, prospective studies limited the conclusions that could be drawn regarding cause-and-effect.

In light of the findings from Systematic Review 1 and 2, cross-sectional Study I was conducted to investigate the validity of self-reported concussion history among professional rugby union players. Following on from this, the large cross-sectional Studies 1I-V were conducted to explore (1) physical health (2) mental health (3) cognitive functioning and (4) multisensory processing among retired professional rugby players compared to retired professional rowers. Reliance on athlete self-reported concussion history is a limitation noted in the literature pertaining to long-term effects of concussion. A sample of 63 professional rugby union players were enrolled in Study I. Agreement between self-reported and clinically diagnosed concussions was found to be fair among the rugby players, with the average player under-reporting the number of clinically diagnosed concussions. Lifetime concussion history was found to be significantly negatively correlated with player self-report accuracy, with recall worsening as the number of lifetime concussions increased. However, the test re-test reliability of the Michigan TBI Identification Method was moderately strong. These findings suggest that there is a need for methodological improvements in concussion reporting and documentation among rugby players.

Ninety-five retired athletes took part in Studies II-V; including 67 retired professional rugby players and 28 retired international rowers. The prevalence of overweight and obesity was found to be higher among the retired rugby players compared to the retired rowers in Study II. Indications of higher visceral and body fat and hypertension were also revealed among the rugby cohort. Significantly higher levels of pain and disability and alcohol usage was found among retried rugby players compared to rowers. Lower levels of exercise was found to be associated with greater levels of pain and disability, indicating that past participation in professional rugby may result in greater levels of pain and functional limitations in retirement. Results from this study highlight modifiable factors such as overweight and obesity and hypertension in retired professional rugby players which are associated with long-term risk of negative health outcomes.

Study III found that the point prevalence of depression among rugby players was 28%, which was higher than the rowers and the general population. The rugby group were found to have a significantly greater sense of athletic identity when compared to the rowers. Concussion history estimates were not associated with mental health indicators. However, multiple regression analysis revealed decreased satisfaction with life, decreased resilience, greater

athletic identity and higher levels of pain and disability were significant predictors of depression among the rugby cohort. These factors were found to account for 67% of the variation in the chance of former rugby players having depression. Results demonstrated that the prevalence of mental health symptoms among former rugby players was 10% higher for alcohol misuse, 17% higher for depression, 13% higher for pain and disability and 20% higher for sleep disturbance compared to rowers. This study provides an insight into the estimate of mental health burden among retired professional rugby players. A combination of factors, including those which are unique to the elite athlete, alongside common stressors which affect the general population, make former professional rugby players an at-risk demographic for experiencing mental health issues. Interventions and strategies to prepare players for career transition may help to mitigate the risk of the occurrence of mental health symptoms and disorders in retirement. The association between the pain disability index and depression indicators suggests that interdisciplinary medical care and support for rugby players should be incorporated into the overall management of the transitioning player. Timely mental health diagnoses and management strategies, which are specific to this rugby population, are required.

In Study IV, the retired rugby players showed no reduction in performance on the CANTAB tests of neurocognitive functioning compared to retired rowers. Cluster-based analysis revealed no association between concussion history estimates and performance on CANTAB tests. Relative to rowers, rugby players performed significantly better in the domains and subdomains of attention and psychomotor speed and working memory assessed by the CANTAB, which revealed that the rugby players performed significantly better on tests of reaction time, motor speed, processing speed and visuospatial memory. Rugby players also performed significantly better than the general population on the same tasks based on normative data. Findings in the CANTAB tests of neurocognitive functioning revealed no overt negative impact of a concussion or years of exposure to rugby on performance.

The fifth and final study of this thesis was conceptualised in response to the findings of the systematic reviews and the need for subtle tests in relation to concussion markers. The insights gained were integrated into completing, for the first time, a novel assessment of multisensory integration among retired professional rugby players using a robust audio-visual illusion paradigm - the ‘Sound Induced Flash Illusion Task’. This task provided a means of assessing multisensory-integration, which may correlate with underlying concussive pathology and functional and structural cerebral disturbances. Compromised audio–visual integration or increased susceptibility to the sound induced flash illusion was found among former rugby players compared to the rowers. Concussion history estimates significantly predicted the odds of an accurate response suggesting that history of concussion

may have a deleterious effect on multisensory integration efficiency. Visual illusions induced by sound may represent a valuable tool to explore the effects of concussion on aging rugby players. However, associations between susceptibility to the sound induced flash illusion and implications of repetitive sports related concussion need to be further investigated using large-scale comparisons.

The current thesis employed comparisons across multiple measures and empirically validated measures of brain health and provides an insight into cognitive-perceptual measures and their applicability to future exploration of cognitive health and multisensory processing within retired professional rugby player cohorts. Healthy brain aging is known to be influenced by multiple factors both inert and environmental. The overall benefits of physical activity associated with sports participation are well established. However, in order to gain continued and optimal brain health benefits from exercise, it should be continued throughout the lifespan. Negative health-related factors and behaviours in retirement identified among rugby players in the current study, including; excessive alcohol usage, physical inactivity, sleep disturbance and pain and disability are known to adversely affect mental and cognitive health and increase the risk of neurodegeneration.

Rugby players are a unique cohort of individuals. The results from the current study suggest that transition from professional rugby may present difficulties for players, particularly due to issues surrounding identity, pain and satisfaction with post professional rugby life. The transitional implications of retiring from professional rugby on brain health need to be explored further. A transitioning program from professional rugby for example could help protect players from the potential adverse consequences of abrupt physical, social and lifestyle changes associated with retirement. A proactive approach to management and education with regard to long-term physical health, particularly musculoskeletal morbidity, within professional rugby is required. Issues such as pain and disability associated with the physicality of professional rugby need to be addressed. The game of rugby is becoming more physical and players are required to have a larger body mass. Therefore, body composition changes which occur in retirement should be viewed in the context of known cardiovascular risk profiles among the general population. The current cross-sectional exploratory research provides information regarding cognitive performance of retired elite rugby players in the early stages of retirement from competition across multiple neurocognitive and perceptual domains. However, long-term follow-up would be required to delineate any negative impacts of concussion in this cohort as they age. Cognitive reserve and resilience owing to the young age of players may have influenced the current results.

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List of Abbreviations

AIMS	Athletic Identity Measurement Scale
APOE e4	Apolipoprotein e4
AUDIT	The Alcohol Use Disorders Identification Test
BESS	Balance Error Scoring System
BMI	Body Mass Index
BSI-18	Brief Symptom Inventory-18
CANTAB	Cambridge Neuropsychological Test Battery
CDC	Centre for Disease Control and Prevention
CD-RISC 25	Connor-Davidson Resilience 25
CNS	Central Nervous System
CTE	Chronic Traumatic Encephalopathy
DAI	Diffuse Axonal Injury
DoD	Department of Defence
DTI	Diffusion Tensor Imaging
EMG	Electromyography
fMRI	functional Magnetic Resonance Imaging
GCS	Glasgow Coma Scale
GLTEQ	Godin Leisure-Time Exercise Questionnaire
HIA	Head Injury Assessment
ICD	International Classification of Diseases
ImPACT	Immediate Post-concussion Assessment and Cognitive Testing
IPAQ	International Physical Activity Questionnaire
IRFU	The Irish Rugby Football Union
K-D Test	King-Devick Test
LEC	Life Events Checklist
LOC	Loss of Consciousness
MCI	Mild Cognitive Impairment
MRI	Magnetic Resonance Imaging
MRS	Magnetic Resonance Spectroscopy
mTBI	mild Traumatic Brain Injury
NART	The National Adult Reading Test
NCAA	The National Collegiate Athletic Association

Neuro-QoL	Quality of Life in Neurological Disorders
NFL	National Football League
PCS	Post-Concussion Syndrome
PDI	Pain Disability Index
PHQ-9	Patient Health Questionnaire-9
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PRUQ	Professional Rugby Union Questionnaire
PSCS	Post-Concussion Symptom Checklist
PSQI	The Pittsburgh Sleep Quality Index
RBT	Repetitive Brain Trauma
RPAQ	Retired Professional Athlete Questionnaire
RPQ	Rivermead Post-Concussion Symptoms Questionnaire
RTP	Return to Play
SAC	Standardised Assessment of Concussion
SCAT-5	Sport Concussion Assessment Tool 5th Edition
SF–12	12-Item Short Form Health Survey
SIFI	Sound-Induced Flash Illusion
SIS	Second Impact Syndrome
SOA	Stimulus Onset Asynchrony
SRC	Sports-Related Concussion
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
TMS	Transcranial Magnetic Stimulation
WHO	World Health Organization

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Chapter 1 Introduction

1.1 Concussion

Concussion is becoming an increasingly significant public health concern, with estimated annual rates of 1 per 200 in individuals 12 years or older (Gordon and Kuhle, 2018). Despite the myriad of benefits attributed to sports participation (Eime et al., 2013, Andersen et al., 2018), engagement in contact or collision sports with high incidences of concussion may put certain athletes at risk of long-term sequelae. Research in the area of sports-related concussion is rapidly evolving. Despite this upsurge in concussion research, consensus statements and media coverage, there remains a lack of synthetisation of concussion literature, standardisation of medical care and many unanswered questions. This is largely due to lack of consensus on the definition of concussion, reliance on athletes to self-report their symptoms, varying study designs and surveillance systems and differing assessments and protocols used in diagnosis and management (Daneshvar et al., 2011, McCrea et al., 2004). The clinical presentation and symptomatology are often non-specific and may mimic other conditions which can frustrate accurate diagnosis and management further. A multidimensional approach to diagnosis and management is required given that concussion is a multi-dimensional injury.

1.2 What is a Concussion?

The ambiguity and controversy surrounding concussion is reflected in the absence of a universal agreement on the definition of concussion. The Centre for Disease Control and Prevention (CDC) and the World Health Organization (WHO) use the term mild traumatic brain injury (mTBI) interchangeably with concussion. The most up to date international consensus guidelines on sports-related concussion (SRC) define concussion ‘as a complex pathophysiological process affecting the brain, induced by traumatic biomechanical forces’

(McCrory et al., 2017). However, uncertainty persists around whether concussion is due to transient and reversible physiological changes, or whether it lies on the traumatic brain injury (TBI) spectrum associated with less structural changes than moderate TBI (McCrory et al., 2017). For the most part, it is regarded as self-limiting and at the less severe end of the brain injury spectrum (Harmon et al., 2019). While the majority of concussed individuals make a relatively quick recovery and return to baseline, some will suffer from persistent affective, somatic, physical or cognitive symptoms (Hiploylee et al., 2017, Rao et al., 2017). It is well established that no two concussions are the same (Oddo et al., 2019), therefore the same injury trajectory or outcome cannot be presumed. In addition to concussion itself, cumulative head impact exposure (i.e. impacts that are below the concussion threshold) may also result in neurological changes (Johnson et al., 2014). The cumulative effects of repetitive impacts have been demonstrated in mouse models, where repeated hits cause greater functional impairments than a single TBI and may potentially lead to more prolonged structural damage and increased risk of long-term neurodegeneration (Longhi et al., 2005, Prins et al., 2013b, Giza and Kutcher, 2014). The clinical signs and symptoms of concussion or the presence of persistent symptoms following concussion should not be explicable by drug, alcohol, medication use, other injuries (such as; cervical injuries or peripheral vestibular dysfunction) or other comorbidities (psychological or medical conditions) (McCrory et al., 2017).

1.3 Evolving Concepts of Concussion

Concussion is recognized as a unique clinical entity (Mullally, 2017). The earliest accounts of concussion derive from ancient literature. The term concussion was first coined approximately 2,400 years ago by Hippocrates and derives from the Latin ‘concussus’, meaning to ‘shake violently’ (Cantu, 2001). An early illustration of a concussed state is described in Homer's Iliad as a “weakness of the knees and clouded vision”, which rapidly subsides allowing return to battle (Wrightson, 2000). By the 13th century AD concussion was a distinct entity described as an abnormal physiologic state as opposed to a brain injury

(McCrory and Berkovic, 2002). During the 20th century concussive injury in boxers was recognised as a cause for concern (Critchley, 1957). Terms such as 'dementia pugilistica, traumatic encephalopathy and punch-drunk syndrome' refer to chronic brain damage and resultant neurological syndromes which have been described in case descriptions of boxers, dating back to the 1920's (Martland, 1928, Parker, 1934). Despite this research, the accepted aim of the sport remains inflicting injury on the opponent, therefore boxing remains a high-risk sport for neurological injury (McCrory, 2001).

Interest in concussion was reignited in contact sports at the turn of the 21st century. Concerns were largely fuelled by autopsy investigations of former professional American National Football League (NFL) players and post-mortem Chronic Traumatic Encephalopathy (CTE) findings. Chronic Traumatic Encephalopathy is a neurodegenerative disease thought to be associated with head trauma (Tharmaratnam et al., 2018). However, the incidence and exact cause remains unknown and the neuropathological and clinical findings related to CTE overlap with aging and many common neurodegenerative diseases (Maroon et al., 2015). Since this, concussion has become one of the most focal and contentious topics in the area of sports medicine. Further, in parallel to post-mortem CTE findings in NFL players, TBI became the signature injury of the wars in Iraq and Afghanistan, which prompted large scale investments from the United States (US) Department of Defence (DoD) towards researching this injury. While previously regarded as an innocuous transient short-lived impairment of neurologic function (McCrory et al., 2009), recent decades of research have sparked reconsideration of this assumption. The modern conception of concussion is a state of cerebral dysfunction, largely without overt signs of injury.

1.4 Epidemiology of Concussion

Gaining reliable incidence figures for SRC is a challenge. Variations in terminology (e.g. TBI, mTBI, concussion), methodological inconsistencies, varying reporting formats such as

injuries per exposure or per hours and under-reporting of symptoms by athletes remain obstacles in understanding the epidemiology of SRC. Traumatic Brain Injury is a major cause of mortality and disability worldwide, generating an estimated one million presentations to the emergency units per year in the European Union (EU) (Popescu et al., 2015). The most common TBI is an mTBI or concussion (Phillips and Woessner, 2015). According to the CDC, an estimated 1.6 to 3.8 million concussions occur in the US annually in sports and recreational activities alone and account for 5-9% of all sports-related injuries (Faul et al., 2010, Langlois et al., 2006, Tommasone and Valovich McLeod, 2006, Koh et al., 2003). These figures are likely underestimated since concussions continue to be underreported and underdiagnosed. The rate of SRC is increasing (Daneshvar et al., 2011), likely due to increased awareness, improvement in the detection of concussion and potentially heightened injury risk associated with contact sports due to increased strength and size of athletes (Kamins and Giza, 2016). Concussion can occur in many sports with the highest incidence reported in rugby, ice hockey and American football (Koh et al., 2003, Pfister et al., 2016). It has been hypothesised that the overall incidence of concussion in sport ranges from 0.1 to 21.5 per 1000 athletic exposures (Clay et al., 2013). It is estimated that between 2-15% of athletes participating in organised sports will suffer a concussion during one season (Harmon et al., 2019) [Table 1-1]. Further, concussions purportedly account for approximately 4–10% of all injuries sustained in The National Collegiate Athletic Association (NCAA) competition (Hootman et al., 2007).

The NCAA Injury Surveillance System (ISS) reported 4.2 concussion injuries per 1000 athletic exposures, with football game injury rates at 2.2 injuries per game for a team of 50 athletes (Guskiewicz et al., 2003). A concussion incidence rate of 0.24 per 1000 hours was found across a variety of high school sports (Lincoln et al., 2011). The authors found that American football accounted for more than half of all concussions, with the highest incidence rate of 0.60 per 1000 hours. Girls' soccer had the most concussions among girls' sports at a rate of 0.35 per 1000 hours. Giza et al. (2013) reported on concussion incidence in high

school and collegiate athletes and found that the highest incidence occurred in male college football with a rate 3.02 per 1000 hours. A more recent study by Baldwin et al. (2018) found concussion risk was greatest for boys in contact/collision sports like football, ice hockey, and lacrosse, and was more likely to occur in competition versus practice settings. The authors also demonstrated that girls had elevated concussion rates in gender-comparable sports. It has been largely accepted in the literature that sex and gender are important factors in concussion risk and recovery (Mollayeva et al., 2018). The evidence suggests that in sex-comparable sports, females have a 1.4 greater incidence of reported concussion than males (Covassin et al., 2016).

Table 1-1 Seasonal Risk of Concussion in Sports-adapted from Harmon et al. (2019).

Reference	Types of sports (Years)	Seasons (n)	Athletes (n)	Concussed athletes (n)	Concussed per athlete/ Season (%)
Football					
Barr and McCrea (2001)	High school and college football (1997–1999)	2	1313	50	1.9
McCrea (2001)	High school and college football (1998–1999)	2	1325	63	2.4
McCrea et al. (2002)	High school and college football (1999–2001)	3	2385	91	3.8
McCrea et al. (2005)	College football (1999–2001)	2	-	94	3.9
Barr et al. (2012)	High school and college football (2008–2009)	2	823	59	7.2
Seidman et al. (2015)	High school football (2013)	1	343	9	2.6
Dompier et al. (2015)	Football (2012–2013)	2	20’479	1178	5.8
	Youth football (2012–2013)	2	4092	136	3.3
	High school football (2012–2013)	2	11’957	767	6.4
	College football (2012–2013)	2	4430	275	6.7
	College football (2011–2014)	4	9718	518	5.3

Houck et al. (2016)	College football (2006–2015)	9	945*	118	12.5
Bretzin et al. (2018)	High school football (2015–2016)	1	39 520	1530	3.9
Total football			67 133	3192	4.8
All sports					
Galetta et al. (2011)	Football, sprint football, men's and women's soccer and basketball (2010–2011)	1	219	10	4.6
Marinides et al. (2015)	College athletes (2011–2012)	1	217	30	13.8
Galetta et al. (2015)	Ice hockey/ lacrosse youth and college	1	332	12	3.6
Leong et al. (2015)	Football, men's and women's basketball (2012–2013)	1	127	11	8.7
Putukian et al. (2015)	College athletes (2011–2012)	1	263	32	12.2
Chin et al. (2016)	High school and college athletes (2012–2014)	3	2018	166	2.7
Kerr et al. (2016b)	NCAA athletes (2011–2014)	4	32 156	1410	4.4
	Men's baseball (2011–2014)	4	1757	13	0.7
	Men's basketball (2011–2014)	4	1889	74	3.9
	College football (2011–2014)	4	9718	518	5.3
	Men's ice hockey (2011–2014)	4	3689	253	6.9
	Men's lacrosse 2011–2014	4	1768	44	2.5
	Men's soccer 2011–2014	4	1810	29	1.6
	Men's wrestling (2011–2014)	4	821	65	7.9
	Women's basketball 2011–2014)	4	1690	90	5.3
	Women's ice hockey 2011–2014	4	1301	94	7.2
	Women's lacrosse 2011–2014	4	1522	49	3.2
	Women's softball (2011–2014)	4	1569	38	2.4
	Women's soccer 2011–2014	4	2831	93	3.3

	Women's volleyball (2011–2014)	4	1791	50	2.8
Dhawan et al. (2017)	Youth hockey	1	141	20	14.2
Tsushima et al. (2018)	Athletes grades 8–12 (2013–2014)	1	10 334	1250	12.1
Bretzin et al. (2018)	High school athletes in 15 sports (2015–2016)	1	193 757	3352	1.7
Total			239 564	6293	2.6

*Total number of athletes estimated using 105 athletes per year on football roster.
NCAA: National Collegiate Athletic Association.

1.5 Pathophysiology of Concussion

An mTBI occurs when a mechanical force is transmitted to the head, neck, or other body part resulting in a complex pathophysiological process, referred to as the neurometabolic cascade of mTBI [Figure 1-1] (Giza and Hovda, 2001). The two main types of injury to the brain associated with TBI are focal and diffuse (McKee and Daneshvar, 2015). Diffuse injury and specifically diffuse axonal injury (DAI) is believed to be the main pathology underlying concussion (Giza and Hovda, 2014). The mechanical forces involved in a concussive impact result in linear and rotational acceleration/deceleration of the brain within the skull (Meaney and Smith, 2011). This causes strain and shearing of the brain tissue (Giza and Hovda, 2014). Such forces lead to a cascade of events within the brain that includes chemical changes, neuronal depolarization, metabolic derangements at the cellular level, and decreased blood flow (Choe, 2016, McKee and Daneshvar, 2015). Concussions are often referred to as an invisible injury, due to the absence of structural abnormalities on conventional neuroimaging modalities (Shenton et al., 2012).

Traumatic Brain Injuries are classified into two events; primary (the initial damage) and secondary (the damage that evolves as a result of the brain's response to the insult), which result in a set of well described acute and subacute pathophysiological changes within the

brain (Romeu-Mejia et al., 2019). The extent of damage varies across the spectrum of injury severity. Primary damage from a sudden impact may include tearing of brain tissue (axonal shearing) in mTBI. Secondary event encompasses the damage that evolves later due to the brain's biological responses following the primary injury (Prins et al., 2013a). The damage and stretching of neuronal tissue that occurs in concussion may be responsible for the clinical syndrome of concussion characterised by transient, yet sometimes persistent, alteration in brain function (McCrory et al., 2017). There has been much scientific endeavour to describe the post-concussive pathophysiology in order to explain the clinical presentation and characteristics of concussion. The perturbations to neuronal membranes and axonal stretching induces ionic channel dysfunction (Giza and Hovda, 2014). The mechanical opening of the voltage gated channels induces uncontrollable ionic flux, comprising of potassium efflux and sodium and calcium influx (Katayama et al., 1990, Takahashi et al., 1981, Nilsson et al., 1990, Astrup et al., 1980). This results in indiscriminate release of the neurotransmitter glutamate, which acts on the N-methyl-D-aspartate (NMDA) receptors causing depolarization of the post-synaptic neuron and a calcium influx. An attempt at restoration of homeostasis ensues, with adenosine triphosphate (ATP)-dependent pumps acting to re-create ionic homeostasis at a maximum capacity. This induces a state of 'hyperglycolysis', associated with the relative decrease of intra-cellular energy stores, and indicative of an energy crisis (Giza and Hovda, 2014). This results in metabolic instability, mitochondrial dysfunction, impaired cerebral glucose metabolism, diminished cerebral blood flow, cytoskeletal damage leading to axonal dysfunction and altered neurotransmission and neuroinflammatory changes (Giza and Hovda, 2014). A state of impaired metabolism can persist over the next 7-10 days due to altered glucose metabolism (Giza and Hovda, 2014), coinciding with the standard symptom resolution time frame (McCrory et al., 2017).

Well documented physiological perturbations such as the initial ionic flux and glutamate release, resulting in increased energy demands and metabolic crisis may now be linked to classic clinical symptoms of concussion such as migraines, cognitive impairment and

vulnerability to repeat concussion [Table 1-2] (Giza and Hovda, 2014). Scientific evidence based on animal models and advances in neuroimaging techniques will allow for non-invasive exploration of the pathophysiological underpinnings of post-concussion syndrome (PCS) and further understanding of the potential mechanisms underlying long-term impairment and neurodegeneration in humans. This has implications for return to play (RTP) protocols as recent evidence suggests that the physiological perturbations may extend beyond clinical recovery and may be responsible for long-term adverse consequences of concussion (Di Battista et al., 2018). A window of vulnerability has been described as a period of diminished brain capacity to sustain a second insult (Prins et al., 2013b). A single concussion is associated with behavioural dysfunction and subcellular alterations that may contribute to a transiently vulnerable state during which a second concussion within a short interval can lead to exacerbated and more prolonged axonal damage and greater behavioural dysfunction (Longhi et al., 2005). The window of risk is greater the shorter the interval between injuries. This can then precipitate 'Second Impact Syndrome' (SIS) (Cantu, 1998). SIS is described as when "an athlete who has sustained an initial head injury, most often a concussion, sustains a second before the symptoms associated with the first have resolved" (Cantu, 1998). However, whether SIS exists as a distinct clinical entity remains controversial due to its rarity (McCrory, 2001).

Table 1-2 Physiological Perturbations after Concussion and Proposed Clinical Correlates. Source directly taken from Giza and Hovda (2014) The new neurometabolic cascade of concussion. Neurosurgery, 75 Suppl 4**,** S24-S33.

Post-TBI pathophysiology	**Acute symptom/clinical correlate**
Ionic flux	Migraine headache, photophobia, phonophobia
Energy crisis	Vulnerability to second injury
Axonal injury	Impaired cognition, slowed processing, slowed reaction time

Impaired neurotransmission	Impaired cognition, slowed processing, slowed reaction time
Protease activation, altered cytoskeletal proteins, cell death	Chronic atrophy, development of persistent impairments

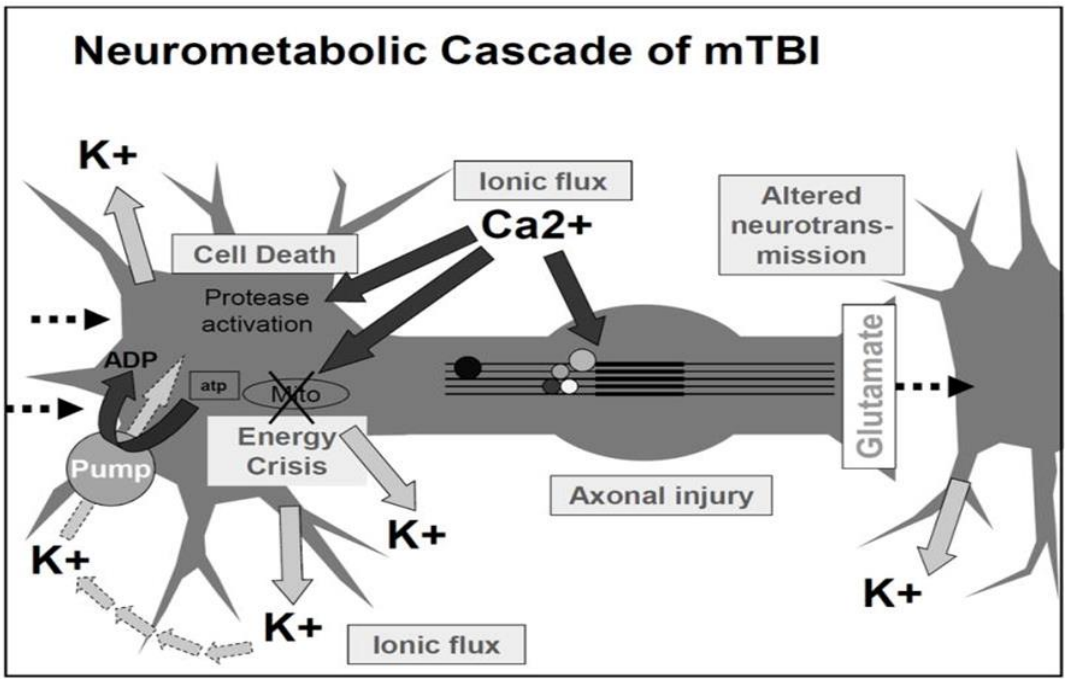

Figure 1-1 *The New Neurometabolic Cascade of mTBI: Diagram of the acute cellular biological processes occurring after concussion/mild TBI. Source directly taken from Giza and Hovda (2014) The new neurometabolic cascade of concussion. Neurosurgery, 75 Suppl 4, S24-S33.*

1.6 Risk Factors for Concussion

Identifying the characteristics that increase concussion risk is essential for prevention and management. Various demographic and medical history factors are associated with increased concussion risk. Predisposing factors for concussion are often stratified into high, moderate and low risk [Table 1-3] (Abrahams et al., 2014). Certain factors (e.g. sex and previous concussion) are consistently associated with increased concussion risk [Table 1-4] (McCrory et al., 2017, Van Pelt et al., 2019). A history of concussion has been associated with a 2–5.8

times higher risk of sustaining another concussion and may result in more self-reported symptoms at baseline than those without a history of concussion (Harmon et al., 2013a). Recent data suggest that in sex-comparable sports, females have a greater incidence of reported concussion than their male counterparts (Baldwin et al., 2018). In addition, female athletes report a higher number and severity of symptoms as well as a longer duration of recovery than male athletes in several studies (Harmon et al., 2013a). There are many proposed explanations for this dichotomy, including; greater willingness to report symptoms among females, hormonal differences, differential cerebral blood flow, neuroanatomy, neck muscle strength and decreased head–neck segment mass contributing to greater angular acceleration of the head after a concussive impact (Mollayeva et al., 2018, Covassin et al., 2016). Certain sports, such as football have a greater risk of concussion. Position and style of play also affect the risk of concussion (Dai et al., 2018) Studies on the association between concussions and genetic polymorphisms such as apolipoprotein e4 (APOE e4) are limited by small sample sizes and a lack of control groups (Panenka et al., 2017). However, presence of the e4 allele of the APOE gene in athletes has been associated with greater reported symptomatology post-concussion (Merritt and Arnett, 2016). Factors such as pre-existing mood disorders, migraine headache, learning disabilities and attention deficit hyperactivity disorder (ADHD) may be risk factors for concussion and may be associated with a prolonged recovery (Harmon et al., 2013a). A recent study from the CARE consortium found that medical history of headaches in the past 3 months, and Brief Symptom Inventory-18 (BSI-18) somatization symptoms increased overall concussion risk (Van Pelt et al., 2019).

Table 1-3 Risk Factors for Concussion- adapted from Abrahams et al. (2014).

High	Match vs practice, previous concussion
Low	Sex, age, genetics, behaviour, match period, mechanisms of injury, playing position, playing level, protective equipment, body checking, environment, anthropometry, fitness, weather season, performance, preseason symptoms, exposure, injury location, disability

Table 1-4 Proposed Concussion Risk Factors – adapted from Finnoff et al. (2011).

Predisposed to Concussion	**Prognosticate Poor Outcome**	**Increase Risk of Catastrophic Injury**
Female gender	Female gender	Young age (<18 years old)
Fatigue	Prior concussion	Recent history of concussion
Prior concussion	Pre-concussion anxiety or depression	Still symptomatic from concussion
Genetic polymorphism	Pre-concussion learning disorder	
	Pre-concussion migraines	
	Post traumatic amnesia	
	Younger athlete (high school > college > professional athletes)	
	Excessive post injury exercise	

1.7 Acute effects of Concussion

1.7.1 Clinical Presentation of Concussion

Concussion results in a host of clinical symptoms that may or may not involve loss of consciousness (McCrory et al., 2017). It is estimated that approximately 90% of concussions in sport occur without loss of consciousness (McCrory et al., 2009). Given the non-specific nature of acute signs and symptoms, detection can be difficult and hence concussions are underdiagnosed (Gardner et al., 2014b). Symptoms of concussion can overlap with other disorders such as sleep disturbances, depression and ADHD. Therefore, it is important to determine whether these symptoms were present prior to the injury or if they are as a result of a concussive episode (Harmon et al., 2013a). The signs and symptoms of an mTBI are often heterogeneous in nature and may appear immediately after the injury or may evolve after several minutes, hours or even days following the trauma (McCrory et al., 2013). The acute signs and symptoms of concussion vary widely and have been well documented in the literature (McCrea et al., 2003). Severity of concussion can range from mild to severe along a clinical and pathological continuum depending upon the patient's symptoms, which can be mild such as a headache or brief change in mental state or very severe with periods of unconsciousness, coma, or death. These symptoms generally fall into four distinct categories: physical (somatic), sleep, cognitive, and emotional (Harmon et al., 2013a) [Table 1-5].

Headache has been cited as the most common presenting symptom, followed by fatigue and dizziness (McCrory et al., 2013). Concussion can have large adverse effects on cognitive functioning and balance in the first 24- hours following injury (McCrea et al., 2003), with deficits still noticeable in postural control and neurocognitive functioning 14- days post-concussion (Broglio and Puetz, 2008). For most injured athletes, cognitive deficits, balance and symptoms improve rapidly during the first two weeks after injury without complication (McCrory et al., 2017). Eighty to ninety percent of athletes have symptom resolution by 7-days following their injury, and only a small percentage have symptoms lasting from weeks

to months (McKeon et al., 2013). However, symptom resolution may not always indicate a complete cognitive recovery as persistent deficits may be present (Makdissi et al., 2010). The time for resolution of symptoms is expected to be longer for children and adolescents (McCrory et al., 2017). Persistent symptoms are defined as failure of normal clinical recovery and symptoms that persist beyond the expected timeframe (McCrory et al., 2017). Headaches lasting longer than 60- hours, three or more symptoms at initial presentation, and the presence of fatigue/tiredness/fogginess have been associated with a longer recovery (Dhawan et al., 2017).

Table 1-5 List of Common Symptoms of mild Traumatic Brain Injury-as organized by category-adapted from Harmon et al. (2013a).

Physical/Somatic	**Affective**	**Cognitive**	**Sleep Dysregulation**
Headache	Mood disruption	Confusion	Drowsiness
Nausea	Irritability	Difficulty concentrating	Fatigue
Vomiting	Emotional lability	Memory deficits	Hypersomnia
Balance problems	Sadness/Depression	Feeling mentally 'foggy'	
Dizziness	Anxiety	Feeling slowed down	Hyposomnia
Decreased playing ability	Inappropriate affect	Slow reaction times	Difficulty falling asleep
Visual disturbances	Emotional outbursts	Cognitive fatigue	
Photophobia	Spontaneous crying	Memory deficits	
Phonophobia	Panic	Loss of focus	
Loss of balance		Difficulty multitasking or completing mental tasks	
Poor coordination		Forgetful of recent information and conversations	
Numbness/Tingling		Repeating questions	
Dazed		Answering questions slowly	
Stunned		Confused about recent events	

1.8 Diagnosis of Concussion

The diagnosis of concussion is clinical, involving careful synthetisation of history, signs and symptoms, physical exam and a battery of tests carried out by a skilled medical professional. It is important to monitor an athlete who has sustained an identified traumatic blow to the head, as symptoms may be delayed in onset as the concussion evolves. Therefore, the concussion may be unrecognised initially. The variety of assessment tools for SRC makes standardisation of concussion assessment challenging (Ma et al., 2012). Consequently, there may be an increased risk for long-term neurological deficits if athletes return to play prematurely due to an undetected mTBI. There are several common features that are used clinically to define the nature of a head injury. Universally, emphasis is placed on four primary diagnostic criteria's for TBI: level of consciousness, post-traumatic amnesia, mental status, and neurological signs (Bodin, 2012). If a sports concussion is suspected, the athlete should be immediately removed from play and a head injury assessment (HIA) ensued. First aid issues should be attended to swiftly including standard medical procedures involving assessment for adequate circulation, an open airway and no cervical spine involvement (McCrory et al., 2017). If there are significant concerns, including presence of red flags which may be indicative of a moderate or severe TBI [Table 1-6], urgent activation of emergency procedures is necessary.

Since an mTBI primarily reflects a transient disturbance in brain functioning, it is not typically associated with structural injuries. Hence, conventional neuroimaging techniques are not routinely recommended (McCrory et al., 2017, Bigler, 2018). However, imaging is important to detect significant pathologies such as intracranial haemorrhage, haematomas, contusions, fractures or other acute neurosurgical emergencies if suspected, or in cases of prolonged symptoms (Harmon et al., 2019). In the absence of red flags, the health professional proceeds with a multimodal approach to diagnose an mTBI; including, signs and symptoms, neurological examination, patient history, and clinical assessment scales [Figure

1-2]. A multitude of assessment tools are available to evaluate a suspected concussion and should be conducted in a standardised fashion. Sideline assessments such as the Sport Concussion Assessment Tool 5th Edition (SCAT-5), the King-Devick (K-D) test, the HIA and the Standardised Assessment of Concussion (SAC) are commonly used. Balance and neuropsychological assessments are a routine part of clinic assessment and monitoring of concussion, common tests used include the Balance Error Scoring System (BESS) and the Immediate Post-concussion Assessment and Cognitive Testing (IMPACT) (Dessy et al., 2017, Guskiewicz et al., 2001).

The emergence of advanced neuroimaging techniques such as multimodal magnetic resonance imaging (MRI) technologies including diffusion tensor imaging (DTI), functional MRI (fMRI) and magnetic resonance spectroscopy (MRS) offer the opportunity to advance research into the neurophysiological effects of concussion (McCrea et al., 2017). Exploration of the role of fluid biomarkers such as blood, saliva and cerebrospinal fluid (CSF) as markers of injury and neurobiological recovery is being conducted. Meier et al. (2017) proposed that two biomarkers; ubiquitin carboxy-terminal hydrolase L1 (UCH-L1) and S100 calcium-binding protein, beta (S100B), offer clinical potential for blood-based biomarkers in the acute detection of concussion. A blood test of two blood biomarkers; glial fibrillary acidic protein (GFAP) and UCH-L1 has recently been Federal Drug Administration (FDA) approved as an indicator for evidence of brain bleeds and hence brain trauma (Bazarian et al., 2018). However, the clinical utility of such makers for concussion is yet to be demonstrated (Harmon et al., 2019).

Table 1-6 Red Flags-SCAT-5- adapted from Echemendia et al. (2017).

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

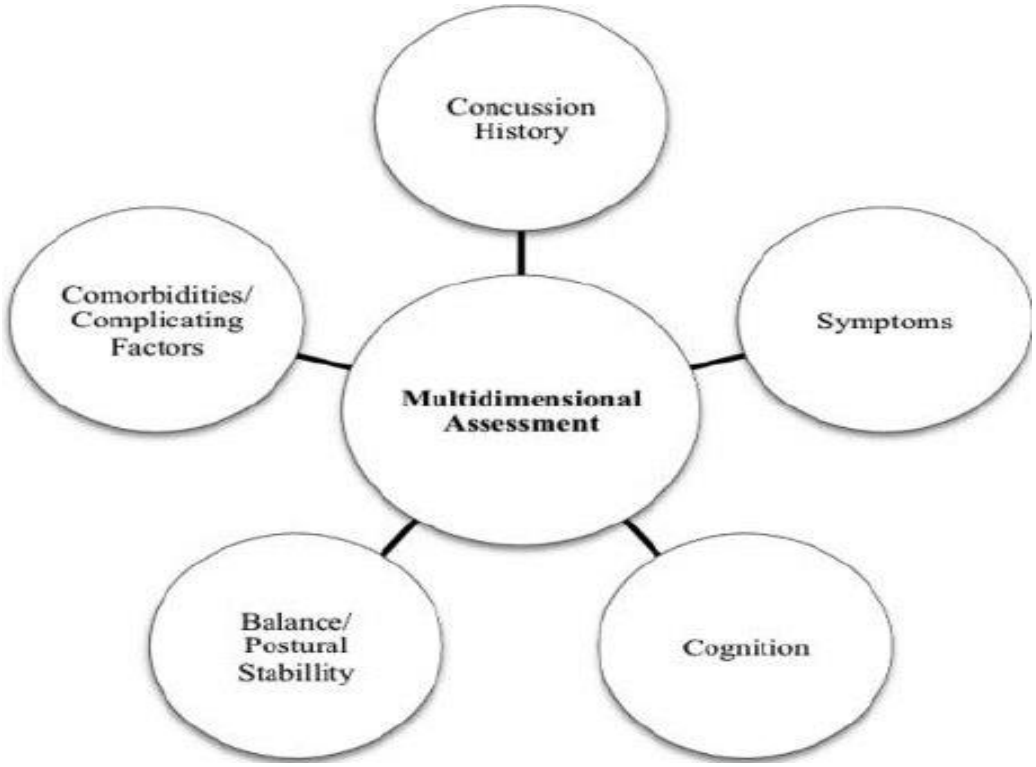

Figure 1-2 *Multidimensional Model of Concussion Assessment. Source taken from Echemendia et al. (2013) Advances in neuropsychological assessment of sport-related concussion. British Journal of Sports Medicine, 47, 294.*

1.9 Predicting Recovery from Concussion

Pre- and post-injury factors should be considered when predicting recovery from concussion [Figure 1-3] (Polinder et al., 2018). Iverson et al. (2017) reported the most consistent post-injury predictor of worse clinical outcome from concussion is the severity of the individual's acute and subacute symptoms, while a low level of acute symptoms is a favourable prognostic indicator. Subacute presence of symptoms including headache and depression may be risk factors for persistent symptoms lasting more than 1- month (Iverson et al., 2017). The evidence regarding specific injury severity characteristics such as loss of consciousness, retrograde amnesia, or post-traumatic amnesia, as predictors of recovery is inconsistent (Iverson et al., 2017). There is also inconsistent evidence regarding pre-injury factors such as history of learning difficulties or neurodevelopmental factors such as ADHD and concussion recovery (Iverson et al., 2017, Harmon et al., 2013a). Factors which strongly predict worse clinical recovery from concussion include previous concussion, younger age, female sex, genetic predisposition, pre-existing mental health or migraine disorder, and certain playing positions (Iverson et al., 2017). Youth athletes may have a more prolonged recovery and may be more susceptible to concussions accompanied by a catastrophic injury [Table 1-4]. This is hypothesised to be related to the physiological differences between younger and older brains (McCrory et al., 2004). The developing brain differs physiologically from the adult brain when comparing the brain water content, degree of myelination, blood volume, blood–brain barrier, cerebral metabolic rate of glucose, blood flow, number of synapses and geometry and elasticity of the skull's sutures (Guskiewicz and Valovich McLeod, 2011). Teenage years has been reported as the most vulnerable time period for having persistent symptoms, with greater risk for girls than boys (Iverson et al., 2017).

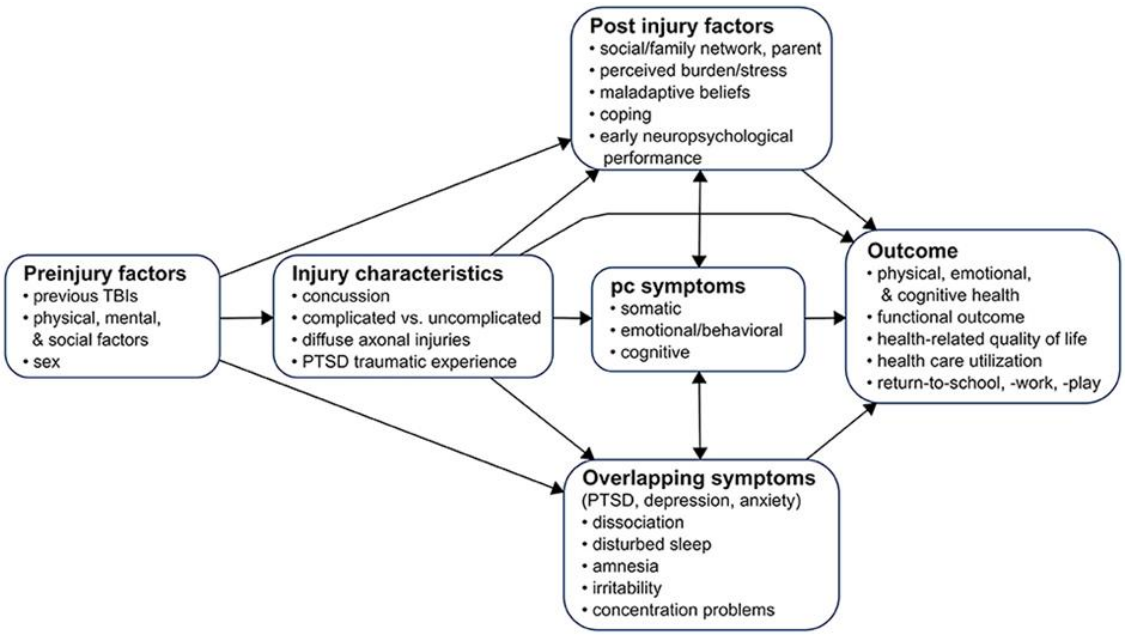

Figure 1-3 *A model for the study of Post-concussion Symptoms after mTBI. Source directly taken from Polinder et al. (2018) A Multidimensional Approach to Post-concussion Symptoms in Mild Traumatic Brain Injury. Frontiers in neurology, 9, 1113-1113.*

1.10 Risks Related to Concussion

There is increasing concerns surrounding the short- and long-term risks of concussion (McAllister and McCrea, 2017, Carman et al., 2015). A history of serious head injury i.e. moderate and severe TBI has been identified for many years as a risk factor for the development of neurodegenerative disease (Graham and Sharp, 2019). However, the long-term consequences of concussion, remain poorly understood. While the term 'mild' might appears to mitigate the seriousness of concussion, given the known catastrophic and often fatal outcome of moderate and severe TBI's (McKee and Daneshvar, 2015), along with the relationship between TBI and dementia (Mendez, 2017), there is grounds for further exploration into the fate of athletes who suffer a single or multiple concussive insults throughout the course of a sporting career. The evidence regarding potential risks of long-

term neurodegenerative changes associated with exposure to repetitive concussions is evolving (Mouzon et al., 2017).

1.10.1 Short-term Risks of Concussion

As noted previously, athletes who return to sports prior to a full recovery are at increased risk of repeat concussions (McCrea et al., 2009). Continuing to play immediately following a concussion is a risk for increased symptom burden, worsening of the injury and prolonged recovery (Asken et al., 2018, Asken et al., 2016a, Elbin et al., 2016a, Howell et al., 2018). Further, continued exposure after concussion may lead to dire consequences. Second Impact Syndrome is considered by some to be a potentially life-threatening complication of concussion (Harmon et al., 2019). However, this syndrome remains controversial due to its rarity. It is not yet fully understood and appears primarily limited to paediatric and adolescent athletes (Stovitz et al., 2017).

1.10.2 Long-term Risks of Concussion

Concussion has been thrust under the spotlight by increased media coverage surrounding long-term sequelae of head impacts in elite athletes. The literature on sports concussion has been largely dedicated to the advancement of RTP criteria in the immediate post-concussion phase (Giza et al., 2013). Given that a concussion is generally considered to be a non-critical, self-limiting condition and a full restoration of functioning generally occurs, the focus has only recently been reverted to the potential long-term repercussions of sports concussion. Short and intermediate term effects have been documented (Broglio and Puetz, 2008, Belanger et al., 2010, Karr et al., 2014). Epidemiology studies have described TBI as a robust environmental risk factor for the occurrence/early expression of neurodegenerative diseases in the general population (Graves et al., 1990, Guo et al., 2000, Lye and Shores, 2000, Plassman et al., 2000, Fleminger et al., 2003). Epidemiological research indicate that

experiencing a moderate or severe TBI in early or midlife is associated with between 2- and 4-fold increased risk of dementia in late life (Shively et al., 2012).

A growing body of literature suggests potential for long-term adverse brain health in certain athletes following a career in contact sports and exposure to head impacts including increase risk of neurodegenerative diseases such as; CTE, Alzheimer's dementia, Parkinson's disease, cognitive impairment and affective disorders such as; depression, decreased mental speed or memory dysfunction (Manley et al., 2017a, Abrahams et al., 2014). Additionally, there is evidence of later life cognitive deficits, neuroimaging abnormalities and altered brain metabolism in former contact sport athletes disproportionate to their age (Manley et al., 2017a, Mez et al., 2017, Stein et al., 2015). Further, studies suggest that multiple concussions may lead to long term sequelae such as depression and cognitive impairment (Manley et al., 2017a, McAllister and McCrea, 2017). However, many of these studies are limited by methodological bias and a retrospective nature. Uncertainty and inconsistency persist in the literature surrounding long-term neurobehavioral and neuropsychological consequences of recurrent concussions/head impact exposure (McCrory et al., 2017). The literature pertaining to the chronic effects of multiple concussions on brain health and neurocognitive functioning in relation to brain matter integrity and pathology in retired athletes is evolving.

1.10.2.1 Post-Concussion Syndrome

Optimal management of the concussed athlete includes identification of those at risk of developing PCS (McAllister and Arciniegas, 2002). Post-concussion syndrome is a complex pathophysiologic process which refers to a collection of somatic, cognitive, emotional, and/or behavioural problems, which persist beyond the expected concussion recovery time (Barlow, 2016). The symptoms of PCS are similar to common symptoms of concussion, however, rather than improving overtime, they persist or worsen (Kamins and Giza, 2016). There is evidence to suggest that 10–25% of mTBI patients may experience PCS, which can develop

into chronic PCS (Hiploylee et al., 2017, Ruff, 2011, Caplain et al., 2017, Cassidy et al., 2014). Post-concussion syndrome can be diagnosed according to the International Classification of Diseases (ICD)-10 or the Diagnostic and Statistical Manual of Mental Disorders (DSM)-5 criteria [Table 1-7] (Polinder et al., 2018). The DSM-5 defines PCS as concussive symptom persistence for more than 3- months, while the ICD-10 does not. DSM-5 also requires objective evidence of memory or attention deficit, but ICD-10 explicitly precludes such evidence. The biopsychosocial model is often applied to explain the onset and persistence of PCS (Silverberg and Iverson, 2011).

Table 1-7 Comparison of three definitions of Post-Concussion Symptoms. Source directly taken from Polinder et al. (2018) A Multidimensional Approach to Post-concussion Symptoms in Mild Traumatic Brain Injury. Frontiers in neurology, 9**,** 1113-1113.

	ICD-10	DSM-IV	DSM-5
Headache	√	√	–
Dizziness	√	√	–
Fatigue	√	√	–
Noise intolerance	√	√	–
Irritability/lability/anxiety/ depression	√	√	–
Sleep problems	√	√	–
Concentration problems	√[A]	√[B]	√[B]
Memory deficit	√[A]	√[B]	√[B]
Intolerance of alcohol	√	–	–
Preoccupation with symptoms	√	–	–
Personality change	–	√	–
Apathy	–	√	–
Perceptual-motor	–	–	√[B]
Social cognition	–	–	√[B]

Table shows symptoms presented in the International Classification of Diseases (ICD)-10 definition of PCS (diagnosis code F07.02), the Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV definition of postconcussional disorder and the DSM-V definition of neurocognitive disorder.
[A]Subjective report.
[B]Objective test.

1.10.2.2 Chronic Traumatic Encephalopathy

Chronic Traumatic Encephalopathy is a degenerative brain disease associated with repetitive head trauma most commonly found in military veterans or professional athletes (Stein et al., 2014). Chronic Traumatic Encephalopathy and other neurodegenerative diseases have been described in former athletes with a history of concussion or repetitive head impact exposure such as American football players and boxers (Corsellis et al., 1973, Tharmaratnam et al., 2018). There are pathological case-studies which suggest increased risk of developing neurodegenerative diseases such as CTE in athletes following a career in contact sports and exposure to head impacts (Martland, 1928, Omalu et al., 2005, McKee et al., 2009, Omalu et al., 2006, Gardner et al., 2014a). Chronic Traumatic Encephalopathy is considered a distinct tauopathy, typically accompanied by behavioural changes (McKee et al., 2013). Currently, CTE can only be confirmed post-mortem. It is also unknown if CTE is a progressive disease, and whether tau protein deposition is the cause of CTE, a by-product or marker of a disease (Stein et al., 2014). Incidence and prevalence of CTE in the general population and in former athletes with and without repetitive head impact exposure is unknown due to the neuropathological diagnosis (Gardner and Yaffe, 2015). CTE has a unique neuropathological signature comprised of accumulation of phosphorylated tau (p-tau) in sulci and peri-vascular regions, microgliosis, and astrocytosis (Fesharaki-Zadeh, 2019).

A cause-and-effect relationship has not yet been established between CTE and SRCs or exposure to contact sports and hence remains controversial (McCrory et al., 2017). As such, the suggestion that repeated concussion or sub-concussive impacts cause CTE remains unknown. Further, a cause and effect relationship between post-mortem CTE changes and antemortem behavioural and cognitive manifestations has not been demonstrated, and asymptomatic players have had confirmed CTE pathology at autopsy (Iverson et al., 2018, McKee et al., 2013). Ideally, well-designed case–control or cohort studies can begin to answer these important questions. The most widely cited risk factor to date is exposure to

multiple concussions/repetitive head impacts, however the required exposure is likely specific to the individual (Asken et al., 2017). There are also suggested factors that may influence the expression of CTE-associated symptoms such as duration of career, underlying genetic factors, or other lifestyle behaviours including alcohol, drug and anabolic steroid use, general health and psychiatric disease (Harmon et al., 2019). More research on CTE is needed to better understand the incidence and prevalence, the extent to which the neuropathological findings cause specific clinical symptoms, the extent to which the neuropathology is progressive, the clinical diagnostic criteria, and other risks or protective factors (Manley et al., 2017a). Particularly given that the neuropathological and clinical findings related to CTE overlap with aging and many common neurodegenerative diseases (Maroon et al., 2015).

1.10.2.3 Mental Health

There is evidence of associations between concussion and long-term mental illness such as depression (Kerr et al., 2014b, Guskiewicz et al., 2007). However, such studies are limited by poor methodological quality and recall bias. There is a growing body of research surrounding mechanisms behind increased risk of mental health problems following mTBI (Rice et al., 2018). Inflammatory pathways may contribute to the development of depression in some individuals (Miller and Raison, 2016). Therefore, long-term issues may arise due to chronic inflammation (Coughlin et al., 2017). However, mental health issues are common in the general population, independent of contact sports participation or head impact exposure. Lifetime prevalence of depression ranges from 20% to 25% in women and 7% to 12% in men (Guilbert, 2003, Wang et al., 2017). Given the multifactorial nature of mental health issues, longitudinal research on athletes with and without concussion exposure which addresses multiple variables is needed to understand the long-term risks associated with sport participation (Harmon et al., 2019).

1.10.2.4 Repetitive Head Impacts

Sub-concussive impacts have been defined as transfer of mechanical energy to the brain causing presumed axonal or neuronal injury in the absence of clinical signs or symptoms (Manley et al., 2017a). They are being increasingly investigated as an entity, which may result in increased long-term neurological sequelae (Lehman et al., 2016, Rubin et al., 2019) such as CTE (Belanger et al., 2016). However, the phenomenon of sub-concussion is poorly understood in terms of definition, characterization and prognosis (Mainwaring et al., 2018). Further, it is difficult to determine if an injury has occurred and the thresholds, which quantify an impact and identify an injury have not been agreed upon (Harmon et al., 2019). Therefore, the hypothesis that sub-concussive impacts may result in long-term neurological injury requires more research before conclusions can be drawn (Manley et al., 2017a).

1.11 The Athlete Brain

1.11.1 Exercise and the Brain

Regular physical activity results in a wide range of health benefits. Physical inactivity is a modifiable risk factor for cardiovascular disease and a widening variety of other chronic diseases (Warburton et al., 2006). Therefore, participation in sports has positive effects on health. Physical activity is a known modifier of brain activity, which influences cognitive functioning and brain health of athletes and those who perform high levels of exercise throughout the lifespan (Horder et al., 2018, Livingston et al., 2017). Significant anatomical and functional brain changes are brought about by acute and chronic exercise (Basso and Suzuki, 2017, Mandolesi et al., 2018). Aerobic exercise has effects on neurophysiology, neurochemistry and cortical excitability (Basso and Suzuki, 2017). The athlete brain may differ to that of a non-athletic control individual in cognitive faculties such as motor, spatial, reaction, perceptual and decision-making abilities due to kinematic patterns, goal orientated

precision, highly complex sporting skills requiring years of practice to gain precision (Yarrow et al., 2009). The further development of skills through training may correlate with structural changes in sensory and motor cortices and neural pathways (Yarrow et al., 2009, Ludyga et al., 2016, Makris, 2014).

1.11.2 Brain Health in Retired Professional Athletes

In spite of the potential benefits attributed to sports participation, as previously stated certain sports expose athletes to a risk of repetitive brain trauma (RBT). Repetitive brain trauma can occur in the form of concussive and/or sub-concussive impacts. Athletes who are involved in contact or collision sports are at the greatest risk of suffering a concussion, which may influence long-term brain physiology, function and structure in certain individuals. Contact sports such as American and Australian football, rugby, soccer, boxing, wrestling, basketball, field hockey and lacrosse are all associated with a relatively high prevalence of concussion (Koh et al., 2003, Baldwin et al., 2018, Giza et al., 2013). There has been significant academic and media focus on the issue of brain health in former professional athletes during the past decade. Recent research has raised controversy and concerns surrounding contact sports with high exposure to head contact (both concussive and sub-concussive impacts). Despite potential long-term neurological consequences of repetitive concussive injuries in contact sport athletes, few studies have investigated the status of living retired professional players at the levels of both brain structure and cognitive functioning.

Tremblay et al. (2013) reported that episodic memory and verbal fluency decline was correlated with neuroimaging findings such as abnormal enlargement of the lateral ventricles, cortical thinning in regions vulnerable to the aging process and various neurometabolic anomalies in former athletes with prior concussions. While Strain et al. (2015) reported prior concussion is a risk factor for increased hippocampal atrophy and the development of mild cognitive impairment among former NFL players. There is evidence of associations between

heading and abnormal brain structure and cognitive impairment among former soccer players (Rodrigues et al., 2016). Despite challenges, emerging imaging modalities represent new and evolving methods of investigating and characterising structural and functional brain alterations that may underpin neurocognitive deficits in retired athletes (Shenton et al., 2012, Eierud et al., 2014). The combined effect of exercise and mTBI on the cerebral cortex grey matter, white and subcortical structures requires further research, given that sport concussions take place in a context where structural/functional plasticity has occurred prior to (and likely after) the concussive event due to exercise (Tremblay et al., 2018). The beneficial effects of exercise on brain health acquired by the athlete may confound the deleterious effects of sports concussion (Tremblay et al., 2018). This is illustrated in the emerging evidence, suggesting that a more expedient return to aerobic exercise is associated with a quicker recovery post-concussion (Lawrence et al., 2018).

1.12 The Aging Brain of an Athlete

1.12.1 The Aging Brain

With age comes a decline in numerous physiological functions including reduced immune function, loss of muscle mass and strength, a decrease in bone mineral density and an increase in fat mass (Boss and Seegmiller, 1981, Nigam et al., 2012, JafariNasabian et al., 2017). Similarly, the natural process of aging results in changes in brain vasculature, size and cognitive function (Peters, 2006). This increases risk of cognitive impairment, dementia and cerebrovascular accident (CVA)(Lo Coco et al., 2016). When investigating brain health in the aging athlete, there are a myriad of factors which need careful consideration. Similar to the general population, equivalent factors are important to mitigate against the risk of cognitive decline in the aging athlete brain. Furthermore, increases in blood pressure and inflammatory load are known to occur in conjunction with the aging process, and are both independently linked to risk of dementia and cognitive decline (Buford, 2016, Singh and

Newman, 2011). There are also several mechanisms that support numerous cognitive processes (processing speed, memory and executive control processes such as inhibition, planning and working memory), which appear particularly sensitive to age-related changes such as, changes in the medial temporal lobe and prefrontal cortex (Singh-Manoux et al., 2012, D'Esposito et al., 2000, Salthouse, 1996, Kausler, 1994, Glisky, 2007). Decreases in neuronal plasticity, particularly of the cortex and hippocampus is attributed to increased susceptibility to learning and memory impairments (Burke and Barnes, 2006, Morrison and Baxter, 2012, Barrientos et al., 2015). Therefore, the brain is extremely vulnerable to the aging process and is constantly undergoing dynamic changes in the presence or absence of concussion.

1.12.2 Protective Factors against Cognitive Decline

Population-based studies demonstrate specific lifestyle factors that are protective against cognitive decline, Alzheimer's disease and dementia which change throughout the lifespan (Livingston et al., 2017) [Table 1-8]. Identified modifiable risk factors encompassing a combination of social, mental, and physical health include physical activity (Colcombe and Kramer, 2003, Beydoun et al., 2014, Fratiglioni et al., 2004); engagement in cognitively stimulating activity (Baumgart et al., 2015, Hughes et al., 2010), social engagement (Holt-Lunstad et al., 2010, Ellwardt et al., 2015), level of education and socioeconomic status (Clouston et al., 2012, Sattler et al., 2012); and cardiovascular risk factors (diabetes, obesity, smoking, and hypertension) (Baumgart et al., 2015, Tervo et al., 2004, Levine et al., 2019). These lifestyle factors may share common pathways and may converge within the major aetiological hypotheses for Alzheimer's disease and dementia (Fratiglioni et al., 2004). There are many documented non-modifiable risk factors for cognitive decline which include; higher age (Tervo et al., 2004), female sex (Sohn et al., 2018, Fratiglioni et al., 2000), a genetic predisposition (ApoE e4 allele) (Rawle et al., 2018), and a lower socio-economic status (Sattler et al., 2012).

Physical inactivity has been identified as one of the strongest modifiable independent risk factor, accounting for up to 12.7% of the risk of Alzheimer's disease (Norton et al., 2014, Barnes and Yaffe, 2011). This statistic is increasingly worrying given the growing worldwide obesity epidemic (Stein and Colditz, 2004). Livingston et al. (2017) estimated that approximately 35% of all dementia cases worldwide could be prevented by targeting nine modifiable risk factors, which are amenable to intervention. The nine identified risk factors included were early life education; midlife hypertension, obesity, hearing loss, old-age smoking, depression, physical inactivity, diabetes, and social isolation. This study also projected that over 3% of dementia cases could be prevented by increasing physical activity alone. Exercise plays a key central role across several of the brain mechanisms involved in preventing dementia including; reduced brain inflammation, vascular, neurotoxic and oxidative stress and increasing cognitive reserve [Figure 1-4] (Livingston et al., 2017). Given that athletes have performed high levels of exercise throughout their career, there may be a potential neuroprotective effect of a career in elite sport. However, it is established that a genetic predisposition and accumulation of exposure to risk factors can only be partially mitigated by modifiable protective factors such as increasing physical activity (Fratiglioni et al., 2004).

Table 1-8 Life-course Model of Contribution of Modifiable Risk Factors for Cognitive Decline; potentially modifiable factors 35%, potentially non-modifiable factors 65%- adapted from Livingston et al. (2017).

Early life	**%**	**Midlife**	**%**	**Later life**	**%**
ApoE E4	7	Hearing loss	9	Smoking	5
Less education	8	Hypertension	2	Depression	4
		Obesity	1	Physical activity	3
				Social isolation	2
				Diabetes	1

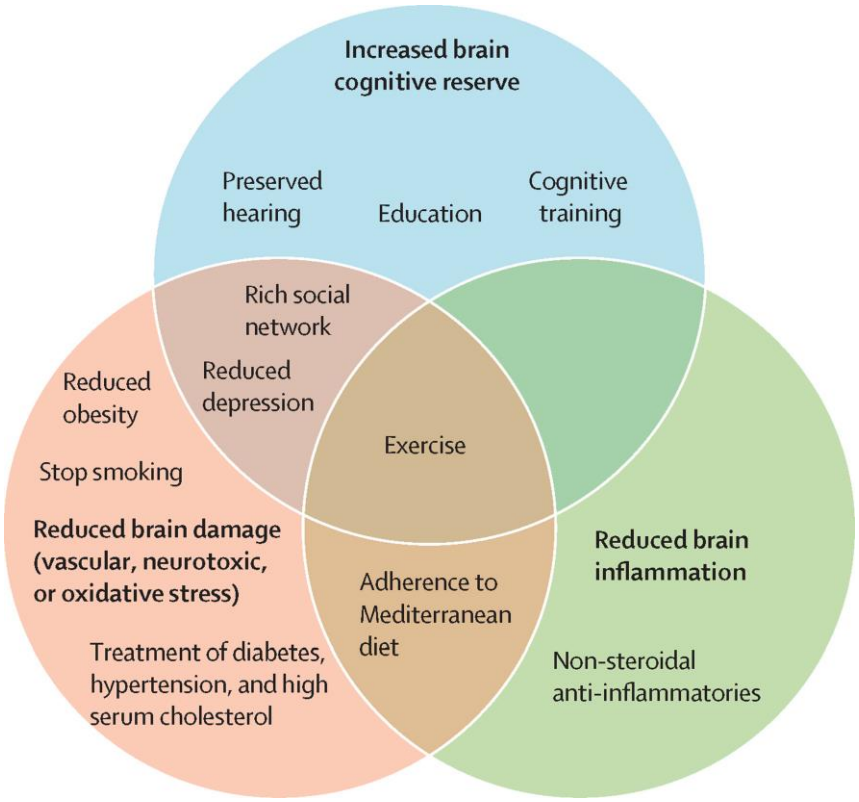

Figure 1-4 *Potential Brain Mechanisms for Preventive Strategies in Dementia. Source directly taken from Livingston et al. (2017) Dementia prevention, intervention, and care. Lancet, 390, 2673-2734.*

1.13 Rugby

Rugby is a popular full-contact sport played throughout the world by male and female players of all ages at varying levels of competition, including at professional level. Rugby is a field-based team game involving two sides of fifteen players (8 forwards, 7 backs). It consists of two forty-minute halves played on a rectangular field with H-shaped goal posts on each try line using an oval shaped ball. Rugby union is a dynamic contact sport, it requires players to perform a variety of open and closed skill activities in a game environment with few stops in play (Reid et al., 2013). A match involves intermittent high-intensity activities, such as sprinting, rucking, mauling, and scrummaging with recovery periods of low-intensity activity. The recovery periods involve not only standing but also include jogging and walking activities. Therefore, it is a physically demanding sport and requires highly developed abilities such as speed, agility, muscle power, maximal aerobic power, aerobic endurance, along with tactical and technical astuteness (Cunniffe et al., 2009, Reid et al., 2013).

Each position requires specific demands, skills, physical attributes and anthropometric profiles due to the specialized nature of the various roles. There has been an unprecedented growth in worldwide rugby participation, with 9.6 million men, women and children playing rugby worldwide. Rugby is particularly popular in Ireland. The Irish Rugby Football Union (IRFU) is the governing body for rugby union in Ireland. The IRFU is divided into five branches. The four main branches represent the four provinces of Ireland: Ulster, Munster, Leinster and Connacht. Each provincial branch organises the sport within its geographic area. The fifth branch is the Exiles Branch, including players living in England, Scotland and Wales who are qualified to represent Ireland through their ancestry. A recent Annual Report by the IRFU totalled the number of registered players at all levels in Ireland at 194,387, including those who play tag and social rugby.

1.13.1 Concussion in Rugby

Owing to the physical nature of the game, players are at risk for concussion. The incidence of concussion in rugby is high (Marshall and Spencer, 2001, King et al., 2014, Shuttleworth-Edwards et al., 2008). Rafferty et al. (2019) reported that on average, a professional rugby union player is more likely than not to sustain a concussion after 25- matches. The English Rugby Football Union (RFU) recently reported a rate of 15.8/1000 player-match-hours in 2015/2016 (RFU, 2017), which is higher than previous estimates of between 4 and 13.4 concussions per 1000 contact hours (Hollis et al., 2009, Hootman et al., 2007, Kemp et al., 2008, Gardner et al., 2014b). This is recognised as one of the highest rates of concussion of all full-contact sports (Gardner et al., 2014b). To date, there has been one case of CTE documented in a deceased former rugby player (Stewart et al., 2016). A review of rugby league concussive injuries found concussion to be much higher in match play than in training; the ball carrier appears to be statistically more likely to get injured than the tackling player, and injury rates are disproportionately high for illegal play (King et al., 2012). There is a lack of research into the long-term brain health of retired professional rugby players (Cunningham et al., 2018). The literature in this area to date will be discussed in detail in Chapter 2. Despite growing evidence regarding the long-term adverse effects of exposure to repetitive concussions among contact sport athletes, few studies have investigated the status of living retired professional rugby players. Large gaps persist in the research into the potential cause-and-effect relationships between concussions, repetitive head impact exposure and long-term brain health among former rugby players.

1.14 Current Gaps and Research Directions

One aspect of concussion research that has garnered much focus in recent times is the development of a diagnostic biomarker. A multitude of biomarker research is ongoing, including investigation into advanced neuroimaging techniques, electrophysiology, fluid

biomarkers and genetics, with the ultimate goal of enhancing clinical decision making and management of a concussed individual (Snyder and Giza, 2019). Another area of sports concussion that is gaining increasing attention is the issue of the long-term effects of concussion/repeated head impact exposure. It is well documented that individuals who suffer single or repeated concussive injuries may be at increased risk of experiencing prolonged and potentially debilitating symptoms or impairments (Manley et al., 2017a), therefore appropriate diagnosis and management of concussion is paramount to mitigate such undesirable sequalae (Kamins and Giza, 2016).

A growing body of research indicates a potential long lasting effect of concussion and increased risk of developing neurodegenerative diseases in a certain sub-sample of individuals (Gavett et al., 2010). The issue of neurodegenerative risk linked to head trauma has long been associated with boxing (McCrory, 2002). However, the potential at risk sporting populations have expanded to include wrestlers, American football players, rugby, soccer and hockey players. Development of neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, and CTE, as a result of participation in contact sports and repetitive head impacts is an ongoing concern (Wilson et al., 2017). A recent retrospective epidemiology study found that mortality from neurodegenerative disease was higher among former Scottish professional soccer players compared to matched controls (Mackay et al., 2019). While the neurocognitive consequences of contact sport participation are uncertain, the overall health benefits of exercise are well documented in the prevention of chronic physical and mental diseases (Celis-Morales et al., 2017, Rovio et al., 2005). Therefore, there is need for balanced reporting where there is uncertainty. However, above all where there is a potential risk of harm, it is best practice to err on the side of caution.

1.15 Summary

As discussed throughout this chapter, the evolving literature suggests that retired athletes who have been exposed to repetitive head impacts throughout a playing career such as professional rugby players may be at increased risk of negative brain health consequences in later life following retirement. However, the neurocognitive sequelae of participation in contact sports and specifically rugby remain uncertain. There has been relatively little research into the long-term health of former professional rugby players, therefore there is a lack clear evidence surrounding the potential long-term effects of concussion in professional rugby players. Different contact sports carry varying risks due to the different degrees of exposure, playing dynamics and rules. Therefore, are likely not directly generalizable to rugby players in terms of potential long-term adverse effects. There is also a lack of research into the potential benefits of being a former professional rugby player. It is known that exercise induces positive changes within the brain which may help reduce the risk of cognitive decline as we age. Furthermore, the overall health benefits of physical activity associated with elite sports in the prevention of chronic diseases and in the reduction in mortality have been established. There are also a number of factors discussed in this chapter which may influence brain health in the aging athlete similar to the general population which are often overlooked and warrant further investigation. The overarching aim of this thesis is to explore long-term brain health among retired professional rugby players and possible associations between concussion in rugby and brain health in retirement.

Chapter 2 The Influence of playing rugby on long-term brain health following retirement: a systematic review and narrative synthesis.

The material presented in this chapter has been disseminated in the following publication:

Cunningham J., Broglio S., and Wilson F. (2018). Influence of playing rugby on long-term brain health following retirement: a systematic review and narrative synthesis. BMJ open sport & exercise medicine. 4(1), e000356.

Please see Appendix A.1 for full manuscript.

2.1 Introduction

Rugby is a full-contact sport played throughout the world at varying levels of competition, including professional level. There are many benefits of engaging in sport, with consistent evidence supporting associations with cognitive vitality, neural functioning and decreased risk of cognitive decline (Szuhany et al., 2015, Roig et al., 2013, Smith et al., 2010, Bherer et al., 2013, Gajewski and Falkenstein, 2016, Prakash et al., 2015). However, the physically demanding nature of rugby exposes players to injury, particularly involving the tackle (Fuller, 2008, Fuller et al., 2010, Gardner et al., 2015), a central tenet of the game (Hume et al., 2017). The frequent engagement in high-velocity collisions and impacts during contact activities such as the tackle and scrum, which varies depending on position, commonly result in musculoskeletal system injuries (King et al., 2010) and place players at risk of head and neck injury (Brown et al., 2014, Gardner et al., 2014b). Given the physical nature of the sport, the incidence of concussion in rugby is high (King et al., 2014, Shuttleworth-Edwards et al., 2008), estimated between 4 and 21.5 concussions per 1000 contact hours (Gardner et al., 2014b, Hollis et al., 2009, Kemp et al., 2008, Hootman et al., 2007, Rafferty et al., 2019).

There is increasing international concern surrounding repetitive concussive injuries and potential development of long-term neurodegenerative disease. Concussion in sport has been a topic of much attention and controversy. There is emerging evidence that certain retired athletes with/without history of concussions may have long-term neurological or neurocognitive impairments (Manley et al., 2017a). Furthermore, a frequency–response relationship between concussions or head impact exposure and depression symptom reporting has been demonstrated among former American NFL players and former collegiate athletes (Manley et al., 2017a). Post-mortem investigations have also raised concerns regarding neurodegenerative diseases, namely CTE in former NFL players, as potential adverse long-term outcomes of exposure to head impacts and concussions in sport (Hay et al., 2016, Mez et al., 2017, McKee et al., 2009, Stern et al., 2013, McKee et al., 2013). Given that rugby has a higher concussion incidence than American football, the issue of neurodegenerative decline is of particular importance (Marshall and Spencer, 2001).

There is some evidence of worse neurocognitive performance associated with school-level participation in rugby. Adolescent male rugby players prospectively investigated have been found to have significantly lower neurocognitive performance over three years and poorer academic achievement over 6 years in comparison with non-contact sport controls (Alexander et al., 2015). To date, there has been one case of CTE documented in a deceased former rugby player (Stewart et al., 2016). However, a paucity of research currently exists exploring the cumulative effects of repeated concussive injuries in rugby. Information on the long-term brain health of living retired rugby players is limited. Considering the high levels of participation in rugby worldwide (McMillan et al., 2017), a formal objective investigation into the long-term cognitive status of retired rugby players is needed.

The specific aim of the review was to:

- Explore the literature examining long-term brain health in living retired rugby players.

2.2 Materials and Methods

This review was conducted according to *'Preferred Reporting Items for Systematic Reviews and Meta-Analyses*' (PRISMA) guidelines (Moher et al., 2009) (www.prisma-statement.org). The review strategy and methods of analysis were registered with PROSPERO, a registry of systematic reviews [Appendix B.1]. Registration is available at: https://www.crd.york.ac.uk/prospero/; registration number: CRD42017081586.

2.2.1 Eligibility Criteria

Details of eligibility criteria are detailed in Table 2-1. Retired rugby players were included in this study. Studies were required to include retired male or female rugby players administered at least one form of brain health measure as an outcome. Studies were excluded if they explored only active rugby players and/or case studies with five or fewer participants. The primary outcomes investigated were brain health measures including cognitive functioning, mental health and neuroimaging outcome measures. Secondary outcome variables included history of sports-related concussion (SRC)/mild traumatic brain injury (mTBI).

Table 2-1 Inclusion/Exclusion Criteria.

Inclusion Criteria	Exclusion Criteria
• Retired male or female rugby players • Administered at least one form of brain health measure as an outcome	• Active rugby players • Case studies with five or fewer participants

2.2.2 Search Strategy

A systematic literature search was undertaken using the electronic databases of MEDLINE/ PubMed, Embase, Cochrane Central Register of Controlled Trials, PyscINFO, CINAHL and Web of Science from their inception to January 2018. The different search terms were adapted for use with each database [Appendix B.2]. The search strategy keywords related to three components: (1) the participant (e.g., retired rugby player), (2) the primary outcome measure (e.g., cognitive functioning) and (3) secondary outcome (e.g., history of sports concussion). No search restrictions were imposed. The electronic database searching was supplemented by searching abstracts of the international conference on sports concussion consensus meetings (2001–2018) along with conducting grey literature searching and a hand search of the reference lists of included studies. Abstracts (n=3) were found, which were not available in full text in the published literature. In this instance the authors were contacted via email/Research Gate seeking access to the full text of relevant studies. The titles and abstracts of the retrieved studies were independently screened by the primary reviewer (Joice Cunningham: J.C) to identify studies that met the eligibility criteria. Following this initial screening, two reviewers (JC and Fiona Wilson: FW) independently assessed for eligibility the full texts of the selected studies. Any disagreements on inclusion of studies were resolved through discussion and consultation with a third reviewer (Steven Broglio: SB) to reach a consensus. Following this process of elimination, nine studies were included in this review.

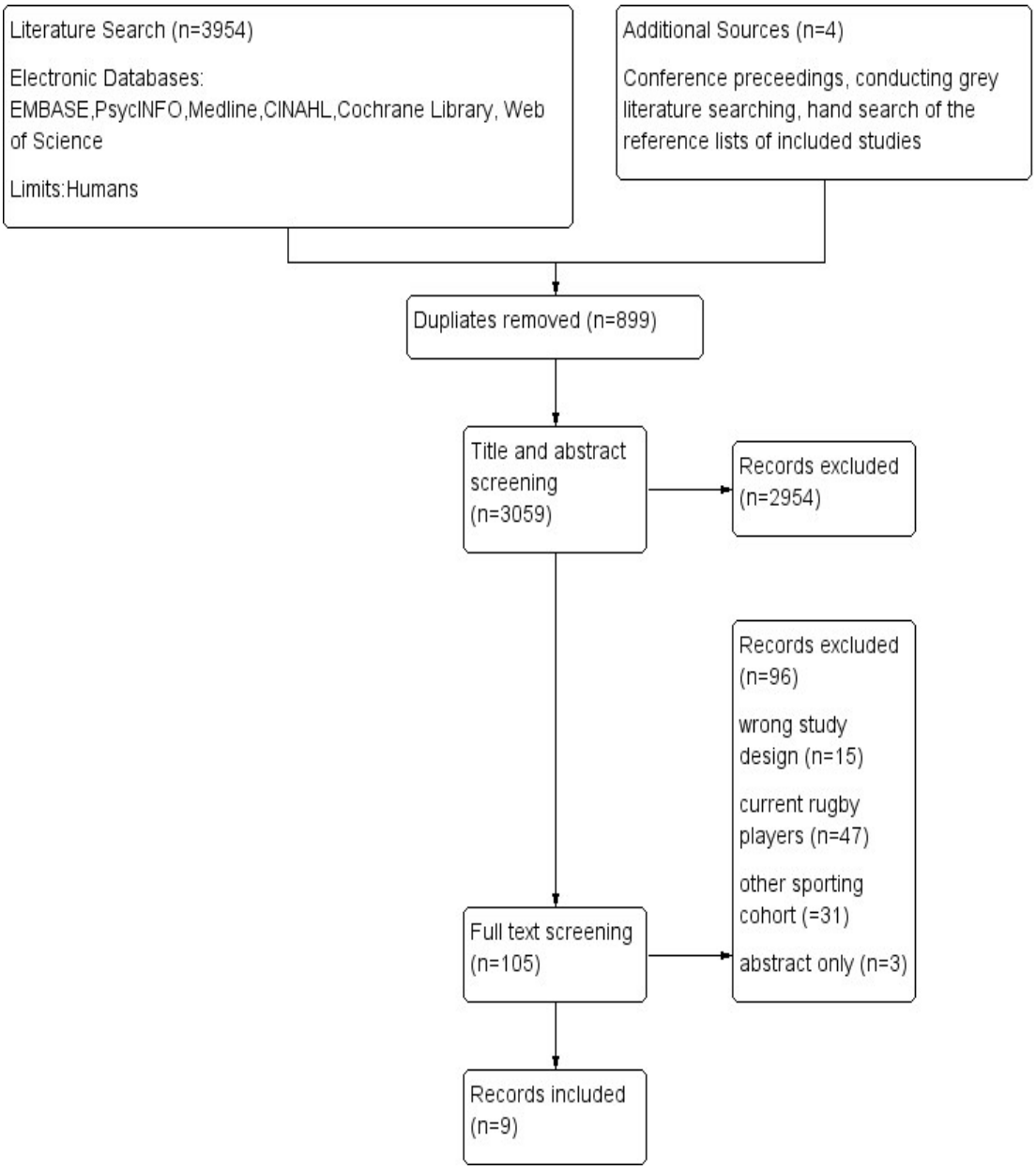

Figure 2-1 *Preferred Reporting items for Systematic Reviews (PRISMA); Flow Diagram of Study Selection Process.*

2.2.3 Data Extraction and Analyses

A data extraction template was used as a checklist of items, which should be included in reports of cross-sectional studies, based on *'Strengthening the Reporting of Observational Studies in Epidemiology*' guidelines (von Elm et al., 2007). Table 2-2 highlights framework for study eligibility criteria: participants, study methodology and outcome measures**.** Key details such as participant characteristics, details of concussion history, outcome measures used and relevant outcome data (group means and SD) were recorded and presented in table format by the primary reviewer (JC) [Table 2-3]. A meta-analysis was deemed inappropriate due to the small number of studies, heterogeneity of study designs and varying cognitive assessments employed.

Table 2-2 Study Eligibility Criteria: Participants, Study Methodology and Outcome Measures**.**

Participant Characteristics **Age** **Sex** **No. of concussions**	 Years Male/female ratio, % Years
Study Methodology **Location** **Study Design** **Eligibility Criteria** **Concussion definition**	 Setting and country Methodological design employed Inclusion & exclusion criteria Description
Objective measures of brain health* **Outcome Measure**	Method (e.g. pen and paper test (MoCA), neuroimaging (MRI))
Subjective measures of brain health* **Questionnaire**	Standardised outcome questionnaire (e.g. RPQ, BRIEF-A)

* Examples listed are not exhaustive but serve to guide the reviewer when extracting data for each variable. Additional/alternate measurement methods and units not listed may be included if they measure the primary outcomes of brain health.

MoCA: The Montreal Cognitive Assessment, MRI: Magnetic Resonance Imaging, RPQ: Rivermead Post-Concussion Symptoms Questionnaire, BRIEF-A: Behavior Rating Inventory of Executive Function - Adult Version.

2.2.4 Methodological Assessment

An adapted Downs and Black checklist was used to evaluate the methodological quality of the studies (Downs and Black, 1998). This was performed independently by two reviewers (JC and FW). Disagreements between the reviewers were resolved through discussion to achieve consensus. Failing agreement, a third reviewer (SB) arbitrated. The checklist was modified to a maximum of 17 applicable questions, which addressed the following methodological components: reporting, external validity, internal validity (bias and confounding) and power [Appendix B.3]. Seventeen items were rated either as yes (=1) or no/unable to determine (=0), and one item was rated on a three-point scale (yes=2, partial=1, and no=0). The maximum achievable score was 18, with higher scores indicating a better methodological quality of the study. Results were categorised according to the adapted Downs and Black checklist (Downs and Black, 1998) from Hartling et al. (2004) and Hignett (2003) [Table 2-4]. Interpretation of results was as follows: strong quality (≥14) represented the top 75%; moderate quality (9–13) represented 50%–74%; limited quality represented (5–8) represented 25%–49%; and poor quality (<5) represented <25%.

Table 2-3 Study Methodologies.

Study	Location	Study Design	Inclusion Criteria	Exclusion Criteria
Imaging studies				
Pearce et al. (2018)	Australia	Cross-sectional	○ Retired professional rugby league player ○ Aged 40-65 years ○ Played in a formal competitive league ○ Last concussion minimum of one decade prior	○ Diagnosed neurological condition ○ Sustained brain injury outside of sport (e.g. motor vehicle)
Gardner et al. (2017)	Wales	Cross-sectional	○ Retired professional rugby league player	○ Medical history of neurosurgery, major psychiatric disturbance, or medical contraindications to MRI
Lewis et al. (2017)	New Zealand	Cross-sectional	○ Retired elite rugby player ○ Aged 30–65 years ○ Male ○ Played at international or national level ○ Retired from competitive sport for at least five years	○ Contraindications to or unwillingness to undertake TMS. ○ Taking medication known to influence corticomotor excitability
Cognitive health studies				
McMillan et al. (2017)	Scotland	Cross-sectional	○ Retired elite rugby player ○ ≥18years of age ○ Fluent in English ○ Capable of giving consent and capable of assessment	○ Those continuing to play
Hume et al. (2017)	New Zealand	Observational cross-sectional	○ Retired elite rugby player ○ Aged 23–72 years ○ Male ○ Played at international or national level ○ Retired from competitive play	○ None reported

Decq et al. (2016)	France	Observational cross-sectional	○ Retired high-level rugby player ○ Aged 45 to 65 years ○ Played rugby for at least 10 years ○ Played at national or international championship level between 1985 and 1990	○ None reported
Thornton et al. (2008)	Canada	Observational cross-sectional	○ ≥18years of age ○ Fluency in English.	○ Being over 66 years of age ○ Diagnosed neurological illness ○ Diagnosed non-sport TBI
Mental health studies				
Gouttebarge et al. (2016)	France, Ireland and South Africa	Observational cross-sectional	○ Retired player and a member of the national Rugby Union players' association from France, Ireland or South Africa. Retired players of these organisations had all competed at a professional level in Rugby Union ○ ≤ 50 years old ○ Male ○ Fluent either in English or French	○ None reported
Brown et al. (2017)	France, Ireland and South Africa	Observational prospective cohort	○ Retired professional rugby players from 3 countries: France, Ireland and South Africa ○ Member as a retired player of the national rugby players' association from France, Ireland or South Africa. Being a member as a retired player of a players' rugby association meant the player had competed at a professional rugby level. ○ < 51 years ○ Male ○ Fluent either in English or French	○ None reported

Table 2-4 Categorization of Total Scores on the adapted Downs and Black Checklist.

Quality Index	Percentage	Methodological Quality Score
Strong	≥75%	≥14
Moderate	50-74%	(9-13)
Limited	25-49%	(5-8)
Poor	<25%	<5

2.3 Results

The search strategy and selection process are summarised in Figure 1, with 3059 records (after the removal of duplicates) initially identified. A total of nine studies published between 2008 and 2018 met our criteria and were included in this review. Two studies included in the review were based on the same cohort of retired rugby players (Gouttebarge et al., 2016, Brown et al., 2017). Studies were cross-sectional or prospective observational studies that explored brain health measures in retired rugby players. Study characteristics are summarised in Table 2-5.

2.3.1 Types of Outcome Measures used

The areas of brain health that were investigated included cognitive functioning, mental health, neurophysiology and neurochemistry. The studies included a wide variety of cognitive tests in order to assess the retired athlete's cognitive capabilities. Some studies used a comprehensive battery of neuropsychological tests that subjectively or objectively explored different aspects of cognition, while others used only one cognitive test. To ease interpretability of tests used, individual neuropsychological tests were categorised according to the predominant cognitive domain they assessed. The eight domains explored were:

attention, executive functioning, information processing, motor speed, verbal ability, verbal memory, visual memory and visuospatial ability.

Neuropsychological tests and their corresponding cognitive domains are displayed in Table 2-6. In addition to the cognitive evaluation, subjective and self-administered questionnaires were used. Four studies used a specific post-concussion questionnaire, for example, the Rivermead Post-Concussion Symptoms Questionnaire and the Post-Concussion Symptom Checklist (PSCS), both of which assess for persistent self-reported symptoms associated with concussion, including cognitive complaints. Symptoms of various aspects of mental health were assessed including distress, anxiety/depression, sleeping disturbance and alcohol misuse. Outcome measures included the Distress Screener, the 12-item General Health Questionnaire (GHQ-12), the Patient-Reported Outcomes Measurement Information System (PROMIS) and the 3-item. The Alcohol Use Disorders Identification Test (AUDIT) was used in five studies to assess for alcohol dependence to investigate the possibility of dual symptoms of mental illness and alcoholism. Brain neurometabolite concentrations were investigated using magnetic resonance imaging (MRS). While transcranial magnetic stimulation (TMS) and electromyography (EMG) were used to explore neurophysiology.

Table 2-5 Data Extraction Table presenting Key Characteristics of each Study.

Reference:	Objective:	Number of Participants (n=); Mean Age (SD)/ Mean 95% [CI]	Number of Concussions: Mean (SD)/Mean 95% CI	Definition of Concussion:	Cognitive Outcome Measures:	Findings	Downs and Black Score; Quality Index
Imaging studies							
Pearce et al. (2018)	To explore the long-term neurophysiological, motor and cognitive changes in retired professional rugby league players with a history of concussion injuries during their career.	Elite rugby players n=25; 48.4 [45.8,51.0], Control n=25; 48.8 [45.9, 51.7]	Retired rugby players 8.5 [4.7,11.3] Controls n/a	Not Defined	CANTAB-VRT, CANTAB-PAL, CANTAB-IED, CANTAB- SWM, O'Connor Finger Dexterity test	Performance on cognitive testing showed that the performance across all tests showed a significant difference between groups (PAL: P < .01; d = 1.06; SWM: P= .02; d= .77; IED: P < .01; d = 1.04).	11; Moderate
Gardner et al. (2017)	To examine brain neurometabolite concentrations in retired rugby league players.	Retired rugby players n=16, 38.3 ± (4.6) Controls n=16, 37.9 ± (4.9)	Retired players reported an average of 33.44 (Median = 20; IQR = 7–20; range 3–100) concussions. Retired players reported an average of 5.9 concussions with LOC sustained during their careers (Median = 3.5; IQR = 3.5–6; range 0–30).	Not Defined	ACS-TOPF, RAVLT, RCFT, TMT A & B, COWAT, WAIS-IV, RPQ, DASS-21, AUDIT.	Retired players did not significantly differ in concentrations of 4 out of 5 neurometabolites tested. A significantly lower concentrations of grey matter glutathione (p = 0.02) in retired players was detected. There were no significant differences between	11; Moderate

						groups on measures of depression, anxiety, or cognitive functioning.	
Lewis et al. (2017)	To assess measures of corticomotor excitability and inhibition in retired rugby players.	Elite Rugby Players n=23, 43 ± (7) Community Level Rugby n=28, 45 ± (8) Retired Non-Contact Sport Controls n=22, 44 ± (9)	Elite Rugby Players: 0 concussions (n= 0; 0%), 1–2 concussions (n=3; 13%), ≥3 concussions (n=20; 87%) Community Level Rugby: 0 concussions (n=1 ; 4%), 1–2 concussions (n=3 ; 11%), ≥3 concussions (n=23 ; 85%) Retired Non-Contact Sport Controls : 0 concussions (n=16 ; 75%), 1–2 concussions (n=5 ; 21%), ≥3 concussions (n=1; 4%)	"A blow to the head followed by a variety of symptoms that may include any of the following: headache, dizziness, loss of balance, blurred vision, 'seeing stars', feeling in a fog or slowed down, memory problems, poor concentration, nausea or throwing-up. Getting 'knocked out' or being unconscious does NOT always occur with a concussion."	RPQ: predominantly early (RPQ-3) and late (RPQ-13) symptoms of brain injury.	RMT was significantly higher and LICI was greater in the elite rugby group compared to the control group.	8; Limited
Cognitive health studies							
McMillan et al. (2017)	To investigate symptoms and a range of cognitive and health outcomes in retired rugby players with history of repeated concussion.	Retired international rugby players n= 52; 53.5 ± (13.0) Controls n = 29; 55.1 ± (9.0)	Retired international rugby players 13.9 ± (18.9) Controls 0.3 ± (0.5)	"being a blow or injury to your head where you may or may not have lost consciousness and then had symptoms, such as dizziness, blurred vision, nausea, vomiting, headache, poor concentration."	MOCA, SDT, TMT, RAVLT SART, JLO Test, Lafayette Grooved Pegboard, SF-36, GOSE, HADS, RPQ, SF-36; questions 1 and 2), AUDIT.	RIRP performed poorer than controls on a test of verbal learning (p=0.022). No significant difference on the other cognitive tests were found (p>.05).	4; Poor

Hume et al. (2017)	To investigate cognitive function in former professional rugby players and assess the association between concussion history and cognitive function.	Retired Elite Rugby n=103, 41.3 ± (7.5) Retired Community Rugby n=195, 44.9 ± (8.4) Retired Non-Contact Sport Group n=65, 42.1 ± (7.7)	Elite Rugby = 3.5 ± (2.0) Community Rugby =2.9 ± (2.2) Non-contact= 0.4 ± (0.8)	"A blow to the head followed by a variety of symptoms (LOC, headache, dizziness, loss of balance, blurred vision "seeing stars", feeling in a fog or slowed down, memory problems, poor concentration, nausea or throwing up."	Online CNS-Vital Signs Test, AUDIT	Elite rugby group performed worse compared to non-contact sports on tests of complex attention -0.67 (-0.07 to -0.26) processing speed -0.51 (-0.89 to -0.12) executive functioning -0.41 (-0.80 to -0.02) and cognitive flexibility -0.37 (-0.74 to 0.00).	11; Moderate
Decq et al. (2016)	To assess the prevalence of major depressive disorder, mild cognitive disorders and headache in a population of retired rugby players.	Age (years) median [IQR] Retired rugby players (RRPs)= 239 52 [49-55.75] Other retired sportsmen (ORS)=138 52 [49-55]	Retired rugby player: n= 3.1 ± (5.01) Other sports: n= .68 ± (1.83)	Not defined	Self-administered Questionnaire F-TICS-m, PHQ-9	A higher rate of major depressive disorder was observed among RRPs compared to ORS (p=0.04). The PHQ-9 score was increased with the number of reported concussions regardless of the type of sport (p=0.026). A higher rate of mild cognitive disorders was observed in RRPs compared to ORS (57% vs 40%) p=0.005.	13; Moderate
Thornton et al. (2008)	To examine the extent to which lifetime concussion exposure is associated with	Male and Female Study Retired players (all male)	Divided participants into no heavy concussion exposure groups [Grade 2 or above] (n=37, 8:29), 1-	Criteria from the American Academy of Neurology. Grade 1- transient confusion that resolves within	ETS Kit, CCFT, WAIS-III, TMT-A and B, WMS-III, RAVLT, WCST, PCSC	Concussion exposure did not predict neurocognitive functioning but did	12; Moderate

	neurocognitive and symptomatic status in competitive vs. recreational/retired players.	n=16 39.25 ± (10.99) Recreational players n=15 50.53 ± (9.80) Older players n=31 44.71 ± (11.75) Competitive players n=80 26.43 ± (6.53)	2 heavy concussions (n=39, 4:35) and 3 or more (n=35, 1:34)	15 mins with no LOC. Grade 2 - transient confusions that persists with for more than 15 minutes with no LOC. Grade 3 - any LOC.		predict PCS. Participants with no heavy concussions reported significantly fewer Memory complaints (d=−0.68), less Distress (d=−0.76), and less overall (Total) PCS (d=−0.65) than did those with three or more heavy concussions.	
Mental health studies							
Brown et al. (2017)	To examine the association between forced retirement and subsequent symptoms of CMDs in former professional rugby players.	Retired Rugby Union players n=293, 39 ± (5), n=173 (voluntary retirement), n=120 (forced retirement)	Not reported	Not defined	4DSQ, GHQ-12, PROMIS, AUDIT-C	Players forced to retire were more than twice as likely to report symptoms of distress in comparison to those that retired voluntarily (odds ratio: 2.1, 95% confidence interval: 1.2–3.6, p< .001). None of the other mental health measures were associated with forced retirement.	12; Moderate
Gouttebarge et al. (2016)	To determine the prevalence of symptoms of CMDs, such as distress, anxiety/depression, sleeping disturbance, adverse nutrition	Retired Rugby Union players n=295, 38 ± (6)	Not reported	Not defined	4DSQ, GHQ-12, PROMIS, AUDIT-C	Prevalence rates were 25% for distress, 28% for anxiety/ depression, 29% for sleeping disturbance, 62% for adverse	11; Moderate

	behaviour, adverse alcohol behaviour, smoking) among retired professional Rugby Union players.					nutrition behaviour, 15% for smoking and 24% for adverse alcohol behaviour.	

AUDIT-C: The Alcohol Use Disorders Identification Test—Consumption, ACS-TOPF: Advanced Clinical Solutions-Test of Premorbid Functioning, CANTAB: The Cambridge Neuropsychological Test Automated Battery, CANTAB-IED: The Intra-Extra Dimensional Set Shift, CANTAB-PAL: Paired Associates Learning, CANTAB- SWM: Spatial working memory, CANTAB-VRT: Visuomotor reaction time, CCFT: Cattell's Culture Fair Intelligence Test, CMD: common mental disorders, COWAT: Controlled Oral Word Association Test, DASS-21: the Depression, Anxiety, Stress Scale 21-item, 4DSQ: Four-Dimensional Symptom Questionnaire, ETS Kit: Educational Testing Service, F-TICS-m: French version of the modified telephone interview for cognitive status, GHQ-12: The General Health Questionnaire-12, GOSE: Extended Glasgow Outcome Scale, HADS: The Hospital Anxiety and Depression Scale, JLO Test: Judgement of Line Orientation, LICI: Long-interval intracortical inhibition, LOC: Loss of consciousness, MOCA: Montreal Cognitive Assessment, PCS(C): Post-concussion Syndrome Checklist, PHQ-9: Patient health questionnaire, PROMIS: Patient-Reported Outcomes Measurement Information System, RAVLT: Rey Auditory Verbal Learning Test, RCFT: Rey Complex Figure Test, RMT: Resting motor threshold, RPQ: Rivermead post-concussion symptoms questionnaire, SART: Sustained Attention to Response Task, SDT: Symbol Digit Test, SF-36: 36-Item Short Form Health Survey, TMT: Trail Making Test, WAIS: Wechsler Abbreviated Scale of Intelligence, WCST: Wisconsin Card Sorting Test, WMS: Wechsler Memory Scale.

Table 2-6 Cognitive Tests and Corresponding Domains.

Domain Measured	***Cognitive Tests Used***	***References***
Intelligence	ETS Kit	Thornton et al. (2008)
	CCFT	Thornton et al. (2008)
Global Cognitive Ability	MOCA	McMillan et al. (2017)
	Cognition Composite T Score	Gardner et al. (2017)
Processing speed	SDMT	McMillan et al. (2017), Thornton et al. (2008)
	Online CNS-Vital Signs Test-Processing Speed	Hume et al. (2017)
Attention and working memory	SART	McMillan et al. (2017)
	Online CNS-Vital Signs Test-Simple Attention	Hume et al. (2017)
	Online CNS-Vital Signs Test-Complex Attention	Hume et al. (2017)
	TMT-A	Thornton et al. (2008)
	WMS-III	Thornton et al. (2008)
Learning	RAVLT- Immediate Recall	McMillan et al. (2017)
Memory	Online CNS-Vital Signs Test- Memory Test	Hume et al. (2017)
	Online CNS-Vital Signs Test-Visual memory	Hume et al. (2017)
	Online CNS-Vital Signs Test-Verbal memory	Hume et al. (2017)
	RAVLT- Delayed Recall	McMillan et al. (2017), Thornton et al. (2008)
	CANTAB-Paired associative learning	Pearce et al. (2018)
	CANTAB-Spatial Working Memory	Pearce et al. (2018)
Executive function	TMT-B	McMillan et al. (2017), Thornton et al. (2008)
	Online CNS-Vital Signs Test- Executive Function Test	Hume et al. (2017)
	Online CNS-Vital Signs Test-Cognitive Flexibility	Hume et al. (2017)
	WCST	Thornton et al. (2008)
	CANTAB- The Intra-Extra Dimensional Set Shift	Pearce et al. (2018)
Fine motor	Lafayette Grooved Pegboard Dominant/Non-Dominant Hand	McMillan et al. (2017), Gardner et al. (2017)
	O'Connor Finger Dexterity test	Pearce et al. (2018)
Psychomotor Ability	Online CNS-Vital Signs Test-Reaction time	Hume et al. (2017)
	Online CNS-Vital Signs Test-Motor Speed	Hume et al. (2017)
	Online CNS-Vital Signs Test-Psychomotor speed	Hume et al. (2017)
	CANTAB- Reaction Time Task	Pearce et al. (2018)
Self-Report Measure	TICS-M	Decq et al. (2016)
	RPQ Total Score	Gardner et al. (2017), McMillan et al. (2017)
	RPQ late (RPQ-13)	Lewis et al. (2017)
	PCSC	Thornton et al. (2008)

2.3.2 Methodological Assessment

Of the eight studies included, the mean methodological quality score was 10.33 (SD 2.58) out of a total score of 18, giving an overall quality score of 'moderate' (percentage 50%–74%; 9–13). See Table 2-7 for individual quality scores.

2.3.3 Study Characteristics

Study characteristics such as participants, outcome measures and findings are summarised in Table 2-5. A total of 992 male retired rugby players (range of mean ages 38–52 years) were included in this review. Participant characteristics varied in age, medical history, socioeconomic background, concussion exposure and number of concussions reported. Six out of the nine included a control group (Hume et al., 2017, McMillan et al., 2017, Decq et al., 2016, Lewis et al., 2017, Pearce et al., 2018, Gardner et al., 2017). While the different cohorts in the study by Thornton et al. (2008) included rugby players across varying participation/competition levels.

Table 2-7 Summary of Quality Appraisal of Included Studies-using the Downs and Black checklist.

Reference	Reporting Total /8	External Validity Total /2	Internal Validity (Bias) Total /4	Internal Validity-Confounding (Selection Bias) Total /3	Power Total /1	Total / 18	Methodological Quality
Pearce et al. (2018)	8	0	2	1	0	11	Moderate
Gardner et al. (2017)	7	2	2	0	0	11	Moderate
Lewis et al. (2017)	6	1	2	0	0	8	Limited
Brown et al. (2017)	8	2	2	0	0	12	Moderate
Hume et al. (2017)	7	0	2	2	0	11	Moderate
McMillan et al. (2017)	3	0	1	0	0	4	Poor
Gouttebarge et al. (2016)	8	1	1	1	0	11	Moderate
Decq et al. (2016)	7	2	2	2	0	13	Moderate
Thornton et al. (2008)	6	2	2	2	0	12	Moderate

2.3.4 Objective Cognitive Tests

Six out of the nine studies investigated cognition in an objective manner (Decq et al., 2016, Hume et al., 2017, McMillan et al., 2017, Gardner et al., 2017, Pearce et al., 2018, Thornton et al., 2008). Four of which found evidence of deficits on certain cognitive tests in retired rugby players (Decq et al., 2016, Gardner et al., 2017, McMillan et al., 2017, Pearce et al., 2018). Gardner et al. (2017), although limited by a small study cohort, found no significant differences in cognitive functioning in retired rugby players in comparison with controls. Thornton et al. (2008) also found no between group differences in cognitive functioning in retired rugby players who were grouped based on self-reported concussion history in a non-controlled study. Decq et al. (2016) found that retired rugby players had a higher rate of mild cognitive disorders ($p=0.005$) based on the French version of the modified telephone interview (F-TICS-m). McMillan et al. (2017) found that retired rugby players performed significantly worse than controls on tests of verbal learning ($p=0.022$), but no significant differences were found in cognitive tests of global cognitive functioning, processing speed, attention, memory and executive function in comparison with controls ($p>0.05$).

Hume et al. (2017) found that a self-reported history of concussion was associated with small to moderate neurocognitive deficits in retired rugby players in areas such as cognitive flexibility, complex attention and executive function relative to the player group with no concussion history. The elite rugby group performed worse on tests of complex attention (effect size (EF) −0.67, 95% CI −1.07 to −0.26) and cognitive flexibility (EF −0.37, −0.74 to 0.00). The community rugby group performed worse than the non-contact group on executive functioning (EF −0.51, 95% CI −0.89 to −0.12). Pearce et al. (2018) found that the retired rugby players were significantly slower at reacting to the stimulus in the visuomotor reaction test ($p<0.01$). The retired rugby group also performed significantly worse in the paired associative learning (PAL) test ($p<0.01$), the spatial working memory (SWM) $p=0.02$ and the

intra-extra dimension (IED) shift test ($p<0.01$), all of which are subtests of the Cambridge Neuropsychological Test Automated Battery (CANTAB).

2.3.5 Fine motor function

Three studies investigated fine motor function using various tests (Pearce et al., 2018, McMillan et al., 2017, Gardner et al., 2017). All three studies found that retired rugby players had significantly decreased dexterity/fine motor co-ordination. Gardner et al. (2017) found that retired rugby players performed significantly worse in a test of manual dexterity with the non-dominant hand only ($p=0.03$). Similarly, McMillan et al. (2017) found that retired rugby players had significantly lower scores on a test of fine coordination of the dominant hand ($p=0.038$). Pearce et al. (2018) found dexterity was significantly reduced in the rugby group compared to controls ($p=0.02$). All three studies compared retired rugby players with healthy community control groups.

2.3.6 Neuroimaging

Gardner et al. (2017) were the only investigators to explore brain health in retired rugby players using a neuroimaging modality. Magnetic resonance spectroscopy was used to detect potential biochemical changes, showing that in comparison with non-sportsperson controls, retired rugby players had significantly lower concentrations of grey matter glutathione ($p=0.02$). No differences were found in grey matter ($p=0.19$) or white matter N-acetylaspartate ($p=0.52$) in retired athletes compared with controls.

2.3.7 Electrophysiology

Lewis et al. (2017) and Pearce et al. (2018) were the only authors to evaluate for electrophysiological changes in retired rugby players using transcranial magnetic stimulation

(TMS). Lewis et al. (2017) found that resting motor threshold was significantly higher (p=0.004) in the elite rugby group compared with the control group. Both Lewis et al. (2017) and Pearce et al. (2018) reported greater long-interval intracortical inhibition (LICI) in the elite rugby groups compared to the control group (p=0.005, p=0.03) respectively. However, Lewis et al. (2017) noted that there was no evidence of altered corticomotor excitation and inhibition found in the retired community rugby group who had experienced a similar number of concussions to the elite group. Pearce et al. (2018) also found that the rugby group had significantly reduced cortical silent period (cSP) at suprathreshold stimulation intensities (p range 0.02 to <0.01) in comparison to the age matched control group.

2.3.8 Subjective cognitive tests

Gardner et al. (2017) and Lewis et al. (2017) found no significant differences in self-report (S-R) measures of post-concussion symptoms (PCS) in retired rugby players compared with controls. In contrast, McMillan et al. (2017) found that persistent symptoms attributed to concussion were more common in retired rugby players who self-reported more than nine concussive events (p=0.028). However, these symptoms were not perceived to affect social or work functioning. Thornton et al. (2008) separated the rugby players into groups based on self-reported concussion exposure. Players with higher past concussion exposure were found to have increased PCS. Participants with no 'heavy' concussions, which included grade 2 or 3 concussions as described by the American Academy of Neurology, 1997) reported significantly fewer memory complaints, less distress and less overall total PCS than did those with three or more heavy concussions.

2.3.9 Mental health

Symptoms of common mental health disorders were assessed in five studies (Gouttebarge et al., 2016, Brown et al., 2017, Decq et al., 2016, McMillan et al., 2017, Gardner et al., 2017),

with three studies including a control group (McMillan et al., 2017, Gardner et al., 2017, Decq et al., 2016). Gouttebarge et al. (2016) and Brown et al. (2017) were based on the same cohort of retired professional rugby players. Gouttebarge et al. (2016) reported prevalence rates among the retired rugby player group of 25% for distress, 28% for anxiety/depression, 29% for sleeping disturbance and 24% for adverse alcohol behaviour. A number of factors such as higher number of life events and higher level of dissatisfaction of the player's rugby union career were associated with mental health symptoms such as distress. Brown et al. (2017) found that players forced to retire were more than twice as likely to report symptoms of distress in comparison to those that retired voluntarily (odds ratio: 2.1, 95% confidence interval: 1.2–3.6, $p<0.001$).

McMillan et al. (2017) found the average scores were in the 'normal' range on the Hospital Anxiety and Depression Scale (HADS) and there was no significant difference between the retired rugby players and controls. Similarly, Gardner et al. (2017) found no differences between groups (all $p >0.05$) on self-report measures of depression, anxiety or stress scores. In contrast, Decq et al. (2016) reported a higher rate of major depressive disorder (Patient Health Questionnaire (PHQ-9) score >9) among retired rugby players compared to controls (9% versus 6%) ($p = 0.04$), the PHQ-9 score also increased with the number of reported concussions ($p = 0.026$). Gardner et al. (2017) found a significant difference in Alcohol Use Disorders Identification (AUDIT) scores ($p < 0.01$) between controls and retired rugby players, with worse scores among the former rugby players.

2.4 Discussion

This review shows modest objective evidence of decreased neuropsychological performance in retired rugby players. Some retired players appear to have persistent subjective post-concussion symptoms complaints, which were associated with the number of reported concussions in two studies. Future studies should investigate the dose-response relationship

between concussion or head impact exposure and persistent symptoms. Fine motor control was found to be decreased in retired players compared with control groups in three studies. The evidence indicating declines in neurophysiological and neurochemical measures among retired rugby players were equivocal. Despite the research in this area being in its infancy, the long-term consequences of SRC remains a controversial topic of continuing interest. Some are now advocating for the banning of collision sports that expose athletes to head impacts, particularly at underage levels (Meehan et al., 2016), but the current body of knowledge surrounding the long-term sequelae of playing rugby is not conclusive. As modern societies are largely inactive, banning a large number of sports is likely to counteract the goal of optimal brain health (Giza et al., 2017).

Notably, investigations into the long-term effects of head impact exposure with/without concussion, associated with rugby participation on later-life brain health, are influenced by methodological biases. Primary among the studies evaluated here is the issue of self-selected participation on which results are based. It is therefore unclear whether the studies presented herein are representative of the entire retired rugby player the population. Five studies provided a concussion definition (Hume et al., 2017, McMillan et al., 2017, Decq et al., 2016, Lewis et al., 2017, Thornton et al., 2008), a wide variety of definitions used differed from international consensus recommended guidelines (King et al., 2009, McCrory et al., 2017).

The lack of standardised criteria may impact accurate injury surveillance (Quarrie and Murphy, 2014, Carney et al., 2014). Pearce et al. (2018), Gardner et al. (2017), Thornton et al. (2008) and McMillan et al. (2017) had the most robust exclusion criteria with participants excluded on the basis of a medical history of neurosurgery, diagnosis of chronic and debilitating neurological or psychiatric disturbance or other major medical conditions. These limitations make it difficult to draw conclusions regarding the long-term sequelae. A control cohort was used in six out of the nine studies, with Thornton et al. (2008), Gouttebarge et al. (2016) and (Brown et al., 2017) being the only authors to exclude a control group.

Instead, Thornton et al. (2008) analysed between-group differences among competitive, older/recreational and retired rugby players based on the number of previous concussions. While the lack of a non-contact control group is a potential bias, investigating groups of rugby players based on number of reported concussions offers an opportunity to evaluate the effect of concussion. However, given that the groups ranged from competitive to recreational to retired rugby players, different levels of head impact exposure without concussion would be expected. This is reflected in the different number of years played, which is highest in the older and recreational players. However, the influence of overall head impact exposure on cognitive tests was not explored. Additionally, the male-to-female ratio differed across the groups, with the 'no concussions' group having the highest percentage of females included. In predicting cognitive functioning based on neurocognitive test batteries, only demographic variables were found to be significant. Greater concussion exposure was found to be associated with total PCSC scores including the memory PCS scale. However, this relationship was only present in retired and recreational players and not competitive players. It is difficult to interpret the associations between self-report concussion history and subjective PCSC scores, given the potential for recall bias in self-report.

Only two out of the nine studies controlled for a history of non-sports-related TBI among participants (Pearce et al., 2018, Thornton et al., 2008), which may influence the results. Investigations in the majority of the studies have been on retired rugby players in comparison with controls who, in many cases, have a previous history of concussion/history of participation in sports that may expose to head impacts (Hume et al., 2017, McMillan et al., 2017, Lewis et al., 2017). For example, 34% of controls in the study by McMillan et al. (2017) had a concussion history and 63% had a history of playing rugby. A more robust comparison would include sport type, years played, position, along with number of concussions among all participants including controls. By failing to do so, there is a risk of biasing between group differences in cognitive tests. Pearce et al. (2018) was the only study to exclude control participants on the basis of having a history of contact sport participation

or a previous concussion. Ideally, former non-contact sport athletes, with and without concussion history, should be employed as a control group to allow for the evaluation of concussion alone and head impact exposure with and without concussion. Length of time since most recent concussion and retirement (i.e., time elapsed since potential head impact exposure) is also of significant importance when trying to differentiate between the potential long-term effects of a career in rugby as oppose to more short-term effects of a recent concussion. This was only assessed in three out of the nine studies. Gardner et al. (2017) included two retired players who had sustained a concussion within the past year, 4 and 6 months prior. Among the retired players, four had retired sometime during the previous 12 months. Whereas, Lewis et al. (2017) required rugby players to be retired from competitive sport for at least 5 years, while Pearce et al. (2018) stipulated that players were to have sustained their last concussion a minimum of ten years prior.

The host of confounding factors that may influence brain functioning in the retired rugby players as they age were controlled to different extents in the studies. Gardner et al. (2017) was the only investigator to evaluate premorbid function. However, two participants who had a history of attendance in special education classes, reading problems and spelling problems were included in this study. Lewis et al. (2017) were the only investigators to control for drugs, physical activity and sleep quality. Importantly, participants were excluded if they were taking medication that are known to influence corticomotor excitability. Gardner et al. (2017) controlled for current prescription medication use among retired rugby players. It is important to view results within a wider context and to consider what implications the observed differences in test performance will have in terms of clinical performance and ongoing neurological function. Hume et al. (2017) found that rugby players performed worse than non-contact sport controls in certain areas of cognition. However, the elite rugby players still performed equally or better than US normative values on 6 out of 11 measures. In the other five measures (cognitive flexibility, processing speed, executive functioning, reaction time and verbal memory), they performed slightly lower (small to moderate EFs) than US

normative values. The elite rugby players performed slightly better than the US norms on motor speed, while the community rugby players performed slightly better than US norms on a measure of complex attention. Collectively, the rugby cohort performed worse on 45% of the measures compared with the controls but were within one SD of normative values. For example, while there was a moderate difference in complex attention between the elite rugby group and the non-contact group, the mean score for the elite players on complex attention was 99, which was near the US standardised average of 100. The moderate between group differences is therefore due to the non-contact sport control group outperforming US standardised average, with a mean score of 106. McMillan et al. (2017) reported decreased performance in retired rugby players in two out of seven cognitive tests. However, the performance of the rugby player group still fell within the normal range for all tests. Where differences were found, they were not associated with a higher number of repeat concussions.

Similarly, results from the study by Gardner et al. (2017) are unclear. The study investigated neurometabolites, based on literature suggesting that they may be indicators of neuronal loss, neuroinflammation, axonal injury and possible neurodegenerative pathologies such as Alzheimer's disease and mild cognitive Impairment (MCI) (Gardner et al., 2017). Biochemical alterations were evident for one out of five of these neurometabolites. The significance of this finding is unclear, particularly given the lack of clinical correlates. Lewis et al. (2017) found some evidence for altered corticomotor excitability and intracortical inhibition in retired elite rugby players in comparison with retired non-contact sport players. Importantly, both rugby groups reported a similar number of concussions and symptom severity compared with the control group, which did not influence the results. Given the absence of findings in the community rugby group, the association with previous concussion is unclear. However, one explanation may be the higher cumulative influence of repeated head impact exposure at the elite-level driving between group results. Pearce et al. (2018) reported increased corticomotor latency among the rugby players, however the authors acknowledge that this was likely due to the significant difference in height, and

subsequent limb length. Further given investigation into long-term effects of concussion using TMS is in its infancy important, the authors note that clinical translation is difficult at this time. There is however evidence to indicate that the motor system may be the earliest clinical manifestation of concussion or head impact exposure and may precede cognitive decline (Rabadi and Jordan, 2001, Pearce et al., 2014, De Beaumont et al., 2009). Therefore, further studies are warranted. There is evidence to suggest that cumulative effect of multiple concussions or repeated head impact exposure may be more influential than the effect of a single concussion (Manley et al., 2017a). An attempt to quantify overall head impact exposure was not undertaken, making it uncertain if long-term exposure to rugby without concussion is associated with alterations in corticomotor function.

Decq et al. (2016) did not find an association between S-R concussion history and cognitive outcome. However, smoking and higher education were factors independently associated with higher and lower S-R cognitive dysfunction, respectively. Among retired rugby players in the study by McMillan et al. (2017) persisting symptoms attributed to concussion were more common if reporting more than nine concussions ($p=0.03$), although these symptoms were not perceived to affect social or work functioning. McMillan et al. (2017) and Gardner et al. (2017) both found significantly poorer performance in rugby players in comparison with controls on test of fine motor function. It is inconclusive whether this deficit can be attributed to a history of head impact exposure. There are also a number of other factors that may contribute to poorer fine motor control and dexterity in retired players, namely musculoskeletal injuries to the upper limb sustained throughout a career, which are extremely common in rugby (McIntosh, 2005, Usman and McIntosh, 2013). Six out of nine studies included alcohol screening (Hume et al., 2017, Gardner et al., 2017, Gouttebarge et al., 2016, Brown et al., 2017, McMillan et al., 2017, Decq et al., 2016). Gardner et al. (2017) found that former rugby players reported significantly greater alcohol consumption in comparison with controls ($p<0.01$). This may have impacted fine-motor performance (Brumback et al., 2007).

The limited number of studies that have investigated symptoms of common mental health disorders in retired rugby players have provided an insight into the potential depression burden on this population. Reasons for this may be due to a combination of factors which warrant further study such as psychological and physical sequelae of playing and retiring from professional rugby union. The association between history of concussion/ repetitive brain impacts, and symptoms of mental health disorders in later life is also poorly understood. Brown et al. (2017) compared former professional rugby players who were and weren't forced to retire, primarily due to injury. This study offers an insight into a subgroup of retired professional rugby players who may be at an increased risk of common mental health symptoms such as distress. Further, factors such as adverse life events and dissatisfaction were associated with greater symptoms of distress (Gouttebarge et al., 2016). Former players should be screened for health-related quality of life and general wellbeing in association with symptoms of common mental health disorders, given the prevalence rates of self-reported sleeping disturbance, adverse nutrition behaviour, smoking and adverse alcohol behaviour among former rugby players (Gouttebarge et al., 2016). There is emerging evidence to suggest that former athletes are just as likely as the general population, if not more at risk, of experiencing anxiety or depression. Given some of the findings in this review further research is warranted to investigate the mental health status of former rugby players (Gorczynski et al., 2017). Awareness of such symptoms among retired rugby players and developing support structures should be a priority among professional rugby alumni bodies.

In addition to concussion, the brain itself is constantly changing primarily because of normal ageing. Six out of the nine studies had an age cut-off as part of the exclusion criteria (Decq et al., 2016, Lewis et al., 2017, Pearce et al., 2018, Hume et al., 2017, Gouttebarge et al., 2016, Brown et al., 2017). Lewis et al. (2017) required former players to be aged 30–65 years, while Pearce et al. (2018) required former players to be aged 40–65 years. Similarly, Decq et al. (2016) excluded retired players over the age of 66 years. Gouttebarge et al. (2016) and Brown et al. (2017) excluded players over the age of 50. It is possible that the relatively

young age of retired rugby players in the included studies and the age cut-off in two studies may have influenced results, given that younger retired rugby players would be expected to be more cognitively resilient. It may be more pertinent to follow players over the age of 65 years, due to the normal effects of the ageing process on cognitive functioning and the suggested role that head impact exposure may play in this process (Moretti et al., 2012). Particularly, in light of the influence of cognitive reserve and neural compensatory mechanisms (Bigler and Stern, 2015, Stern, 2002, Levi et al., 2013), which begin to diminish with age. Therefore, the exclusion of players in this age bracket in both studies may have limited the potential for greater observed between group differences. Follow-up studies are required on these rugby players as they enter older age. The neurocognitive findings in the study by Thornton et al. (2008) present an interesting finding, given there were minimal differences across the three concussion exposure groups in neuropsychological functioning. If there was a cumulative effect of head impact exposure on neuropsychological performance, a difference would be expected in the form of decreased performance in retired players in comparison with younger players.

The nature of rugby has changed over time and will continue to evolve. The modern game has larger, faster, stronger players, experiencing greater impact forces (Hume et al., 2017). Therefore, the nature of long-term health in former players may change over time. Equally, major strides in the awareness of SRC, availability of side-line medical assessment and treatment of players are evident across the board and specifically within the sport of rugby. The rigour with which concussion is identified and return to play managed has greatly improved (McMillan et al., 2017). This may positively influence the long-term brain health of retired athletes and minimise any potential adverse long-term effects of rugby on brain functioning. Hence, findings from this review may not generalise to the modern rugby era but do not preclude additional investigation. Whether repeated concussions associated with playing rugby can be partly or completely responsible for longer term neurological disorders in older retired rugby players remains unanswered.

2.5 Conclusion

This review highlights the need for additional research to clarify the long-term influence of playing rugby on the brain health of retired rugby players. Despite the call for bans, the evidence is inconclusive and poorly developed. This review does offer positive findings in relation to objective neuropsychological performance in retired rugby players, the majority of which were normal, apart from fine motor control. Reliability of player self-reported concussion and the evidence of increased self-reported cognitive difficulties among some retired rugby players must be further investigated, along with mental health burden in this population. In the absence of prospective epidemiological studies to establish a direct relationship between playing rugby and long-term brain health, the neurocognitive and neurobehavioral status of living retired rugby players remains unclear. Further research is required to investigate whether decreased cognitive functioning, both objectively and subjectively, may become more apparent in retired rugby players as they age. Equally, additional research is necessary to investigate evidence of neurochemical changes and fine motor functioning in retired rugby players and the aetiology and pathophysiology behind findings.

Chapter 3 History of Sport-Related Concussion and Long-Term Clinical Cognitive Health Outcomes in Retired Athletes: A Systematic Review.

The material presented in this chapter has been disseminated in the following publication:

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Please see Appendix A.2 for full manuscript.

Neuropsychological Test Abbreviations

ACS-TOPF	Advanced Clinical Solutions-Test of Premorbid Functioning
AD8	Eight-Item Informant Interview to Differentiate Aging and Dementia
AMNART	American version of the National Adult Reading Test
BGT	Bender Visual-Motor Gestalt Test
BNT	Boston Naming Test
BRI	Behavioral Regulation Index
BRIEF-A	Behavior Rating Inventory of Executive Function - Adult Version
B–SIT	Brief Smell Identification Test
BTACT	Brief Test of Adult Cognition by Telephone
BVMT–R	Brief Visuospatial Memory Test–Revised
CANTAB- TOTSPT	One Touch Spatial Planning Task
CANTAB–IED	Intra-Extra Dimensional Set Shift
CANTAB-MOT	Motor Screening Task
CANTAB–PAL	Paired Associates Learning
CANTAB–RTI	Reaction Time
CANTAB-RVP	Rapid Visual Information Processing
CANTAB-SSP	Spatial Span
CANTAB–SWM	Spatial Working Memory
CANTAB–VRT	Visuomotor Reaction Time
CCFT	Cattell's Culture Fair Intelligence Test
CDS	Cognitive Difficulties Scale
CFQ	Cognitive Failures Questionnaire

CNS Vital Signs Online	Central Nervous System Vital Signs Online computerized neurocognitive assessment software
COWAT	Controlled Oral Word Association Test
CPT	Conners Continuous Performance Test
CVLT–II	California Verbal Learning Test, second edition
DASS-21	The Depression, Anxiety, Stress Scale 21-item
D-KEFS	Delis-Kaplan Executive Function System
DQ	Dysexecutive Questionnaire
DSM-5	Diagnostic and Statistical Manual of Mental Disorders
DST	Digit Symbol Test
DWR	Delayed Word Recall
EFT	Eriksen Flanker Task
ETS Kit–V2 and –V3	Educational Testing Service Kit V2 and V3 vocabulary items
FAS	Verbal phonemic fluency test
F–TICS–m	French version of the modified Telephone Interview for Cognitive Status
FTT	Finger Tapping Test
GPT	Grooved Pegboard Test
HADS	The Hospital Anxiety and Depression Scale
ImPACT	Immediate Post-Concussion Assessment and Cognitive Testing
JLO Test	Judgement of Line Orientation
LF	Letter Fluency task
MCIS	Mild Cognitive Impairment Screen
MCS	Mental Component Summary
MMSE	Mini-Mental State Examination
MoCA	The Montreal Cognitive Assessment
NAB-LL	Neuropsychological Assessment Battery List Learning test
Neuro–QoL	Neurological Quality of Life in Neurological Disorders
PASAT	Paced Auditory Serial Addition Test
PCS	Physical Component Summary
PCSC	Postconcussion Syndrome Checklist
PROMIS	Patient-Reported Outcomes Measurement Information System
RAVLT	Rey Auditory Verbal Learning Test
RBANS	Repeatable Battery for the Assessment of Neuropsychological Status
RCFT	Rey Complex Figure Test
ROCFT	Rey-Osterreith Complex Figure Test
RVDLT	Rey Visual Design Learning Test
SART	Sustained Attention to Response Task
SDMT	Symbol Digit Modalities Test
SDT	Symbol Digit Test
SF–12/36	12/36-Item Short Form Health Survey
SOPT	Self-Ordered Pointing Task
SORT	Semantic Object Retrieval Test
SRTT	Serial Reaction Time Test
TCFT	Taylor Complex Figure test
TMT	Trail Making Test

TOMM	Test of Memory Malingering
TYM	Test Your Memory
VRST	Verbal Selective Reminding Test
WAIS–III/IV	Wechsler Adult Intelligence Scale, third/fourth edition
WASI	Wechsler Abbreviated Scale of Intelligence scale, revised version
WASI	Wechsler Abbreviated Scale of Intelligence
WCST	Wisconsin Card Sorting Test
WMS	Wechsler Memory Scale
WMS-III/IV	Wechsler Memory Scale, third/fourth edition
WRAT–4	Wide Range Achievement Test, fourth edition
WTAR	Wechsler Test of Adult Reading

3.1 Introduction

There is increasing demand and necessity to understand the relationship between a history of concussions or head-impact exposure and development of later-life cognitive impairment. The current dialogue around this topic has largely stemmed from post-mortem investigations of athletes, particularly retired American NFL players, with a history of substantial head-impact exposure throughout their careers. In the last decade, a dramatic shift in both public and scientific perception around the long-term consequences of concussion is evident. An injury that was once viewed as a short-lived impairment of neurologic function and often trivialized is now implicated in a number of long-term neurologic sequelae (Mez et al., 2017, Stein et al., 2015, Pearce et al., 2015, Manley et al., 2017a, Solomon, 2018). However, the long-term consequences of concussion, which is on the mild end of the TBI spectrum (McCrory et al., 2017), remain poorly understood. Whereas a full recovery of cognitive functioning is generally the norm (Dougan et al., 2014, Rohling et al., 2011, Broglio and Puetz, 2008), the clinical pathway to recovery and return to sport is much more prolonged and less clear for a minority of athletes (McCrory et al., 2017). Given the limited studies found pertaining to retired rugby players specifically in the previous chapter, a broader scope of the literature was undertaken in the current chapter.

The specific aim of the review was to:

- Explore the literature on the long-term cognitive health status of retired athletes.

3.2 Materials and methods

This review was conducted in accordance with *'Preferred Reporting Items for Systematic Reviews and Meta-Analyses'* (PRISMA) guidelines (www.prisma-statement.org). The

review strategy and methods of analysis was registered with PROSPERO, a registry of systematic reviews [Appendix B.4]. Registration is available at https://www.crd.york.ac.uk/prospero/; registration number: CRD42016050750.

3.2.1 Eligibility criteria

Details of eligibility criteria are detailed in Table 3-1. Studies were included if the authors evaluated retired male or female athletes who participated in organized sport from the amateur to professional level. At least one form of cognitive testing must have been used as an outcome measure. Studies were excluded if the investigators explored only athletes still actively involved in sport or did not report retired athlete data as a subgroup or if they were case studies with five or fewer participants. Neurocognitive testing must have been conducted with the participants and not gained through reports from friends or family. The primary outcomes of interest were a variety of cognitive domains, such as attention, memory, executive function, intelligence, processing speed, visuospatial abilities, and psychomotor speed. The secondary outcome variable of interest was history of sport-related concussion (SRC).

Table 3-1 Inclusion/Exclusion Criteria.

Inclusion Criteria	**Exclusion Criteria**
• Retired male or female athletes who participated in organized sport from the amateur to professional level. • At least one form of cognitive testing must have administered as an outcome measure	• Athletes still actively involved in sport. • Case studies with five or fewer participants. • Neurocognitive status gained through reports from friends or family.

3.2.2 Search strategy

Electronic databases were searched, including EMBASE, PsycINFO, MEDLINE/PubMed, CINAHL, Cochrane Central Register of Controlled Trials, and Web of Science, from their inception to April 2018 using the relevant database search engines. Common key words and medical subject headings were related to 3 components: (1) the participant (e.g., retired athlete), (2) the primary outcome measure (e.g., cognitive test used), and (3) the secondary outcome (e.g., history of sport concussion). No search restrictions for date or language were imposed. The search strategy for each database and corresponding number of hits per database are presented in Appendix B.5. The electronic database searching was supplemented by searching the abstracts of the International Conference on Sports Concussion consensus meetings (2001–2018) and conducting a gray literature search and a hand search of the reference lists of the included studies. Two reviewers (J.C. and F.W) independently screened the titles and abstracts to identify studies that potentially met the eligibility criteria. Full texts of these reports were retrieved and independently assessed for eligibility by the same two reviewers. Any disagreements on inclusion of studies were resolved through discussion and consultation with a third reviewer (S.B) to reach a consensus. Following this process of elimination, 46 studies were included for this review.

3.2.3 Data extraction and analysis

A data extraction template was used as a checklist of items that should be included in reports of cross-sectional studies, based on *'Strengthening the Reporting of Observational Studies in Epidemiology*' guidelines (von Elm et al., 2007). Key details such as participant characteristics, details of concussion history, outcome measures used and relevant outcome data (group means and standard deviations) were recorded and presented in table format by the primary reviewer (JC) [Table 3-2].

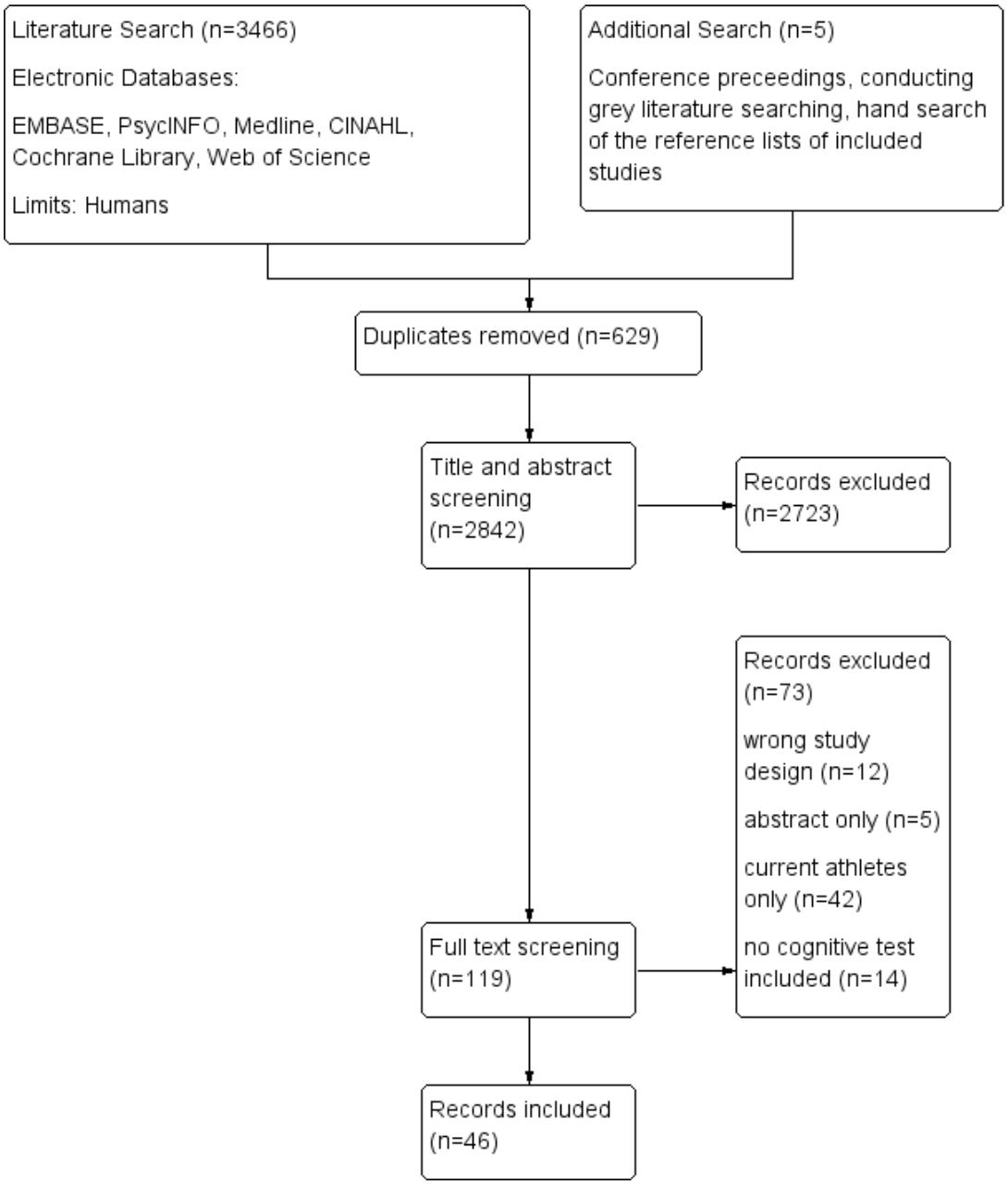


Figure 3-1 *Preferred Reporting items for Systematic Reviews (PRISMA); Flow Diagram of Study Selection Process.*

Table 3-2 Summary of Extracted Data of Included Studies (n=46); Main Characteristics, Concussion Reports, Types of Cognitive Measures Used and Primary Results.

References	Objectives	Number of Participants (n =); Mean Age ± (SD)	Number of Concussions: Mean (SD)	Cognitive Measures:	Primary Findings
Pearce et al. (2018)	Investigate long-term neurophysiological and cognitive effects of repeated concussion injuries in former professional rugby players	Former professional rugby athletes: n = 25 (CI) 48.4 (45.8, 51.0), Controls: n = 25, 48.8 (45.9, 51.7)	Athletes Mean, CI 8.5 (4.7,11.3) Controls n/a	CANTAB- VRT, PAL, IED, SWM, RTI, O'Connor Finger Dexterity test	Performance on cognitive testing showed that the performance across all tests showed a significant difference between groups (PAL: $P < .01$; d = 1.06; SWM: $P = .02$; d = 0.77; IED: $P < .01$; d = 1.04)
Clark et al. (2018)	Investigate the relationship between exposure to concussive/ subconcussive head impacts, white matter integrity, and functional task-related neural activity in former U.S. football athletes	Players (n = 61); 58.5 ± (3.66), College players (n = 31), professional players (n = 30)	Overall (n = 61); 3.87 ± (5.85)	RBANS, WAIS, MMSE	No group differences were observed across the concussion history–career duration stratifications for any neuropsychological test (all $P > 05$)
Lewis et al. (2017)	Assess measures of corticomotor excitability and inhibition in retired rugby players	Elite Rugby Players: n = 23; 43 ± (7), Community Level Rugby: n = 28; 45 ± (8), Retired Controls: n = 22; 44 ± (9)	Elite Rugby Players: 0 concussions (n = 0; 0%), 1–2 concussions (n = 3; 13%), ≥3 concussions (n = 20; 87%). Community Level	RPQ: predominantly early (RPQ-3) and late (RPQ-13) symptoms of brain injury	No significant between group differences in RPQ

			Rugby: 0 concussions (n = 1; 4%), 1–2 concussions (n = 3; 11%), ≥3 concussions (n = 23; 85%). Controls: 0 concussions (n = 16; 75%), 1–2 concussions (n = 5; 21%), ≥3 concussions (n = 1; 4%)		
Esopenko et al. (2017)	Characterise retired professional ice hockey players' cognitive and psychosocial functioning in relation to concussion exposure and APOEε4 status	Retired professional ice hockey players: n = 33; 54.3 ± (10.4) Controls: n = 18; 53.5 ± (10.2)	Retired professional ice hockey players: Mean ± (SD); 4.8 ± (2.7), Controls: 0.6 ± (0.8)	RCFT, WASI, BVMT-R, SDMT, JLO, RAVLT, SOPT, PASAT, FAS, TMT A & B, WCST, Cambridge Brain Sciences, CogState, CFQ, DQ	Reliable group differences in cognitive performance were observed on 1 test of executive (WCST) and 3 tests of intellectual function (WASI vocabulary, similarities and matrix reasoning)
Gardner et al. (2017)	Examine brain neurometabolite concentrations in retired rugby league players who had a history of self-reported concussions	Retired rugby players: n = 16; 38.3 ± (4.6), Controls: n = 16; 37.9 ± (4.9)	Retired players reported an average of 33.44 (Median = 20; IQR = 7–20; range 3–100) concussions. Retired players reported an average of 5.9 concussions with LOC sustained during their careers (Median = 3.5; IQR = 3.5–6; range 0–30)	ACS-TOPF, RAVLT, RCFT, TMT A & B, COWAT, WAIS-IV, RPQ, GPT	There were no significant differences between groups on measures of depression, anxiety, or cognitive functioning
Deshpande et al. (2017)	Estimate the association of playing high school football with cognitive impairment and depression at 65 years of age	Retired high school players: n = 3904; 64.4 ± (0.8) Football (n=834), Non-sport and other sport (n=1858)	Not specified	LF, DWR	Football players did not have significantly different composite cognition scores than all controls; including non-sports controls and non-collision sport controls (–0.04; 97.5% CI: –0.14 to 0.05; *P*= .37)

Kuhn et al. (2017)	Investigate relationships between neuroimaging, neuropsychological and symptoms in a cohort of retired NFL players	NFL players: n = 45 46.7 ± (9.1)	NFL players: 6.9 ± (6.2) concussions and 13.0 ± (7.9) "dings" in the NFL	TOMM, BVMT-R, CVLT-II, TMT A and B, WAIS-3, COWAT, WTAR IQ, ImPACT	There were minimal and statistically nonsignificant correlations among the neuroimaging, neurocognitive, and symptom scores examined in this cohort of NFL retirees
Montenigro et al. (2017)	Develop a metric to quantify cumulative RHI exposure from football and to examine the association between RHI exposure and long-term clinical outcomes	Former high school and collegiate football players: n = 93; 47.3 ± (13.9)	Concussion history median (IQR) 20 ± (3)	BTACT, BRIEF-A	Mean scores on the BTACT indicated that the entire sample was, on average, cognitively normal
Strain et al. (2017)	Assess the relationship of white matter integrity and performance on the BNT in a group of retired professional football players and a control group	Retired NFL n = 25; 59.4 ± (11.8), Control n = 22; 61.1 ± (12.2)	Not Specified	BNT	The mean BNT T-score of the retired athletes was significantly lower than the mean performance of the control group (P = .005)
McMillan et al. (2017)	Investigate symptoms and a range of cognitive and health outcomes in retired rugby players with history of repeated concussion	Retired International Rugby Players (RIRP): n = 52; 53.5 ± (13.0), Controls: n = 29; 55.1 ± (9.0)	RIRP: 13.9 ± (18.9) Controls: 0.3 ± (0.5)	MOCA, SDMT, TMT-B, RAVLT, SART, GPT, JLO Test, RPQ, SF-36	RIRP performed poorer than controls on a test of verbal learning (P = .022). No significant difference on all other cognitive tests was found (P > .05)
Alosco et al. (2017)	i) Examine olfactory function in former NFL players compared to controls. ii) Investigate the association between the B-SIT and	Former NFL Players n = 95; 55.29 ± (7.88) (Original sample 96, 1 player was excluded due to poor effort on testing). Controls: n = 28 57.14 ± (6.94)	NFL players: median of 50 concussions. The players reported a mean of 4.63 ± (16.45) concussions that resulted in LOC	TMT-A & B, WAIS-R, WSCT, COWAT, DKEFS, ROCF, NAB-LL, Map Reading Test, Naming	In the former NFL players, lower olfactory test scores correlated with worse neuropsychological and neuropsychiatric functioning

	behavioural/mood and neuropsychological tests in the former NFL players			Test, Animal Fluency, BSIT, BRIEF-A, BRI	
Solomon et al. (2016)	Investigate an association between years of exposure to pre-high school football <12 years and neuroradiological, neurological and neuropsychological outcomes in later life	Retired NFL players: n = 45; 46.7 ± (9.1)	Retired NFL players: 6.9 ± (3.2)	TOMM, BVMT-R, CVLT-II, TMT A & B, WAIS-III, COWAT, WTAR IQ, ImPACT, MMSE	Neurocognitive test scores did not demonstrate a significant relationship with years of exposure to pre-high school football
Multani et al. (2016)	To evaluate the impact of repetitive concussions in retired professional football players on white-matter tracts, self-reported symptomology and neuropsychological assessment	Retired professional football players: n = 18; 49.6 ± (12), Healthy male controls: n = 17; 46.7 ± (10)	Retired professional male football players: 5.4 ± (4), Healthy male controls: 0	RVDLT, WTAR, cognitive self-report questionnaire	Retired players reported significantly higher neuropsychiatric and cognitive symptoms than healthy controls and worsening of these symptoms since their last concussion
Koerte et al. (2016a)	Characterize, neuroimaging features of CSP in former NFL players who present with cognitive, mood, and behavioural symptoms compared to asymptomatic non-contact sport athletes	Former NFL players n = 72; 54.53 (7.97). Former professional non-contact sport athletes n = 14; 57.14 (7.35)	Not specified	NAB-LL, NAB Map Reading, NAB Naming, ROCF, TMT Parts A and B, WAIS-R, WRAT-4, WCST, BRIEF-A, BRI	Former professional NFL players demonstrated significantly lower outcome scores in most tests of cognitive functioning and higher scores in behavioural evaluations

Koerte et al. (2016b)	Evaluate cortical thickness in former professional soccer players using high resolution structural MRI	Former soccer players: n = 15; 49.3 ± (5.1). Controls: n = 15; 49.6 ± (6.4)	Not specified	TMT A & B, ROCFT	All soccer players and controls tested within normal range for age for all cognitive tests
Gardner et al. (2016)	Characterize MRI features of the septum pellucidum in retired NFL players with a history of repeated concussive/sub concussive head traumas compared with controls	Retired NFL players n= 17; 54.6 ± (15.8), Controls n = 17; 54.7 ± (15.8)	Not specified	MMSE	There was no significant difference in MMSE score (mean score, SD; SD 27.1 ± (1.7) versus 25.9 ± (3.3), *P* = .3
Wright et al. (2016)	Determine whether concussion history and cognitive reserve could be used to create an index to predict cognitive outcomes in retired American football players	Retired NFL players: n = 40; 46.38 ± (10.75)	Retired NFL players: 3.93 ± (3.95)	AMNART, CVLT-II, ROCFT, SDMT, TMT A & B, F-A-S	Retired NFL players displayed deficits in attention and processing speed, verbal memory, non-verbal memory and executive ability
Wilde et al. (2016)	Evaluate the effects of boxing on brain structure and cognition	Boxers: n = 10; (8 retired, 2 active); 45.7 ± (9.71), Control: n = 9; 43.44 ± (9.11)	Not Specified	VSRT, SRTT	Word list recall was impaired in the boxers (*P*= .006), implicit memory was preserved (*P*< .04)
Amen et al. (2016)	Determine whether low perfusion in specific brain regions on neuroimaging can accurately separate	Retired NFL: n = 161; 52 ± (14.2), For SPECT control group n = 124; 44 ± 16.6	Not Specified	Connors' Continuous Performance Test II, Micro-Cog or WebNeuro	Neuropsychological assessments showed 92% of players had decreased general cognitive proficiency, 86% had decreased information processing speed, 83% had memory loss, 83% had

	professional football players from healthy controls				attentional deficits, and 85% had executive function impairment
Hume et al. (2017)	Investigate cognitive function in former professional rugby players and assess the association between concussion history and cognitive function	Retired Elite Rugby: n = 103; 41.3 ± (7.5), Retired Community Rugby: n = 195; 44.9 ± (8.4), Retired Non-contact sport group: n = 65; 42.1 ± (7.7)	Elite Rugby: 3.5 ± (2.0) Community Rugby: 2.9 ± (2.2), Noncontact: 0.4 ± (0.8)	Online CNS-Vital Signs Test	Elite rugby group performed worse compared to non-contact sports on tests of complex attention, processing speed, executive functioning and cognitive flexibility
Vann Jones et al. (2014)	Investigate the hypothesis that chronic low-level head trauma as a result of heading is associated with persistent cognitive decline	Former professional players: n = 92, 67.45 ± (6.96)	Not specified	TYM	In comparison to the only large UK-based MCI prevalence study of men; it was demonstrated that there was no statistical significance between MCI among the sample of ex-professional footballers and a large sample of men in Wales
Decq et al. (2016)	Assess the prevalence of major depressive disorder, mild cognitive disorders and headache in retired rugby players and to explore the link between scores and the number of reported concussions	median (IQR) Retired rugby players (RRPs): n = 239; 52 (49-55.75), Other retired sportsmen (ORS): n = 138; 52 (49-55)	RRP: 3.1 ± (5.01), Other sports: 0.68 ± (1.83)	F-TICS-m	A higher rate of mild cognitive disorders was observed in RRPs compared to ORS (57% versus 40%) *P* = .005
Meehan et al. (2016)	Determine whether the exposure to the sub-concussive blows that occur during Division III collegiate collision sports	Male and Female Study n = 3656 n (%), <40: 538 (14.7), 40–44: 452 (12.4), 45–49: 571 (15.6), 50–54: 744 (20.4), 55–59:551 (15.1),60–64: 382	Diagnosed Concussion: n (%) Collision sport; athletes: 283 (7.6), Contact sport athletes: 121 (3.3), Non-contact; sport athletes: 177	PROMIS, Neuro-QOL	Athletes with a history of concussion had lower scores (indicating worse self-reported health) on measures of general

	affect later life neurobehavioral quality-of-life measures	(10.5), 65–70: 367 (10.0), >70: 47 (1.3)	(4.8), Non-athletes: 255 (6.9). Undiagnosed Concussion: n (%) Collision sport; athletes: 396 (10.7), Contact sport athletes: 134 (3.6), Noncontact sport athletes: 102 (2.8), Nonathletes: 113 (3.1)		concerns regarding cognition, executive function, and positive affect
Coughlin et al. (2015)	Investigate cognitive, molecular and structural markers in former NFL players	Retired NFL: n = 9; 64.81 Control: n = 9; 58.33	Retired NFL players: n = 12.90	CVLT-II	Former players had varied performance on a test of verbal learning and memory
Stamm et al. (2015)	Determine the relationship between exposure to repeated head impacts through tackle football prior to age 12 and later-life executive function, memory, and estimated verbal IQ	Former NFL Players AFE < 12 years: n = 21; 51.95 ± (1.33) Former NFL Players AFE ≥ 12 years: n = 21; 52.33 ± (1.33)	AFE < 12 years: 392.00 ± (145.40), AFE ≥ 12 years: 370.30 ± (234.90)	WCST, NAB-LL, WRAT-4	Former NFL players in the AFE < 12 years group performed significantly worse than the AFE ≥ 12 group on all measures of the WCST, NAB-LL, and WRAT-4
Koerte et al. (2015)	Evaluate neurochemistry by using MRS along with neurocognitive performance in former professional soccer players without a known history of concussion, but with a history of extensive heading	Former soccer players n = 11; 52.0 ± (6.8), Former noncontact sport athletes n = 14; 46.9 ± (7.9)	Not specified	TMT A & B, ROCF	All soccer players and controls tested within the normal range for age for TMT parts A and B, ROCF test

	compared with former noncontact sport athletes				
Strain et al. (2015)	Assess the relationship of memory performance with hippocampal volume and concussion history in retired NFL athletes with and without a diagnosis of mild cognitive impairment	Retired NFL: n = 28 (MCI n = 8); 58.1 ± (13), Control: n = 27; (MCI=6); 59 ± (12)	NFL MCI: 3.8 ± (3.5) NFL Athletes with MCI and Concussion History; 4.6 ± (3.6)	CVLT-II, ROCFT, BNT, SORT	No significant differences were found on the ROCFT. The CVLT scores were significantly worse in athletes compared to controls (*P* = .002), athletes with no MCI versus athletes with MCI (*P* < .001) and athletes with MCI compared to control (*P* < .001)
Terry et al. (2015)	Examine neural activation, verbal memory and behavioural scores on the fMRI paradigm in individuals who sustained at least 2 football related concussions compared to a control	Football players: n = 25; 52.0 ± (8.05), Control group: n = 16; 49.1 ± (8.3)	4.3 ± (3.7)	WTAR, CVLT-II, WMS-IV	Concussive history was not associated with worse memory functioning on neuropsychological tests or worse behavioural performance
Casson et al. (2014)	Perform clinical neurological, neuropsychological and neuro-radiological examinations on a group of retired NFL players.	Retired NFL players: n = 45; 45.6 ± (8.9) years	6.9 ± (6.2)	MMSE, ImPACT	The majority of retired players had normal clinical mental status and CNS. Neuropsychological testing revealed isolated impairments in 11 players (24%), but none had dementia
Tremblay et al. (2014)	Investigate white matter integrity and cognitive and motor function in retired athletes with a history of concussions	Retired athletes: n = 15; 60.87 ± (7.51), Control group: n = 15 58.13 ± (5.28)	Retired athletes: 2.08 ± (1.31)	MMSE, RAVLT, TCFT, Eriksen Flanker Task, TMT A & B, SDMT, SRTT	The majority of neuropsychological tests did not reveal clinically significant differences between athletes and controls. Retired athletes showed reduced semantic verbal fluency (*P* = .04) and delayed recall and recognition

					conditions of the TCFT (*P* = .03, *P* = .02)
Hart et al. (2013)	Assess for the presence of cognitive impairment and depression in aging former NFL players, and identify neuroimaging correlates of these dysfunctions	Retired NFL players n = 34; mean 61.8 range 41 to 79, Control n = 26; 60.1 range 41–79	32/34 had sustained at least 1 concussion with an average of 4.0 (mean 2.0 Grade 1, 0.5, Grade 2 and 1.6 Grade 3 per participant)	WASI, TMT-A & B, WAIS-IV, COWAT, BNT, ROCFT, CVLT-II, SORT	Significant differences were found on BNT, SORT, ROCFT and CVLT. No significant differences were found on the TMT, WAIS-IV and COWAT
Hampshire et al. (2013)	Evaluate the performances and brain activation patterns of retired NFL players relative to controls using an f MRI-optimised neuropsychological test of executive function	NFL alumni: n = 13, Controls: n = not specified	Not specified	CANTAB-TOTSPT	Behaviourally, the NFL alumni showed sub-clinical and modest performance deficits on the executive function
Pearce et al. (2014)	To investigate corticomotor excitability and inhibition, cognitive functioning and fine motor dexterity in retired elite and amateur Australian football players (AFPs), with a history of concussions	AFPs = 40. Elite players: n =20; 49.7 ± (5.7). Amateur players n = 20; 48.4 ± (6.9). Controls n = 20; 47.56 ± (6.85)	Elite Players: 3.70 ± (2.89). Amateur players: 2.40 ± (1.56)	CANTAB-PAL, CANTAB-SWM, CANTAB- RT	Reaction time showed significant differences between the healthy control group and the combined AF groups (*P* = .003), with no differences between the 2 AF groups (*P* = .061). No differences were observed when comparing the healthy control group to the combined football groups on the PAL and SWM. However, within the AFPs, the amateur player group performed significantly worse compared to elite group

Seichepine et al. (2013)	Examine executive function in current and retired college and professional football players	Retired college and professional football players n = 64; 47 ± (13.6) (range 25–81)	56/64 participants: ≤55 concussions. 6/64 participants: 100–140 concussions.1/64 participants: ~350 concussions. 1/61 reported ~20000 concussions	BRIEF-A	Significant group differences were observed between football players and normative data for healthy adults on the BRIEF-A in the following areas – Global Executive Composite ($P < .05$), Metacognition Index ($P < .05$) and Behavioral Regulation Index ($P < .05$). ($P < .006$)
Randolph et al. (2013)	Explore the prevalence of cognitive impairment in a sample of retired NFL players	Retired NFL players (n = 41) were selected from 513 players who completed surveys from a previous study; 64.2 ± (5.5), Cognitively normal subjects (=41) extracted from RBANS normative data; 64 ± (5.8)	Not specified	RBANS	RBANS total score mean for the NFL players was significantly below the healthy control sample ($P = .002$)
Tremblay et al. (2013)	Investigate the neuroimaging profile of former university athletes with concussions in relation to cognition	Former university athletes: n = 30, Experiment group: n = 15; 60.87 ± (7.51), Controls: n = 15; 58.13 ± (5.28)	Experiment Group: 24.00 ± (4.55), Controls: no history of concussion	MMSE, TCFT, RAVLT, SDMT, Colour trails test (A and B)	Relative to controls, former athletes showed a reduced semantic verbal fluency ($P = .040$) and altered episodic memory on both delayed recall ($P = .026$) and recognition ($P = .015$) conditions of the TCFT, while performance on the copy trial did not different across groups ($P > .15$)
Ford et al. (2013)	Examine long-term neural changes associated with multiple sport related concussion using event-related fMRI	Retired NFL players: n = 27 Low concussion: (n= 15); 64.1 ± (6.8), High concussion;(n = 12); 62.6 ± (5.0), Control: n = 14; 62.2 ± (6.3)	Low concussion history: 0,1,2 concussions: 1.07 ± (.96). High concussion history: 3 or more concussions: 6.5 ± (5.1)	MMSE, WAIS-3, COWAT, TMT B, BNT, WTAR, TICS, Memory Paradigm	Both concussion groups demonstrated relational memory impairments relative to the age-matched group $P < .05$

Willeumier et al. (2012)	Investigate the effects of body mass as measured by waist to height ratio (WHtR) on regional cerebral blood flow using single photon emission CT imaging	Retired NFL athletes: (n = 76), n=38 healthy weight; 58 ± (9.6), n = 38; overweight 58 ± (13.3)	Not specified	Microcog	Between-group differences were found in general cognitive proficiency and general cognitive function ($P < .025$). Overweight athletes had significant decrease in attention ($P = .01326$), general cognitive proficiency ($P = .012$) and memory ($P = .005$)
Amen et al. (2011)	Determine whether relative to a healthy control group, retired NFL players as a group would exhibit significant decreases in regional cerebral blood flow in the, consistent with previous brain trauma, and compromised neuropsychological functioning	Active and retired NFL players n = 100, 57.27 ± (12.37), For SPECT control group n = 20; 50.0 ± (16.1)	Not specified, LOC episodes mean= 2.693, 0 n = 37, 1 n = 15, 2 n = 15, 3-5 n = 18, >5 n = 14	Microcog, CPT-II, MCIS	Players scored in the bottom half of the percentile placements on all measures including general cognitive functioning, general cognitive proficiency, processing speed, processing accuracy, attention, reasoning and memory except spatial processing and reaction-time, which were both in the top half of the percentile placements
Hinton et al. (2011)	Determine the relative influence of current exercise and diet on the late-life cognitive health of former Division 1 collision-sport collegiate athletes (i.e., football players) compared with non-collision sport athletes and non-athletes	Former Division I Collision-sport athletes (football players): n = 214 Former Division I non-collision sport athletes (other athletes): n = 136 Former non-athletes (non-athletes) n = 50	Not specified	CDS	Former football players reported more cognitive difficulties, as well as worse physical and mental health than controls

De Beaumont et al. (2009)	Investigate electrophysiological, motor and cognitive measures in former athletes who sustained their last sports concussion > 30 years ago	Former Canadian University level athletes n = 19; 60.79 ± (5.16), Controls: n = 21; 58.89 ± (9.07)	Former Canadian University level athletes: range 1–5, Controls: no prior history of concussion or neurological insult	MMSE RCFT	Former athletes with concussion obtained an equivalent total score at the MMSE to that of former athletes with no prior history of concussion ($P > .05$). Every participant from both groups scored within the normal range at the MMSE
Thornton et al. (2008)	Examine the extent to which lifetime concussion exposure is associated with neurocognitive and symptomatic status in competitive versus recreational/retired rugby players and differential complications between groups	Male and Female Study Retired players: No concussions n = 37; 32.14 ± (12.41), 1–2 concussions n = 39; 28.72 ± (10.20), 3 or more: n = 35; 34.03 ± (12.06)	Divided participants into no heavy concussion exposure groups Sample size (Female/Male): Grade 2 or above: n = 37, 8:29) 1–2 heavy concussions: n = 39, 4:35) 3 or more (n = 35, 1:34)	ETS Kit - V2 and V3, CCFT, WAIS-III, TMT-A and B, WMS-III, RAVLT, WCST, PCSC	Participants with no heavy concussions reported significantly fewer Memory complaints (d = −0.68), less Distress (d = −0.76), and less overall (Total) PCS (d = −0.65) than did those with 3 or more heavy concussions
Guskiewicz et al. (2005)	Investigate the association between recurrent concussion and late-life cognitive impairment in retired professional football players	Retired professional footballers: n = 2552; 53.8 ± (13.4)	At least 1 concussion n = 1513; 3+ concussions n = 597	SF-36 (including MCS)	Retired players with 3 or more reported concussions had a fivefold prevalence of MCI diagnosis and a threefold prevalence of reported significant memory problems compared with retirees without a history of concussion
Downs and Abwender (2002)	Investigate neuropsychological function in older and retired soccer players in comparison to swimmers	Male and female soccer players: n = 32 (males n = 15, females n = 11); 19.81 ± (1.50). Older male soccer players (current/ retired professionals): n = 6; 41.5 ± (9.77).	Not specified	WCST, CPT, PASAT	Soccer players performed worse than swimmers on tests of conceptual thinking. The older soccer group performed particularly poorly on

		Control groups: Male and female swimmers n = 22; (male n = 7, females n = 15); 19.50 ± (1.22) and adult male swimmers (n = 7) 42.86 ± (15.09)			measures of concentration, reaction time and conceptual thinking
Murelius and Haglund (1991)	Analyse possible chronic brain damage in 47 former amateur boxers who started their career after the introduction of stricter Swedish amateur boxing rules	High match boxers (HM): n = 25; 30.5 ± (5.1), Low match boxers (LM): n = 25; 32.3 ± (5.6) Soccer players: n = 25; 33.0 ± (6.0) Track and Field: n = 25; 33.4 ± (5.4)	Not specified	Synonyms test of verbal understanding, Block Design Test (Koh's cubes), TMT A & B, FTT Tests from Claeson-Dahl, Luria and tests of construction-memory- verbal learning, verbal retention, memory for designs, motor functions of the hand.	In only one test did the groups differ significantly. Boxers who had participated in a large number of bouts had slightly inferior finger-tapping performance. None of the boxers were considered to have definite signs of intellectual impairment
Casson et al. (1984)	Dispute the claims that chronic encephalopathy occurs in only an occasional poorly skilled fighter, or those that are poorly educated or abusing drugs and alcohol	Retired athletes n = 18 (n = 13 former boxers, n = 2 active professional boxers, n = 3 active Golden Glove boxers), mean age 36	Not specified	TMT, DST, WMS, Bender Gestalt Test	All former and active professional boxers had abnormal results on at least 2 of the 4 main tests. 8/17 had abnormal CT scans - these had a significantly higher mean impairment index on neuropsychological testing than those with normal CT scans ($P < .001$)

3.2.4 Methodological assessment

An adapted Downs and Black Checklist was used to evaluate the methodological quality of the studies (Downs and Black, 1998). This was performed independently by two reviewers (JC and FW). Disagreements between the reviewers were resolved through discussion to achieve consensus. Failing agreement, a third reviewer (SB) arbitrated. The checklist was modified to a maximum of 17 applicable questions which addressed the following methodological components: reporting, external validity, internal validity (bias and confounding) and power. Seventeen items were rated either as yes (=1) or no/unable to determine (=0), and one item was rated on a 3-point scale (yes = 2, partial = 1, and no = 0). The maximum achievable score was 18, with higher scores indicating a better methodological quality of the study [Appendix B.3]. Results were categorized according to the adapted Downs and Black Checklist (Downs and Black, 1998) from Hartling et al. (2004) and Hignett (2003) and were interpreted as follows: strong quality (≥14) represented the top 75%; moderate quality (scored 9–13) represented 50%–74%; limited quality represented (5–8) represented 25%–49%; poor quality (<5) represented <25%.

3.3 Results

3.3.1 Literature Search

After removing duplicates, this review yielded a total of 2842 records. The titles and abstracts of these records were screened, and 119 studies identified that potentially met the inclusion criteria and, hence, were subject to full review. Of these, a total of 46 cross-sectional studies published between 1984 and 2018 met the criteria and were included in a quantitative synthesis. Given the heterogeneity of the study design and outcome measures, a meta-analysis

could not be conducted for all studies. Where possible, depending on the homogeneity of the included studies a meta-analysis was performed.

3.3.2 Methodological Assessment

A detailed breakdown of the quality appraisal of the 46 studies is presented in Table 3-3. A total of n=11; 24% of studies had a methodological quality score of poor or limited. The mean methodological quality score was 10.3 ± (2.9) out of a total score of 18, giving an overall quality score of moderate (percentage 50%–74%; 9–13).

3.3.3 Study Characteristics

Key study characteristics and findings of the 46 cross-sectional studies are summarised and presented in Table 3.2. The total sample included 12'763 participants; this included 4'317 collision sport athletes, 662 contact sport athletes, 3346 non-contact athletes and 4'438 participants classified as controls. Collision sports included rugby, football, boxing and ice-hockey. All contact sport athletes included were soccer players. Sports classified as non-contact were swimming, cricket, field hockey, track and field, running, table tennis, ball-room dancing, athletics, badminton, canoeing, horseback riding, rock climbing, fencing, golf, weightlifting, paragliding, pelota, skiing, squash, archery, triathlon, sailing and gliding. The majority 43/46 (94%) studies excluded female participants, with only three studies including female athletes (Meehan et al., 2016, Thornton et al., 2008, Downs and Abwender, 2002). Participant characteristics varied in age, medical history, socioeconomic background, concussion exposure, number of concussions reported, and types of sports played.

A large proportion of these studies (n = 20) included retired NFL players (Wright et al., 2016, Solomon et al., 2016, Kuhn et al., 2017, Gardner et al., 2016, Strain et al., 2017, Strain et al., 2015, Amen et al., 2016, Casson et al., 2014, Coughlin et al., 2015, Stamm et al., 2015, Hampshire et al., 2013, Hart et al., 2013, Ford et al., 2013, Willeumier et al., 2012, Guskiewicz et al., 2005, Alosco et al., 2017, Koerte et al., 2016a, Randolph et al., 2013, Amen et al., 2011, Clark et al., 2018). Seven studies investigated retired rugby players (Thornton et al., 2008, Lewis et al., 2017, Hume et al., 2017, Gardner et al., 2017, Decq et al., 2016, McMillan et al., 2017, Pearce et al., 2018). Participants in the other studies included boxers (n=3) (Wilde et al., 2016, Casson et al., 1984, Murelius and Haglund, 1991) and soccer athletes (n=4) (Downs and Abwender, 2002, Koerte et al., 2015, Koerte et al., 2016b, Vann Jones et al., 2014), while other authors investigated a combination of former professional/amateur athletes including university and high school football and hockey athletes (n = 12) (Meehan et al., 2016, Esopenko et al., 2017, Deshpande et al., 2017, Alosco et al., 2017, Multani et al., 2016, Terry et al., 2015, Tremblay et al., 2014, Hinton et al., 2011, De Beaumont et al., 2009, Tremblay et al., 2013, Pearce et al., 2014, Seichepine et al., 2013, Montenigro et al., 2017).

Table 3-3 Summary of Quality Appraisal of Included Studies- using the adapted Downs and Black checklist.

References	Reporting: Total/8	External Validity: Total/2	Internal Validity (Bias): Total/4	Internal Validity- Confounding (Selection Bias) Total/3	Power: Total/1	Total Quality: Score/18	Methodology Quality
Pearce et al. (2018)	8	0	2	1	0	11	Moderate
Clark et al. (2018)	6	2	2	1	0	11	Moderate
Lewis et al. (2017)	6	1	2	0	0	9	Moderate
Esopenko et al. (2017)	8	2	2	0	0	12	Moderate
Gardner et al. (2017)	7	2	2	0	0	11	Moderate
Deshpande et al. (2017)	6	2	3	3	0	14	Strong
Kuhn et al. (2017)	7	2	2	3	0	14	Strong
Montenigro et al. (2017)	6	0	2	2	0	10	Moderate
Strain et al. (2017)	5	2	2	0	0	9	Moderate
McMillan et al. (2017)	3	0	1	0	0	4	Poor
Alosco et al. (2017)	6	0	2	0	0	8	Limited
Solomon et al. (2016)	7	2	2	2	0	13	Moderate
Multani et al. (2016)	7	0	2	0	0	9	Moderate
Koerte et al. (2016a)	5	0	2	0	0	7	Limited
Koerte et al. (2016b)	6	2	2	1	0	11	Moderate
Gardner et al. (2016)	6	0	2	1	0	9	Moderate
Wright et al. (2016)	8	2	3	2	0	15	Strong
Wilde et al. (2016)	6	0	2	0	0	8	Limited
Amen et al. (2016)	4	0	2	1	0	7	Limited
Hume et al. (2017)	7	0	2	2	0	11	Moderate
Decq et al. (2016)	7	2	2	2	0	13	Moderate

Meehan et al. (2016)	8	2	2	2	0	14	Strong
Coughlin et al. (2015)	7	2	2	2	0	13	Moderate
Stamm et al. (2015)	7	0	2	2	0	11	Moderate
Koerte et al. (2015)	7	2	2	0	0	11	Moderate
Strain et al. (2015)	8	2	2	3	0	15	Strong
Terry et al. (2015)	8	2	2	3	0	15	Strong
Casson et al. (2014)	7	2	2	1	0	12	Moderate
Vann Jones et al. (2014)	4	2	2	2	0	10	Moderate
Tremblay et al. (2014)	5	0	2	1	0	8	Limited
Hart et al. (2013)	7	2	2	2	0	13	Moderate
Hampshire et al. (2013)	3	0	2	0	0	5	Limited
Pearce et al. (2014)	7	0	2	0	0	9	Moderate
Seichepine et al. (2013)	5	0	2	1	0	8	Limited
Randolph et al. (2013)	1	0	2	0	0	3	Poor
Tremblay et al. (2013)	7	0	2	0	0	9	Moderate
Ford et al. (2013)	7	2	2	0	0	11	Moderate
Willeumier et al. (2012)	7	2	2	1	0	12	Moderate
Amen et al. (2011)	6	2	2	1	0	11	Moderate
Hinton et al. (2011)	7	2	2	3	0	14	Strong
De Beaumont et al. (2009)	6	0	2	1	0	9	Moderate
Thornton et al. (2008)	6	2	2	2	0	12	Moderate
Guskiewicz et al. (2005)	6	0	2	1	0	9	Moderate
Downs and Abwender (2002)	4	0	2	2	1	9	Moderate
Murelius and Haglund (1991)	2	0	2	2	0	6	Limited
Casson et al. (1984)	5	0	2	0	0	7	Limited

A total of 32 studies out of 44 included a control group (Meehan et al., 2016, Thornton et al., 2008, Downs and Abwender, 2002, Gardner et al., 2016, Strain et al., 2017, Strain et al., 2015, Coughlin et al., 2015, Hampshire et al., 2013, Hart et al., 2013, Ford et al., 2013, Alosco et al., 2017, Koerte et al., 2016a, Clark et al., 2018, Hume et al., 2017, Gardner et al., 2017, Decq et al., 2016, McMillan et al., 2017, Pearce et al., 2018, Wilde et al., 2016, Murelius and Haglund, 1991, Koerte et al., 2015, Koerte et al., 2016b, Esopenko et al., 2017, Multani et al., 2016, Terry et al., 2015, Tremblay et al., 2014, Hinton et al., 2011, De Beaumont et al., 2009, Tremblay et al., 2013, Pearce et al., 2014, Willeumier et al., 2012, Deshpande et al., 2017); the remaining 12 studies did not use a control group (Wright et al., 2016, Solomon et al., 2016, Kuhn et al., 2017, Amen et al., 2016, Casson et al., 2014, Guskiewicz et al., 2005, Randolph et al., 2013, Amen et al., 2011, Casson et al., 1984, Vann Jones et al., 2014, Seichepine et al., 2013, Montenigro et al., 2017). A wide variety of cognitive tests were reported.

The tests and their corresponding cognitive domains are displayed in Table 3-4. Objective neuropsychological tests alone were used in 30 studies to assess different aspects of cognition (Downs and Abwender, 2002, Solomon et al., 2016, Kuhn et al., 2017, Gardner et al., 2016, Strain et al., 2017, Strain et al., 2015, Amen et al., 2016, Casson et al., 2014, Coughlin et al., 2015, Stamm et al., 2015, Hampshire et al., 2013, Hart et al., 2013, Ford et al., 2013, Willeumier et al., 2012, Amen et al., 2011, Clark et al., 2018, Hume et al., 2017, Decq et al., 2016, Pearce et al., 2018, Wilde et al., 2016, Casson et al., 1984, Murelius and Haglund, 1991, Koerte et al., 2015, Koerte et al., 2016b, Deshpande et al., 2017, Terry et al., 2015, Tremblay et al., 2014, De Beaumont et al., 2009, Tremblay et al., 2013, Pearce et al., 2014). A total of five studies used subjective cognitive tests alone (Guskiewicz et al., 2005, Lewis et al., 2017, Vann Jones et al., 2014, Hinton et al., 2011, Seichepine et al., 2013).The remaining nine studies included a combination of objective/subjective tests

(Thornton et al., 2008, Alosco et al., 2017, Koerte et al., 2016a, Randolph et al., 2013, Gardner et al., 2017, McMillan et al., 2017, Esopenko et al., 2017, Multani et al., 2016, Montenigro et al., 2017). Cognitive tests were categorized according to the predominant cognitive domain which they assessed.

3.3.4 Cognitive Domains

A breakdown of cognitive domains assessed in the studies is displayed in Table 3-4. The nine categories included global cognitive ability, attention, memory, executive function, language, intelligence, psychomotor function, perception and S-R cognitive functioning. Memory was the most commonly studied cognitive health outcome (67%, n=31 studies), followed by attention (37%, n=17) and global cognitive ability (37%, n = 17). Two studies Kuhn et al. (2017) and Tremblay et al. (2014) were excluded from the analysis as the cognitive results were duplicates of those in Solomon et al. (2016) and Tremblay et al. (2013) respectively. A breakdown of cognitive results is displayed in Table 3-5.

Table 3-4 Summary of Cognitive Tests Used Across Studies and Corresponding Cognitive Domains of Interest.

Domain	Domain Description	Cognitive Tests	References
Global Cognitive Ability (16)	A broad array of cognitive domains.	MMSE, Modified MMSE, Online CNS-Vital Signs, MOCA, RBANS, BTACT, Micro-Cog, WebNeuro, Cambridge Brain Sciences, ImPACT, CogState, FTICS-m, Composite Cognition Score	Clark et al. (2018), McMillan et al. (2017), (Deshpande et al., 2017), Hume et al. (2017), Esopenko et al. (2017), Montenigro et al. (2017), Decq et al. (2016), Amen et al. (2016), Solomon et al. (2016), Gardner et al. (2016), Casson et al. (2014), Tremblay et al. (2013), Randolph et al. (2013), Ford et al. (2013), Willeumier et al. (2012), Amen et al. (2011), De Beaumont et al. (2009)
Attention (17)	Ability to concentrate and focus on specific stimuli. Attention has multiple subprocesses specialized for different aspects of attentional processing and complex attention tasks, such as selective and divided attention.	TMT, SDMT, Colour Trails Test (A and B), PASAT, EFT, CPT-II, SRTT, SART, WAIS	Clark et al. (2018), McMillan et al. (2017), Gardner et al. (2017), Hume et al. (2017), Alosco et al. (2017), Esopenko et al. (2017), Wright et al. (2016), Wilde et al. (2016), Solomon et al. (2016), Koerte et al. (2016a), Koerte et al. (2015), Casson et al. (2014), Tremblay et al. (2013), Ford et al. (2013), Hart et al. (2013), Thornton et al. (2008), Murelius and Haglund (1991)
Memory (31)	Involves the registration, storage, recognition and retrieval of information.	CVLT-II, WMS-IV, TOMM, BVMT-R, DWR, LF, VSRT, NAB-LL, RAVLT, ROCFT, TCFT, SOPT, RVDLT, TYM, CANTAB-PAL, CANTAB-SWM, SORT, NAB-Map Reading Test, Animal Fluency	Pearce et al. (2018), McMillan et al. (2017), Hume et al. (2017), Esopenko et al. (2017), Alosco et al. (2017), Deshpande et al. (2017), Gardner et al. (2017), Amen et al. (2016), Wright et al. (2016), Multani et al. (2016), Wilde et al. (2016), Strain et al. (2015), Solomon et al. (2016), Koerte et al. (2015), Coughlin et al. (2015), Stamm et al. (2015), Terry et al. (2015), Koerte et al. (2016a), Koerte et al. (2016b), Casson et al. (2014), Pearce et al. (2014), Vann Jones et al. (2014), Tremblay et al. (2013), Hart et al. (2013), Ford et al. (2013), Willeumier et al. (2012), Amen et al. (2011), De Beaumont et al. (2009), Thornton et al. (2008), Casson et al. (1984), Murelius and Haglund (1991)
Executive Function (11)	Includes planning, decision making, working memory, responding to feedback, inhibition and mental flexibility.	CANTAB-IED, CANTAB-TOTSPT, WCST, D-KEFS	Pearce et al. (2018), Esopenko et al. (2017), Alosco et al. (2017), Hume et al. (2017), Wright et al. (2016), Koerte et al. (2016b), Stamm et al. (2015), Casson et al. (2014), Hampshire et al. (2013), Thornton et al. (2008), Downs and Abwender (2002)

Language (8)	Includes object naming, word finding, fluency, grammar, syntax and receptive language.	BNT, COWAT, F-A-S Verbal Phonemic Fluency Test, Letter Fluency	Esopenko et al. (2017), Gardner et al. (2017), Alosco et al. (2017), Strain et al. (2017), Solomon et al. (2016), Strain et al. (2015), Ford et al. (2013), Hart et al. (2013)
Psychomotor function (6)	The relationship between cognitive functions and physical movements.	Lafayette Grooved Pegboard Test, O'Connor Finger Dexterity test (Lafayette Instrument, USA), Finger tapping test, CANTAB-VRT, CANTAB-RTI, CNSVS domain-Motor Speed	Pearce et al. (2018), McMillan et al. (2017), Hume et al. (2017), Gardner et al. (2017), Pearce et al. (2014), Downs and Abwender (2002)
Intelligence (12)	Premorbid intelligence quotient (IQ) refers to one's intellectual ability level previous to the onset of disorders like mild cognitive impairment (MCI) and Alzheimer's disease (AD) and it is important to estimate disease severity.	WTAR IQ, WRAT-4, WAIS- III, IV, WASI, ACS-TOPF, ETS Kit - V2 and V3, CCFT	Clark et al. (2018), Esopenko et al. (2017), Gardner et al. (2017), Solomon et al. (2016), Multani et al. (2016), Koerte et al. (2016b), Stamm et al. (2015), Terry et al. (2015), Casson et al. (2014), Ford et al. (2013), Hart et al. (2013), Thornton et al. (2008)
Perception (3)	Recognition and interpretation of sensory information from the environment. Also includes response to this information in order to interact with the environment.	B-SIT, JLO	Alosco et al. (2017), Esopenko et al. (2017), McMillan et al. (2017)
Self-reported cognitive functioning (14)	The 'self-experience' of cognition. A self-report is any method (e.g., survey, questionnaire or poll) which involves asking a participant about their feelings, attitudes, beliefs and so on.	PROMIS, Neuro-QOL, BRIEF-A, BRI, CDS, SF36 (including MCS), RPQ, Dysexecutive Questionnaire, Cognitive Failures Questionnaire, MCIS, PCSC, AD8, cognitive self-report questionnaire	Gardner et al. (2017), Lewis et al. (2017), Alosco et al. (2017), Esopenko et al. (2017), McMillan et al. (2017), Montenigro et al. (2017), Multani et al. (2016), Koerte et al. (2016b), Meehan et al. (2016), Randolph et al. (2013), Seichepine et al. (2013), Hinton et al. (2011), Thornton et al. (2008), Guskiewicz et al. (2005)
*Kuhn et al 2017 excluded as cognitive results were taken from Solomon et al 2016. *Tremblay et al 2014 excluded as cognitive results were taken from Tremblay et al 2013.			

3.3.4.1 Global Cognitive Ability

Global cognitive ability was assessed in 17 studies (Solomon et al., 2016, Gardner et al., 2016, Amen et al., 2016, Casson et al., 2014, Ford et al., 2013, Willeumier et al., 2012, Randolph et al., 2013, Amen et al., 2011, Clark et al., 2018, Hume et al., 2017, Decq et al., 2016, McMillan et al., 2017, Esopenko et al., 2017, De Beaumont et al., 2009, Tremblay et al., 2013, Montenigro et al., 2017, Deshpande et al., 2017). Thirteen out of the 17 studies found no significant evidence for increased global cognitive difficulties in retired athletes compared to controls/normative data (Solomon et al., 2016, Gardner et al., 2016, Casson et al., 2014, Ford et al., 2013, Willeumier et al., 2012, Clark et al., 2018, McMillan et al., 2017, Esopenko et al., 2017, De Beaumont et al., 2009, Tremblay et al., 2013, Montenigro et al., 2017, Hume et al., 2017, Deshpande et al., 2017), while the other four studies did (Amen et al., 2016, Randolph et al., 2013, Amen et al., 2011, Decq et al., 2016).

Decq et al. (2016) found that retired rugby players had a significantly higher rate of mild cognitive disorders on a modified version of the Telephone Interview for Cognitive Status (F-TICS-m) than others from a variety of sporting disciplines. However, cognitive results were not associated with reported concussions. Retired NFL players were assessed by Amen and colleagues (2011) and the same cohort by Willeumier et al. (2012) the following year. Significant decreases from normal values were found in cognitive functioning and proficiency tests. A large number of the same participants were used by Amen et al. (2016) who found significant relationships between position and body mass measured by waist-to-height ratio (WHtR) and cognitive function among retired NFL players. Randolph et al. (2013) found that retired NFL players scored significantly below that of the healthy control sample in the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) (p= .002). The meta-analysis of three studies measuring global cognition using the MMSE is presented in Figure 3-2. This showed no significant difference between groups for this outcome (p = .68); mean difference (MD) 0.09 and 95% confidence interval (CI) -0.35, 0.54.

Overall, the majority of studies do not support decreased global cognitive functioning/proficiency in retired athletes.

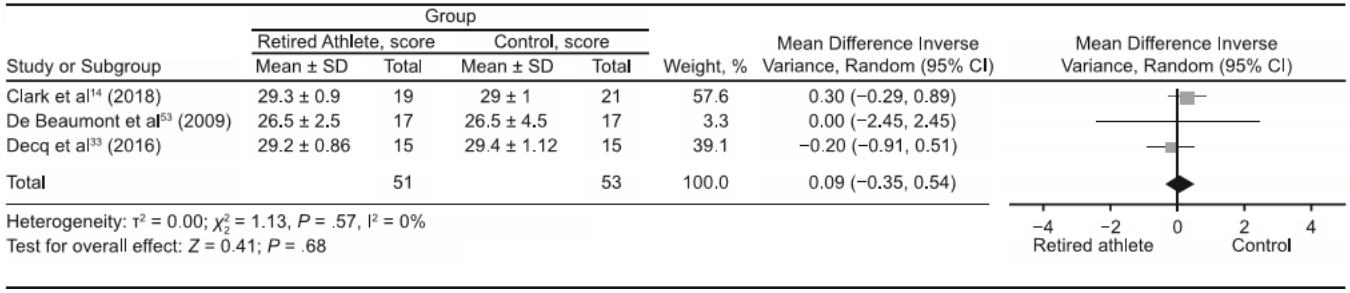


Figure 3-2 *Forest Plot of between-group Comparisons for The Mini-Mental State Examination. Retired athletes compared with controls:* [a] *The total does not equal 100% because percentages were rounded.*

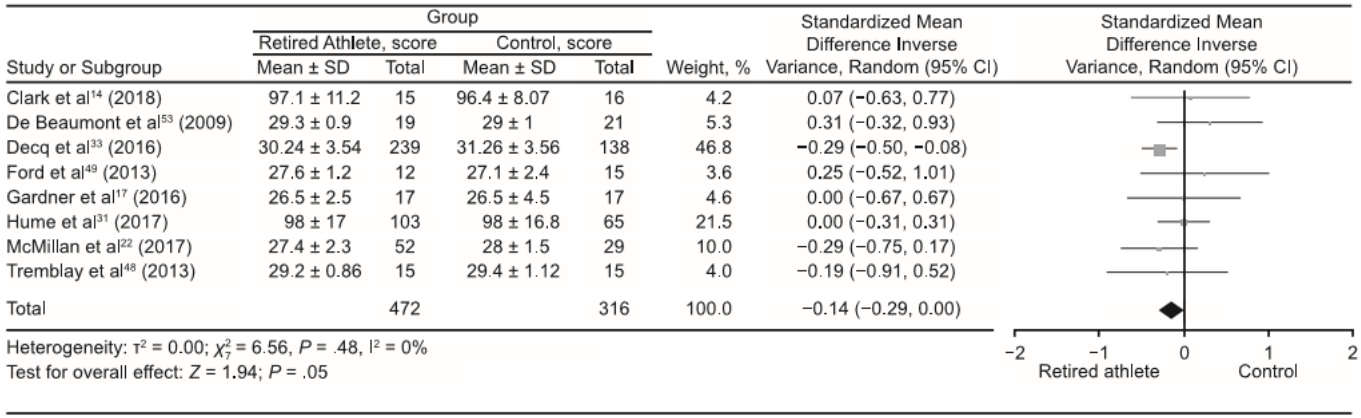


Figure 3-3 *Forest Plot of between-group Comparisons for Global Cognitive Ability. Retired athletes compared with controls:* [a] *The total does not equal 100% because percentages were rounded.*

3.3.4.2 Attention

Tests of attention were administered by 17/46 investigators (Thornton et al., 2008, Wright et al., 2016, Solomon et al., 2016, Casson et al., 2014, Hart et al., 2013, Ford et al., 2013, Alosco et al., 2017, Clark et al., 2018, Hume et al., 2017, Gardner et al., 2017, McMillan et al., 2017, Wilde et al., 2016, Murelius and Haglund, 1991, Koerte et al., 2015, Koerte et al., 2016b, Esopenko et al., 2017, Tremblay et al., 2013). Three studies found that retired athletes had decreased attention scores (Wright et al., 2016, Alosco et al., 2017, Hume et al., 2017). Alosco et al. (2017) found retired NFL players performed significantly worse than controls on the Trail Making Test (TMT) (p = .005). Wright et al. (2016) found retired NFL players had attentional and processing speed deficits on the TMT and the Symbol Digit Modalities Test (SDMT) in comparison to normative values. Hume et al. (2017) found the elite-rugby group performed worse on the CNS Vital Signs test of complex attention than the non-contact sport athletes (effect size -0.67, 95 % confidence interval [CI]: 1.07 to -0.26). From the variety of tests administered to investigate attention, the balance of evidence does not support decreased functioning in retired athletes. Results from six studies assessing attention using the TMT are illustrated in Figures 3-4 and 3-5. Neither tests revealed significant between group differences on pooling results (TMT-A: P = .72; MD: -0.52; 95% CI: -3.40, 2.36; TMT-B: P = .38; MD: -1.41; 95% CI: -4.58, 1.76).

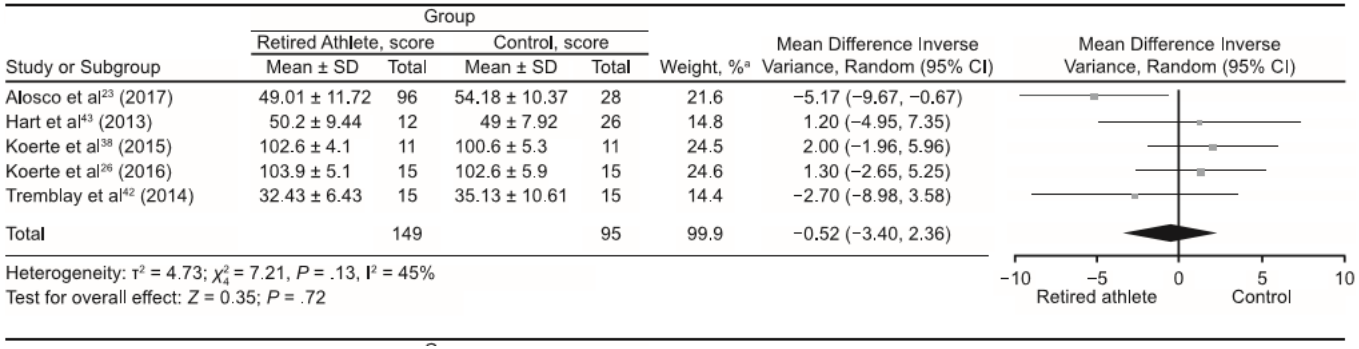


Figure 3-4 *Forest Plot of between-group Comparisons for The Trail Making Test-A. Retired athletes compared with controls:* [a] *The total does not equal 100% because percentages were rounded.*

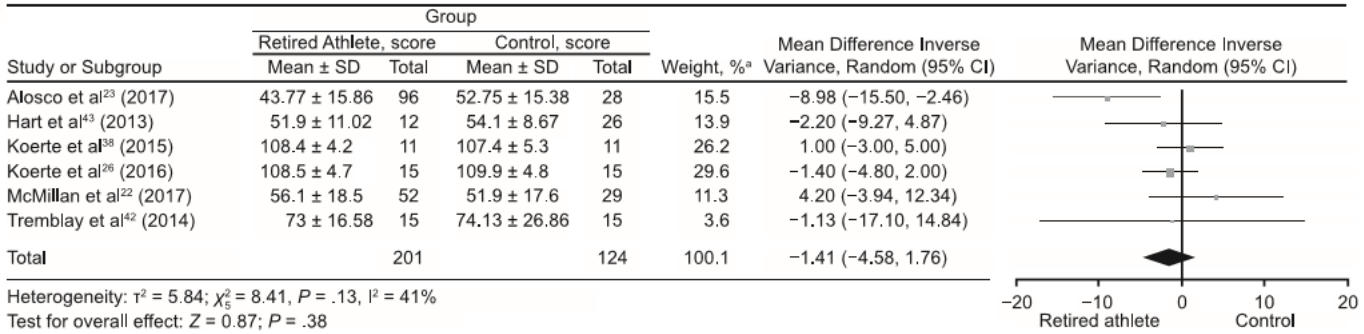


Figure 3-5 *Forest Plot of between-group Comparisons for The Trail Making Test-B. Retired athletes compared with controls:* [a] *The total does not equal 100% because percentages were rounded.*

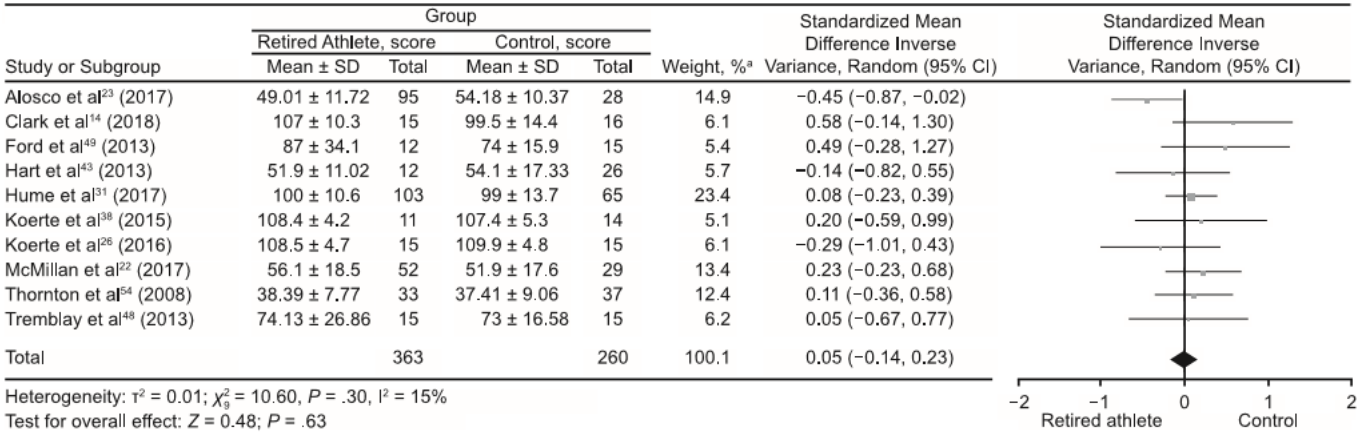


Figure 3-6 *Forest Plot of between-group Comparisons for Attention. Retired athletes compared with controls on.* [a] *The total does not equal 100% because percentages were rounded.*

3.3.4.3 Memory

Memory was assessed in 31 studies (Thornton et al., 2008, Wright et al., 2016, Solomon et al., 2016, Strain et al., 2015, Amen et al., 2016, Casson et al., 2014, Coughlin et al., 2015, Stamm et al., 2015, Hart et al., 2013, Ford et al., 2013, Willeumier et al., 2012, Alosco et al., 2017, Koerte et al., 2016a, Amen et al., 2011, Hume et al., 2017, Gardner et al., 2017, McMillan et al., 2017, Pearce et al., 2018, Wilde et al., 2016, Casson et al., 1984, Murelius and Haglund, 1991, Koerte et al., 2015, Koerte et al., 2016b, Vann Jones et al., 2014, Esopenko et al., 2017, Deshpande et al., 2017, Multani et al., 2016, Terry et al., 2015, De Beaumont et al., 2009, Tremblay et al., 2013, Pearce et al., 2014). Various tests were used to investigate memory which are summarised in Table 3-4. Fourteen studies reported normal functioning in memory tests (Thornton et al., 2008, Solomon et al., 2016, Casson et al., 2014, Coughlin et al., 2015, Alosco et al., 2017, Gardner et al., 2017, Murelius and Haglund, 1991, Koerte et al., 2015, Vann Jones et al., 2014, Esopenko et al., 2017, Deshpande et al., 2017, Multani et al., 2016, Terry et al., 2015, Pearce et al., 2014).

Seventeen of 31 studies (55%) found significant decreases in memory functioning among retired athletes compared to controls/normative data (Wright et al., 2016, Strain et al., 2015, Amen et al., 2016, Stamm et al., 2015, Hart et al., 2013, Ford et al., 2013, Willeumier et al., 2012, Koerte et al., 2016a, Amen et al., 2011, Hume et al., 2017, McMillan et al., 2017, Pearce et al., 2018, Wilde et al., 2016, Casson et al., 1984, Koerte et al., 2016b, De Beaumont et al., 2009, Tremblay et al., 2013). Two studies found that retired NFL players performed worse than control participants on the California Verbal Learning Test (CVLT) (Strain et al., 2015, Hart et al., 2013). McMillan et al. (2017) identified worse performance on the Rey Auditory Verbal Learning Test (RAVLT) by retired rugby players compared with the control group. Wilde et al. (2016) found that word list recall on the Verbal Selective Reminding Test

(VRST) was significantly worse in the boxers compared to controls while Koerte et al. (2016a) found that retired NFL players had significantly decreased performance on a list learning task.

Tremblay et al. (2013) reported that retired American football athletes had significantly decreased scores on the RAVLT and Taylor Complex Figure Test (TCFT). Pearce et al. (2018) used the Spatial Working Memory (SWM) and Paired Associates Learning (PAL) CANTAB subtests to assess memory and found significant differences between groups with the retired rugby players performing poorer than controls. The remaining four studies reported significant deficits in memory tests; however, no control group was employed (Wright et al., 2016, Coughlin et al., 2015, Stamm et al., 2015, Casson et al., 1984). The same group of retired NFL players used by Amen and colleagues (2011) and Willeumier et al. (2012) displayed significant decreases in memory on the Microcog memory subset. Similar results were reported by Amen et al. (2016) using a large proportion of the same players.

Ford et al. (2013) reported relational memory impairments in retired athletes and found that the high concussion group was significantly worse at recognizing intact pairs as ‘‘old’’ (intact pair hits) relative to the age-matched group ($p < .05$). Overall, results are mixed. However, there is preliminary evidence of memory decline in retired athletes. Meta-analysis of three studies using the CVLT-II outcome measure found that retired athletes performed significantly worse than controls (MD = -6.48; 95% CI -10.07, -2.88; P < 001; Figure 3-7). Meta-analysis of five studies using the ROCFT outcome measure also found that controls outperformed retired athletes significantly (ROCFT-Immediate: $p < .0001$; MD: -4.85; 95% CI: -7.15, -2.54; ROCFT-Delay: $p < .0001$; MD: -5.36; 95% CI: -7.79, -2.94; Figures 3-8 and 3-9).

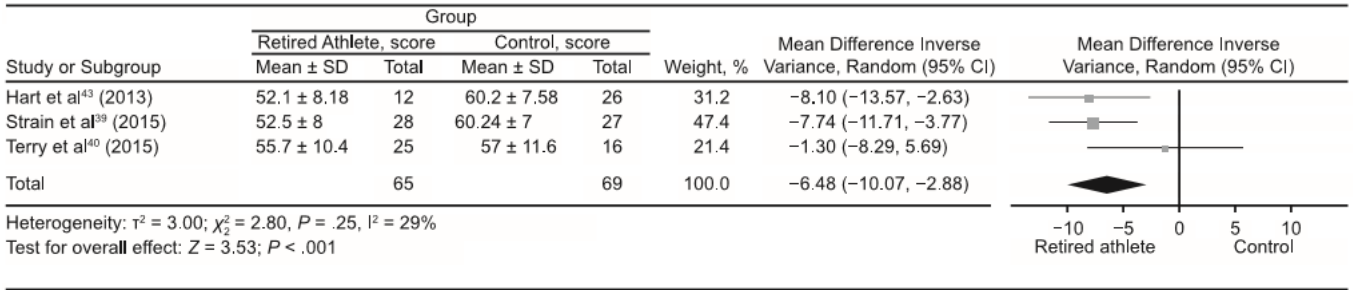


Figure 3-7 *Forest Plot of between-group Comparisons for The California Verbal Learning Test-II. Retired athletes compared with controls.* [a] *The total does not equal 100% because percentages were rounded.*

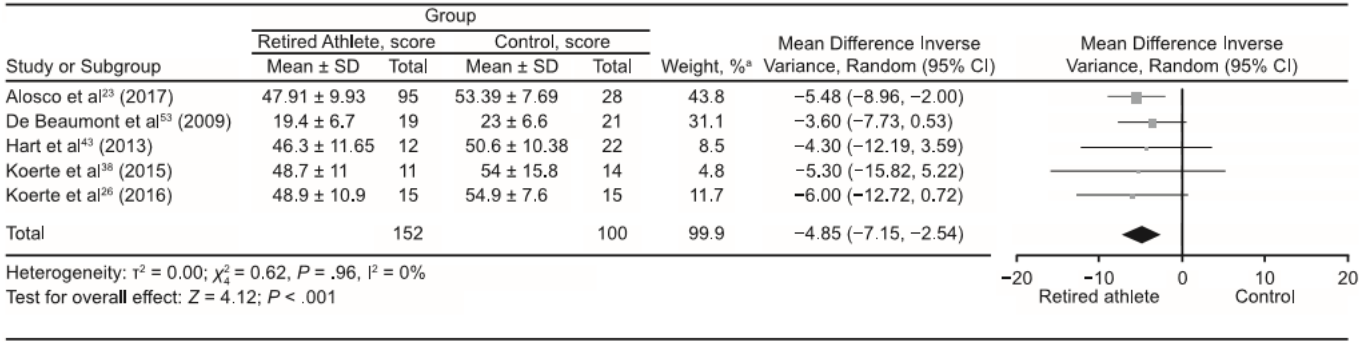


Figure 3-8 *Forest Plot of between-group Comparisons for The Rey-Osterrieth Complex Figure Test Copy and Immediate Recall. Retired athletes compared with controls.* [a] *The total does not equal 100% because percentages were rounded.*

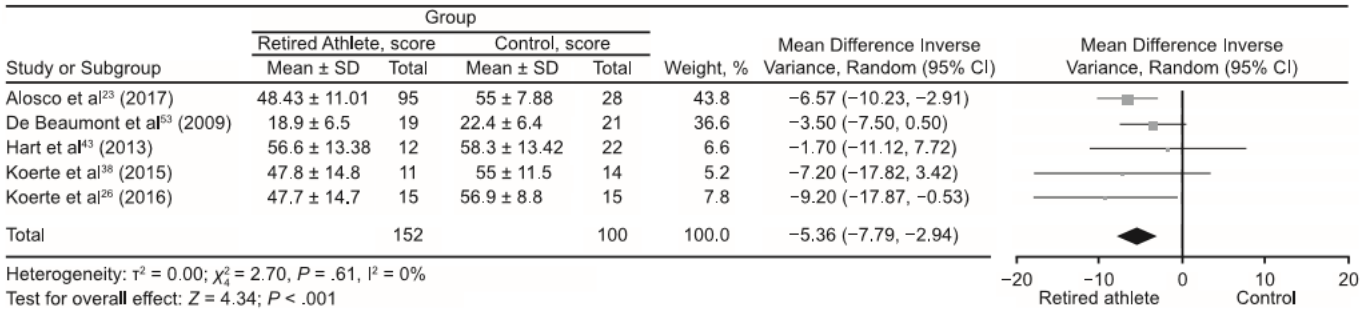


Figure 3-9 *Forest Plot of between-group Comparisons for The Rey-Osterrieth Complex Figure Test Delayed Recall. Retired athletes compared with controls on.* [a] *The total does not equal 100% because percentages were rounded.*

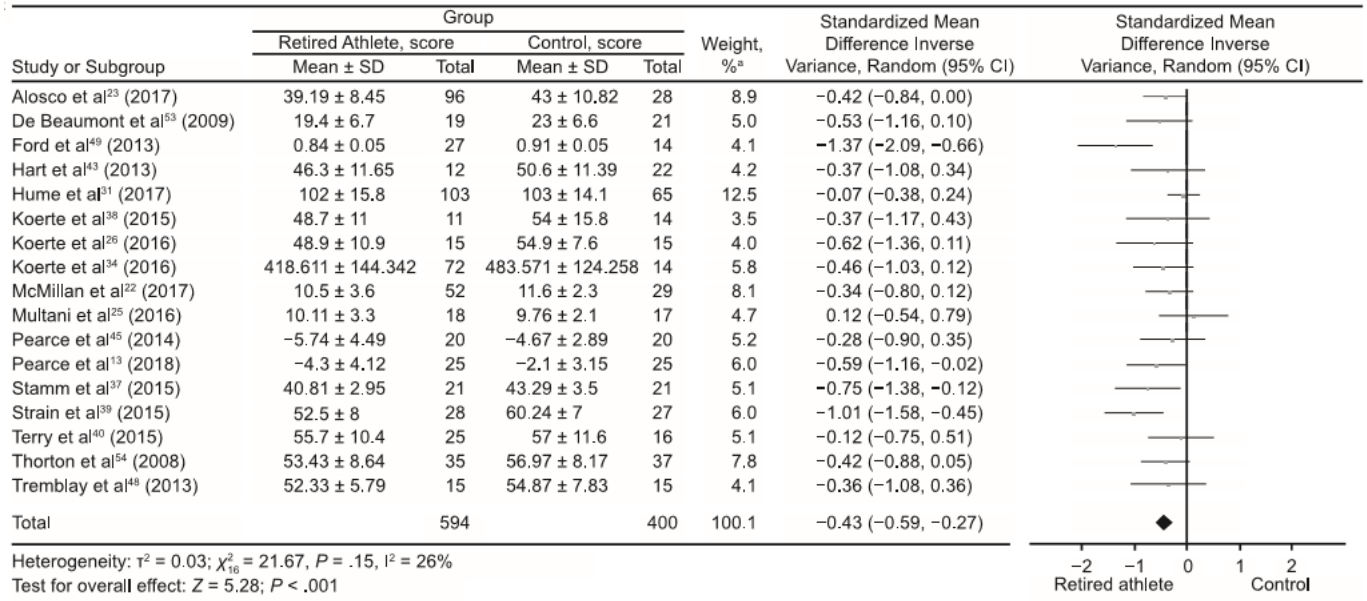


Figure 3-10 *Forest Plot of between-group Comparisons for Memory. Retired athletes compared with controls: [a] The total does not equal 100% because percentages were rounded.*

3.3.4.4 Executive Function

Tests of executive function were employed by 11 investigators (Thornton et al., 2008, Downs and Abwender, 2002, Wright et al., 2016, Casson et al., 2014, Stamm et al., 2015, Hampshire et al., 2013, Alosco et al., 2017, Koerte et al., 2016a, Hume et al., 2017, Pearce et al., 2018, Esopenko et al., 2017). The most common test used was the Wisconsin Card Sorting Test (WCST)(Koerte et al., 2016a, Thornton et al., 2008, Downs and Abwender, 2002, Stamm et al., 2015, Esopenko et al., 2017). Six out of the 11 found significantly decreased executive function in retired athletes (Wright et al., 2016, Downs and Abwender, 2002, Stamm et al., 2015, Hume et al., 2017, Pearce et al., 2018, Esopenko et al., 2017), while the remaining five studies did not (Thornton et al., 2008, Casson et al., 2014, Hampshire et al., 2013, Alosco et al., 2017, Koerte et al., 2016a).

Three studies found significantly decreased performance on the WCST in retired athletes compared to controls (Downs and Abwender, 2002, Stamm et al., 2015, Esopenko et al., 2017). Wright et al. (2016) found retired NFL players displayed deficits in executive ability in comparison to normative data (Heaton system: 37.5%; Wechsler system: 20.0%). Pearce et al. (2018) reported that retired rugby players performed significantly worse than controls on the Intra-Extra Dimensional Set Shift (IED) CANTAB subtest. Hume et al. (2017) found that retired elite-rugby group performed worse on tests of executive functioning (effect size -0.41; 95% CI: -0.80 to -0.02) on the online Computerized Neurocognitive Assessment Software-Vital Signs (CNS-VS). Overall, results are mixed. However, there is evidence of executive function decline in retired athletes.

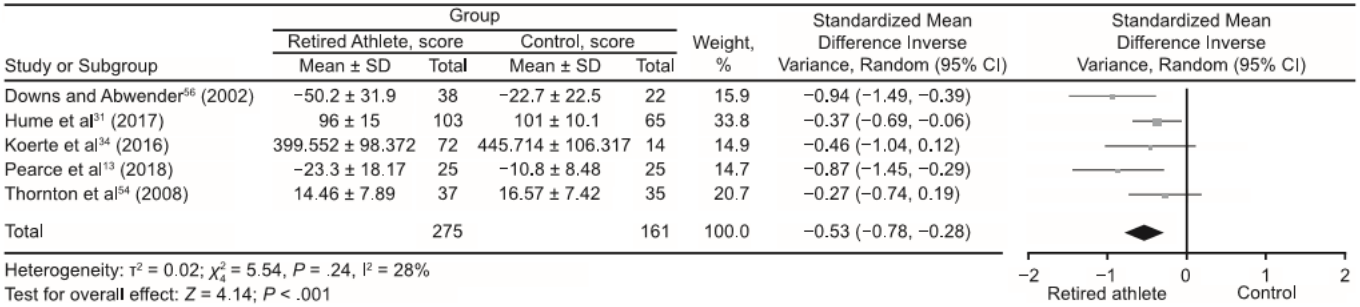


Figure 3-11 *Forest Plot of between-group Comparisons for Executive Function. Retired athletes compared with controls:* [a] *The total does not equal 100% because percentages were rounded.*

3.3.4.5 Language

Language tests were reviewed including tests of naming, speech production and verbal fluency by eight investigators (Solomon et al., 2016, Strain et al., 2017, Strain et al., 2015, Hart et al., 2013, Ford et al., 2013, Alosco et al., 2017, Gardner et al., 2017, Esopenko et al., 2017). The Boston Naming Test (BNT) was employed in four studies (Strain et al., 2017, Strain et al., 2015, Hart et al., 2013, Ford et al., 2013). Two of the four found that the mean BNT t-score of the retired athletes was significantly lower than the mean performance of the control group (Strain et al., 2017, Hart et al., 2013), while the other two studies found

no significant differences (Strain et al., 2015, Ford et al., 2013). Phonemic Word List Generation (FAS) was used by Esopenko et al. (2017) and found no significant differences between retired contact sport athletes and controls. The Controlled Oral Word Association Test (COWAT) was used in five studies (Solomon et al., 2016, Hart et al., 2013, Ford et al., 2013, Alosco et al., 2017, Gardner et al., 2017), none of which found significant differences between retired athlete and control. Overall, this review shows mixed evidence for language deficits in retired athletes.

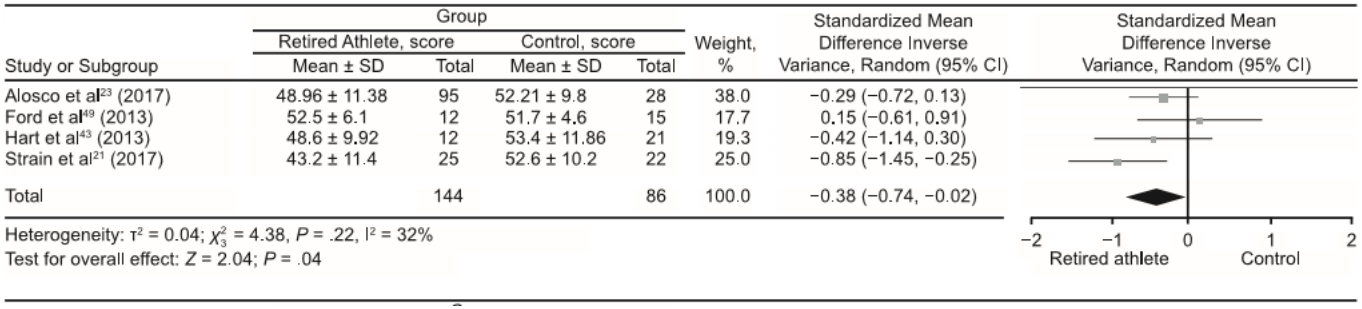


Figure 3-12 *Forest Plot of between-group Comparisons for Language. Retired athletes compared with controls: [a] The total does not equal 100% because percentages were rounded.*

3.3.4.6 Psychomotor Function

Psychomotor function was assessed by six investigators (Pearce et al., 2018, McMillan et al., 2017, Downs and Abwender, 2002, Hume et al., 2017, Gardner et al., 2017, Pearce et al., 2014), four of which found significant decreases in retired athletes in comparison to controls (Pearce et al., 2018, McMillan et al., 2017, Gardner et al., 2017, Pearce et al., 2014). Pearce et al. (2018) used the visuomotor reaction time (VRT) CANTAB subtest and found that the retired rugby players were significantly slower at reacting to the stimulus than the control group ($p < .01$). McMillan et al. (2017) found that retired rugby players had decreased fine motor coordination in the dominant hand on the Grooved Pegboard test; a measure of visual motor coordination. While Gardner et al. (2017) reported significantly worse scores among retired rugby players using their non-dominant hand ($p = .03$). Pearce et al. (2014) assessed fine motor control and found that reaction time (both reaction to stimulus and movement time on the O'Connor Finger Dexterity Test was better in the healthy control group compared to retired elite and amateur Australian football players ($p= .003$). The other two studies did not find decreases in psychomotor function in retired athletes in comparison to controls (Downs and Abwender, 2002, Hume et al., 2017). There appears to be evidence of increased difficulties in psychomotor functioning in retired athletes.

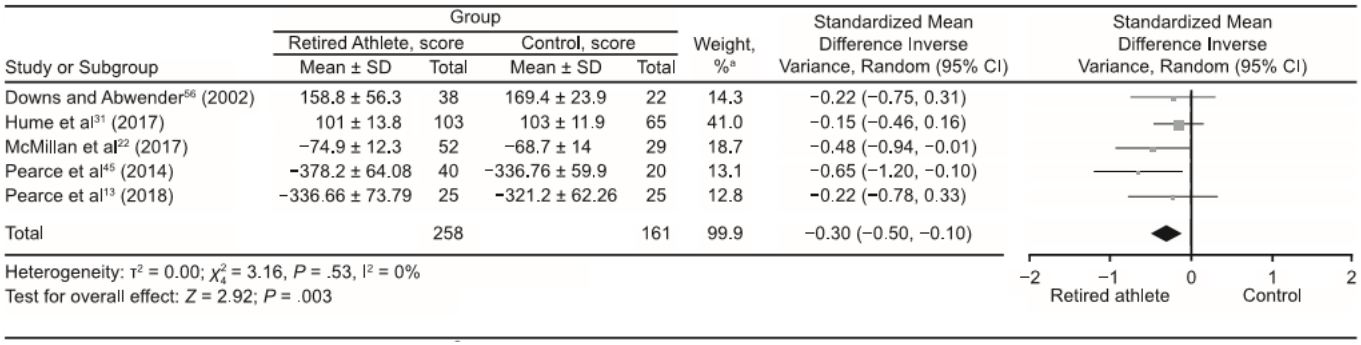


Figure 3-13 *Forest Plot of between-group Comparisons for Psychomotor Function. Retired athletes compared with controls: [a] The total does not equal 100% because percentages were rounded.*

3.3.4.7 Intelligence

Pre-morbid intelligence was assessed in 12 studies (Terry et al., 2015, Multani et al., 2016, Esopenko et al., 2017, Gardner et al., 2017, Clark et al., 2018, Koerte et al., 2016a, Ford et al., 2013, Hart et al., 2013, Stamm et al., 2015, Casson et al., 2014, Solomon et al., 2016, Thornton et al., 2008). A total of nine studies found no significant difference in intellectual ability in retired athletes in comparison to controls (Thornton et al., 2008, Solomon et al., 2016, Casson et al., 2014, Hart et al., 2013, Ford et al., 2013, Clark et al., 2018, Gardner et al., 2017, Multani et al., 2016, Terry et al., 2015). Two investigators found that retired athletes performed significantly worse than controls on intellectual function tests (Koerte et al., 2016a, Esopenko et al., 2017). While Stamm et al. (2015) found that former NFL players exposed to tackle football prior to age 12 performed significantly

worse on the Wide Range Achievement Test 4 (WRAT-4) than former NFL players exposed to tackle football age 12 or older. Overall, there does not appear to be evidence of decreased intellectual functioning in retired athletes.

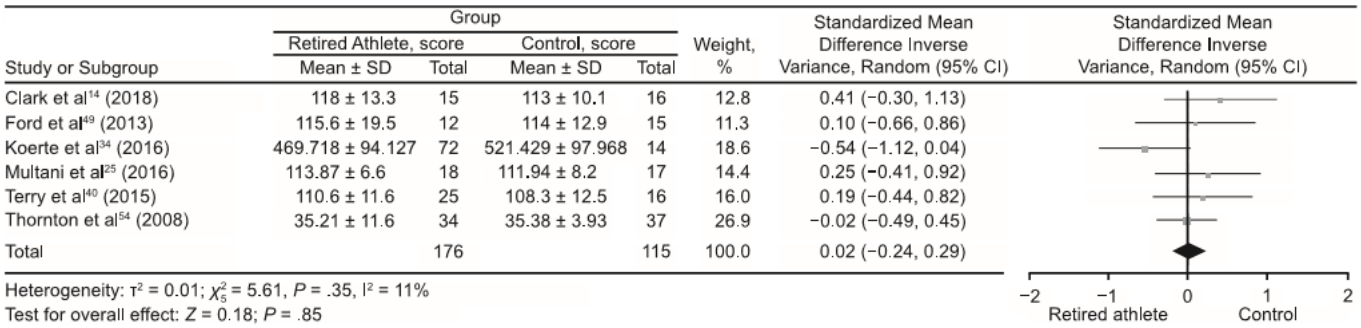


Figure 3-14 *Forest Plot of between-group Comparisons for Intelligence. Retired athletes compared with controls:* [a] *The total does not equal 100% because percentages were rounded.*

3.3.4.8 Perception

The Brief Smell Identification Test (B-SIT) was employed by Alosco et al. (2017). B-SIT scores were significantly lower among former NFL players in comparison to non-contact control athletes. Visuospatial perception was assessed in two studies which employed the Judgement of Orientation test (JLO) (Esopenko et al., 2017, McMillan et al., 2017). No significant group differences were found between retired athletes and controls.

3.3.5 Self-Reported Cognitive Functioning

Fourteen studies employed subjective self-reported (S-R) cognitive functioning tests (Thornton et al., 2008, Meehan et al., 2016, Guskiewicz et al., 2005, Alosco et al., 2017, Koerte et al., 2016a, Randolph et al., 2013, Lewis et al., 2017, Gardner et al., 2017, McMillan et al., 2017, Esopenko et al., 2017, Multani et al., 2016, Hinton et al., 2011, Seichepine et al., 2013, Montenigro et al., 2017) to compare retired athletes to control groups/normative data. A variety of S-R measures were employed [Table 3-4]. Eleven studies found significantly increased subjective reports of cognitive difficulties experienced by former athletes (Meehan et al., 2016, Thornton et al., 2008, Montenigro et al., 2017, Guskiewicz et al., 2005, Randolph et al., 2013, Koerte et al., 2016a, Alosco et al., 2017, McMillan et al., 2017, Esopenko et al., 2017, Multani et al., 2016, Seichepine et al., 2013). The remaining three studies found no significant increase in S-R complaints among retired athletes (Montenigro et al., 2017, Gardner et al., 2017, Lewis et al., 2017). This review found evidence for increased S-R cognitive issues among retired athletes.

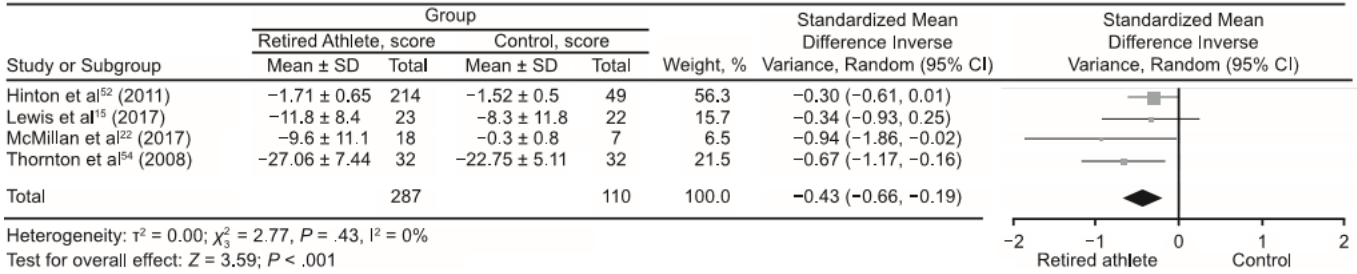


Figure 3-15 *Forest Plot of between-group Comparisons for Self-Reported Cognitive Functioning. Retired athletes compared with controls:* [a] *The total does not equal 100% because percentages were rounded.*

3.3.6 Rate of Mild Cognitive Impairment in Retired Athletes

Three studies implemented S-R, rather than formal diagnosis, to investigate mild cognitive impairment (MCI) in retired athletes (Guskiewicz et al., 2005, Randolph et al., 2013, Vann Jones et al., 2014). Guskiewicz et al. (2005) found that 35% of the retired NFL players self-reported cognitive difficulties, which were deemed consistent with MCI. Randolph et al. (2013) found indications of possible cognitive impairment in retired NFL players whereby a subsample of the players was compared to a clinical sample of MCI patients, revealing similar profile of impairments. Conversely, Vann Jones et al. (2014) found that the prevalence of possible MCI or dementia in former professional soccer players was not statistically different from a large control sample. No association was demonstrated between low-risk and high-risk playing positions or length of playing career and a positive MCI screening result, with age being the only risk factor across both groups.

3.3.7 Pooled Summaries

Meta-analyses were conducted where possible for outcome measures using different scales and tools to assess the cognitive domains. A number of meta-analyses were conducted for outcome measures using different scales and tools to assess domains of cognition, global cognitive ability and self-report cognition. Data were pooled using standardized mean difference and a random effects model according to Cochrane guidelines Higgins and Green (2011). Global cognitive ability was borderline statistically significant between groups (p= .05; SMD: -0.14; 95% CI: -0.29, 0.00) [Figure 3-3]. Retired athletes performed significantly worse than controls on tests of memory (p < .00001; standardized mean (difference (SMD): -0.43; 95% CI: -0.59, -0.27) [Figure 3-10]. Assessment of executive function also revealed that retired athletes were significantly outperformed by controls (p < .0001; SMD: -0.53; 95% CI: -0.78, -0.28) [Figure 3-11]. Tests of language (p= .04; SMD: -0.38; 95% CI: -0.74,

-0.02) [Figure 3-12] and psychomotor function (*p*= .003; SMD: -0.30; 95% CI: -0.50, -0.10) [Figure 3-13] were also statistically significant favouring controls. Domains of intelligence (*p*= .85; SMD: 0.02; 95% CI: -0.24, 0.29) [Figure 3-14] and attention (*p*= .63; SMD: 0.05; 95% CI: -0.14, 0.23) [Figure 3-6] showed no between-group statistical significance Pooling of S-R tests also revealed that retired athletes reported significantly more cognitive difficulties compared to controls (*p*= .0003; SMD: -0.43; 95% CI: -0.66, -0.19) [Figure 3-15].

3.3.8 Summary of Main Results

This review focused on a qualitative synthesis of the studies. Fourteen studies employed a subjective S-R cognitive functioning test from mixed sporting populations (Meehan et al., 2016, Thornton et al., 2008, Guskiewicz et al., 2005, Koerte et al., 2016a, Alosco et al., 2017, Randolph et al., 2013, Lewis et al., 2017, McMillan et al., 2017, Gardner et al., 2017, Esopenko et al., 2017, Multani et al., 2016, Hinton et al., 2011, Seichepine et al., 2013, Montenigro et al., 2017), 11 of which found significantly increased subjective reports of cognitive difficulties experienced by former athletes in comparison to control groups/normative data (Alosco et al., 2017, Thornton et al., 2008, Meehan et al., 2016, Randolph et al., 2013, Koerte et al., 2016a, McMillan et al., 2017, Esopenko et al., 2017, Multani et al., 2016, Hinton et al., 2011, Seichepine et al., 2013, Guskiewicz et al., 2005). Synthesis of studies demonstrated more evidence for cognitive deficits in the areas of memory, executive function, psychomotor function and S-R cognition. The balance of evidence to date does not support a significant association between cognitive deficits in retirement and concussion history and exposure. The majority of studies (n=33) failed to find any significant association between concussion history/exposure to concussion and cognitive deficits. However, 13/46 studies did report a frequency-response relationship, with greater cognitive impairments (subjective or objective) in those with greater levels of exposure to

head impacts or concussions (Montenigro et al., 2017, Seichepine et al., 2013, Thornton et al., 2008, Downs and Abwender, 2002, Stamm et al., 2015, Ford et al., 2013, Guskiewicz et al., 2005, Hume et al., 2017, McMillan et al., 2017, Wilde et al., 2016, Casson et al., 1984, Murelius and Haglund, 1991, Esopenko et al., 2017). The cross-sectional nature of the studies included in this review and an insufficient number of longitudinal studies limit the ability to make causal inferences about the relationship between concussion and long-term cognitive outcomes.

Table 3-5 Evaluation of Cognitive Outcome Measures by Cognitive Domain Effect Size- MD: Mean difference, IV: Interval Variable; Random Effect Model; 95% CI: 95% Confidence Interval (CI).

References	Retired Athletes (N=)	Controls (N=)	CGA	A	M	EF	L	PF	I	P	S-R C
Pearce et al. (2018)	25	25			CANTAB-SWM [MD (CI): 2.20 (4.23, 0.17)]	CANTAB-IED [MD (CI): 12.50 (4.64, 20.36)]		CANTAB-RTI [15.46 (-22.39, 53.31)]			
Clark et al. (2018)	31	30	RBANS [MD (CI): 0.70 (-6.21, 7.61)]	RBANS [MD (CI): 7.50 (-1.27, 16.27)]					WAIS [MD (CI): - 5.00 (-3.35, 13.35)]		
Lewis et al. (2017)	51	22									RPQ [MD (CI): 3.50 (-2.51, 9.51)]
Esopenko et al. (2017)	33	18	*	*	*	*	*		*	*	*
Gardner et al. (2017)	16	16		✢	✢		✢	✢	✢		✢
Deshpande et al. (2017)	834	1858	**		**						
Montenigro et al. (2017)	93	ND	**								**
Strain et al. (2017)	25	22					BNT [MD (CI): -9.40 (-15.58, -3.22)]				
McMillan et al. (2017)	52	29	MOCA [MD (CI)-0.60 (-1.43, 0.23)]	TMT-B [MD (CI): 4.20 (-3.94, 12.34)]	RAVLT [MD (CI): -1.10 (-2.39, 0.19)]			Grooved Pegboard Test [MD (CI): 6.20 (0.11, 12.29)]		JLO [MD 0.10 (-0.88, 1.08)]	RPQ [MD (CI): 9.30 (4.14,14.46)]

Alosco et al. (2017)	95	28		TMT-A [MD (CI): -5.17 (-9.68, -0.66)]	NAB-LL [MD (CI): -3.81 (-8.16, 0.54)]	DKEFS [MD (CI): -1.40 (-2.55, -0.25)	COWAT [MD (CI): -3.25 (-7.54, 1.04)]			*	BRIEF-A [MD (CI): 1.32 (0.87, 1.78)]
Hume et al. (2017)	301	65	CNS-VS [MD (CI): 0.00 (-5.24, 5.24)]	CNS-VS [MD (CI): 1.00 (-2.91, 4.91)]	CNS-VS [MD (CI): -1.00 (-5.59, 3.59)]	CNS-VS [MD (CI)-5.00 (-8.80, -1.20)]		CNS-VS [MD (CI): -2.00 (-5.93, 1.93)]			
Solomon et al. (2016)	45	ND	**	**	**		**		**		
Multani et al. (2016)	18	17			RVDLT [MD (CI): 0.35 (-1.47, 2.17)]				WTAR [MD (CI): 1.93 (-3.02, 6.88)]		*
Koerte et al. (2016a)	72	14			NAB-LL [MD (CI) -64.96 (-138.09, 8.17)]	WCST [MD (CI): -46.16 (-106.31, 13.99)]			WAIS-R [MD (CI): -51.71 (-107.44, 4.02)]		BRI [MD (CI): 162.76 (157.58, 167.94)]
Koerte et al. (2016b)	15	15		TMT-B [MD (CI): -1.40 (-4.80, 2.00)]	ROCFT [MD (CI): -6.00 (-12.72, 0.72)]						
Gardner et al. (2016)	17	17	MMSE [MD (CI): 0.00 (-2.45, 2.45)]								
Wright et al. (2016)	40	ND		**	**	**					
Wilde et al. (2016)	10	9		*	*						
Amen et al. (2016)	161	ND	**		**						
Decq et al. (2016)	239	138	F-TICS-m [MD (CI): -1.02 (-1.76, -0.28)]								
Meehan et al. (2016)	1335	2321									*
Coughlin et al. (2015)	9	9			**						

Stamm et al. (2015)	21	21			NAB-LL [MD (CI): -2.48 (-4.44, -0.52)]	WCST [MD (CI)-7.52 (-8.94, -6.10)]			WRAT-4 [MD (CI): -8.55 (-10.06, -7.04)]		
Koerte et al. (2015)	11	14		TMT-B [MD (CI): 1.00 (-2.72, 4.72)]	ROCFT [MD (CI): -5.30 (-15.82, 5.22)]						
Strain et al. (2015)	28	27			CVLT-II [MD (CI): -7.74 (-11.71, -3.77)]						
Terry et al. (2015)	25	16			CVLT-II [MD (CI): -1.30 (-8.29, 5.69)]				WTAR [MD (CI): 2.30 (-5.33, 9.93)]		
Casson et al. (2014)	45	ND	**	**	**	**			**		
Vann Jones et al. (2014)	92	ND			**						
Tremblay et al. (2014)	15	15	MMSE [MD (CI): -0.20 (-0.91, 0.51)]	Color Trails Test B [MD (CI):1.13 (-14.84, 17.10)]	RAVLT [MD (CI): -2.54 (-7.47, 2.39)]						
Hart et al. (2013)	34	26		TMT-B [MD (CI): -2.20 (-11.32, 6.92)]	ROCFT [MD (CI): -4.30 (-12.43, 3.83)]		BNT [MD (CI): -4.80 (-12.37, 2.77)]		*		
Hampshire et al. (2013)	13	NS				*					
Pearce et al. (2014)	20	20			CANTAB-PAL [MD (CI): 1.07 (-1.27, 3.41)]			CANTAB-RTI [MD (CI): 41.44 (8.52, 74.36)]			
Seichepine et al. (2013)	64	ND									**
Randolph et al. (2013)	513	ND	**								**
Ford et al. (2013)	27	14	MMSE [MD (CI): 0.50 (-0.89, 1.89)]	TMT-B [MD (CI): 13.00 (-7.90, 33.90)]	Memory Paradigm [MD (CI): -0.07 (-0.10, -0.04)]		BNT [MD (CI): 0.80 (-3.36, 4.96)]		WAIS-III [MD (CI): 1.60 (-11.22, 14.42)]		
Willeumier et al. (2012)	38	38	*		*						
Amen et al. (2011)	100	ND	**		**						

Hinton et al. (2011)	214	186									CDS [MD (CI): 0.19 (0.03, 0.35)]
De Beaumont et al. (2009)	19	21	MMSE [MD (CI): 0.30 (-0.32, 0.92)]		ROCFT [MD (CI): -3.60 (-7.73, 0.53)]						
Thornton et al. (2008)	74	37		WAIS-III [MD (CI): 0.98 (-2.96, 4.92)]	RAVLT [MD (CI): -3.54 (-7.43, 0.35)]	WCST [MD (CI): -2.11(-5.65, 1.43)]			WAIS-III [MD (CI): -0.17 (-2.01, 1.67)]		PCSC [MD (CI): 4.31 (1.18, 7.44)]
Guskiewicz et al. (2005)	2552	ND									**
Downs and Abwender (2002)	38	22				WCST [MD (CI): 27.50 (13.67, 41.33)]		PASAT [MD (CI): -10.60 (-31.10, 9.90)]			
Murelius and Haglund (1991)	50	50		*	*						
Casson et al. (1984)	18	ND			**						

Abbreviations: A, Attention; EF, Executive Function; GC, Global Cognitive Ability; I, Intelligence; L, Language; M, Memory; ND, Normative Data; NS, Not Specified; P, Perception; PF, Psychomotor Function; S-R C, Self-report Cognition.

*Kuhn et al 2017 excluded as cognitive results were taken from Solomon et al 2016.

*Tremblay et al 2014 excluded as cognitive results were taken from Tremblay et al 2013.

Key:

*** Data not provided**

**** No control**

✢ Composite cognition score

White square: test/domain

Dark grey square: athletes significantly worse

Light grey: athletes not significantly worse.

3.4 Discussion

This review appraised the literature regarding SRC and cognitive health outcomes in retired athletes and was unique in that it focused on clinical cognitive outcomes in living retired athletes. Findings suggest that certain areas of cognition may be affected by SRC history. However, there appears to be bias towards assessment of certain areas of cognition such as memory, attention and global cognition, with a neglect of other aspects of cognition such as psychomotor function, perception and language. Further, epidemiological studies are confounded by individual differences in susceptibility to age related neurocognitive decline or dementia-related pathology. Therefore, lifetime exposure to concussion is more than likely one of myriad of environmental and predetermined risk factors for diminishing cognitive reserve and promoting early expression of neurocognitive decline. Premorbid intellectual function and factors relating to cognitive reserve were not controlled for in the studies. An important issue is the significant overlap between normal age-related neurocognitive downturn and the manifestation of sports concussion in later life (Asken et al., 2016b).

From this review, there is emerging evidence of increased S-R cognitive difficulties. There was a significant number of studies who found S-R cognitive complaints among retired athletes (11/15 studies which tested for S-R symptoms: 73%). However, conclusions drawn from S-R data should be made with caution, particularly in the absence of clear associations between S-R symptoms and previous head impact exposure/reported number of concussions and the potential recall bias which continues to be a limitation of all retrospective studies in this area. Furthermore, external factors such as the media may influence former athletes reporting (Mittenberg et al., 1992, Gunstad and Suhr, 2001). Among the studies that investigated objective as well as subjective cognition in the retired athletes (Thornton et al., 2008, Gardner et al., 2017, McMillan et al., 2017, Esopenko et al., 2017, Multani et al., 2016, Montenigro et al., 2017), there was a lack of clear agreement between the two measures. The

majority of studies (n = 6) failed to support the subjective complaints when referencing to neuropsychological test results (Thornton et al., 2008, Gardner et al., 2017, McMillan et al., 2017, Esopenko et al., 2017, Multani et al., 2016, Montenigro et al., 2017) Ideally, the clinical significance of findings should be carefully considered in the overall context of the individual's performance on neuropsychological and cognitive testing and symptom S-R. The emerging disparity between subjective and objective tests may indicate that more sensitive cognitive test measures are required to identify subtle changes, which may then result in S-R difficulties translating to anomalies on cognitive tests. Meta–analysis of the cognitive domains of memory, psychomotor function, language and executive function, along with self-report cognitive functioning, revealed that retired athletes performed statistically significantly worse than controls. Despite the statistically significant difference noted, the magnitude of the effect sizes is small and therefore whether or not the effect size is clinically meaningful is unclear.

Further methodological shortcomings of the reviewed studies include a paucity of studies using a prospective, longitudinal design and biased recruitment. Study designs also raise important issues, along with retrospective recall bias and lack of controlling for confounding variables - namely lack of controlling for history of non SRCs. A further issue was lack of a suitable control group. Important factors that are associated with professional team sports, such as high levels of physical fitness, high income and potential drug use (e.g., opioid analgesics) were not considered. The influence that late impact of upper limb orthopaedic injuries may have on psychomotor tests was also overlooked. A total of 12 studies did not include a control group which greatly limits the conclusions that can be drawn (Solomon et al., 2016, Montenigro et al., 2017, Seichepine et al., 2013, Vann Jones et al., 2014, Casson et al., 1984, Randolph et al., 2013, Guskiewicz et al., 2005, Willeumier et al., 2012, Stamm et al., 2015, Casson et al., 2014, Kuhn et al., 2017, Wright et al., 2016) as they were unable to provide context to population normative data. Among the studies that used a control group (n = 32), only a small number of studies (n = 9) included an appropriate noncontact athlete

control cohort (Meehan et al., 2016, Downs and Abwender, 2002, Hume et al., 2017, Koerte et al., 2016a, Lewis et al., 2017, Murelius and Haglund, 1991, Koerte et al., 2015, Koerte et al., 2016b, Deshpande et al., 2017); the majority of investigators (n = 22) failed to accurately match controls to retired non-contact athletes (Tremblay et al., 2013, Tremblay et al., 2014, Randolph et al., 2013, De Beaumont et al., 2009, Terry et al., 2015, Multani et al., 2016, Esopenko et al., 2017, McMillan et al., 2017, Decq et al., 2016, Gardner et al., 2017, Pearce et al., 2018, Wilde et al., 2016, Amen et al., 2011, Alosco et al., 2017, Gardner et al., 2016, Strain et al., 2017, Strain et al., 2015, Amen et al., 2016, Coughlin et al., 2015, Hampshire et al., 2013, Hart et al., 2013, Ford et al., 2013).

It is also important to consider that a large proportion of investigators (n = 19) failed to provide a concussion definition (Deshpande et al., 2017, Vann Jones et al., 2014, Casson et al., 1984, Downs and Abwender, 2002, Kuhn et al., 2017, Gardner et al., 2016, Casson et al., 2014, Hampshire et al., 2013, Ford et al., 2013, Koerte et al., 2016a, Randolph et al., 2013, Lewis et al., 2017, Gardner et al., 2017, Decq et al., 2016, Wilde et al., 2016, Murelius and Haglund, 1991, Koerte et al., 2015, Koerte et al., 2016b, Hinton et al., 2011), which reduces player recall validity (Robbins et al., 2014). Others have noted both underreporting (e.g., lack of understanding about concussion) and exaggeration of head impacts (Llewellyn et al., 2014, Baugh et al., 2017). The ability to accurately quantify participants' exposure to sub concussive blows was a further difficulty.

Just over 50% of the studies (n=24) controlled for history of neurological or psychiatric conditions (Ford et al., 2013, Hart et al., 2013, Thornton et al., 2008, Wright et al., 2016, Solomon et al., 2016, Kuhn et al., 2017, Casson et al., 2014, Koerte et al., 2016a, Clark et al., 2018, Decq et al., 2016, Gardner et al., 2017, McMillan et al., 2017, Wilde et al., 2016, Pearce et al., 2018, Casson et al., 1984, Koerte et al., 2015, Koerte et al., 2016b, Multani et al., 2016, Terry et al., 2015, Tremblay et al., 2014, Hinton et al., 2011, De Beaumont et al., 2009, Tremblay et al., 2013, Pearce et al., 2014). History of head impact exposure or concussion

are one of myriads of factors which may lead to neurocognitive decline in former athletes and therefore inclusion/exclusion criteria must be robust, and these factors controlled appropriately in studies. Individuals with premorbid psychiatric or other health problems or life stressors are more likely to experience post-concussion syndrome (PCS)(Binder, 1986, Ponsford et al., 2012). Similarly, only a minority of studies (n=14) reported past or present alcohol or drug use (Meehan et al., 2016, Kuhn et al., 2017, Casson et al., 2014, Stamm et al., 2015, Alosco et al., 2017, Hume et al., 2017, Tremblay et al., 2014, De Beaumont et al., 2009, Tremblay et al., 2013, Terry et al., 2015, Decq et al., 2016, Casson et al., 1984, Esopenko et al., 2017, Deshpande et al., 2017). Downs and Abwender (2002) reported screening for alcohol abuse but did not report findings in the results section. Certain studies reported significantly higher alcohol consumption among retired athletes compared to controls (Gardner et al., 2017, Decq et al., 2016, McMillan et al., 2017, Meehan et al., 2016), which can negatively influence cognition (Rehm et al., 2019). Substance abuse has been associated with sustained deficits in executive functioning, especially inhibition (van Holst and Schilt, 2011).

Long-term high-dose anabolic steroid exposure may cause cognitive deficits, notably in visuospatial memory (Kaufman et al., 2015). Epidemiologic and intervention studies suggest that overall physical activity preserves or improves cognitive function during aging (van Praag, 2009, Deslandes et al., 2009); therefore, the lack of controlling for current activity levels among retired players versus controls in the majority of studies presents a potential bias. Yet, modifiable risk factors such as diet and physical activity are controlled for in only a minority of studies (Meehan et al., 2016, Tremblay et al., 2014, Koerte et al., 2015, Koerte et al., 2016b, De Beaumont et al., 2009, Tremblay et al., 2013), who accounted for physical activity engagement/exercise frequency. Similarly, only a small proportion examined factors such as BMI, weight-height ratio or cardiovascular health (Wright et al., 2016, Amen et al., 2016, Willeumier et al., 2012, Alosco et al., 2017, Amen et al., 2011, McMillan et al., 2017, Hinton et al., 2011). These factors may potentially impact cognitive functioning, with data

from a meta-analysis showing that categorization in the overweight or obese range in midlife is a risk factor for dementia later in life (Albanese et al., 2017b). A large proportion of the studies (n = 20) evaluated included retired NFL players. With a propensity towards being overweight in this population (Tucker et al., 2009), there may be an escalated risk of cognitive impairment (Anstey et al., 2011). Hinton et al. (2011) found that dietary fat intake was more significantly associated with S-R cognitive difficulties than exposure to football alone among former collegiate football players. Wright et al. (2016) found that BMI was significantly associated with cognitive reserve outcomes in retired NFL players.

Aside from the proposed negative relationship between concussion and cognitive function, the potential causes of cognitive issues in retired athletes are diverse. Factors such as genetics (Deary et al., 2004), diet and nutrition (Freeman et al., 2014), exercise (Blondell et al., 2014), obesity (Nguyen et al., 2014), chronic pain and life stress (Hart et al., 2003), childhood adversity (Richards and Wadsworth, 2004), personality factors (Luchetti et al., 2016), family history of neurological conditions (Hayden et al., 2009) steroid use (Kanayama et al., 2010), drug and alcohol use (Gould, 2010), depression and anxiety (Baumgart et al., 2015), general medical history e.g., hypertension, diabetes, heart disease (Cooper et al., 2015, Aarsland et al., 2017), and neurodegenerative diseases (e.g., Alzheimer's disease, Parkinson's disease and ALS) (Phukan et al., 2007, Kelley and Petersen, 2007, Houck et al., 2018) have all been implicated in exacerbated cognitive decline with aging (Aarsland et al., 2017). The vast majority of studies did not control for the above variables. Parent socioeconomic status (SES), race and medical history have been found to independently predict baseline memory scores among collegiate athletes, while concussion history and years exposed to sport were not predictive of baseline memory scores (Houck et al., 2018). None of the studies accounted for socioeconomic status (SES) during childhood which could affect cognitive reserve later in life and could potentially account for differences among athlete groups with a history of concussion/head impact exposure versus controls or norms. The importance of premorbid information, intellectual level and learning disabilities such as ADHD, which is known to be

high among athletes, should also be considered. Athletes with a history of multiple concussions and a premorbid learning disability are vulnerable to neurocognitive impairment (Collins et al., 1999).

Measures of individual differences in baseline intelligence and education status have not been included in the majority of studies. Stamm et al. (2015) reported 14% of the < 12 year group, compared with 0% of the >12 group, had a learning disability along with significant differences in premorbid intellectual functioning (i.e., WTAR scores), with the less than 12 year group representing those who were exposed to tackle football prior to the age of 12 years old and the greater than 12 year group representing those who were not exposed until a later age. This casts doubt as to whether the group differences were reflections of premorbid impairment as opposed to the effects of concussion. Many studies included participants in control groups who were still exposed to considerable concussion risk, albeit a lower risk of head impacts. Alosco et al. (2017) and Murelius and Haglund (1991) included participants in the control group with a history of playing soccer in both the former and latter and one with a history of amateur wrestling in the former study. While McMillan et al. (2017) included participants in the control group, 34% of whom had a history of concussion and rugby participation. The inclusion of current and retired athletes in some studies, without distinction between the two, may skew results (Seichepine et al., 2013, Thornton et al., 2008), as results may reflect effects of recent concussions or current head impact exposure.

The assessment of cognition should ideally capture all domains of cognition. The tests used varied greatly between studies and only a small proportion of the authors employed a comprehensive battery which explored all aspects of cognitive functioning. Most studies focused on specific domains such as tests of executive function and memory and attention. Further, many of the assessments employed in the studies were designed to detect gross cognitive impairments, possibly overlooking subtle changes in cognitive function that may be associated with concussion history. Given the media interest in this topic and public

perceptions, studies with negative findings are potentially less likely to be published. Publication bias was not assessed in this review; it was not possible to perform a funnel plot due to the heterogeneity of outcome measures used. Large-scale prospective longitudinal studies, showing a high level of control on confounding factors are required to confirm the effects of aging with a history of concussion on cognitive functioning in retired athletes.

3.5 Limitations

The self-selected convenience samples limit conclusions that can be drawn. This issue is exacerbated in some studies by limiting inclusion criteria to retired NFL players with a minimum of 6 month history of S-R complaints of cognitive, behavioural and mood symptoms prior to the study (Stamm et al., 2015, Alosco et al., 2017, Koerte et al., 2016a) and recruiting of players presenting to memory clinics with cognitive/ behavioural symptoms (Gardner et al., 2016). Participants who are self-selected are potentially non-representative of the retired athlete population. Due to the retrospective nature of the studies, the investigation into the long-term effects of concussion is influenced by methodological biases, making it difficult to draw conclusions regarding the long-term sequelae. A large proportion of the studies (n = 43) were based on solely retired male athletes, with only 3 studies recruiting retired female athletes. There is a particularly large NFL alumni representation among a high number of the studies (n = 20), a unique cohort whose career path and level of head impact exposure makes it impossible to infer results outside of that elite group. Aside from the level of head impact exposure, a host of factors separate NFL players from the general population at large, including income, education level and various lifestyle factors. This exposes large gaps in the knowledge of the effect of concussion on a range of other sportspeople who participate at different sporting levels. This should include female athletes, given the potential sex influences on concussion recovery (Baker et al., 2016, Stone et al., 2017).

A further limitation is the fact that concussions were often not well documented in the past. Therefore, all studies included reliance on the athlete's self-report for concussion histories, making this information subject to retrospective recall bias. Only one investigator, Wright et al. (2016) corroborated patients' self-report with verifiable reports. Sole reliance on player's self-report history of concussion and the retired athlete's response to a survey-based questionnaire regarding subjective memory difficulties is potentially unreliable. This is compounded by the fact that SRC that occurred in the past were potentially overlooked by clinicians unless associated loss of consciousness (LOC) took place (Ward, 1964). History of non SRC, which constitute the majority of concussion (Sojka, 2011, Browne and Lam, 2006), needs to be considered in future study designs.

3.6 Conclusion

A total of 46 studies evaluated nine different aspects of cognitive functioning. Relative to the control groups or normative data, five areas showed significant declines: memory, executive function, psychomotor function, language and S-R cognitive function. The four other areas: global cognitive ability, attention, intelligence and perception were, on balance, neutral. The preliminary evidence of a dose-response association between cognitive health outcomes and past concussion exposure warrants further study, in order to determine the complex interaction between previous head impact exposure and factors which may influence cognitive health in the aging retired athlete. As detailed throughout this review, confounding variables, case ascertainment, recall bias on behalf of the participants and publication bias in the SRC field at large may have inflated these significant findings.

Chapter 4 Methods

4.1 Introduction

In this chapter, the various methods employed to complete the cross-sectional studies detailed in this thesis will be described. Study designs, background to assessment procedures, sampling, methods and data analyses will be explained. The methodologies and procedures used across studies will be described below and are presented in Chapters 5-9. There are a number of outcome measures and assessments that are common to all studies. They will be described in detail and will be referred to in subsequent chapters thereafter when describing individual study methodologies to avoid duplication. The research projects in this thesis were led by Trinity College Dublin in collaboration with Leinster Rugby, Rugby Players Ireland and Rowing Ireland. Study I of this thesis was a validation study investigating the agreement between self-reported and clinically documented concussion histories in current rugby union players. The purpose of Study I was to address a significant limitation noted in the literature relating to the reliability and validity of self-reported concussion history. This led into cross-sectional studies II-V which were a part of the 'Brain Health in Retired **PRO**fessional Rugby **P**layers' (PROP) studies. This project investigated long-term brain health in retired professional rugby union players. It was conducted as part of a multidisciplinary project which involved researchers in the Trinity Institute of Neuroscience, Departments of Psychology, Physiology and Physiotherapy, Trinity College Dublin and the Michigan Concussion Center, University of Michigan. It was rolled out in collaboration with Rugby Players Ireland and Rowing Ireland. There is overlap in the methodologies used for studies II-V. The overall aim of the 'PROP' study was to investigate history of concussion among retired professional rugby players and long-term mental and cognitive health status. Secondary outcomes included measures of cardiovascular health, physical activity, chronic pain, sleep and quality of life. A longitudinal study design would be desirable in the future.

4.2 Background Research Methods

4.2.1 Study Designs

Studies I-V were observational. Observational studies dominate the literature regarding preventative medicine as they are used to assess potential causation in exposure-outcome relationships. Observational studies are a vital part of epidemiological research. All studies contained in this thesis are cross-sectional in nature. A cross-sectional study design involves simultaneous measurement of exposure and outcome in the study participants (Setia, 2016). Cross-sectional studies are used to examine the prevalence of a disease or health related characteristics in a defined population at a particular point in time (Mann, 2003). Therefore, they have been described as taking a snapshot of the prevalence and health status of a population in society (Liamputtong, 2013). Cross-sectional study design also facilitates investigation of the relationship between diseases (or other health-related characteristics) and other variables of interest. Since exposure and disease status are measured simultaneously, it may not be possible to distinguish whether the exposure preceded or followed the disease. Therefore cause and effect relationship cannot be inferred (Levin, 2006). One of the main limitations of observational studies is the inability to control for confounding variables. However, the major advantage of this study design is that participants do not undergo any intervention. This generally reduces costs and simplifies the ethical process. Multiple outcome measures are usually employed, hence cross-sectional studies often generate large amounts of data at a specific once off time point (Sedgwick, 2014). Given that the science in this area is in its infancy, it was deemed appropriate to use a variety of outcome measures in order to assess brain health.

4.2.2 Sampling

Important components of quantitative research include an adequate sampling method and sample size. This is necessary to ensure that meaningful statistical results can be detected (Fox and Mathers, 1997). Clinical research often involves a group of people referred to as a "sample population" who have shared or common characteristics such as a particular medical condition or certain exposure types (Martínez-Mesa et al., 2016). This sample population are used to infer conclusions about a larger population with the same characteristic. This is the practical approach to clinical research, when access to the entire population also referred to as the "target population" is not possible or feasible (Elfil and Negida, 2017). Therefore, it is imperative to limit the risk of introduced bias while reducing the number of participants. This is achieved by selecting a sample that is representative of the target population as much as possible. The generalizability of the findings in these clinical studies are based on factors such as the internal and external validity of the research methods (Elfil and Negida, 2017).

All studies in this thesis employed a non-probability convenience sampling method. Convenience sampling is also referred to as haphazard or accidental sampling (Etikan, 2016). It is a type of nonprobability or non-random sampling that involves recruiting participants from the target population based on practical criteria, such as geographical proximity, accessibility, availability at a given time, or willingness to partake in a study (Dörnyei, 2007).

The main advantages associated with convenience sampling include availability of participants, ease of access, time efficiency and affordability (Etikan, 2016). The obvious disadvantage with convenience sampling is the likely introduction of bias into a study (Mackey, 2005). It is impossible for the researcher to be certain that the convenience sample represents the target population regarding the specific characteristics under investigation. This is primarily due to the high possibility of self-selection and hidden biases in non-probability sampling (Leiner, 2014). When designing a research study, a consideration is the sample size; i.e. the number of participants required to answer the research question

sufficiently. A lack of a sufficient number of observations reduces the overall power of the study (Suresh and Chandrashekara, 2012). As all studies in this thesis were explorative in nature, a power calculation was not performed. A power calculation is understood to be of little value in exploratory studies, where the data available to base calculations is sparse (Jones et al., 2003).

4.2.3 Reliability and Validity

Psychometrics and validation studies play a fundamental role in public health research. Evidence-based clinical practice is achieved through implementation of findings of well conducted quality research studies. Therefore, rigour of research and execution of study designs must be carefully examined and critically analysed. Measurement of reliability and validity is an important of aspect of high-quality quantitative research. Reliability is concerned with the consistency and credibility of research findings, while validity refers to the truthfulness of the findings (Bannigan and Watson, 2009). This was considered when choosing outcome measures to ensure the instrument was appropriate and had relevant items. The reliability and validity of the various methods and outcome measures for the studies contained in this thesis will be presented and discussed in this chapter.

4.3 Overview of Studies I-IV

4.3.1 Introduction

Study I was designed to explore the validity and reliability of self-reported concussion history in current rugby union players. This was recognised as a significant limitation in the broader literature pertaining to long-term cognitive health and associated concussion history in retired elite athletes as detailed in systematic review II (Chapter 3). To date there is no research into the validity and reliability of self-reported concussion history among rugby players

specifically. The rationale for cross-sectional studies II-V was based on the findings of the systematic review described in Chapter 2 (Cunningham et al., 2018). This review found a pertinent need for research examining the long-term brain health of living retired professional rugby players. The evolving literature in this area highlights the gap in the understanding of a potential cause-and-effect relationship between participation in rugby, concussion history and long-term brain health. Due to the scarcity of research pertaining to the long-term health of living former professional rugby players, a broader investigation into the long-term brain health of retired professional rugby union players was conducted. Two protocols will be presented in this chapter which have been devised for the purpose of this thesis. Protocol I pertains to Study I which explored self-reported concussion history in current rugby players. Protocol II was employed in a cross-sectional study (Studies II-V) investigating former rugby players and subsequent markers of aging and specifically brain aging. These methods will include assessment of cognitive functioning, mental health, concussion history and various aspects of overall general health that were deemed clinically relevant. Although this study focusses on retired rugby union players specifically, the general study design and the methods for assessing brain health are likely to be relevant to other studies of former elite sportspersons. The domains of assessment and the instruments used in their measurement are summarised in Table 4-1 and described in detail in Table 4-2 and throughout this chapter.

4.4 Study I Protocol

4.4.1 Materials and Methods

4.4.1.1 Study Design

This study was a cross-sectional cohort design. Current professional rugby players in an Irish rugby union club (Leinster Rugby) were invited to partake in the study. Participants were primarily recruited via email advertisement through team managers. The study was launched in the host club by presentations for players and staff, along with flyers and general word of

mouth. Recruitment and data collection for the study began in January 2017 and concluded in January 2018. This study was registered with ClinicalTrials.gov, a database of privately and publicly funded clinical studies conducted around the world. Registration is available at https://clinicaltrials.gov/; registration identifier: NCT03544372.

4.4.1.2 Eligibility Criteria

The inclusion criteria included player's age >18 years old and a current contract to be a professional rugby player. Players were included if they provided written informed consent and were freely willing to participate in the study.

4.4.1.3 Recruitment

A convenience sample of current professional rugby union players contracted to Leinster Rugby were recruited to take part in the study. The study was rolled out at the host club. Members were recruited via mass email inviting them to participate in the study. This contained information on the study along with a participant information leaflet [Appendix C.1] and was distributed via a gatekeeper at the host club (the administration officers for Leinster Rugby) to advertise the study to current players. Potential participants were also recruited via word of mouth, flyers, and advertisements and presentations at Leinster Rugby and events. Those participants agreeing to take part were then contacted by the lead investigator in order to schedule a testing time that was convenient for the participant. Recruitment for the study commenced in January 2017 and concluded in September 2017.

4.4.1.4 Ethics Approval

Ethical approval for the Study I was obtained from the Faculty of Health Sciences Research

Ethics Committee, Trinity College Dublin [Appendix C.2]. In addition, approval was obtained from Leinster Rugby which was the testing location for the study [Appendix C.3]. All procedures were performed in accordance with the 1964 Helsinki declaration (WMA., 1964) and its later amendments (WMA., 2013). All participants provided written informed consent [Appendix C.4].

4.4.1.5 Participants and Test centre

A sample of 63 current professional rugby players were recruited (members of Leinster Rugby Ireland). The location for testing was at the host club, Newstead Building A, Belfield, University College Dublin. The lead investigator individually screened players' eligibility prior to commencing the study. The 62 willing recruits signed an informed consent form to participate following a seven-day time to reflect and withdraw if desired. This included all professional rugby players contracted to the club, excluding one player who declined to participate.

4.5.1.6 Assessment protocol

Participants enrolled in this study attended a once-off testing at the host club. Data collection took place at the rugby training facility. Participants completed a sociodemographic and concussion history questionnaire. The testing was organized and conducted by physiotherapist and lead investigator (JC).

4.4.1.4 Outcome Measures

The primary outcome measure was the National Institute of Health Common Data Element;

the Michigan Traumatic Brain Injury (TBI) Identification Method [Appendix C.5] (Broglio et al., 2018). This questionnaire was used to obtain concussion history. A demographic questionnaire; the Professional Rugby Union Questionnaire (PRUQ) was also administered to capture detailed demographics, current physical and mental health, medical history, and sports history such as player's rugby playing career, age of debut, career duration, and number of seasons played [Appendix C.6]. Medical records of documented concussion history at the host club were gained via KitMan (KitMan Labs Dublin) and ImPACT (Covassin et al., 2009).

4.5 Study II-IV Protocol

4.5.1 Materials and Methods

4.5.1.1 Study Design

As part of the 'PROP' project, cross-sectional, controlled studies II-V were conducted between August 2018 and June 2019. The study protocol was registered with a trial registry (ClinicalTrials.gov; identifier: NCT03544346) prior to recruitment and remained unchanged for the trial duration. Retired professional rugby players (members of Rugby Players Ireland) and former international rowers (members of Rowing Ireland) were recruited. General and brain health-related measures through validated assessments were collected. Participants enrolled in the studies attended the designated test centre on one occasion to complete sociodemographic and clinical questionnaires, to undergo physical examination and to complete a battery of cognitive functioning tests. All equipment was calibrated as per manufacturer recommendations prior to each session.

4.5.1.2 Eligibility criteria

Participants were required to be a retired professional rugby player or retired international rower (no age limit); male or female. Participants were required to have played at least one season of professional rugby or in the case of the rowers, completed and trained full time as an international athlete for at least one season. Participants were excluded if they had been diagnosed with a moderate/severe brain injury (e.g. a motor vehicle accident). A recent concussion diagnosis (in the last year) also precluded entry into the study, along with treatment of chemotherapy or radiotherapy in last 12 months. Non-English speakers were also excluded.

4.5.1.3 Recruitment

A convenience sample of retired professional rugby players and retired international rowers were recruited to take part in the 'PROP' studies, which was rolled out in various testing centres located across Ireland. Members were recruited via mass email inviting them to participate in the study. This contained information on the study along with a participant information leaflet [Appendix C.7] and was sent through a gatekeeper (the administration officers for Rugby Players Ireland and Rowing Ireland). Potential participants were also recruited via media reports, word of mouth, flyers, posters, and advertisements and presentations at Rugby Players Ireland and Rowing Ireland alumni events [Appendix C.8]. Those participants agreeing to take part were then contacted by the research team in order to schedule a testing time that was convenient for the participant. Prior to the organised time of testing, each participant was emailed/posted a package which contained a demographic/medical history/sporting history questionnaire; the Retired Professional Athlete Questionnaire (RPAQ) [Appendix C.9]. Along with six health-related questionnaires [Appendix C.10-C.15]; two sports specific questionnaires for the former rugby players

[Appendix C.16-C.17] and one for the former rowers [Appendix C.17]. The athletes returned this package to the lead investigator at the time of testing. Participation in the study was completely voluntary and players were informed that they could withdraw from the study at any time. Written informed consent [Appendix C.18] was gained by all participants prior to testing. Recruitment for the 'PROP' study commenced in August 2018 and concluded in July 2019.

4.5.1.4 Ethics Approval

Approval for all studies was granted by the local appropriate research ethics committee; the Faculty of Health Science Ethics Committee at Trinity College Dublin [Appendix C.19]. Ethical approval was also granted by Rugby Players Ireland [Appendix C.20] and Rowing Ireland [Appendix C.21]. Written informed consent was obtained for each subject prior to participation, in compliance with the Declaration of Helsinki (WMA., 1964) and all later amendments (WMA., 2013).

4.5.1.5 Participants and Test centres

A sample of 68 retired professional rugby players were recruited (members of Rugby Players Ireland). The primary location for testing was the Exercise Laboratory in the Faculty of Health Sciences, St James's Hospital, County Dublin. However, testing was also conducted in different centres in each province throughout the country. This included Ravenhill Stadium, Ulster Rugby, Belfast, County Antrim; the Sportsground, Connacht Rugby, County Galway; Munster Rugby, High Performance Centre, University of Limerick, County Limerick; Affidea Clinic, The Elysian, County Cork; Leinster Rugby, Newstead Building, Belfield, County Dublin.

4.5.1.7 Assessment protocol

Participants enrolled in this study attended a once-off testing in the Trinity Centre for Health Sciences, Dublin, or another designated location around the country. A standardised test protocol was used for all assessments. Participants were asked to refrain from smoking, eating or drinking during the assessment. Participants completed sociodemographic and clinical questionnaires, physical assessment and underwent cognitive functioning testing. All measures were taken by the same physiotherapist and lead investigator (JC). The testing lasted approximately 2 hours 10 minutes per participant.

4.6 Stimuli and Apparatus

4.6.1 Outcome Measures

The various outcome measures used across studies I-V will be described in this section. The majority of the outcome measures described were employed in studies II-V. Study I assessed concussion history primarily. The 'PROP' project was a once-off test comprising clinical questionnaires, a brief health screen and objective cognitive assessments [Table 4-1]. In all studies, the testing protocol was explained to the participant prior to commencing the test. Demographic, medical and sporting history information was gained [Appendix C9]. Concussion history was then collected [Appendix C5]. This was followed by questionnaires enquiring into a host of overall health and lifestyle questionnaires [C10-C15] and a list of mental health questionnaires [Appendices C.22-C27]. The participants then underwent a brief health screen including resting heart and blood pressure, height, weight and body composition [Table 4-2]. The participant was then taken through the cognitive assessment portion of the test procedure. The administration test order of the three objective cognitive assessments the NART, CANTAB and SIFI was randomized using Microsoft Excel randomization tools.

Table 4-1 Framework for Studies II-V Data Collection.

General Questionnaires	Cognitive Ability	Concussion History	Physical Health
Retired Professional Athlete Questionnaire (RPAQ) Lifestyle and confounder questionnaires Mental health questionnaires	The Cambridge Neuropsychological Test Automated Battery (CANTAB) The National Adult Reading Test (NART) Sound Induced Flash Illusion Test (SIFI)	The Michigan Traumatic Brain Injury (TBI) Identification Method	Body composition Blood Pressure

Table 4-2 Domains and Instruments used in Studies I-V.

Domain	Instrument	Approximate time for administration
Clinical Questionnaires (General Information)		
Demographics/ Medical History/ Sporting History	Retired Professional Athlete Questionnaire (RPAQ) Professional Rugby Union Questionnaire (PRUQ)	5 minutes
Concussion History	The Michigan Traumatic Brain Injury (TBI) Concussion Questionnaire	5 minutes
Clinical Questionnaires (Overall Health)		
Pain	Pain Disability Index (PDI)	5 minutes
Alcohol	The Alcohol Use Disorders Identification Test (AUDIT)	5 minutes
Physical Activity	The International Physical Activity Questionnaire (IPAQ)	5 minutes
Exercise	Godin Leisure-Time Exercise Questionnaire (GLTEQ)	5 minutes
Sleep	The Pittsburgh Sleep Quality Index (PSQI)	5 minutes
Cognitive Function	Neuro-QOL Item Bank v2.0 – Cognition Function-Short Form	5 minutes
Clinical Questionnaires (Athlete Specific)		
Athletic Identity	Athletic Identity Measurement Scale (AIMS)	5 minutes
Rugby	Satisfaction with Rugby Playing Career	5 minutes
Clinical Questionnaires (Mental Health and Psychological Well-being)		
Events	Life Events Checklist (LEC)	5 minutes
Overall Physical and Mental Health	Short Form 12 (SF-12)	5 minutes
Resilience	Connor-Davidson Resilience 25 (CD-RISC 25)	5 minutes
Depression/Anxiety	Patient Health Questionnaire (PHQ-9) Brief Symptom Inventory (BSI)	5 minutes
Satisfaction with Life	Satisfaction with Life Scale	5 minutes
Physical Assessment		

Body composition	Body mass index (BMI) Bio-impedance analysis	5 minutes
Blood Pressure	Sphygmomanometer	5 minutes
Objective Cognitive Function		
Premorbid Intelligence (IQ)	The National Adult Reading Test (NART)	6 minutes
Multisensory Integration	Sound Induced Flash Illusion Test (SIFI)	10 minutes
The Cambridge Neuropsychological Test Automated Battery (CANTAB)		
Sensorimotor Ability	CANTAB-Motor Screening Task (MOT)	2 minutes
Motor and Mental Response Speeds	CANTAB-Reaction Time (RTI)	3 minutes
Visual memory and New Learning	CANTAB-Paired Associates Learning (PAL)	8 minutes
Spatial Working Memory	CANTAB-Spatial Working Memory (SWM)	4 minutes
Visuospatial Working Memory	CANTAB-Spatial Span (SSP)	5 minutes
Sustained Attention	CANTAB-Rapid Visual Information Processing (RVP)	7 minutes

4.7 Clinical questionnaires

Self-report questionnaires pertaining to physical, mental and overall health were deemed relevant to the overall general health of the retired rugby players in study II-V. This section will detail the questionnaires used to measure domains including sleep, pain, athlete identity, satisfaction with sporting career, alcohol use, cognitive functioning, exercise and physical activity levels and mental health. The questionnaires were simple, quick to administer and score and were chosen to assess factors other than concussion history that may confound long-term brain health.

4.7.1 Demographic/Medical History/Sporting History

A Professional Rugby Union Questionnaire (PRUQ) [Appendix C.6] and a Retired Professional Athlete Questionnaire (RPAQ) [Appendix C.9] were specifically designed for the studies I-V. Both of which acquired information regarding organized professional sport history, medical, occupational and demographic information.

4.7.2 Concussion History

The Michigan Traumatic Brain Injury (TBI) Identification Method was used to obtain athlete concussion history [Appendix C.5]. This is a self-report pen and paper questionnaire that investigates lifetime history of concussion, including sports-related and non-sports-related concussions. It assesses each concussive event across common criteria such as mechanism and date of injury, presence or absence of associated loss of consciousness (LOC) and symptoms experienced. This Michigan TBI Identification method is a NIH Common Data Element (Broglio et al., 2018). This questionnaire was used to assess concussion history in studies I-V. Study I used the Michigan TBI Identification Method to validate self-reported concussion history against medically documented concussion history. In studies II-V, lifetime history of concussion was gained in order to facilitate investigation into relationships between history of sports-related concussion and subsequent measures of brain health.

4.8 General Health Questionnaires

Self-report questionnaires pertaining to physical, mental and overall health were deemed relevant to athlete general health. All questionnaires described below were part of the 'PROP' studies II-V. This section will detail the questionnaires used to measure domains including sleep, pain, athletic identity, satisfaction with rugby paying career, alcohol use, cognitive functioning, exercise and physical activity levels and mental health. The questionnaires were

simple, quick to administer and score and were chosen to assess factors other than concussion history that may confound long-term brain health. The participants were requested to complete all questionnaires independently. The lead investigator (JC) was available in the event of any questions or issues arising.

4.8.1 The Pain Disability Index

In order to assess pain-related disability associated with chronic musculoskeletal pain, the widely used Pain Disability Index (PDI) was employed (Tait et al., 1990) [Appendix C.10]. This instrument is designed to assess self-reported levels of disability experienced on a day to day basis while carrying out essential life activities (Chibnall and Tait, 1994). The rating scales measure the degree to which aspects of life are disrupted by chronic pain. The various activities measured by the PDI include: (1) family and home responsibilities: activities related to home and family, (2) recreation: hobbies, sports and other leisure time activities, (3) social activity: participation with friends and acquaintances other than family members, (4) occupation: activities partly or directly related to working including housework or volunteering, (5) sexual behaviour: frequency and quality of sex life, (6) self-care: personal maintenance and independent daily living (bathing dressing etc.) and (7) life-support activity: basic life-supporting behaviours (eating sleeping breathing etc.). Higher scores indicate greater levels of pain and disability. Reliability and validity of the PDI have been supported by several studies (Tait et al., 1987, Jerome A, 1991, Gronblad et al., 1993). Long-term elite sports participation has been found to be associated with adverse health related outcomes including higher incidence of osteoarthritis and joint replacement among former rugby union players (Davies et al., 2017). Hence, assessment of disability associated with chronic pain was deemed to be pertinent in this cohort. Furthermore, associations between the concurrent prevalence of chronic pain and mental disorders have been frequently documented (Pereira et al., 2017).

4.8.2 The Alcohol Use Disorders Identification Test

The Alcohol Use Disorders Identification Test (AUDIT) is a 10-item screening tool developed by the World Health Organization (WHO) (Daeppen et al., 2000) [Appendix C.11]. This questionnaire is used to assess alcohol consumption, drinking behaviours, and alcohol-related problems. Participants were encouraged to answer the AUDIT in terms of standard drinks. They referred to a chart illustrating the approximate number of standard drinks in different alcohol beverages for reference. A score of 8 or more is considered to indicate hazardous or harmful alcohol use. The AUDIT has been identified as a reliable and valid screening instrument to identify at-risk drinkers and patients with an alcohol-use disorder (AUD) (Dybek et al., 2006, Osaki et al., 2014, Moussas et al., 2009). It has been validated across genders and in a wide range of racial/ethnic groups and is well suited for use in primary care settings (Kaner et al., 2007, Källmén et al., 2014). Research suggests higher rates of alcohol use or dependence in athlete populations when compared to non-athlete populations (Sonderlund et al., 2014). This may be exacerbated by the transition into retirement and potential loss of self-identity (Park et al., 2013). Alcohol misuse is known to be a confounding factor in cognitive functioning (Kim et al., 2016), and can predispose to psychiatric disorders and poor mental health (Boden and Fergusson, 2011, Pereira et al., 2013). Recent research also suggests that even moderate levels of alcohol consumption may be associated with adverse brain outcomes (Topiwala et al., 2017).

4.8.3 Subjective Assessment of Physical Activity

Physical activity was measured subjectively using two questionnaires; the International Physical Activity Questionnaire (IPAQ) and the Godin Leisure-Time Exercise Questionnaire [Appendix C.12 and Appendix C.13]. Despite the limitations with using physical activity questionnaires, they remain the most extensively used method of recording physical activity.

Exercise is a known protective factor for neurodegeneration (Liu et al., 2019). Research suggests that exercise is a strong modulator that induces structural and functional changes in the brain (Mandolesi et al., 2018), incurring benefits on both cognitive functioning and wellbeing (Fernandes et al., 2017). Hence it was deemed an important factor that could influence brain heath in retired professional rugby players.

4.8.3.2 The International Physical Activity Questionnaire

The International Physical Activity Questionnaires (IPAQ) was developed to obtain internationally comparable data on health-related physical activity (Craig et al., 2003) [Appendix 4.12]. The IPAQ is a 7-day recall questionnaire with two versions available in 21 languages including English, French, Spanish, Arabic, and Korean. The self-administered short form IPAQ (IPAQ-SF) was used. The IPAQ-SF has been recommended for population prevalence studies, where time is limited, because it is easier and more feasible to complete than the long form (Craig et al., 2003, Lee et al., 2011). This measure assesses the types of intensity of physical activity and sitting time that people do as part of their daily lives. These measures are considered to estimate total physical activity in MET-min/week and time spent sitting. The short version assesses frequency (days in the past week) and duration (minutes and/or hours per day) of walking, moderate, and vigorous intensity physical activity. The participants are instructed to only report activity that was done in at least 10-minute bouts. The IPAQ is for use with young and middle-aged adults. The IPAQ questionnaires have been validated across 12 countries (Wolin et al., 2008, Craig et al., 2003). The IPAQ-SF has been validated against accelerometery in different samples (Ekelund et al., 2006, Macfarlane et al., 2006, Mader et al., 2006).

4.8.3.1 The Godin Leisure-Time Exercise Questionnaire

The Godin Leisure Time Exercise Questionnaire (GLTEQ) is a commonly used self-report measure of physical activity (Sikes et al., 2019) [Appendix C.13]. It is a simple and quick self-administered, four item questionnaire that assesses an individual's leisure-time activity during a typical week. It is a two-part questionnaire, containing two separate sections. The first section prompts the respondent to report the number of bouts of strenuous, moderate, or mild physical activity in which they engage in over a typical week. It is stipulated that the exercise bouts must be greater than 15 minutes in duration. Strenuous exercise is described as "heartbeat is rapid" and includes examples such as running or vigorous swimming. Moderate exercise is described as "not exhausting" and includes examples such as fast walking, easy bicycling, and tennis. Mild exercise is described as "requiring minimal effort" and includes examples such as yoga, bowling and easy walking (Godin and Shephard, 1985). The second part of the questionnaire is also known as the Sweat Index. The respondent is asked how often during a typical week in their leisure time they engage in any regular activity long enough to work up a sweat (heart beats rapidly).

The GLTEQ summary score (i.e., the total leisure activity score (TLS)) is calculated as the sum of weekly frequencies of strenuous, moderate and vigorous intensity activity by their corresponding MET values; [TLS= (9 METS x strenuous activity time] + [5 METS x moderate activity time] + [3 METS x light activity time)]. Having summed those values, an overall score ranging between 0 and 119 in arbitrary units will be gained. Higher scores reflect participation in a greater volume of physical activity. It can be used for classifying healthy adults into active and insufficiently active categories. The health contribution score corresponds with health-promoting physical activity recommendations, and can classify individuals into categories of sufficiently active, moderately active, or insufficiently active based on public health guidelines (Amireault and Godin, 2015). The TLS has been found to

be positively correlated with maximal oxygen uptake and body fat percentage (Godin and Shephard, 1985). The strongest correlation was between VO2 max (percentile) and reported strenuous exercise (r = 0.35). The validity and reliability of the GLTEQ has been established among many cohorts (Motl et al., 2018, Miller et al., 1994, Jacobs et al., 1993, Eisenmann et al., 2002).

4.8.4 The Pittsburgh Sleep Quality index

The Pittsburgh Sleep Quality Index (PSQI) is an effective self-rated questionnaire used to assess the quality and patterns of sleep over a 1-month time interval (Buysse et al., 1989) [Appendix C.14]. It differentiates "poor" from "good" sleep by measuring seven domains: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction over the last month. **S**leep is an important aspect of maintaining the body's circadian rhythm. Inadequate sleep contributes to heart disease, diabetes, depression, falls, accidents, impaired cognition, and a poor quality of life. Normal aging changes interfere with the quality of sleep. The respondent self-rates each of these seven areas of sleep. Scoring of the answers is based on a 0 to 3 scale, whereby 3 reflects the negative extreme on the Likert scale. A global sum of "5" or greater indicates a "poor" sleeper. The PSQI has internal consistency and a reliability coefficient (Cronbach's alpha) of 0.83 for its seven components. The scale has been translated into over 56 languages. Several studies in a variety of adult populations have supported high validity and reliability for the PSQI (Backhaus et al., 2002, Spira et al., 2012, Popevic et al., 2018, Grandner et al., 2006, Marques et al., 2013). Sleep is a known important modulator of cognitive functioning and mental wellbeing (Colrain, 2011, Hudson et al., 2019, Freeman et al., 2017). Both of which can suffer as a result of sleep deprivation.

4.8.5 Neuro-QOL-Cognition Function-Short Form

The Neuro-QoL questionnaire used in this study is a standardised approach to measuring health-related quality of life (HRQOL) of adults and children across a wide range of common neurological disorders [Appendix C.15]. The development of Neuro-QoL was instigated by the National Institute for Neurological Disorders and Stroke (NINDS) (Cella et al., 2011). Neuro-QoL is a self-report measure, comprised of item banks and scales that evaluate symptoms, concerns, and issues that are relevant across neurological disorders (generic measures) along with instruments that assess areas most relevant for specific patient populations (targeted). Lower scores indicate poorer cognitive health. The NeuroQoL instruments lend themselves to use in both clinical practice and research to assess within-disease as well as cross-disease comparisons. The Neuro-QoL measure has demonstrated good reliability and validity (Cella et al., 2012, Miller et al., 2016, Victorson et al., 2014, Nowinski et al., 2016). Many studies to date have used self-reported cognitive measures to investigate associations between long-term cognition and history of head impact exposure in retired athletes (Guskiewicz et al., 2005). However, a limitation of these studies is that conclusions drawn from self-reported data should be cautious. Investigations of objective and subjective cognition in retired athletes and associations between self-reported symptoms and performance on neuropsychological tests need to be investigated further. Therefore, the clinical importance of the self-reported cognitive findings should be carefully considered in the overall context of the individual's performance on neuropsychological and cognitive testing and symptom self-report.

4.8.6 Athlete specific Questionnaires

4.8.6.1 The Athlete Identity Measurement Scale

The Athlete Identity Measurement Scale (AIMS) is a widely used instrument which was

developed by Brewer et al. (1993) [Appendix C.16]. It is designed to evaluate levels of athletic identity. The concept of athletic identity was described by the developers as 'how athletes who practice a sport in a professional manner build the notion of themselves, in relation to the emotions of their interpersonal living resulting from sporting practices' (Brewer et al., 1993). Therefore, it refers to the degree of importance, strength and exclusivity that is attached to the athlete's role by him/herself and his/her context (Cabrita et al., 2014). Athlete Identity is a social construct which is influenced by friends, family, colleagues, coaches and the sporting context (Tušak et al., 2005). This interaction allows athletes to form identities that distinguishes themselves from others, yet simultaneously gives them a feeling of belonging to a defined group (Anderson and Coleman, 2008).

This questionnaire is comprised of ten statements to which the individual responds on a 7-point Likert scale varying from 1 (entirely agree) to 7 (entirely disagree). These are subdivided into three subscales; including social identity (items 1, 2 and 3), exclusivity (items 4, 5) and negative affectivity (items 6, 7). This results in a total athletic identity score, ranging from 10 to 70. A lower score indicates stronger athletic identity. The AIMS instrument has been found to have high internal stability and test-retest validity (Brewer et al., 1993) and validity (Proios, 2012). This questionnaire was administered to the retired athlete cohort as former elite athletes have been shown to have emotional difficulties upon retirement.

Changes in athletic identity have been found to be significant determinants of adjustment for athletes upon career termination (Lavallee et al., 1997).

4.8.6.2 Satisfaction with Rugby Playing Career Questionnaire

This questionnaire was adapted from a previously used questionnaire on rugby players (Davies et al., 2017) [Appendix C.17]. A question was added to the original form which asked players whether they believe that their rugby career has impacted on their long-term cognitive functioning in any way. If the player answered yes, they were asked to detail how

they felt it had. This questionnaire is designed to gauge rugby player's reflections and sentiments on their playing career given their experience. Rugby players were asked to reflect on various statements: (1) considering the benefits and risks of my previous participation in rugby, I would do the same again and (2) considering the benefits and risks of my previous participation in rugby, I would recommend this to my children, relatives or close friends. The players responded on a five-point Likert scale that ranged from one "strongly agree" to five "strongly disagree". The third statement asked players to reflect on the question; did your rugby career enrich your life? Again, a five-point Likert scale was used which ranged from one "dramatically" to five "not at all". Finally, they were asked whether they believe that their rugby career has impacted on their long-term cognitive functioning in anyway. This was a simple yes or no question. However, if the player indicated yes, they were asked to detail how they believed it had.

4.9 Mental Health Questionnaires

A list of six self-reported questionnaires pertaining to mental health and psychological well-being were administered [Appendices C.22-C.27]. All questionnaires described below were part of the 'PROP' study (studies II-V). The Brief Symptom Inventory Index (BSI), the Patient Health Questionnaire (PHQ-9), the 12-Item Short Form Health Survey (SF-12), the Connor-Davidson Resilience Scale (CD-RISC-25), the Life Events Checklist (LEC) and the Satisfaction with Life Scale were all completed. Investigation into mental health was deemed very important as this is a key aspect of overall brain health. There is evidence to suggest an increased risk of mental health issues among elite athlete populations (Souter et al., 2018, Wolanin et al., 2015). Reasons for potential psychological issues in retired elite athletes are plentiful and may include injury, involuntary retirement (Wolanin et al., 2015), life events (Gouttebarge et al., 2016), disordered eating (McArdle et al., 2016), substance abuse (Dietze et al., 2008) and transition into retirement (Martin et al., 2014). Further common mental health disorders such as depression and anxiety have been linked to repetitive head impacts

and concussion in contact sport athletes (Gouttebarge et al., 2016). The concept of subjective wellbeing encompasses two major components; emotional and cognitive (Diener and J. Larsen, 1993, Diener et al., 1985). Affective components include positive and negative affect, while the cognitive component pertains to satisfaction with life.

4.9.1 The Brief Symptom Inventory-18

The BSI-18 a widely-used standardized screening instrument which quantitatively assesses psychological distress and psychiatric disorders [Appendix C.22]. It is the most recent and shortened version in a series of similar instruments developed by Derogatis (1983). The BSI-18 consists of 18 descriptions of emotional and physical complaints. The shortened scale comprises three six-item scales; somatization, depression and anxiety, along with a Global Severity Index (GSI). Respondents are asked to indicate on a scale; (zero being not at all and four being very much), to what extent they are troubled by the complaints. Depression, anxiety and somatization over the previous week is gauged. Each subscale of the BSI-18 contains six items from the three corresponding subscales of the BSI; six each on the Somatization, Depression, and Anxiety dimensions. The Global Severity Index (GSI) represents the global or total score, which summarizes the respondent's overall level of psychological distress.

The GSI is a concise/ quantitative indication of the respondent's current level or depth of psychological dysphoria. Generally, the GSI is the single best indicator of the respondent's overall emotional adjustment or psychopathologic status. The Somatization (SOM) items reflect distress caused by the perception of bodily dysfunction/ focusing on symptoms arising from cardiovascular, gastrointestinal and other physiologic systems that have powerful autonomic mediation. In addition, symptoms included on the Somatization dimension are often observed in highly somaticized presentations of anxiety and depressive disorders. The Depression items represent core symptoms of various syndromes of clinical depression.

Symptoms of disaffection and dysphoric mood are included as are those reflecting self-deprecation, anhedonia, loss of hope, and suicidal ideation. These symptoms retain core loadings in repeated factor analyses across multiple populations. The original BS-56 has been used in a variety of settings, and its psychometric properties have been widely investigated and appraised (Adawi et al., 2019). Psychometric evaluation of the BSI-18 reveals it to be an acceptable short alternative to the complete scale (Recklitis et al., 2017, Spitzer et al., 2011, Franke et al., 2017).

4.9.2 The Patient Health Questionnaire

Depression is a major public health issue and is one of the leading causes of disease burden and disability worldwide (Consortium, 2004, Moussavi et al., 2007). The PHQ-9 is a commonly used instrument for screening and monitoring depression in primary care and other medical and non-medical settings (Smarr and Keefer, 2011) [Appendix C.23]. It is a nine-item questionnaire that has been translated into various foreign languages for use in other countries. It requires minimal time to administer and is easily understood. The respondent is asked to reflect on symptoms they may have experienced in the preceding two weeks and indicate to what extent they have been bothered by these symptoms on a scale; (zero being not at all and three being nearly every day). There is pre-identified cut-off thresholds to classify respondents as being within the normal range, having minor depressive symptoms or having major depression (Kroenke and L Spitzer, 2002). The reliability and validly of the PHQ-9 has been widely researched and appraised (Kroenke et al., 2001). The internal validly has also been found to be high (Udedi et al., 2019).

4.9.3 The Short Form Health Survey-12

The widely used SF-12 survey was used assess to physical and mental health [Appendix C.22]. The items of the SF-12 produce two summary measures, Physical Component

Summary (PCS) and Mental Component Summary (MCS). It was developed for the Medical Outcomes Study (MOS), a multi-year study of patients with chronic conditions (Ware and Sherbourne, 1992). The SF-12 is a shortened version of the SF-36, a common health-related quality of life (HRQoL) measure (Ware et al., 1996). The SF-12 is a short generic self-report measure of overall health status. The instrument consists of 12 items taken from the 36-item short-form (SF-36), covering the same eight domains of health outcomes, enquiring about aspects of physical and mental health These include physical functioning (PF), role-physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role-emotional (RE), and mental health (MH). Each question is scored on a numerical rating scale (NRS). Lower scores represent poorer mental health on both the PCS and MCS components. The reliability and construct validity of the measure have previously been established (Huo et al., 2018, Shou et al., 2016, Hayes et al., 2017).

4.9.4 The Connor-Davidson Resilience Scale-25

Resilience has been described as the ability to positively adapt in the face of adversity and significant life stressors (Fletcher and Sarkar, 2013). Resilience is a pivotal part of determining how an individual reacts to and copes with trauma, tragedy, threats or various other unfavourable life events (Connor, 2006). Resilience is also described as the ability to remain functionally stable and well despite this stress (Bonanno, 2004). The importance of resilience to a person's overall mental health and psychological well-being is becoming increasingly apparent (Färber and Rosendahl, 2018, Joyce et al., 2018). The CD-RISC-25 is a self-report questionnaire developed to assess resilience [Appendix C.23]. This version of the CD-RISC comprises of 25 items, each rated on a 5-point scale (0-4), with higher scores reflecting greater resilience. All three versions of the CD-RISC have been deemed to have sound psychometric properties (Kuiper et al., 2019).

4.9.5 The Life Events Checklist

The Life Events Checklist (LEC) was used and was developed at the Center for Posttraumatic Stress Disorder (PTSD) in the United States [Appendix C.24]. It was developed concurrently with the Clinician-Administered PTSD Scale (CAPS) (Weathers et al., 2018). It was designed to be administered before the CAPS, which is a clinician led structured interview and the gold-standard for diagnosing PTSD. Exposure to potentially traumatic events is often associated with significant psychological and emotional distress. The LEC gauges exposure to potentially traumatic events in a respondent's life and is the most commonly used self-report tool for general post traumatic events (Elhai et al., 2005). It investigates exposure to 16 events that are known to potentially result in PTSD or distress. It concludes with one additional item assessing any other extraordinarily stressful event not captured in the first 16 items. The varying levels of exposure are assessed on a six-point nominal scale, first scale being "happened to me" and final scale being "doesn't apply". The respondent may have been exposed at multiple levels to the same trauma type. The LEC has demonstrated adequate test-retest reliability and good convergent validity and therefore is deemed as a useful stand-alone assessment of exposure to traumatic life events (Gray et al., 2004). The checklist does not have a formal scoring protocol or interpretation as it does not yield a composite score. However, it identifies whether a person has experienced one or more of the events listed and the varying levels of exposure to each type of potentially traumatic event included.

4.9.6 Satisfaction with Life Scale

Life satisfaction is a key component of the broader concept of subjective wellbeing. An individual's satisfaction with their life is a cognitive process of judgement in which they assess the quality of their life on the whole, based on their own criteria (Shin and M. Johnson, 1978). It has been shown in studies investigating self-reported mental health and well-being that a happy person has increased life-expectancy, has improved health outcomes and better

established interpersonal relationships (Diener and Chan, 2011, Kimm et al., 2012). The Satisfaction with Life Scale is a commonly used five item scale which measures global cognitive judgements of subjective life satisfaction (Diener et al., 1985) [Appendix C.25]. This a five-item scale designed to measure global cognitive judgments of one's life satisfaction. The individual specifies the degree to which they agree or disagree with each of the five statements. On a seven-point Likert scale that ranges from seven "strongly agree" to one "strongly disagree". The scale does not assess satisfaction with life domains such as health or finances but allows subjects to integrate and weight these domains in whatever way they choose. The Satisfaction with Life Scale does not discriminate between various domains of the individual's life such as occupation, health or finance, but rather enables the individual to weigh in all aspects of their life, good and bad, and judge it as a whole in terms of satisfaction levels (Pavot and Diener, 2008). It has been shown to be suitable for different age groups and applications and to have good psychometric properties (Pavot and Diener, 2008, 1993). This includes high internal consistency and temporal reliability and moderate to high correlation with other measures of subjective well-being (Pavot, 1993). It has been used and validated extensively in diverse samples regarding age, sex, occupation and has been validated in numerous languages (López-Ortega et al., 2016).

Table 4-3 Selected Questionnaires and Rationale for Inclusion.

Questionnaire	Rationale for Inclusion
Pain Disability Index (PDI)	Long-term elite sports participation may be associated with chronic pain and disability associated with higher incidence of osteoarthritis and joint replacement among former rugby union players. Chronic pain can be associated with poorer mental health outcomes.
The Alcohol Use Disorders Identification Test (AUDIT)	Research suggests higher rates of alcohol use or dependence in athlete populations when compared to non-athlete populations. Further, alcohol misuse is known to be a confounding factor in cognitive functioning and can predispose to poor mental health.
The International Physical Activity	Research suggests that physical activity is a strong modulator of long-term brain health, incurring benefits on both cognitive functioning and wellbeing. Hence it was deemed an important factor that could influence brain heath in retired professional rugby players.

Questionnaire (IPAQ)	
Godin Leisure-Time Exercise Questionnaire (GLTEQ)	As above, exercise is a known protective factor for neurodegeneration and is also an important moderating factor in mental health and wellbeing. Hence it was an important factor to consider when investigating brain health in aging retired professional rugby players.
The Pittsburgh Sleep Quality Index (PSQI)	Sleep is a known important modulator of cognitive functioning and mental health and general wellbeing. Therefore, it was deemed an important confounding factor to include when investigating brain health in former rugby players.
Neuro-QOL Item Bank v2.0 – Cognition Function-Short Form	Given that many studies have focused solely on self-reported cognitive functioning, it was deemed important to include both subjective and objective cognitive tests. The clinical importance of self-reported cognitive findings should be carefully considered in the overall the context of rugby player's performance on neuropsychological and cognitive testing and symptom self-report and history of head impact exposure in retired athletes.
Athletic Identity Measurement Scale (AIMS)	Athletic identity has been found to be an important factor for successful career termination in elite athletes. Loss of athletic identity may be associated with increased distress on retirement.
Satisfaction with Rugby Playing Career	This questionnaire was included as it was deemed important to gauge rugby player's reflections and sentiments on their playing career given their experience.
Brief Symptom Inventory (BSI)-18	As above investigation into mental health was deemed very important as this is a key aspect of overall brain health and has been linked in some studies to concussion. The BSI-18 was included to investigate depression, anxiety and somatization.
Patient Health Questionnaire (PHQ-9)	Investigation into mental health was deemed very important as this is a key aspect of overall brain health. There is evidence to suggest an increased depression risk among elite athlete populations. Therefore, the PHQ-9 was selected to investigate prevalence of depression. It was also included in order to investigate any associations between concussion or repetitive head impact exposure and depression.
Short Form 12 (SF-12)	The SF-12 survey was included to assess physical and mental functioning in retired professional rugby players in order to get an idea of overall health and wellbeing.
Connor-Davidson Resilience 25 (CD-RISC 25)	Resilience is increasingly noted as an important factor to a person's overall mental health and general well-being. Therefore, it was deemed an important confounding factor to include when investigating mental health in former rugby players.
Life Events Checklist (LEC)	Exposure to traumatic events is often associated with significant psychological and emotional distress. The LEC was chosen in order to gauge exposure to potentially traumatic events which may have impact upon mental health among former rugby players.
Satisfaction with Life Scale (SWLS)	Satisfaction with life was investigated as self-reported happiness and satisfaction with life has been linked to improved health outcomes in physical and mental health and increased life-expectancy. Hence, it was deemed an important confounding factor to include when investigating brain health and general wellbeing in former rugby players.

4.10 Objective Cognitive Assessment

Cognitive health was examined as a large component of the 'PROP' study through studies II-V. The Cambridge Neuropsychological Test Automated Battery (CANTAB), the Sound Induced Flash Illusion (SIFI) and the National Adult Reading Test (NART) were administered. The cognitive measures were administered in a quiet room in order to enhance optimal testing conditions. The CANTAB test was performed on an iPad. The test order of the six CANATB subtests was predetermined by the Cambridge Cognition Consultancy based on empirical investigation of the relationships of test sequence and practice and fatigue effects (Clark et al., 2012). Instructions were provided by the CANTAB interface and delivered auditorily prior to practice and test blocks. The SIFI task was performed on a laptop. Prior to administering the SIFI task, participants were informed that they would be presented with a series of flashes accompanied by auditory beeps and their task was to count and report the number of flashes while ignoring the beeps. Furthermore, subjects were instructed to maintain fixation for the full duration of the task. Instructions were repeated on the screen prior to practice and test blocks. Each trial was initiated by a white fixation cross in the middle of a black screen followed by the appearance of one or two flashes paired with 0, 1 or 2 beeps. Upon disappearance of the fixation cross, participants were required to input the number of flashes they perceived using response keys on the keyboard. For the second part of the task, auditory beeps only were presented, and subjects were instructed to report the number of beeps.

4.11 The Cambridge Neuropsychological Test Automated Battery (CANTAB)

The cognitive health of the participants was assessed using the Cambridge Neuropsychological Test Automated Battery (CANTAB) software package. The CANTAB is a computer based cognitive assessment system consisting of a battery of

neuropsychological tests, administered to participants using a touch screen computer or tablet. It is considered one of the most validated and widely used computerised measures of cognition (Robbins et al., 1998). There are 25 tests in the CANTAB repertoire which provide an evaluation of various areas of cognitive function including visual memory, visual attention, working memory and planning (Spreen et al., 2006). The CANTAB tasks can be ordered and applied individually or as a battery to measure specific domains of cognitive function. It is a standardised and empirically validated computerized neuropsychological battery of tests that assesses cognitive performance across an array of neuropsychological domains and clinical conditions. It was originally written and developed at Cambridge University in the 1980s (Fray et al., 1996, Luciana and Nelson, 2002, Sahakian et al., 1988).

The CANTAB is a user-friendly, non-verbal cognitive test battery that can be tailored to a specific target population (Parsey and Schmitter-Edgecombe, 2013). The initial purpose of CANTAB was to assess the patterns of cognitive decline in dementia in elderly individuals (Fray et al., 1996). Since its inception, it has been used in the assessment of a wide variety of clinical populations across different ages and cognitive abilities (Levaux et al., 2007, Rasmussen et al., 2009, Sahakian et al., 1988, Sahakian and Owen, 1992, De Luca et al., 2003). The relationships between the scores on component tests of CANTAB and evidence of impairment in specific cognitive functions and psychiatric disorders have been extensively demonstrated (Hadwin et al., 2005, Liotti et al., 2007, Owen et al., 1995, Pantelis et al., 1997, Palade and Benga, 2007, Sweeney et al., 2000, Steele et al., 2007, Torgersen et al., 2010, Yun et al., 2011). The CANTAB has also been shown to be sensitive to cognitive changes associated with the natural aging process and neurodegenerative processes (Clark et al., 2012, Robbins et al., 1994, Torgersen et al., 2012, Muhlert et al., 2014, de Rover et al., 2011).

Intrinsic advantages of using computerized tests over conventional pen and paper measures include millisecond timing accuracy, reliable and randomized presentation of stimuli over multiple trials and repeated administration, and the unobtrusive measurement of cognitive skills and response times during all aspects of the assessment process (Schatz and Browndyke, 2002a). It has been suggested that computerized batteries reflect the activity of developing neural networks with more sensitivity than can be achieved with traditional tests (Berger, 2006, Luciana, 2003, Strauss et al., 2006, Schatz and Browndyke, 2002b). Having gained expert advice from Cambridge consultancy for traumatic brain injury research, six tests from this platform were chosen for the 'PROP' study. These included the Motor Screening Test (MOT), the Reaction Time (RTI), the Paired Associates Learning (PAL), the Spatial Working Memory (SWM), the Spatial Span Test (SSP) and the Rapid Visual Information Processing (RVP) [Figure 4-1]. The software was ordered from Cambridge Cognition, Tunbridge Court, Bottisham, Cambridge, CB25 9TU, United Kingdom (www.cambridgecognition.com).

The CANTAB tests are recommended to be administered using a computer with a touch-sensitive screen. In accordance with CANTAB recommendations participants were instructed to adjust positioning to their convenience. The task instructions are delivered to participants through an automated voice within the CANTAB programme which provides standardised tests. Computerized administration does not require extensive training and limits the interaction between the subject and examiner. However, the lead investigator (JC) was trained for CANTAB testing and was present to supervise all testing procedures in the event of any issues arising with the computerized neuropsychological testing because of hardware and software interactions. Responses are recorded and analysed automatically. Application of the test and feedback are given in a standardized manner (Fray et al., 1996). Prior to each task the participant was administered orientation/training trials to familiarize themselves with the requirements of each task prior to the actual test. All procedures recommended for software use by Cambridge Cognition were followed.

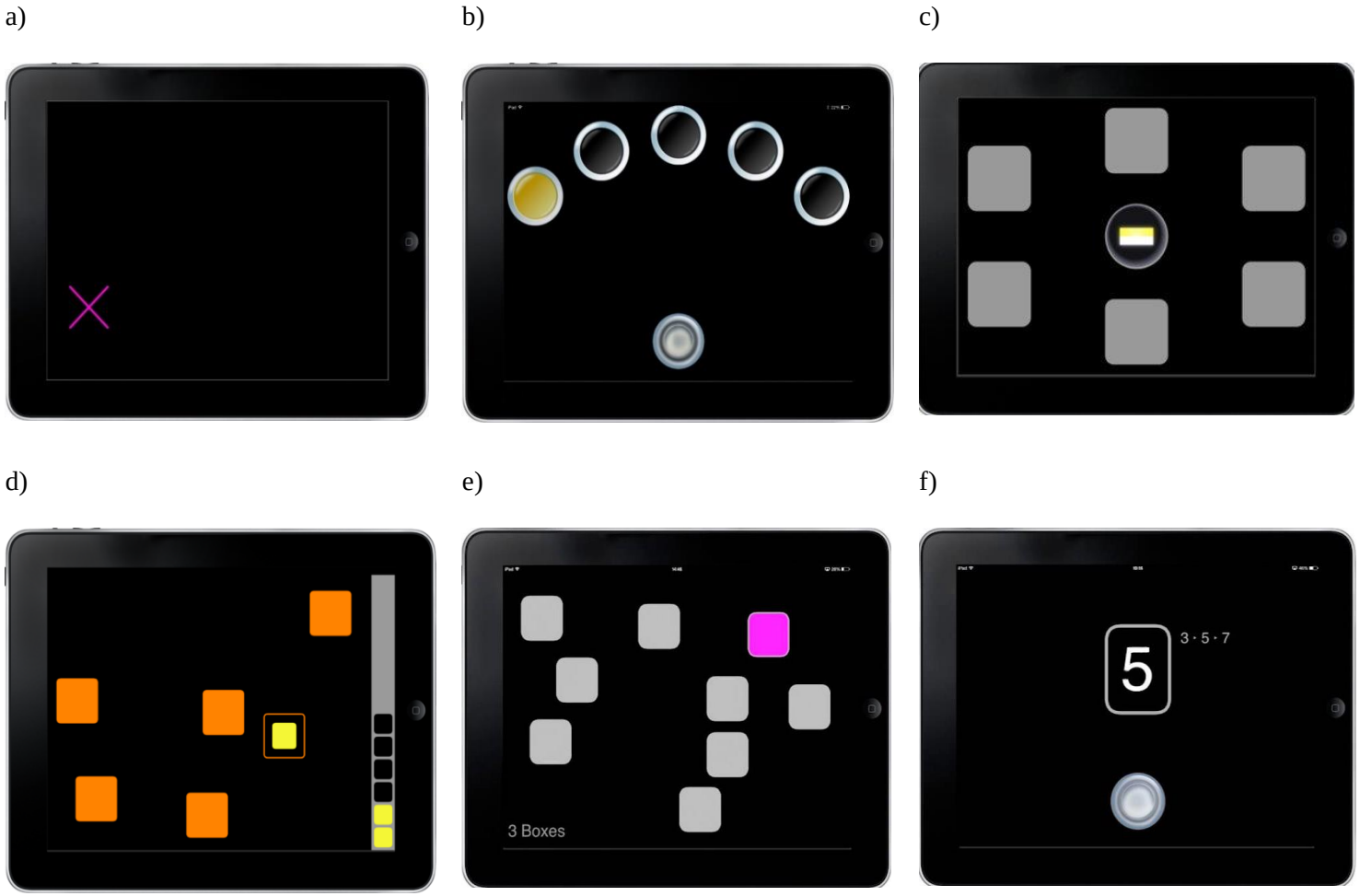


Figure 4-1 *Schematic and Chronological Representation of Selected CANTAB Tasks. a) MOT. b) RTI. c) PAL. d) SWM. e) SSP. f) RVP.*

4.11.1 The Cambridge Neuropsychological Test Automated Battery-Motor Screening Task

4.11.1.1 Background

The Motor Screening (MOT) task is used to assess psychomotor function and to screen for visual, movement and comprehension difficulties. It is recommended in research studies as an initial test of sensorimotor skills. In this way, it is used as a general assessment and screening for any visual, movement or language impairments that could confound the more cognitively challenging tasks of the CANTAB test battery which it precedes. It is also a useful introduction to CANTAB tests for the participant. The presence of sensorimotor deficits or lack of comprehension on the Motor Screening Task will limit the collection of valid data from the participant. Reduced speed in the MOT task can be indicative of neurodegenerative processes or age related changes (Salthouse, 1993). The Motor Screening (MOT) The motor screening test is common to all the CANTAB batteries and should be given at the beginning of a test session.

4.11.1.2 Task Format

Coloured crosses are presented in different locations on the screen, one at a time. There is an initial demonstration of the correct way to point using the forefinger of the dominant hand. During the MOT test the participant is instructed to touch the coloured crosses appearing in various locations on screen as quickly and as accurately as possible [Figure 4-2]. The administration time of this task is two minutes.

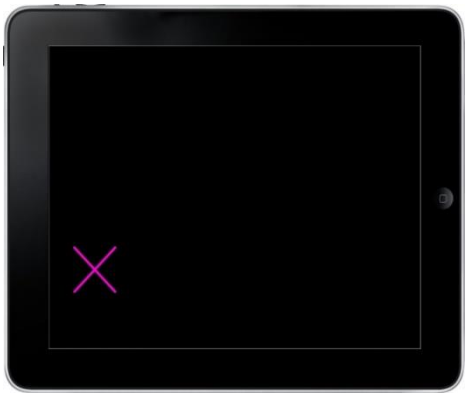


Figure 4-2 *iPad interface of The Motor Screening Task.*

4.11.1.3 Scoring

The primary purpose of the MOT task is to act as a training procedure to ensure that the participant can point accurately and to provide measures of both speed and accuracy that provide an index of the participants' motor skill. The core outcome measures assess the participant's speed of response and the accuracy of pointing (selecting the cross). Results are expressed as the standard score of mean latency (MOTML) [Table 4-4].

Table 4-4 Motor Screening Task Outcome Measure.

MOT score	Description
MOT Mean Latency (MOTML)	The mean latency for a participant to correctly respond to the stimulus on screen during assessed trials, measured in milliseconds. A higher score indicates poorer performance on the task.

4.11.2 The Cambridge Neuropsychological Test Automated Battery-Reaction Time

4.11.2.1 Background

The Reaction Time (RTI) is a test of processing speed and visuomotor reaction time encompassing choice reaction time, movement time and vigilance. It provides assessments of motor and mental response speeds. It also measures movement time, reaction time, response accuracy and impulsivity. Visuomotor reaction time is assessed through reaction time (difference in time of stimulation presentation and initiation of movement by releasing the button on the press pad); and movement time (time from release of press pad to touching the target displayed on the tablet screen). This test of attention and reaction and movement time is based on a 5-choice serial reaction time task derived from continuous performance tests (Mirsky et al., 1960, Rosvold et al., 1956), which has been shown to be sensitive to lesions on the medial prefrontal cortex and nucleus basalis in rats (McGaughy et al., 2002). The 5-choice paradigm in contrast to a simple selection task, increases the cognitive load and requires enhanced attention (Robbins, 2002). It can differentiate between motor and cognitive slowing by individually measuring motor release speed and correct selection speed.

4.11.2.2 Task Format

The participant is instructed to select and hold a button at the bottom of the screen. Participants are instructed to keep their finger on the button at the bottom of the screen until a target appears. Circles are presented inside one of five circles above as the target (in the five-choice RTI variant). A yellow dot will appear in one of the circles, and the participant must react as quickly as possible, releasing the button at the bottom of the screen, and selecting the circle in which the dot appeared [Figure 4-3]. The administration time of this task is three minutes.

Figure 4-3 *iPad interface of The Reaction Time Task.*

4.11.2.3 Scoring

The measures that were analysed were the five-choice reaction time (time to release the button after yellow spot onset) and five choice movement time choice (time to touch the circle after button release) [Table 4-5].

Table 4-5 Reaction Time Task Outcome Measure.

RTI score	Description
RTI Median Five Choice Reaction Time (RTIFMDRT)	The median duration it took for a participant to release the response button after the presentation of a target stimulus. Calculated across correct, assessed trials in which the stimulus could appear in any one of five locations. Measured in milliseconds. A higher score indicates poorer performance on the task.
RTI Median Five Choice Movement Time (RTIFMDMT)	The median time taken for a participant to release the response button and select the target stimulus after it flashed yellow on screen. Calculated across correct, assessed trials in which the stimulus could appear in any one of five locations. Measured in milliseconds. A higher score indicates poorer performance on the task.

4.11.3 The Cambridge Neuropsychological Test Automated Battery-Paired Associates Learning

4.11.3.1 Background

The Paired Associates Learning (PAL) task is a non-verbal test of episodic memory performance and is considered a visuospatial memory task (Sahakian et al., 1988). Episodic memory is the ability to learn, store, and retrieve information (Dickerson and Eichenbaum, 2010). It is often referred to remembering 'what, when and where'(Barnett et al., 2015). The task assesses visual memory and new learning through the testing of conditional learning and recall of discrete pattern locations concealed behind boxes on the screen (Strauss et al., 2006). The object-location memory of the PAL task is sensitive to medial temporal lobe impairment (Soldan et al., 2016) and is particularly dependent on integrity of the hippocampal area (de Rover et al., 2011).

4.11.3.2 Task Format

Six white boxes appear equally distributed on the screen and the boxes then open one at a time, for three seconds each in a random order [Figure 4-4]. One or more of them will contain a pattern within. The patterns are then displayed in the middle of the screen, one at a time and the participant must select the box in which the pattern was originally located. Initially, only one box contains a pattern with the remaining boxes empty. Once all six boxes have opened and closed, displaying either a pattern or an empty box, the displayed pattern appears in the middle of the screen. The participant is required to touch the box in which the pattern was located. If the participant chooses the correct box, the task proceeds to the next set of patterns. After two correct sets with a single pattern the number of patterns is increased to two for two sets, then to three for two sets. Finally, the number of patterns is increased to six,

and then to eight for one set. If the participant makes an error, the boxes are opened again, and all pattern locations are revealed in sequence again to remind the participant of the locations of the patterns and the trial is repeated (to a maximum of 10 trials). By increasing the number of patterns and therefore the length of the sequence, both visual episodic memory and learning can be assessed using the total error score adjusted for the longest sequence reached (a maximum of eight patterns). If a correct response has not been made after 10 trials in any set, the test is terminated. Increased difficulty levels can be used to test high-functioning, healthy individuals. Administration time is approximately eight minutes to complete.

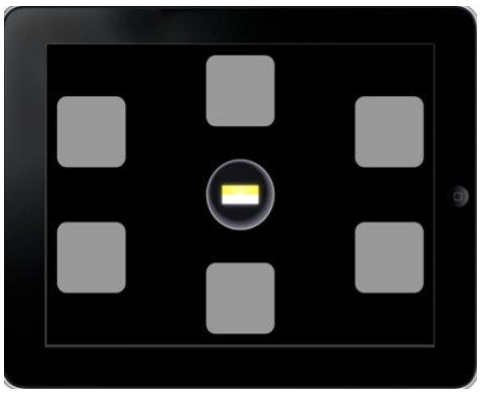


Figure 4-4 *iPad interface of The Paired Associates Learning Task.*

4.11.3.3 Scoring

The measures that were analysed for the purpose of this thesis were the PAL Total Errors Adjusted (PALTEA) and the PAL First Attempt Memory (PALFAMS) scores. The PAL Total Errors Adjusted (total errors for all stages attempted plus an adjustment for each stage not reached), refers to the number of times a participant chose the incorrect box for a stimulus on assessment and an adjustment is made for the estimated number of errors they would have made on any problems, attempts and recalls they did not reach. Therefore, the PALTEA value represents the same level attempted for each individual (Sahakian et al., 1988). As this outcome indicates the number of errors made before the completion of the test; a larger score

indicates greater difficulty with the task. PAL first attempt memory score (sum of patterns correctly located in the first trial for all stages completed) is the frequency with which participants chose the correct box on their first attempt, with lower scores denoting poorer performance [Table 4-6].

Table 4-6 Paired Associates Learning Task Outcome Measure.

PAL score	**Description**
PAL First Attempt Memory Score (PALFAMS)	The number of times a participant chose the correct box on their first attempt when recalling the pattern locations. Calculated across all assessed trials. A higher score indicates a better performance.
PAL Total Errors Adjusted (PALTEA)	The number of times the participant chose the incorrect box for a stimulus on assessment problems, plus an adjustment for the estimated number of errors they would have made on any problems, attempts and recalls they did not reach. This allows to compare performance on errors made across all subjects regardless of those who terminated early versus those completing the final stage of the task. A higher score indicates poorer performance on the task.

4.11.4 The Cambridge Neuropsychological Test Automated Battery-Spatial Working Memory

4.11.4.1 Background

The Spatial Working Memory (SWM) task is a test of spatial working memory and executive function, by requiring participants to find tokens revealed behind boxes, whilst remembering boxes previously containing found tokens (Owen et al., 1990). This self-ordered test has notable executive function demands and provides a measure of strategy as well as working memory errors. Spatial Working Memory requires retention and manipulation of visuospatial information and manipulation of remembered items in working memory (van Asselen et al., 2006). The SWM task has been demonstrated to be sensitive to frontal-lobe dysfunctions (Owen et al., 1995), particularly in the dorsolateral prefrontal cortex (Manes et al., 2002).

4.11.4.2 Task format

The aim of this test is that by selecting the boxes and using a process of elimination, the participant should find one yellow 'token' in each of a number of boxes and use them to fill up an empty column on the right-hand side of the screen. The test begins with a number of coloured squares (boxes) shown on the screen [Figure 4-5]. Participants find tokens in coloured boxes presented on the screen and move them to a collection bank on the right-hand side of the screen. The key task instruction is that tokens will not be located in the same box twice in each trial. Depending on the difficulty level used for this test, the number of boxes can be gradually increased until a maximum of 12 boxes are shown for the participants to search. The colour and position of the boxes used are changed from trial to trial to discourage the use of stereotyped search strategies. The administration time of this task is four minutes.

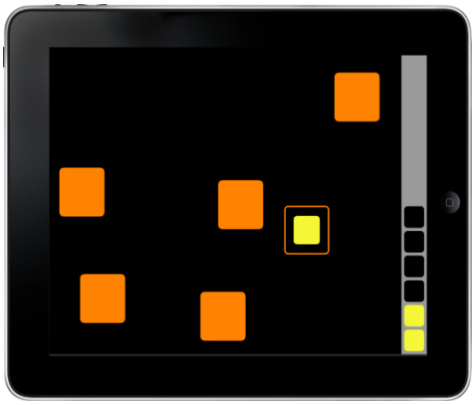


Figure 4-5 *iPad interface of The Spatial Working Memory Task*

4.11.4.3 Scoring

Outcome measures include SWM between errors: the number of times the participant incorrectly revisits a box, calculated across all assessed 4, 6, and 8 token trials; and SWM strategy: the number of unique boxes from which a participant starts a new search in the 6 and 8 box trials. Scores are calculated for errors detected at the 4-shape 6-shape and 8-shape stages. Outcome measures are described in Table 4-7.

Table 4-7 Spatial Working Memory Task Outcome Measure.

SWM score	Description
SWM Between Errors BE468	The number of times the participant incorrectly revisits a box in which a token has previously been found. Calculated across all assessed four, six and eight token trials. A lower score indicates a better performance.
SWM Strategy (6-8 Boxes)	The number of times a participant begins a new search pattern from the same box they started with previously. If they always begin a search from the same starting point, it is inferred that the participant is employing a planned strategy for finding the tokens. Therefore, a lower score indicates high strategy use and better performance.

SWM Between Errors 4 Boxes	The number of times a participant revisits a box in which a token has previously been found. Calculated across all trials with 4 tokens only. A low score indicates a better performance. Calculated across all trials with 4 tokens only. A lower score indicates a better performance.
SWM Between Errors 6 Boxes	The number of times the participant revisits a box in which a token has previously been found. Calculated across all trials with 6 tokens only. A lower score indicates a better performance.
SWM Between Errors 8 Boxes	The number of times the subject revisits a box in which a token has previously been found. Calculated across all trials with 8 tokens only. A lower score indicates a better performance.

4.11.5 The Cambridge Neuropsychological Test Automated Battery-Spatial Span

4.11.5.1 Background

Spatial Span (SSP) assesses visuospatial working memory capacity and therefore the cognitive ability to store, manipulate and manage non-verbal information on a transient basis (Della Sala et al., 1999). Memory span is the ability to grasp a number of discrete units in a single moment of attention and to reproduce them immediately (Blankenship, 1938). Memory span assessment measures the ability to recall series of discrete stimuli, such as digits, letters, words, sounds, immediately after their presentation (Teixeira et al., 2011). The Spatial Span Test is a nonverbal analogue of the commonly used Digit Span Test, which measures the capacity of visuospatial memory (Kessels et al., 2008). It is also described as the computerized version of the Corsi block tapping task, which is a widely-used neuropsychological tool that involves asking participants to tap wooden blocks in the same order that an administrator did (Kessels et al., 2000). The SSP task is a useful tool to assess non-verbal memory deficits. It is sensitive to damage to the parieto-occipital region of the brain (Koenigs et al., 2009).

4.11.5.2 Task Format

White squares are shown on the screen, some of which briefly change colour in a variable sequence [Figure 4-6]. The participant must then select the boxes which changed colour in the same order that they were displayed by the computer (for the forward variant) or in the reverse order (for backward variant). The number of boxes in the sequence increases from two at the start of the test, to nine at the end and the sequence and colours are varied through the test. The administration time of this task is five minutes but can vary depending on the participant's performance.

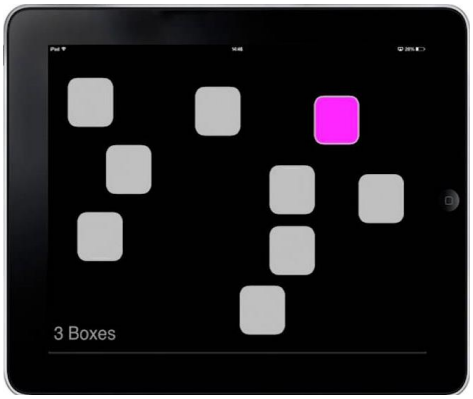


Figure 4-6 iPad interface of The Spatial Span Task.

4.11.5.3 Scoring

Participants are required to memorize the forward sequence of colour changes across a pattern of squares over increasing sequence length throughout the task [Table 4-8].

Table 4-8 Spatial Span Task Outcome Measure.

SSP score	Description
SSP Forward Span Length (SSPFL)	The longest sequence of boxes successfully recalled by the participant. Applicable to Forward variants only. A higher score indicates a better performance.

4.11.6 The Cambridge Neuropsychological Test Automated Battery-Rapid Visual Information Processing

4.11.6.1 Background

The Rapid Visual Information Processing (RVP) is primarily a measure of sustained attention. Besides examining selective and sustained attentional processes, the RVP task assesses processing speed. Participants need to employ working memory, inhibitory control and sustained attention to avoid selecting incorrect responses and detect target sequences (Gau and Huang, 2014). The RVP visual sustained attention test is sensitive to frontal- and parietal-lobe dysfunctions (Coull et al., 1996).

4.11.6.2 Task Format

A white box is shown in the centre of the screen, inside which digits from 2 to 9 appear in a pseudo-random order, at the rate of 100 digits per minute [Figure 4-7]. Participants are requested to detect target sequences of digits (for example, 2-4-6, 3-5-7, and 4-6-8). When the participant sees the target sequence, they must respond by selecting the button in the centre of the screen as quickly as possible. The level of difficulty varies with either one- or three-target sequences that

the participant must watch out for at the same time. The administration time of this task is seven minutes.

Figure 4-7 *iPad interface of The Rapid Visual Processing Task.*

4.11.6.3 Scoring

Outcome measures used for the purpose of this thesis cover sensitivity to the target sequence (RVP A Prime), the latency/speed of response (Median Response Latency) and the probability of false alarms (RVPPFA) [Table 4-9].

Table 4-9 Rapid Visual Processing Task Outcome Measure.

RVP score	Description
RVP A Prime (RVPA)	The signal detection measure of a participant's sensitivity to the target sequence (string of three numbers), regardless of response tendency (the expected range is 0.00 to 1.00; bad to good). This metric is a measure of how good the participant is at detecting target sequences.
RVP Probability of False Alarm (RVPPFA)	The number of sequence presentations that were false alarms divided by the number of sequence presentations that were false alarms plus the number of sequence presentations that were correct rejections (False Alarms ÷ (False Alarms + Correct Rejections)). A lower score indicates a better performance.

RVP Median Response Latency (RVPMDL)	The median response latency on trials where the subject responded correctly. Calculated across all assessed trials. A lower score indicates a better performance.

4.11.7 Reliability and validity of CANTAB subtests

The Cambridge Neuropsychological Test Automated Battery (CANTAB) is widely used in different populations. The CANTAB is a validated, reliable neuropsychological battery (Wild et al., 2008), consisting of memory, learning, attention, problem solving, and executive function tests (Robbins et al., 1994). A large number of discriminating power and predictive validity studies have suggested that four CANTAB tests are particularly suitable for assessing mild cognitive impairment (MCI) and Alzheimer's disease (AD) dementia including; the Rapid Visual Information Processing (RVP), Paired Associates Learning (PAL), Reaction Time (RTI), and Spatial Working Memory (SWM) tests (Fowler et al., 1995, Juncos-Rabadán et al., 2014, Saunders and Summers, 2010, Summers and Saunders, 2012).

The majority of psychometric studies have limited their investigation to two or three of the most frequently researched subtests. The Paired Associates Learning (PAL), Spatial Working Memory (SWM), Rapid Visual Information Processing, and Reaction Time tests have been demonstrated to have high-to-adequate test–retest correlations (.71–.89) (Gonçalves et al., 2016). The psychometric properties and neural validation, including studies on large samples of healthy volunteers, and patients with mild cognitive impairment and Alzheimer's Disease have demonstrated consistent validity and reliability of CANTAB subtests including the Paired Associates Leaning (PAL), Spatial Working Memory (SWM), Spatial Span (SSP) and Reaction Time (RTI) tasks (Robbins et al., 1994, Fowler et al., 2002, Blackwell et al., 2004, Kim et al., 2014, Torgersen et al., 2012).

4.11.8 The Cambridge Neuropsychological Test Automated Battery procedure

In this study the CANTAB was presented on an Apple 2018 (9.7 inch) IPAD [Figure 4-8]. In accordance with CANTAB recommendations participants were instructed to adjust positioning to their convenience. The test order of the CANTAB subtests was predetermined by the Cambridge Cognition Consultancy based on empirical investigation of the relationship of test sequence and practice and fatigue effects (Clark et al., 2012). Each test was initiated by a practice test. Instructions were delivered auditorily prior to practice and test blocks. No feedback is given to participants for any of the subtests.

Figure 4-8 *Apple IPAD 2018 (9.7 inch) on which the CANTAB was presented.*

4.12 The Sound-Induced Flash Illusion Task (SIFI)

The Sound-Induced Flash Illusion Task (SIFI Task short version) was administered to investigate cross-modal multisensory integration efficiency. Multisensory Integration is a process by which information from different sensory systems is combined to influence perception, decisions, and overt behaviour (Stein et al., 2009). The SIFI is a particularly useful tool in measuring multisensory integration as it is susceptible to the fission illusion and can be employed to differentiate between sensory acuity and sensory processing ability (Setti et al., 2011, Shams et al., 2005). In the SIFI Task incongruent number of auditory and visual stimuli are paired across multiple stimulus onset asynchronies (SOAs) in close temporal proximity to induce the fission illusion [Figure 4-9] (Shams et al., 2000a).

More specifically, pairing a singular visual flash with two auditory beeps can create an erroneous percept of two visual flashes (Shams et al., 2000a) and susceptibility to the range of SOAs was found to widen across neurocognitive decline (Setti et al., 2011, McGovern et al., 2014). Uni-sensory visual and auditory conditions were introduced to control for visual-auditory deviations from the norm. Multisensory congruent and incongruent illusory trials across multiple auditory SOAs at 230ms, 150ms and 70ms pre (A-V/A) and post (V/A-A) visual flash presentation were used to induce the fission illusion (Setti et al., 2011). Neurons in the superior colliculus of the midbrain synthesize information from different senses and hence play an integral role in multisensory integration (Stein et al., 2002). An age-related increased susceptibility to the fission illusion across wider ranges of SOA's has been demonstrated (McGovern et al., 2014, Diederich et al., 2008, Peiffer et al., 2007, Laurienti et al., 2006).

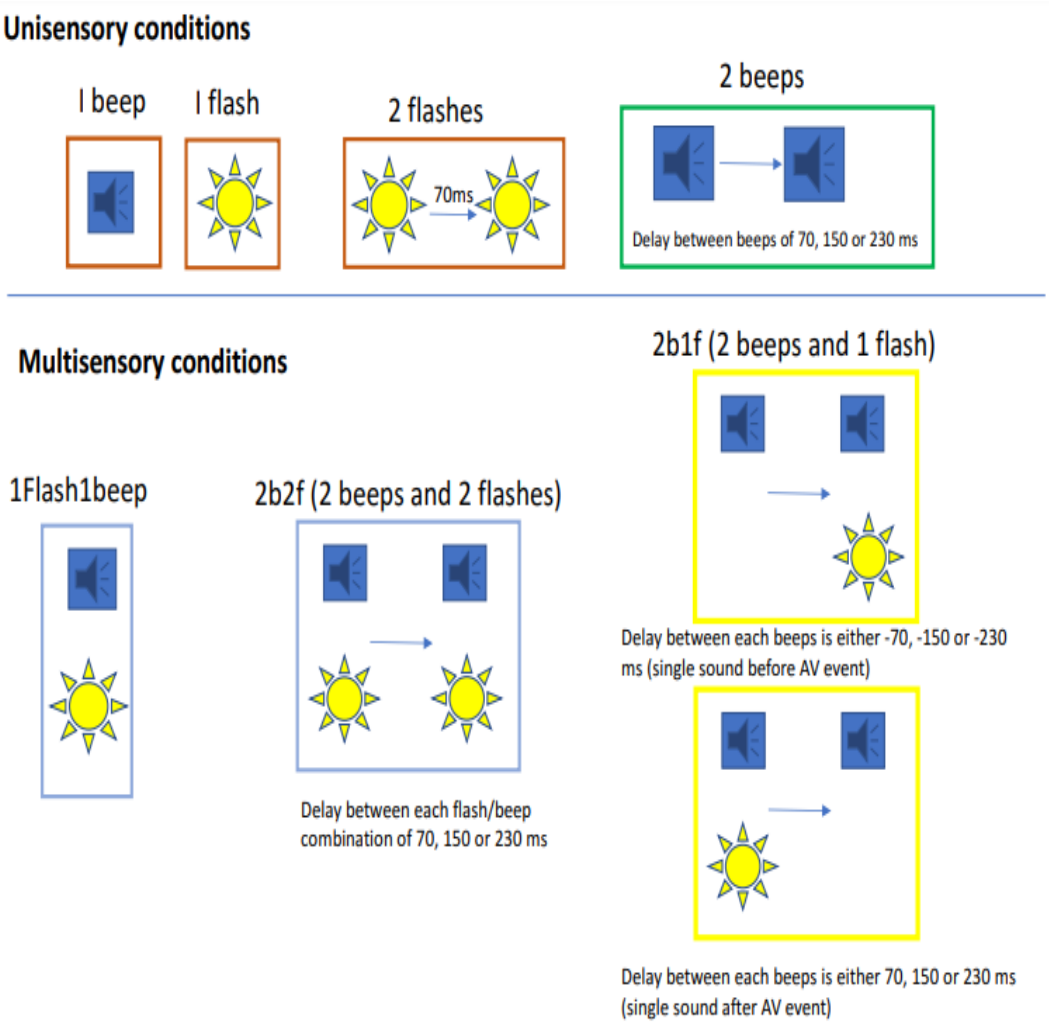


Figure 4-9 *Schematic Representation of the Sound Induced Flash Illusion Task.*

4.12.1 The Sound Induced Flash Illusion Procedure

It was deemed unnecessary to assess visual or hearing acuity in the current study. Participants included were presumed to have thresholds within the normal limits due to the age range. However, all participants were screened for any sensory impairments or cognitive disability. The task was programmed using DMDX software and consisted of a total of 64 test trials preceded by a practice block of 10 trials. It was presented on a DELL laptop with 1366x768 pixel spatial resolution. Participants were seated comfortably approximately 60cm from the computer screen. The inter-individual presentation of the visual and auditory stimuli was randomly generated and presented in order to reduce the possibility of a learning effect. The visual stimulus was displayed as a hard-edged white annulus presented at a luminance of 31.54 foot-lambert on a black background 17 milliseconds. The inner and outer edges of the annulus stimulus extended 8.5 and 10◦ below a white fixation cross at the centre of the screen, respectively. The auditory stimulus was a brief auditory tone with a frequency of 3500 hertz, which was presented for 10 milliseconds at a sound pressure level of 65 decibel.

Each participant was given information about the task prior to administering the test. Each trial was initiated by a white fixation cross in the middle of a black screen followed by the appearance of one or two brief visual flashes accompanied by one, two or no auditory beeps. Participants were instructed to maintain fixation throughout each trial. They were instructed to input the number of flashes they perceived using response keys on the keyboard. If they perceived no flashes (such as in the auditory-only trials), then they were instructed to report perceiving no flashes and to report the number of auditory beeps instead. Thus, there were six conditions in total, representing all possible combinations of flashes and beeps. All conditions were presented in randomized order. At the end of each trial, the fixation cross disappeared, and the participant was instructed to press a response key to initiate the next trial. The experiment began with a training phase to familiarize the participant with the test procedure. Instructions were repeated on screen prior to the practice and participants could repeat the presentation of ten practice trials until they felt comfortable with the task. The practice included trials with one or two unimodal flashes;

one flash with one beep; one flash with two beeps across different SOAs. The participant was informed that the experiment was not time dependent and hence should be self-paced. The experiment lasted approximately 5 minutes.

4.12.2 The Sound Induced Flash Illusion Reliability and Validity

The Sound Induced Flash Illusions, was first described by Shams et al. (2002). Sound-induced flash illusion provides a valid example of perception as a multisensorial experience where all sensorial modalities work together. It is a widely used validated psychophysical paradigm (Shams et al., 2005). Audio-visual illusions can be classified into ‘fission’ (where one flash is accompanied by two or three auditory stimuli (or beeps) and ‘fusion’ illusions (where one beep is accompanied by two or more visual stimuli (flashes) (Maccora et al., 2013). Although vision has been often considered as the dominant sensory modality in

humans, sound-induced flash illusions underline the leading role of acoustic stimuli in the cross-modal perception. The sound induced flash illusion has been found to be a robust percept (Abadi and Murphy, 2014, Rosenthal et al., 2009). Advanced neuroimaging studies have shown that the percept of the sound-induced flash illusion is correlated with modulation of activity in early visual cortical areas (Arden et al., 2003, Bhattacharya et al., 2002, Mishra et al., 2007, Shams et al., 2002).

4.13 The National Adult Reading Test (NART)

The National Adult Reading Test (NART) was used to estimate premorbid intelligence (PMIQ) by using full-scale intelligence quotients (Nelson, 1991). It comprises a list of 50 words printed in order of increasing difficulty [Figure 4-10]. The words are 'irregular' with respect to the common rules of pronunciation in order to minimise the possibility of reading by phonemic decoding rather than word recognition. Since being devised in 1982, the NART has become a widely used method in neuropsychological research for estimating PMIQ (Bright et al., 2018). It has been highly validated and standardized in terms of psychometric testing to measure full-scale intelligence quotient (FSIQ) and verbal and performance intelligence quotients (Nelson, 1982). It assesses the individual by testing reading ability of phonetically irregular words. The estimates of PMIQ are derived from the Wechsler Adult Intelligence Scale Version III (Wechsler, 1997). The NART is suitable for male or females between the ages of 20 to 70 (Nelson and McKenna, 1975).

CHORD	SUPERFLUOUS
ACHE	SIMILE
DEPOT	BANAL
AISLE	QUADRUPED
BOUQUET	CELLIST
PSALM	FAÇADE
CAPON	ZEALOT
DENY	DRACHM
NAUSEA	AEON
DEBT	PLACEBO
COURTEOUS	ABSTEMIOUS
RAREFY	DÉTENTE
EQUIVOCAL	IDYLL
NAÏVE	PUERPERAL
CATACOMB	AVER
GAOLED	GAUCHE
THYME	TOPIARY
HEIR	LEVIATHAN
RADIX	BEATIFY
ASSIGNATE	PRELATE
HIATUS	SIDEREAL
SUBTLE	DEMESNE
PROCREATE	SYNCOPE
GIST	LABILE
GOUGE	CAMPANILE

Figure 4-10 *The National Adult Reading Test.*

4.13.1 The National Adult Reading Test procedure

The participant was screened for any learning disability such as dyslexia or ADHD prior to the testing. The NART word card was given to the participant. The investigator had a NART answer sheet, containing the correct pronunciation of each word. The investigator explained the test to the participant. They were instructed to read slowly down through the list of words, beginning at the top left of the card. The participant was instructed to pause after each word until the instructor said next before reading the next word. The participant was advised that there may be many words that they would more than likely not recognise and to try to attempt to pronounce each word as best they could. The investigator recorded the number of errors on the NART answer sheet.

4.13.2 Reliability and Validity of the National Adult Reading Test

The National Adult Reading Test (NART) has become a widely accepted method for estimating premorbid levels of intelligence in neuropsychological research. The NART as a valid measure of premorbid ability rests upon the assumptions that reading ability is relatively independent of brain damage, and that it is a strong predictor of intelligence in the normal population. Its validity has been demonstrated in many studies (Bright et al., 2002, Crawford et al., 1989, O'Carroll, 1987, McGurn et al., 2004, Sharpe and O'Carroll, 1991). It has also been demonstrated to have sound test-re-test reliability (Smith et al., 1998), as well as inter-rater reliability (O'Carroll, 1987). The NART has been standardised against the most recent revisions of the Wechsler Adult Intelligence Scale (WAIS-III) (Bright et al., 2018).

4.14 Anthropometry

Anthropometry is easy, feasible and time efficient and the most commonly used measure of body composition (van der Kooy and Seidell, 1993). Measures recorded included body mass and height. Body Mass Index gives an estimation of ideal weight based on an individual's height by using the formula (weight (kg)/height (m)^)(WHO, 2000). It is a simple method of indirectly assessing fatness which is widely employed in clinical research settings due to its straightforward application. The primary disadvantage of BMI usage is the fact that this measure cannot distinguish between fat and muscle mass. This can lead to erroneous classification of those with a high muscle mass as either overweight or obese (Cornier et al., 2011). However, several systematic reviews have demonstrated that higher BMI, specifically being classified as obese, is associated with significantly higher all-cause mortality (Berrington de Gonzalez et al., 2010, Flegal et al., 2014, Flegal et al., 2013, Whitlock et al., 2009, Winter et al., 2014, McGee, 2005). The individual can be classified as: (1) underweight BMI: less than 18.5 (2) normal weight BMI: 18.5 to 24.9 (3) overweight BMI: 25 to 29.9 and (4) obese BMI: 30 or more. Despite the outlined limitations of BMI, it is widely used as a

risk factor for the development of or the prevalence of several health issues such as cardiovascular disease (Nuttall, 2015, Khan et al., 2018).

4.14.1 Anthropometry Measurement Protocols Anthropometry: Standing height, body mass and body mass index

4.14.1.1 Standing Height

Barefoot standing height was measured using a Leicester portable height measure stadiometer (Invicta Plastics Ltd, Leicester, United Kingdom) [Figure 4-11]. Participants were asked to stand, without shoes, on the footplate, with their back against the stadiometer, legs together, arms down by their sides and mid-axillary line in parallel to the stadiometer. The participant's head was positioned in the Frankfort horizontal plane [Figure 4-12], the standard plane used for the correct orientation of the head, established by a line passing through the tragion (front of the ear) and the lowest point of the eye socket. It was ensured that the participant's legs were straight and that their shoulder blades and buttocks were touching the uprights. The participant was instructed to place their arms by their side in a relaxed manner. The headboard was lowered until it touched the crown of the head, compressing the hair. Measurements were taken to the nearest 0.1cm.

Figure 4-11 *Height Measure Stadiometer.*

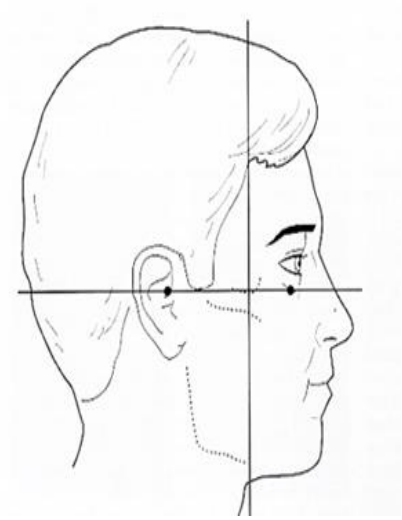


Figure 4-12 *Position of the Head in the Frankfort Horizontal Plane*

4.14.1.2 Body Mass

The body mass of each participant was measure using the Tanita Multi-Frequency Body Composition Analyser (MC-180 MA, Tanita Corp, Tokyo, Japan)**.** Body mass was measured to the nearest 0.1 kg. Participants were measured in one layer of light clothes. The machine deducted a predetermined weight, equivalent to one layer of light clothing, from the participants recorded weight. Participants were asked to void before the measurement if they hadn't done so in the previous 30 minutes.

4.14.1.3 Body Mass Index

Body Mass Index was calculated according to the formula: mass (kg) divided by height squared (m^2). Participants were then classified according to their BMI as underweight, normal weight, overweight or obese.

4.15 Body Composition

Measurement of body composition is an important component of assessing overall body fat, visceral fat and muscle mass in relation to overall general health. Body composition measurements influence overall health outcomes and is increasingly valuable in clinical practice (Wells and Fewtrell, 2006). Body composition measures such as bioimpedance analysis is preferable over other anthropometric methods such as BMI due to the provision of estimates of fat free mass (FFM) and body fat percentage (%BF)(Duren et al., 2008).

4.15.1 Bioimpedance analysis (BIA)

Along with anthropometric measures, bio-impedance analysis (BIA) can was used to assess body composition and to gain estimate components of body composition, including fat percentage, fat-free mass and total body water percentage. Bio-impedance analysis is a quick, easy to perform, cheap, non-invasive measure of body composition, commonly used in the clinical setting (Ward, 2012, Jaffrin, 2009). It operates on the principle of impedance; i.e. the opposition that a circuit presents to the passage of a current when a voltage is applied. Electrolytes within various bodily tissues are naturally conductive to differing degrees (Wagner and Heyward, 1999). Adipose tissue is a poor conductor of electrical current (due to its' relatively small water content) and consequently the resistance to current flow is greater in individuals with large amounts of body fat. In contrast, lean tissue contains large amounts of water and electrolytes and is a good electrical conductor. Therefore, the higher the fat mass, the greater the resistance to the flow of the electric current.

An individual's total body water can be estimated from the impedance measurement; other measures including body fat percentage, fat mass and fat-free mass can subsequently be derived from total body water. Bio-impedance analysis has been found to be reliable when a standardised protocol is followed, and valid compared to DEXA (Jackson et al., 1988). This model uses 8-electrodes which allows segmental measurement (trunk, arms and legs), use of multi-frequency electrical levels to estimate both intra- and extra-cellular water and the incorporation of a body scales to measure body weight (Volgyi et al., 2008, TANITA, 2005). The validity of the 8-electrode model of Tanita BIA has been established (Bosy-Westphal et al., 2008). Similarly, Volgyi et al. (2008) reported moderate-to-high correlations between BIA and DEXA measurements in men and women. Pietrobelli et al. (2004) compared BIA to DEXA in normal healthy males and females, reporting no significant difference between any of the body segments measured by BIA versus DEXA ($r>0.95$). The validity of

commercial Bioelectrical Impedance scales has also been demonstrated (Wang and Hui, 2015, Karelis et al., 2013, Barreira et al., 2013).

Figure 4-13 *Tanita MC 180 MA Multi-Frequency Body Composition Analyser.*

4.15.2 Body Impendence Analysis Procedure

Participants were screened for presence of medical devices such as electronic cardiac device, like pacemaker (PM) and implantable cardiac defibrillator (ICD) prior to testing. Body Impendence Analysis was measured using the Tanita. The BIA system used for the 'PROP' study was the MC-180 MA Multi-Frequency Body Composition Analyzer (Tanita Corp, Tokyo, Japan) [Figure 4-13]. Participants were instructed to stand on the machine in bare feet, ensuring correct placement on the footplates. Participants were weighed with one layer of light clothing. The machine deducted a predetermined weight (equivalent to one layer of clothing) from the participant's recorded mass. The body composition analyser was prepared

as follows. Information including gender, age, body height and standard body type was inputted. The level gauge on the base of the analyser was checked to ensure the machine was level with the floor. The investigator ensured that the feet of the machine were adjusted accordingly.[1] On the touchscreen, '*body composition*' mode was selected. Following the onscreen instructions, participants were instructed to grasp the hand-held paddles and to stand upright, ensuring that their thighs were not touching and that their arms were straight down by their sides. Of the generated output, the following details were recorded: mass, BMI, percentage body fat and visceral fat.

4.16 Resting heart rate and blood pressure

Blood pressure was assessed in study II as part of the 'PROP' project. Blood pressure is measured and expressed in millimetres of mercury (mmHg) (ACSM, 2010b). Two phases of blood pressure are assessed: systolic blood pressure (SBP); the maximum pressure recorded in the arteries during the contraction phase of the heart, and diastolic blood pressure (DBP); the minimum pressure in the arteries recorded during the relaxation phase of the heart (ACSM, 2010a). Invasive (intra-arterial) blood pressure (IBP) monitoring is considered the gold standard method of measuring blood pressure This method is not appropriate pressure for asymptomatic individuals (ACSM, 2010b). Therefore, indirect measurement methods, such as auscultation and oscillometric methods, are employed clinically (Bonnafoux, 1996). For the purpose of this study, an electronic device using the oscillatory method for measuring blood pressure was used (Alpert et al., 2014). The speed and simplicity of these devices has made their use in clinical practice widespread. A cuff is inflated to a target pressure, and systematically decreased using a valve. Small oscillations of intra-cuff pressure, which are caused by heartbeat-induced pulse volume changes, are sensed by the cuff and measured by a pressure transducer. A proprietary algorithm then calculates values for SBP and DBP.

The guidelines for blood pressure have changed recently (Williams et al., 2018). Hypertension is a key risk factor for cardiovascular disease, the most important cause of morbidity and mortality worldwide (Lim et al., 2012). The detection and subsequent management of hypertension requires appropriate monitoring, and self-monitoring of blood pressure (SMBP) is increasingly used for this purpose with endorsement by guidelines worldwide. Hypertension is a modifiable risk factor for cardiovascular disease, stroke and all-cause mortality (Sardarinia et al., 2016). Electronic blood pressure monitor devices have been validated against mercury reference sphygmomanometers (Coleman et al., 2006, Cho et al., 2013). Monito accuracy is reported as ± 3 mmHg for blood pressure, and ± 5% beats per minute (bpm) for heart rate.[2]

4.16.1 Resting heart rate and blood pressure procedure

The participant was instructed to be seated in a supported chair, feet uncrossed, flat on the floor relaxed. Following a five-minute relaxed and quiet period, the investigator (JC) proceeded with the blood measure measurement. Participants were asked to remove any clothes from the left arm. It was ensured that the participant's arm was supported on a table, and the cuff was positioned on the upper left arm at heart-level. Resting blood pressure and HR was take using an automated oscillometric upper arm blood pressure machine (Omron 705IT, Omron Corporation, Kyoto, Japan) [Figure 4-14]. Resting heart rate and blood pressure were taken on the left arm (unless contraindicated). The correct cuff size was chosen depending on the participant's arm circumference. Participants were instructed not to speak or move while the measurement was being taken. The investigator pressed 'start' to inflate the cuff and begin the measurement process. An automatic pressure release valve-controlled

1 Multi-frequency Body Composition Analyzer MC-180MA: Instruction Manual
2 Omron 705IT: Instruction Manual

deflation of the cuff. A proprietary algorithm then calculates values for SBP and DBP. The values for SBP and DBP were then recorded by the lead investigator. SBP and DBP were reported in mmHg, and HR was reported in bpm. SBP/DBP measurements were provided to the patient both verbally and on paper. This process was then repeated three times, with each repeat measurement separated by 1-2 minutes. These readings were then averaged to gain an estimate of the participant's level of BP and average HR.

Figure 4-14 *Omron 705-IT Upper Arm Blood Pressure Monitor.*

4.17 Statistical Approach in this Thesis

Data analysis was performed in all studies in this thesis using IBM Statistical Package for the Social Sciences (SPSS) Version 26.0 statistic software package (SPSS Inc, Chicago, IL) and R version 3.6.0 with package lme4. For all studies, preliminary analyses included assessment of normality by visual inspection of histogram and Q-Q plots and using Kolmogorov-Smirnov test ($p>.05$). Normally distributed data are presented as mean and standard deviation (SD) and non-normally distributed data as medians and interquartile range (IQR). Non-parametric tests were used if data was not normally distributed. Pearson Product Moment

correlations or Spearman's rho correlations as appropriate. Significance was taken at $p<0.05$. In study I, Cohen's kappa coefficient (k) was used to assess the inter-rater reliability between documented and self-reported concussions. The intraclass correlation coefficient ($ICC_{2,1}$) was used to assess the test re-test reliability of the Michigan TBI Identification Method. A mixed effects logistic regression was used to explore variables such as number of lifetime concussions, age of player at the time of interview, length of time since the concussion diagnosis and position of play as possible predictors of player self-report accuracy. For analysis of the 'PROP' studies II-V, cognitive performance of rugby players vs rowers was examined using independent sample t-tests for parametric data and Mann-Whitney U for non-parametric data to compare the two groups. Correlations between outcomes of interest such as cognitive and perceptual outcomes and concussion history were examined using Pearson Product Moment correlations or Spearman's rho correlations as appropriate. Simple Linear regression models were used to show or predict the relationship between variables of interest. As all studies within this thesis were considered exploratory work and nested within a power calculation was not performed. Full details of statistical analysis for each study is presented in the relevant chapters. A Logistic Regression model was used to investigate the probability of a correct response in the SIFI task, allowing this to vary according to group (rugby vs rowing) and condition (SOAs).

Chapter 5 Athlete concussion history recall is underestimated: a validation study of self-reported concussion history among current professional rugby union players.

The material presented in this chapter has been disseminated in the following publication:

Cunningham J., Broglio S., Wyse J., Farrell G., Denver K and Wilson F. (2019). Reliability of self-reported concussion history in current professional rugby union players. Journal of Neurotrauma, Vol. 36, No. 13, Abstracts.

Please see Appendix A.3 for full abstract.

5.1 Introduction

The physical nature of rugby can expose players to risk of brain and spinal injury (Gardner et al., 2014b). Despite significant advancement in concussion research, concussive injury remains one of the most ambiguous sports-related injuries (Sharp and Jenkins, 2015). Clinically diagnosed concussions that are recorded in medical documentation remain the gold standard for identifying concussion history. However, much research includes concussion history gained via player self-report. The use of self-report concussion history is potentially subject to inaccuracies, given symptoms such as impaired cognitive functioning, memory loss and amnesia are often associated with concussion (McCrory et al., 2017). This is the first study to investigate the validity and reliability of self-reported concussion history in professional rugby union players. The Michigan TBI Identification method is a National Institutes of Health (NIH) Common Data Element (Broglio et al., 2018) and has been implemented in large scale concussion studies (Broglio et al., 2017b). Therefore, research on its validity compared to the gold standard clinical documentation of concussion history is required. There has been escalating concern regarding the long-term effects of concussion in

rugby. Given the high incidence of concussion associated with the sport, there is need for research into the concussion history identification methods used before conclusions are made regarding studies using concussion self-report history. As previously discussed in chapters 2 and 3, reliance on athlete self-reported concussion history is a limitation noted in the literature. Therefore, the aims of this study are to i) estimate current professional rugby player self-report concussion history validity by investigating agreement between self-reported and clinically diagnosed concussion histories and ii) evaluate the test re-test reliability of the Michigan TBI Identification Method questionnaire.

5.2 Materials and Methods

5.2.1 Study Design

This study was a cross-sectional validation study design. Current professional rugby players in an Irish rugby union club were invited to partake in this study. Participants were primarily recruited via email advertisement through team managers. The study was launched in the host club by presentations for players and staff, along with flyers and general word of mouth. Recruitment and data collection for the study began in January 2017 and concluded in January 2018. This study was registered with ClinicalTrials.gov, a database of privately and publicly funded clinical studies conducted around the world. Registration is available at https://clinicaltrials.gov/; registration identifier: NCT03544372.

5.2.2 Eligibility Criteria

The inclusion criteria included player's age > 18 years old and a current contract to be a professional rugby player. Players were included if they provided written informed consent and were freely willing to participate in the study. The lead investigator individually screened players' eligibility prior to commencing the study. The 62 willing recruits signed an informed consent form to participate following a seven-day time to reflect and withdraw if desired.

5.2.3 Participants

A sample of 63 professional rugby players were recruited. This included all professional rugby players contracted to the club, excluding one player who declined to participate. The lead investigator individually screened players' eligibility prior to commencing the study. The 62 willing recruits signed an informed consent form to participate following a seven-day time to reflect and withdraw if desired.

5.2.4 Outcome Measures

The primary outcome measure was the National Institute of Health Common Data Element; the Michigan Traumatic Brain Injury (TBI) Identification Method (Broglio et al., 2018). This questionnaire was used to obtain concussion history in a cohort of professional rugby players (n=62) during their lifetimes with an emphasis on their professional rugby career [see Chapter 4; Section 4.7.2]. A demographic questionnaire was also administered to capture detailed demographics, current physical and mental health, medical history, and sports history such as player's rugby-playing career, age of debut, career duration, and number of seasons played [see Chapter 4; Section 4.7.1]. Data collection took place at the rugby training facility.

5.2.5 Approvals

The Faculty of Health Science Research Ethics Committee at Trinity College Dublin approved all aspects of this study [see Chapter 4; Section 4.4.1.4].

5.2.6 Retrospective Self-report Concussion History

Concussion was defined as a 'traumatic brain injury induced by biomechanical force'. Further information provided included that 'concussion may be *caused either by a direct*

blow to the head, face, neck or elsewhere on the body with an impulsive force transmitted to the head', 'concussion results in a range of clinical signs and symptoms that may or may not involve loss of consciousness'. The variety of symptoms may include any of the following: 'headache, dizziness, loss of balance, blurred vision, 'seeing stars,' feeling in a fog or slowed down, memory problems, poor concentration, nausea, or throwing-up'. This definition was adapted from the one put forth by the international Concussion in Sport Group in 2017 (McCrory et al., 2017).

Player self-reported concussion history gained through the concussion questionnaire included information about all past concussive injuries, including diagnosed and undiagnosed sport and non-sport related concussions. Players were first asked to report the number of concussions they sustained specifically during their professional rugby playing careers within the club. The process was then repeated for non-SRCs (e.g. from an automobile accident, fall, or violence) and overall life-time concussion history. The Michigan TBI Identification Method gains quantitative and qualitative information around the incident including the date of injury, age at time of injury, associated loss of consciousness, information on memory before and after the injury, the mechanism of injury and symptoms related to the injury. Additional qualitative information that specified the circumstances of the injury and specific competition during which the injury occurred were probed. Players were encouraged to answer the questions to the best of their ability and to provide estimates where specific information could not be recalled.

5.2.7 Prospective Concussive Injury Records

Clinically documented concussions, extracted from the club's ImPACT (Covassin et al., 2009) and KitMan (KitMan Labs Dublin) medical files, served as the reference standard and were available for a nine year (2008 to 2017) interval. Medically documented concussions were diagnosed by one or more of a team of medical professionals (e.g., physician or

physiotherapists). Each documented concussion diagnosis was linked using name, birth date, and approximate date of injury to a player self-reported concussion. As it is unrealistic to expect players to precisely recall the exact concussion date, and given the dearth of literature on this topic, a system was devised to match clinically diagnosed concussions with player self-reported concussions. A match between the questionnaire and medical documentation was made when the date on which the player reported sustaining the concussion and the date recorded in the medical documentation were within the same playing season (i.e. 10 months). Self-reported concussion information was compared to medical record (i.e., ImPACT and KitMan) data captured between 2008 and 2017. Concussions were deemed 'Match' or 'No Match' based on details such as approximate injury date and characteristics.

5.2.8 Test Re-test Reliability

To evaluate the stability of the Michigan TBI Identification Method questionnaire, a random subset (*n*= 20) of players were re-administered the questionnaire six months following the initial interview. Concussions incurred following the initial interview were disregarded.

5.3 Statistical Analysis

Data analysis was performed using SPSS Version 25.0 statistic software package and R version 3.6.0 with package lme4. Cohen's kappa coefficient (k) was used to assess the interrater reliability between documented and self-reported concussions. The intraclass correlation coefficient ($ICC_{2,1}$) was used to assess the test re-test reliability of the Michigan TBI Identification Method. Players (n=24) who had no self-reported or clinically diagnosed concussions registered were removed from the analyses. The remaining 38 were current professional rugby union players who were able to provide self-reported concussion and had medically documented concussion history records within the club. Concussion history sources were categorized by those self-reported only, those clinically diagnosed only and

those both reported by the player and clinically diagnosed. A mixed effects logistic regression was used to explore variables such as number of lifetime concussions, age of player at the time of interview, length of time since the concussion diagnosis and position of play as possible predictors of player self-report accuracy. Initial exploration suggested number of lifetime concussions and controlling for time elapsed since diagnosis as predictors. A bootstrap approach with 1000 bootstrap replicates was used to carry out inference on fixed effect parameters.

5.4 Results

Ninety-nine unique concussions; including 63 reported by the players and 92 in the medical records were recorded for 38 players (all male; age 28.0 [4.2 years]). Seventeen players self-reported at least one undiagnosed concussion. A small number of players (n=5) reported one or more non-SRCs. The mean number of concussions in the medical records per player was 1.48 [1.96], 30% more than the mean number of diagnosed sports-related concussions which occurred at the host club reported per player (1.03 [1.20] events). Twenty-one players (34%) reported at least one concussion, nine reported two concussions, and six reported three or more. One player self-reported six concussions, all of which were diagnosed. In contrast, medical documentation indicated that 58% (n=36) players had at least one diagnosed concussion over the nine-year period. Fourteen players (23%) had one clinically diagnosed concussion, seven had two clinically diagnosed concussions, eleven reported three or more and three players had five or more concussions. One player had ten documented concussions. Data stratified by year between 2008 and mid 2017 [Table 5-1] indicated both self-reported and diagnosed concussions steadily increased over time.

Table 5-1 Clinically Diagnosed and Self-reported Concussions Stratified by Year.

Year	2007-2008	2009-2010	2011-2012	2013-2014	2015-2016	2017-(midseason)	Total
Total Diagnosed Concussions	2 (2.2%)	2 (2.2%)	9 (9.8%)	22 (23.9%)	47 (51.1%)	10 (10.9%)	92 (100%)
Total Self-Reported Concussions	1 (1.6%)	0 (0%)	6 (9.5%)	13 (20.6%)	38 (60.3%)	5 (7.9%)	63 (100%)

For comparison analyses, all self-reported undiagnosed concussions and/ or any concussions which did not occur at the host club (n = 22) were excluded from the analysis as these would not be expected to be documented in the medical records. Implementing our matching criteria, of the 63 athlete reported concussions, 46 were also clinically documented (73%); while the athletes only recalled 46 of the 92 documented concussions (50%). In other words, based on this matching criterion, athletes failed to recall 50% of clinically documented concussions and there were no clinical data associated with 27% of the concussion's players identified. The majority of athlete reported and documented concussions (n=34, 74%) were time matched within three months.

The number of player self-reported and diagnosed concussions while a professional player at the host club had a 'fair' level of agreement (k = .292; SE [.076]), p < .001). Lifetime concussion history was found to be significantly negatively correlated with player self-report accuracy, with recall worsening as the number of lifetime concussions increased (b = - .187; SE [.081]), p= .022). The ability to accurately recall concussions declined with time [Table 5-2]. However, this did not achieve significance (p = .166). The test re-test reliability of the concussion history questionnaire was moderately strong ($ICC_{2,1}$= 0.70; 95% CI [0.38-0.87]).

Table 5-2 Logistic Regression Model; Table showing 2.5% and 97.5% confidence limits (quantiles of refitted estimates of fixed effects) for the bootstrap fitting of the mixed effects logistic regression model.

	2.5%	97.5%
(Intercept)	0.662	3.737
Number lifetime concussions	-0.566	-0.021
Time elapsed since concussion diagnosis	-0.541	0.088

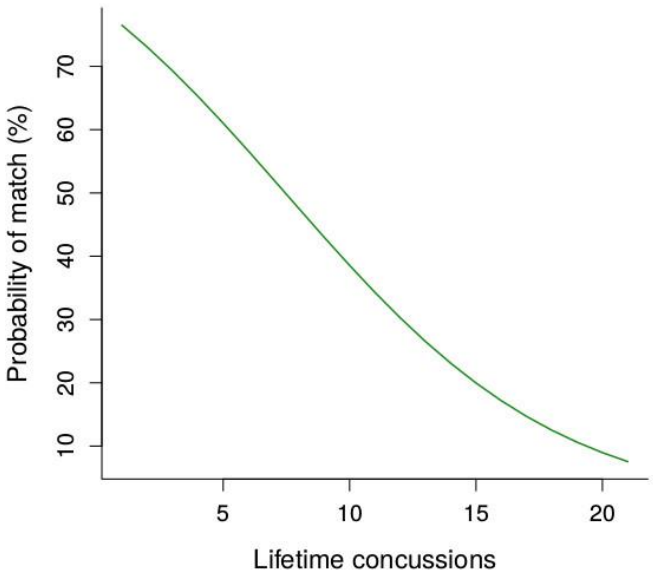


Figure 5-1 *Model: Predicted Probability of Match versus Number of Lifetime Concussions.*

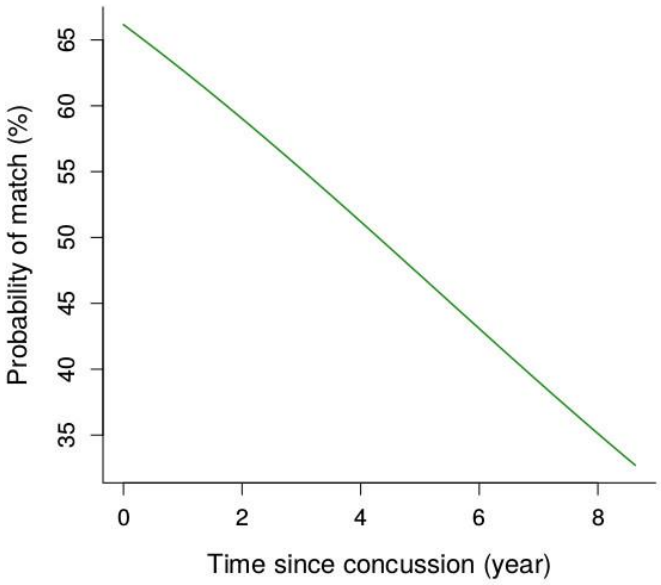


Figure 5-2 *Model: Predicted Probability of Match versus Time between Diagnosis of Concussion and Self-report.*

5.5 Discussion

This is the first study to investigate the accuracy of self-reported concussion history among professional rugby union players by establishing the validity against medical documentation. The overall level of agreement between the two sources was fair. While a high proportion of self-reported concussions (46/63, 73%) could be matched to clinical documentation, athletes failed to recall 50% of concussions documented in the medical records. The poor overlap between the two concussion history sources suggests that player self-report is significantly less reliable than clinical documentation, which generally serves as the gold standard. Large epidemiological studies on sports injuries in general have employed athlete self-reports to study an injury (Clarsen et al., 2013, Pons-Villanueva et al., 2010, Soo Hoo et al., 2018) .While the use of self-reported measures is commonplace in studies collecting data on sports injuries in general, recall will always be imperfect, placing bias into research findings. Despite this, there are many noted benefits of using self-reports of injury including ease of administration, practical feasibilities, time efficiency, availability and cost-effectiveness (Lovalekar et al., 2017, Saw et al., 2016, Englert et al., 2010).The athlete perspective is always of value and supplements reports by medical professionals.

The reasons for divergence between the self-report and documented concussion history is not entirely clear, but concepts and understanding of what constitutes a concussion evolved significantly over the nine-year period of document review, with significant strides in awareness, diagnosis and management. Diagnosis of concussion in the past was often reliant on associated loss of consciousness and amnesia (Clark and Guskiewicz, 2016). We noted that seven concussions self-reported by players lacked corresponding medical data, suggesting that more concussions may not have been documented. The symptoms of concussion are highly variable in presentation, duration and outcome and some concussions still go unrecognized and therefore undocumented (Sharp and Jenkins, 2015). This is due to a myriad of reasons including the latent onset of symptoms (Sahler and Greenwald, 2012),

limitations of diagnostic tools (Dessy et al., 2017), and failure of athletes to disclose concussive symptoms to the medical personnel (Asken et al., 2016a, Kroshus et al., 2015). Therefore, undiagnosed or undisclosed concussions may result in an incomplete concussion history (Baugh et al., 2017). Athletes may not seek medical care for injuries, which suggests that medical records may underestimate true injury frequency (Register-Mihalik et al., 2013). One study found that 30% of athletes reported at least one previously undiagnosed concussion (Meehan et al., 2013).

Reasons for nondisclosure of concussion among athletes may include athletes not realizing they had sustained concussions, not believing concussions were serious enough to warrant disclosure, and not wanting to leave the game and let down their teams (Kerr et al., 2016a). We found that n =14 (37%) of the rugby players were able to self-report their concussion history 100% accurately according to the medical documentation. Many factors may affect reporting including the method used to gain self-reported concussion history (Kurowski et al., 2014); this study used an interviewer administered questionnaire. The most effective method of retrospective injury data acquisition remains unknown. A face to face interview was chosen to increase response rates and facilitate the likelihood of obtaining accurate and complete self-report histories. The Michigan TBI Identification Method questionnaire was chosen as it is a standardized concussion injury specific surveillance questionnaire. This has been shown to promote a more effective and consistent approach to reporting injuries due to the systematic and structured nature of such questionnaires (Mukherjee, 2015), mainly due to the interview style allowing for provision of prompts, cognitive anchors and clarification in relation to concussion education and symptomology. Therefore, we were able to ensure that player self-report concussion met the clinical definition and criteria for concussion in accordance with international Concussion in Sport Group in 2017 (McCrory et al., 2017). Providing a definition including education around concussion symptomatology was employed to facilitate players in providing accurate histories (Robbins et al., 2014). However, there is also the possibility that players may have felt more comfortable disclosing

information anonymously, rather than in an interview style. Other documented factors influencing athlete self-reported concussion history include gender (Kurowski et al., 2014) and anatomical location of the injury (Mukherjee, 2015).Various factors may influence reliability of recall including age, number of concussions and learning difficulties such as attention-deficit hyperactivity disorder (ADHD)(Wojtowicz et al., 2017).

By re-testing the players using the Michigan TBI Identification Method, we wanted to ascertain the reliability of the questionnaire to inform future implementation. This is the first study to investigate the reliability of this tool on a cohort of professional rugby union players signed to one club. The reliability was found to be moderately strong, as such the result provides preliminary support for its use. This should be considered by future researchers using this questionnaire for identifying concussions. Further research into the reliability of this and other concussion history tools commonly used on rugby players is required in varying settings to limit potential selection bias. Of note was the exponential increase in the number of concussions both self-reported and clinically diagnosed from 2008-2017. It is likely this resulted from an evolution in concussion understanding and clinical practice including increased awareness, clinical detection, clinical management, diagnosis, and education. Some concussions that were not identified by medical professionals in a previous era might be diagnosed today because of improvements in clinician training and heightened awareness of concussion. It is possible that past concussions were misdiagnosed or undiagnosed because of the more restricted understanding of what constitutes a concussion, according to the most up to date guidelines. It is therefore unsurprising that the number of self-reported concussions also increased, the more proximate the event. Research on athletes and non-athletes illustrates that recall accuracy may decline as the level of detail requested and the time elapsed since the injury increases (Jenkins et al., 2002). This study corroborates results from such studies in that recall accuracy was negatively correlated with the time elapsed since injury and this was approaching significance [Figure 5-1]. Interestingly, lifetime concussion history was found to be significantly negatively correlated with player

self-report accuracy [Figure 5-2]. There may be many explanations for recall worsening as the number of lifetime concussions increased, including a fatigue effect whereby after a certain threshold is reached several concussive injuries may blend into one. Obtaining accurate concussion histories from former athletes is an important methodological issue in studies investigating history of concussion and health outcomes such as cognition.

5.6 Limitations

The basis on which concussion diagnoses were made in this study would ideally have remained constant through the nine-year study period. However, there was considerable evolution in the detection and management of concussion over the players' professional careers. Therefore, this may have introduced heterogeneity into our sample due to improvements in clinical staff members' detection and diagnoses of clinically documented concussions over time. Team clinical staff members relied on previously published definitions of concussion, symptoms and signs reported and exhibited by the athlete, and reports by medical staff members and other witnesses regarding the condition of the injured player. We also lacked clinical data from prior to 2008. Therefore, our findings may not be generalizable to non-respondents, respondents without clinical data, and other athlete populations. Given that our sample was all male and in light of significant differences in concussion reporting between male and female athletes (Bagley et al., 2012), our research is not generalizable to all professional rugby players.

While clinically diagnosed concussion history and medical documentation may be as close to a gold-standard concussion history measure, medical records also have several shortcomings. The quality of medical data is undeterminable and inevitably open to error. Accurate data about injuries will only be included in medical records if medical care was sought and the concussion diagnosis was made correctly. Clinically documented concussion histories are often limited because medical records have been inconsistent, hard to access, or

non-existent in the past. An advantage of this study was the easy access to data. However, it is possible that the medically documented concussions in the club of the players' playing careers may have been incomplete or inaccurate due to errors in concussion diagnosis. There are a number of reasons for this, namely diagnosis of concussion relies heavily on varying health professionals' knowledge and clinical skill in the absence of an objective diagnostic measure. A positive to this study is the fact that the core medical team at the host club, involved in diagnosis and management of concussions, remained the same over the nine-year period.

Current best clinical practice may still potentially erroneously omit some concussions and may heavily rely on athletes to state that they feel symptomatic to initiate concussion management protocols. Therefore, regardless of agreement between the two measures, both measures may not be completely accurate in how they are capturing and measuring concussions. It is also possible that players may retrospectively confuse concussion with other injuries or conditions that share similar symptoms such as overexertion, dehydration, cervical injuries, cardiac, neurological or psychiatric conditions (McCrory et al., 2017). Time-constraints and pressure may have also impacted on the players self-reports. There is also the possibility of non-disclosure of concussion. Additionally, there will be baseline variation in recall levels amongst players due to unmeasured factors which were not accounted for such as natural memory ability. Random effects modelling aims to capture such variation where present. Finally, for this study we devised a system whereby self-reported and clinically diagnosed concussions that were found to be within the same playing season were deemed a "match". Other studies have devised other grading systems (Kerr et al., 2015).

5.7 Conclusion

Agreement between player self-reported and clinically diagnosed concussion histories was fair. Players were found to under-report concussion history, failing to account for 50% of concussions identified in the clinical records. These findings have important implications for study design of future scientific studies that rely heavily on findings that involve self-reported concussion history among professional rugby players as a variable of interest. Retrospective studies relying on player-recalled concussion history data should interpret findings with caution and within the context of the validity and reliability of concussion history sources. An improved understanding of the reliability of player self-reported and clinically documented concussion histories will help develop more accurate estimates of concussion history and drive future clinical and research efforts.

Chapter 6 Lifestyle factors and general health status following a career in professional rugby union: a cross-sectional study.

Foreword

The following chapter is the first of four chapters which describe the cross-sectional 'PROP' studies. The overall aim of which was to investigate brain health in former professional rugby players. This chapter will provide an overview of participant characteristics and general health status. Some of the measures used will be included or referred to in Chapters 7-9. Rugby union and rugby will be referred to interchangeably hereafter.

6.1 Introduction

Health is defined as a 'a state of complete physical, mental and social wellbeing and not merely the absence of disease or infirmity'(WHO, World Health Organization, 1946). A wide range of physical and mental benefits, increased longevity and the prevention or delay of the onset of chronic diseases are among the myriad of improved health outcomes attributed to regular physical activity in the general population (Ruegsegger and Booth, 2018, Warburton and Bredin, 2017). Rugby is regarded as a form of moderate-to-vigorous physical activity (Griffin et al., 2019). Due to the high physical demands of the sport, it is plausible to surmise that playing rugby should confer significant health benefits on players. Participation in rugby as a physical activity intervention has been shown to be effective at improving metabolic risk factors associated with Type 2 Diabetes (Mendham et al., 2015) and reducing adiposity and improving submaximal oxygen consumption at the amateur recreational level (Mendham et al., 2014). Despite these recognized benefits of exercise and physical activity, the literature to date has focused on the potential negative long-term effects of participation in professional rugby (McMillan et al., 2017). Furthermore, evidence of the risks of adverse health outcomes

associated with long-term sports participation, particularly at the elite level, have been documented (Davies et al., 2017). Given the physical nature of the game of rugby, injury rates remain high relative to other sports (Gardner et al., 2014b, Williams et al., 2013, Viviers et al., 2018). The long-term consequences of this higher injury incidence in rugby on longer-term health-related quality of life are poorly understood (Davies et al., 2017). There is evolving evidence of poorer long-term physical, mental and neurological health associated with elite rugby (Lee et al., 2001, Cunningham et al., 2018, Stewart et al., 2015, Davies et al., 2017). Research has demonstrated strong links between certain sports such golf and improved physical health and mental well-being, and potential contribution to increased life expectancy (Murray et al., 2017). However, there is little investigation to date into long-term health outcomes following retirement from professional rugby.

The primary aim of this study was to:

i) objectively measure physical fitness, including cardiovascular health and body composition in retired professional rugby players (RUG) compared to a control group of retired international rowers (ROW).

The secondary aim of the study was to:

i) explore self-reported general health among retired professional rugby players (RUG) compared to the rowing control group (ROW).

6.2 Methods

6.2.1 Study design

This was a cross-sectional, control study undertaken as part of the 'PROP' project and conducted between August 2018 and June 2019. The research was conducted in accordance with the Declaration of Helsinki (WMA., 1964) and all subsequent amendments (WMA.,

2013). The ‘Strengthening the Reporting of Observational studies in Epidemiology’ (STROBE) guidelines for reporting observational studies were used as a template in shaping this chapter (von Elm et al., 2007). The study protocol was registered with a trial registry (ClinicalTrials.gov; identifier: NCT03544346) prior to recruitment and remained unchanged for the trial duration. Detailed information regarding participants, recruitment, eligibility criteria, assessment protocol and ethical approval for ‘PROP’ is described in detail in Chapter 4.

6.2.4 Outcome Measures

6.2.4.1 Sociodemographic Outcomes

Information regarding participant age, handedness, sex, employment status, education level achieved, and income was gained using the RPAQ questionnaire [see Chapter 4; Section 4.11]. Details of sporting history was also gained such as position, number of years playing participating at their chosen sport at the professional level and at any level. Information regarding smoking history was also gained in the RPAQ (i.e. current / former / non-smoker) [Chapter 4; Section 4.11].

6.2.4.2 Physical Fitness Outcomes

Participant height, weight and BMI were measured using the anthropometric methods outlined in Chapter 4 Section 4.14. Body Composition was also measured using bio-impedance analysis (BIA) [see Chapter 4; section 4.15], along with resting heart rate (HR) and blood pressure (BP) [See Chapter 4; section 4.16].

6.2.4.3 Health related questionnaires

The following health-related self-reported questionnaires, previously described in Chapter 4, were completed:

- The Pain and Disability Index (PDI) (See Section 4.8.1)
- The Alcohol Use Disorders Identification Test (AUDIT) (see Section 4.8.2)
- The International Physical Activity Questionnaire (IPAQ) (see Section 4.8.3.1)
- The Godin Leisure-Time Exercise Questionnaire (see Section 4.8.3.2)
- The Pittsburgh Sleep Quality Index (PSQI) (see Section 4.8.4)

6.3.5 Statistical Analysis

Statistical analyses were performed with SPSS for Windows version 26 (IBM, Armonk, New York, USA). Descriptive statistics of participant characteristics for continuous data were reported as mean (SD) or median (IQR), as appropriate. The Shapiro-Wilk normality test was used to analyse distributions for normality using (with a $p > .05$ indicative of normal distribution). Histograms and normal Q-Q plots of residuals were also visually evaluated. Group differences were examined by independent samples t-tests for normally distributed variables. Mann-Whitney U tests were used to assess non-parametric continuous variables, while $\chi 2$-tests were used to explore group differences for categorical variables. Correlational analyses and regression were used to investigate associations between variables of interest. Correlations between outcomes of interest were examined using Pearson Product Moment correlations or Spearman's rho correlations, as appropriate. For all analyses, $p < .05$ (two-tailed) was taken as statistically significant.

6.4 Results

6.4.1 Recruitment & Participant Characteristics

Ninety-five retired athletes took part in this study; 67 retired professional rugby players (58 males and 9 females) and 28 retired international rowers (21 males and 7 females). Demographic details for rugby and rowers are detailed in table 6-1. The mean age of retired rugby players (RUG: 39.16 SD (5.65) years) was significantly younger than the rowers (ROW: 43.89 SD (9.18) years; p = .016). The two groups did not statistically differ in the majority of demographic characteristics such as handedness, marital status and level of education [Table 6-1]. However, rowers had a statistically lower annual income when compared to the rugby group (p = .001). Rugby players also reported having undergone significantly more general anaesthetics compared to the rowers (p = .003). The mean numbers of years played at professional level rugby (RUG: 9.14 (SD 4.44)) was not statistically different to number of years rowing at an international level (ROW: 7.62 SD (5.44); p = .592). The mean duration of engagement in rugby at any level (RUG: 23.13 SD (7.49) years) was also not statistically significantly different to the mean duration of participation in rowing at any level among the controls (ROW: 22.14 SD (9.36); p = .498).

Table 6-1 Descriptive Characteristics of the RUG and ROW groups. The results are expressed as number (%) other otherwise stated.

Characteristic	RUG (n=67)	ROW (n=28)	p-value
Sex			.170
Male	58 (87%)	21 (75%)	
Female	9 (13%)	7 (25%)	
Age			
Mean (SD)	39.16 ± (5.65)	43.89 ± (9.18)	**.016**
Median [IQR]	38.00 [25.00]	44.50 [30.00]	
20–29	2 (3%)	2 (7%)	
30–39	35 (52%)	6 (21%)	
40–49	28 (42%)	10 (36%)	

50–59	2 (3%)	10 (36%)	
White race – no. (%)	68 (100%)	68 (100%)	-
Handedness			.644
Left	5 (7%)	1 (3.5%)	
Right	62 (91%)	26 (93%)	
Ambidextrous	1 (2%)	1 (3.5%)	
Position played			
Forward	38 (57%)	-	-
Back	29 (43%)	-	-
Total no. years of professional play			
Mean (SD)	9.14 (4.44)	7.62 (5.46)	.592
Total no. years playing at any level			
Mean (SD)	23.13 (7.49)	22.14 (9.36)	.498
Marital status			.460
Single/never married	10 (15%)	6 (21%)	
Married/engaged	52 (78%)	21 (75%)	
Separated	2 (3%)	1 (4%)	
Divorced	3 (4%)	0 (0%)	
Widowed	0 (0%)	0 (0%)	
Other	-	-	
Highest Level of Education			.505
Secondary school education only	2 (3%)	0 (0%)	
At least one year of university completed but no degree	11 (16%)	3 (11%)	
University graduate (BA or BSc)	23 (34%)	9 (32%)	
Master's degree (MA or MSc)	26 (39%)	11 (39%)	
Higher degree (PhD, M.D)	5 (8%)	5 (18%)	
Income			**.001**
<10'0000	3 (4%)	1 (3.5%)	
10-20'000	1 (2%)	3 (11%)	
20-40'000	4 (6%)	9 (32%)	
40-70'000	23 (34%)	6 (21%)	
70-100'000	14 (21%)	8 (29%)	
100-200'000	17 (25%)	1 (3.5%)	
>200'000	5 (8%)	0 (0%)	
No. of general anaesthetics			
Mean (SD)	4.34 (3.77)	2.11 (1.91)	**.003**
Smoking Status			.517
Never smoked	45 (69%)	22 (79%)	
Past smoker	16 (25%)	5 (18%)	
Current smoker	4 (9%)	1 (4%)	

6.4.2 Anthropometrics & body composition

6.4.2.1 Body Mass Index, Fat Percentage and Basal Metabolic Rate

Body composition characteristics are illustrated in Table 6-2. Mean Body Mass Index (BMI) among the rugby group (RUG: 28.99 SD (3.37) kg.m-2) was significantly higher than the mean rower BMI (ROW: 25.11 SD (3.10); p <.001). Seven players (11%) were in the normal BMI range (BMI 18.5 to 24.9). Thirty-nine rugby players (59%) had a BMI classification of overweight (BMI 25 to 29.9 kg.m-2), while 20 rugby players (30%) had a BMI classification of obese (BMI ≥ 30.0 kg.m-2). Fourteen rowers (52%) were in the healthy BMI range. Twelve rowers (44%) had a BMI of overweight, while one rower (4%) was classified as obese. In terms of mean visceral fat, the rugby group (RUG: 8.79 SD (3.49)) had a higher level than the rowers (ROW: 7.31 SD (3.77); p = .057), which was approaching statistical significance. The mean Basal Metabolic Rate (BMR) for the rugby group (RUG: 2192.55 SD (344.15)) was statistically greater than the mean rower BMR (ROW: 1907.63 SD (285.63); p = <.001). Positional differences among the rugby player cohort were explored. However, no significant difference between forwards and backs in body composition was revealed [Table 6-3].

Table 6-2 Anthropometrics and Body Composition (Mean, standard deviation in parenthesis).

Measures	RUG (n=66)	ROW (n=27)	p-value
Body Mass Index	28.99 (3.37)	25.11 (3.10)	**<.001**
Body fat (%)	24.16 (6.6)	21.84 (5.92)	.118
Visceral fat	8.79 (3.49)	7.31 (3.77)	.057*
Basal Metabolic Rate	2192.55 (344.15)	1907.63 (285.63)	**<.001**

*approaching statistical significance

Table 6-3 Body Composition and Cardiorespiratory Fitness among the RUG group based on Position (Mean, standard deviation in parenthesis).

Measures	Forwards (n=37)	Backs (n=28)	p-value
Body Mass Index (BMI)	29.65 (3.70)	28.30 (2.65)	.545
Body Fat %	25.32 (7.51)	22.87 (4.92)	.150
Visceral Fat	8.84 (3.87)	8.82 (3.01)	.157
Systolic Blood Pressure (mmHg)	134.61 (13.85)	133.93 (12.63)	.920
Diastolic Blood Pressure (mmHg)	78.67 (11.90)	80.36 (7.46)	.394

6.4.3 Cardiovascular Fitness

6.4.3.1 Resting Heart Rate and Blood Pressure

At rest, heart rate was not significantly different between groups (RUG: 63.00 (SD 7.75) bpm, ROW: 62.00 SD 10) bpm; p = .599). Systolic blood pressure was not significantly different between groups (RUG: 134.12 (SD 13.15) mmHg, ROW: 136.30 (SD 17.96) mmHg; p = .790). Diastolic blood pressure was also not significantly different (RUG: 79.11 (SD 10.15) mmHg, ROW: 79.41 (SD 11.8) mmHg; p = .900) [Table 6-4]. The prevalence of elevated, Hypertension Stage 1 and Hypertension Stage 2 was analysed based on the most up to date American Heart Association guidelines (Whelton Paul et al., 2018) [Figure 6-1]. Among the rugby players, seven were in the normal range for blood pressure. Fourteen players (21%) were in the elevated range. Twenty-two players (33%) were in the Hypertension Stage 1 category, while the remaining twenty-three players (35%) were in the Hypertension stage 2 category. Among the rowers, three (11%) were in the normal category. Six rowers (22%) had elevated blood pressure as per the guidelines. Eleven rowers (17%)

were in the Hypertension Stage 1 category, while six (22%) were in the Hypertension stage 2 category. Among the rugby players, no significant difference between forwards and backs in terms of blood pressure was revealed.

Table 6-4 Cardiorespiratory Fitness across RUG and ROW groups (Mean, standard deviation in parenthesis).

Measures	RUG (n=66)	ROW (n=27)	p-value
Systolic Blood Pressure (mmHg)	134.12 (13.15)	136.30 (17.96)	.790
Diastolic Blood Pressure (mmHg)	79.11 (10.15)	79.41 (11.18)	.900
Resting Heart Rate (bpm)	63.0 (7.75)	62.0 (9.54)	.599

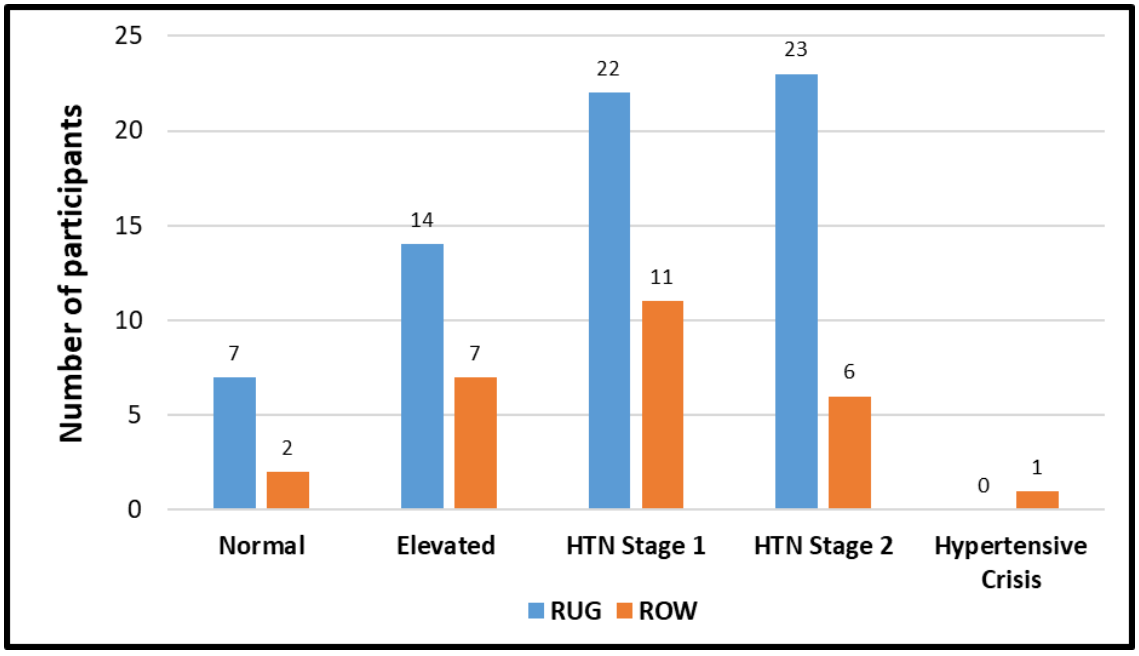


Figure 6-1 *Blood Pressure results across RUG and ROW groups- according to the most up to date American Heart Association Guidelines 2017.*

6.4.4 General health related measures

A summary of results across the two groups is provided in Table 6-5. The 12-Item Short Form Health Survey (SF-12) revealed no significant difference between the RUG and RUG groups on physical and overall health-related-quality of life. Lower scores represent poorer health on the Physical Component Score (PCS). The level of self-reported pain and disability was significantly higher among the rugby players (Mean 6.88 SD (9.01)) in comparison to the rowers (Mean 3.61 SD (5.58); p = .045). Present level of alcohol consumption was explored using the Alcohol Use Disorders Identification Test (AUDIT). Hazardous alcohol use is defined by a score of ≥ 8 on the AUDIT. The rugby group reported significantly higher alcohol usage (Mean 8.50 SD (4.91)) compared to the rowing group (Mean 6.26 SD (5.08); p = .006). There was a point prevalence of hazardous or harmful alcohol of 45.5% (95% CI: 33.1-58.2) among the rugby group, while the rowers had a point prevalence of 35.7% and 95% CI: 18.6-55.9. The PSQI revealed no significant between group differences in terms of sleep disturbance. The point prevalence of sleep disturbance among the RUG group was 55.9% [95% CI 42.4-68.8] compared to 35.7% [95% CI 18.6-55.9] among the ROW group.

Table 6-5 General Health-related Measures across RUG and ROW groups (Mean, standard deviation in parenthesis).

Measures	RUG (n=67)	ROW (n=28)	p-value
SF-12 PCS	17.12 (5.55) $^{+}$	18.57 (1.50)	.679
Pain/Disability	6.88 (9.01) *	3.61 (5.58)	**.045**
Alcohol Use	8.50 (4.91) *	6.26 (5.08)	**.006**
Sleep Quality	4.95 (2.77) **	4.32 (2.42)	.289
Activity Levels	298.96 (340.74) *	267.86 (163.89)	.448
Exercise Levels	46.66 (25.58) *	60.30 (24.94)	**.020**

*n-2, ** n-3, $^{+}$ n-6

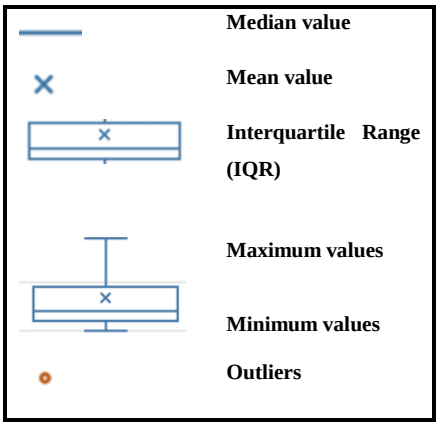


Figure 6-2 *Box and Whisker Plot Key.*

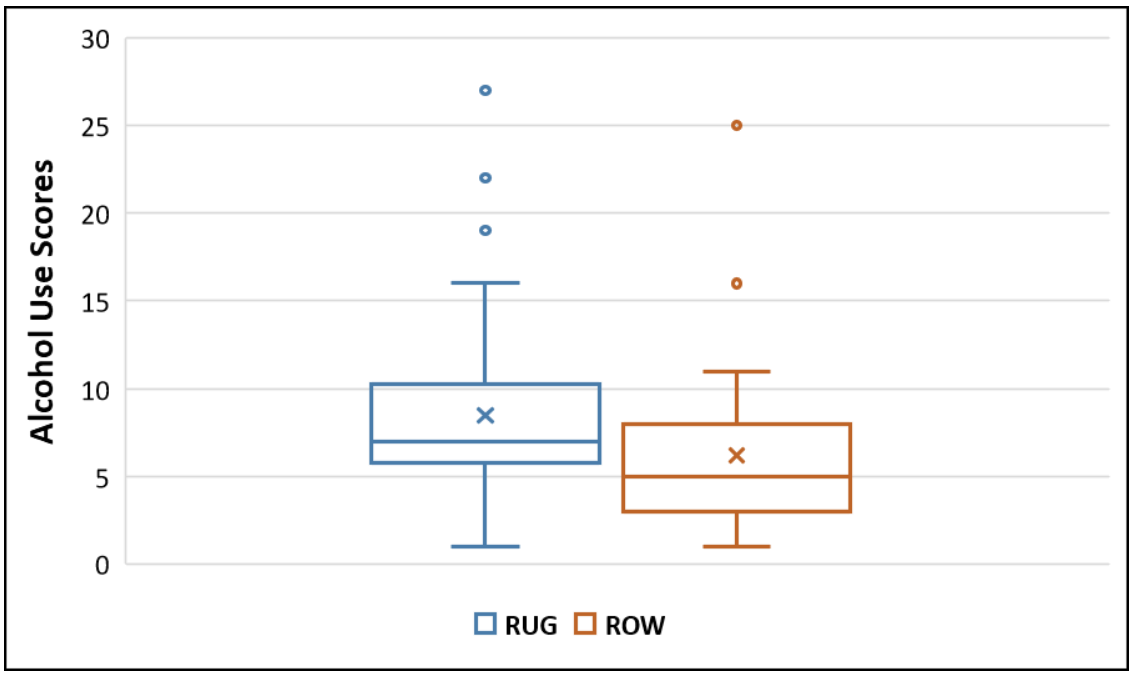


Figure 6-3 *Alcohol Usage (AUDIT); Box and Whisker Plots for RUG and ROW groups.*

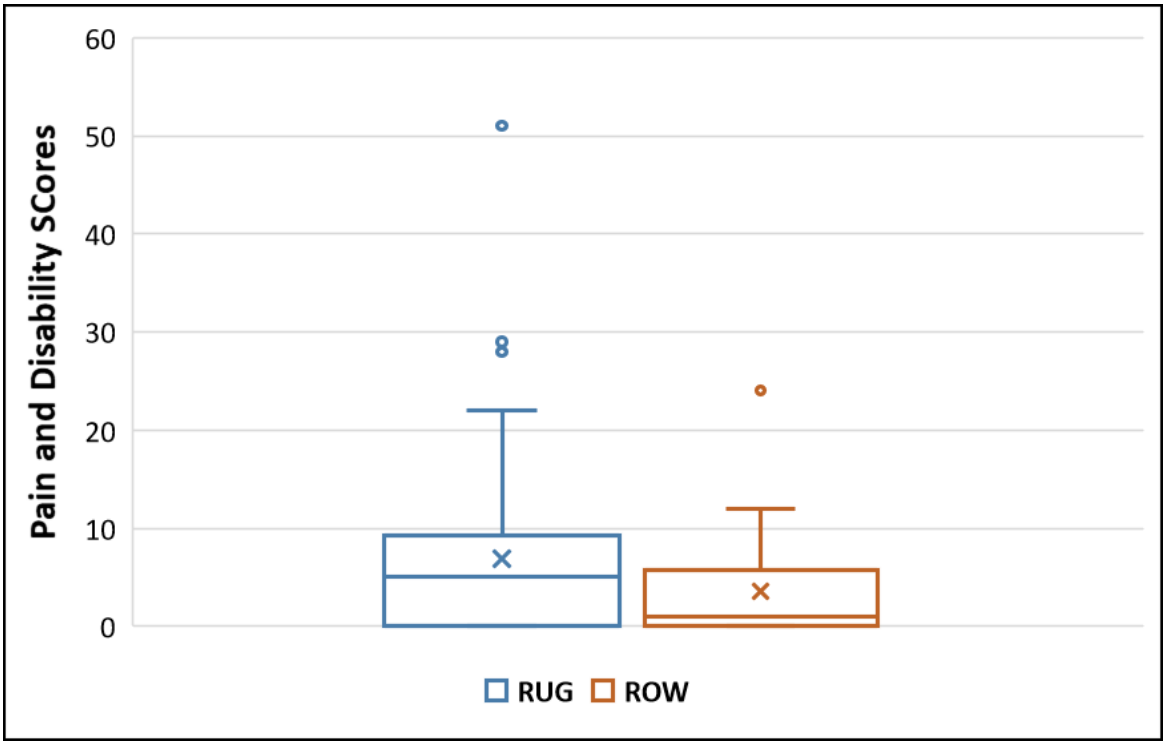


Figure 6-4 *Pain and Disability; Box and Whisker Plots for RUG and ROW groups.*

Table 6-6 Bivariate Correlations (Spearman's rho) between Anthropometric, Body Composition Variables and Years Exposure to Professional Sport for RUG and ROW groups.

RUG group							
		Years Pro	SBP	DBP	RHR	BMI	BF%
Years Pro	Spearman's rho						
	p-value						
SBP	Spearman's rho	-.166					
	p-value	.183					
DBP	Spearman's rho	-.170	**.565****				
	p-value	.173	**.000****				
RHR	Spearman's rho	-.067	-.121	.127			
	p-value	.593	.333	.308			
BMI	Spearman's rho	.001	.137	**.328****	.034		
	p-value	.995	.271	**.007****	.784		
BF%	Spearman's rho	-.167	-.113	.076	.226	**.448****	
	p-value	.181	.367	.542	.068	**.000****	
VF	Spearman's rho	.064	.151	**.374****	.171	**.720****	**.441****
	p-value	.714	.227	**.002****	.169	**.000****	**.000****
ROW group							
Years Pro	Spearman's rho						
	p-value						
SBP	Spearman's rho	.219					
	p-value	.283					
DBP	Spearman's rho	.197	**.370**$^{+}$				
	p-value	.261	**.057**$^{+}$				
RHR	Spearman's rho	.213	-.119	.239			

	p-value	.297	.556	.231			
BMI	Spearman's rho	.361	**.532****	**369**+	-.337		
	p-value	.070	**.004****	**.058**+	.085		
BF%	Spearman's rho	.187	-.026	.328	.134	.299	
	p-value	.360	.896	.095	.504	.129	
VF	Spearman's rho	.345	**.670****	**.472***	-.286	**.774****	.234
	p-value	.085	**.000****	**.013***	.148	**.000****	.240

*Correlation is significant at the 0.05 level (2-tailed).
**Correlation is significant at the 0.01 level (2-tailed).
+ Approaching statistical significance

SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, RHR: Resting Heart Rate, BMI: Body Mass Index, BF%: Body Fat %, VF: Visceral Fat

Table 6-7 Bivariate Correlation (Spearman's rho) between Pain and Disability and Exercise Variables for RUG and ROW groups.

RUG group		
		Exercise
Pain and Disability	Spearman's rho	**-.289***
	p-value	**.022***
ROW group		
	Spearman's rho	-.176
	p-value	.371

*Correlation is significant at the 0.05 level (2-tailed).

Table 6-8 Retired Rugby Player Reflections on their Playing Career Satisfaction.

Considering the benefits and risks of my previous participation in rugby, I would do the same again. (n = 62)	**Frequency**	**Percent**
Strongly agree	47	75.8
Agree	9	14.5
Undecided	4	6.5
Disagree	1	1.6
Strongly disagree	1	1.6
Total	62	100
Considering the benefits and risks of my previous participation in rugby, I would recommend this to my children, relatives or close friends. (n = 61)		
Strongly agree	24	39.3
Agree	22	36.1
Undecided	13	21.3
Disagree	-	-
Strongly disagree	2	3.3
Total	61	100.0
Did your rugby career enrich your life? (n = 61)		
Dramatically	49	80.3
Somewhat	9	14.8
Undecided	2	3.3
Not Really		
Not at all	1	1.6
Total	61	100.0

6.4.4 Reflection on Rugby Playing Career

The Satisfaction with Rugby Playing Career Questionnaire was administered in order to gauge former rugby players opinions on their playing career [Table 6-8]. Players were asked to consider the benefits and risks of professional rugby and answer whether they would undertake the same participation again and or recommend it to their family or friends. When asked whether they would do the same again regarding choosing a career in professional

rugby, 78.8% of the players strongly agreed that they would. However, when asked whether they would recommend the game of rugby to children, relatives or close friends, 39.3% strongly agreed, 36.1% agreed, 21.3% disagreed and 3.3% strongly disagreed. A large proportion of players strongly agreed that playing rugby had enriched their life (80.3%). However, 23.6% believed that playing rugby had impacted negatively upon their long-term cognitive functioning, while 14.5% were unsure and 61.8% did not.

6.5 Discussion

This study provides an insight into physical and cardiovascular health among former retired rugby players compared to retired international rowers. The aim of this chapter was to describe the study participants in terms of sociodemographic characteristics and general health status. It was found that retired rugby players had a statistically higher BMI when compared to rowers. The mean rugby BMI was 29, which is in the overweight, borderline obese category. In rugby as in certain other sports a large body mass is an advantage (Walsh et al., 2018). This is particularly true in certain positions at elite level rugby where body composition and physical fitness positional differences have been demonstrated in body weight, agility, speed, strength and endurance (Meir et al., 2001). Forwards (i.e. all players involved in the scrum) generally have a higher body mass (Brazier et al., 2018) due to positional specific game demands such as significantly more physical collisions and tackles when compared to backs (Gissane et al., 2001). However, we did not find significant positional differences among the rugby players [Table 6-3]. The requirement to gain weight in order to advance their rugby career, may be leading players to overweight or obesity as per the World Health Organization classification for BMI; [normal ($18.5 \leq$ BMI $<$ 25 kg/m2), overweight ($25 \leq$ BMI $<$ 30 kg/m2) and obese (BMI $\geq$ 30 kg/m2)). The current study suggests that BMI remains high among the rugby players in retirement. Current rugby players have been shown to have higher muscle and bone mass than the general population

(Gavarry et al., 2018, Hind et al., 2015). However, we found that visceral fat levels were also higher among rugby players when compared to the rowers, with the between group difference approaching statistical significance ($p = .057$). There is ample evidence to demonstrate that overweight and obesity and high body fat is associated with an elevated risk of developing chronic diseases including, cardiovascular disease, metabolic disorders, hypertension (HTN), osteoarthritis, and certain cancers (Reilly et al., 2003, Lu et al., 2014, Meigs et al., 2006, Basen-Engquist and Chang, 2011). Furthermore, given that rugby players self-reported exercise levels were significantly less than rowers [Table 6-5], it is likely that the body composition of players alters during retirement.

A recent review based primarily on American National Football League players, found that retired athletes had a comparable cardiovascular risk profile with the general population (McHugh et al., 2019). In this study it was found that similarly to the general population, retired athletes with a high BMI had an increased prevalence and severity of risk factors for cardiovascular disease such as high blood pressure, glucose intolerance, elevated body and visceral fat and high low-density lipoprotein and total cholesterol levels. While there are concerns regarding the utility of BMI as a measure in current athletes due to high muscle mass (Walsh et al., 2018), it has been shown to be a valid biometric measure in medical research for the general population (Chernenko et al., 2019). Our findings corroborate the viewpoint that retired athletes fall in line with the general population on retirement. Body Mass Index accordingly becomes a useful indicator of cardiovascular health once more with Spearman's Rho correlational analysis revealing BMI was positively correlated with important measures such as diastolic blood pressure, visceral and total body fat among the rugby players [Table 6-6]. Therefore, BMI was found to be an important indicator of overall cardiovascular risk profile among retired professional rugby players.

The results from the study suggest that further investigation into blood pressure among former rugby players is warranted. Findings indicate that the prevalence of both

prehypertension and hypertension may be high among former professional rugby union players [Figure 6-1]. This finding deserves exploration given the significant adverse health consequences of hypertension. Pain and disability was found to be significantly correlated with self-reported exercise levels on the Godin Leisure Time Exercise Questionnaire among the rugby cohort only ($p < .022$) [Table 6-7]. Reduced exercise among the retired rugby players is likely contributing to higher BMI, body and visceral fat levels when compared to rowers. The prevalence of musculoskeletal injuries such as joint, ligament, muscular and tendinous injuries, along with fractures and dislocation are high among rugby union players (Brooks and Kemp, 2008). This is unsurprising given the nature of the game involving high-impact body contact being commonplace due to multiple physical collisions and tackles which occur at high speed, along with regular twisting and manoeuvring (Brazier et al., 2019). Furthermore, a large proportion (89%) of the former rugby players in the current study reported having undergone at least one general aesthetic associated with their rugby playing career. Therefore, it is likely that their past rugby career has contributed to the significantly greater levels of pain and disability among rugby players compared to their rowing counterparts.

Musculoskeletal injuries and multiple surgeries leading to secondary osteoarthritis and chronic pain (Neuman et al., 2008, Roos et al., 1998) in former players may put them at risk of long-term diseases associated with sedentary lifestyle and overweight/obesity. It is well known that pain and disability associated with osteoarthritis in the general population can become a barrier to exercise (Petursdottir et al., 2010). This is of particular concern given the young mean age of the rugby cohort and the significant correlation between pain and disability and exercise levels among rugby players revealed [Table 6-7]. Sports career termination coupled with cessation of regular exercise has been found to significantly increase cardiovascular risk profile in former power sport athletes compared to nonathletes based on values such as BMI, diastolic blood pressure, low-density lipoprotein and insulin (Emami et al., 2018). The beneficial effects of exercise on health and general wellbeing are

well documented. However, exercise is needed on a regular basis throughout the lifespan to reap the benefits (Allan, 1992, Cheng and Mao, 2016).

Benefits from sports participation generally outweigh any potential adverse effects that may occur such as injury (Scully et al., 1998, Blair and Connelly, 1996, Melzer et al., 2004). The majority of retired players strongly agreed that playing rugby had enriched their life (80%) and that they would do the same again regarding choosing a career in professional rugby (79%). However, less players (39.3%) strongly agreed that they would recommend playing professional rugby to their family or friends. Degenerative joint disease takes years to develop (Lee et al., 2001). Therefore, players require follow-up and the level of self-reported pain and disability at this point may indicate the need for proactive osteoarthritis management within this population. It is important to identify and manage barriers to continued participation in sporting and physical activities upon retirement. Barriers such as pain and disability identified in the current study need to be addressed in order to enable rugby players to continue to be active in retirement. Given the overall negative effects of obesity on cardiovascular health, body composition changes in retirement from elite rugby need to be considered. Longitudinal follow-up of players is required in order to delineate the effects of a career in rugby on physical health and whether higher levels of pain and disability leads to premature degenerative disease being more common in former rugby players than in the general population. Future interventions should evaluate body composition and incorporate weight management strategies and appropriate detraining from elite rugby programmes as appropriate for rugby players transitioning into retirement.

6.6 Limitations

The cross-sectional methodology resulted in measurement of multiple health related factors which enabled us to present a relatively comprehensive overview of health within this retired professional rugby player population. However, a limitation of the cross-sectional design

employed includes reduced capacity to infer causality and risk of recall bias. Therefore, the self-report nature of questionnaires used to gain information on health and lifestyle behaviours such as exercise, alcohol use and smoking status may be open to bias. While the findings indicated hypertension in certain athletes, caution is needed when interpreting the blood pressure results. As this was a once off testing, it is not diagnostic and further twenty-four monitoring for players would be required by a medical professional to reach a diagnostic threshold and establish the true burden of hypertension in this cohort. The limited number of female participants included in the study analyses needs to be considered, given different sex-related risks of morbidity.

6.7 Conclusion

Little is known about the potential relationships between professional rugby and physical and general health status in retirement. Global participation figures in rugby are estimated at over eight million and any potential negative effects in health-related quality of life following participation in rugby could present a significant public health burden. However, application of these findings to lower levels of participation and rugby exposure is also required. The prevalence of overweight and obesity was higher among the retired rugby players compared to the retired rowers. Indications of higher visceral and body fat and hypertension were also revealed among the rugby cohort. Lower levels of exercise was found to be associated with pain and disability, indicating that past participation in professional rugby may result in greater levels of pain and functional limitations in retirement. Results from this study highlight modifiable risk factors such as overweight and obesity and hypertension in retired professional rugby players which are associated with long-term risk of negative health outcomes. Introduction of detraining protocols for professional rugby players transitioning into retirement should be considered. A proactive approach to management and education with regard long-term physical health, particularly musculoskeletal morbidity, within professional rugby players is required.

Chapter 7 An investigation into the mental health status of retired professional rugby union players and its association with a history of concussion: a cross-sectional study.

The material presented in this chapter has been disseminated in the following publication:

Cunningham J., Broglio S., Mc Cabe., E and Wilson F. (2019). Depression indicators in former professional rugby players are related to number of playing years and not concussion history. Journal of Neurotrauma, Vol. 36, No. 13, Abstracts.

Please see Appendix A.4 for full abstract.

7.1 Introduction

Mental health problems are a major public health issue globally, with depression being a leading cause of disability and disease burden worldwide (Consortium, 2004, Moussavi et al., 2007, Friedrich, 2017). Mental health problems are present in one in three adults throughout their lifetime (Steel et al., 2014).While there is relatively little research available on the psychological wellbeing and mental health of elite athletes, it has become an area of growing concern (Rice et al., 2016, Glick et al., 2009). Exercise is cited as a protective factor against mental health issues due to the well-documented biochemical and physiological effects of exercise, including inflammation reduction and neurotransmitter release (Mikkelsen et al., 2017, Stanton and Reaburn, 2014). Therefore, it may have been thought that athletes would be less likely to experience depression, anxiety and other common mental health disorders which affect the general population due to the noted benefits of exercise (Basso and Suzuki, 2017, Anderson and Shivakumar, 2013).

However, while physical exercise is recommended as treatment for mental health problems such as depression (NICE., 2009), a straightforward and reliable dose-response relationship between exercise and mood has not been established (Mikkelsen et al., 2017). Greater amounts of exercise may not always be more effective for reducing mental health burden. Chekroud et al. (2018) and others have shown that further investigation into the specific types, durations, and frequencies of exercise is required (Patsou et al., 2017, Nebiker et al., 2018, Chekroud et al., 2018). The prevalence of mental health problems in elite athletes remains unclear (Wolanin et al., 2015, Bar and Markser, 2013). Kessler et al. (2007) demonstrated that mental health problem onset often overlaps with participating years for elite athletes, but a clear picture of mental health among elite athletes is not available. Gorczynski et al. (2017) suggested that overall incidence of mental health problems in this population is similar to non-athletic populations, while Souter et al. (2018) and Wolanin et al. (2015) suggest it may be higher. These studies were conducted predominantly among current/former National Collegiate Athletic Association (NCAA) athletes, American National Football League players and soccer players, with a lack of research addressing mental health among retired professional rugby union players.

Rugby has a high injury burden due to the physicality and impacts associated with the sport, leaving players vulnerable to musculoskeletal and brain injuries. Emerging evidence suggests an association between concussion and or repeated head impact exposure and long-term mental health problems (e.g. depression) among former American NFL players and collegiate athletes (Manley et al., 2017a). Chronic Traumatic Encephalopathy (CTE) has been described in NFL players with a history of repeated head trauma, characterised by an abnormal accumulation of tau protein (Horstemeyer et al., 2019). The described clinical signs of CTE include impaired judgment, aggression, mental illness, such as depression and anxiety, and suicidality (Baugh 2012). However, this has not been empirically investigated in retired rugby players. Given the elevated risk of concussion in rugby, there is a need to investigate long-term mental health outcomes in this population.

Therefore, the primary aim of this study was to

i) determine the prevalence of symptoms of common mental problems (anxiety, depression, somatization, sleep disturbance, adverse alcohol behaviour) among retired professional rugby union players (RUG) compared to retired international rowers (ROW).

The secondary aims of this study were to

i) explore the associations between sports-related concussion (SRC) history or head impact exposure and symptoms of depression in retired professional rugby union players, and ii) explore the associations between factors which may be associated with mental health (pain and disability, alcohol use, sleep disturbance) and the symptoms of mental health conditions under study in retired professional rugby union players.

7.2 Methods

This was a cross-sectional, controlled study undertaken as part of the 'PROP' project and conducted between August 2018 and June 2019. The 'Strengthening the Reporting of Observational studies in Epidemiology' (STROBE) guidelines for reporting observational studies were used as a template in shaping this chapter (von Elm et al., 2007). The study protocol was registered with a trial registry (ClinicalTrials.gov; identifier: NCT03544346) prior to recruitment and remained unchanged for the trial duration. Rowers, as former non-contact sport athletes without concussion history, were included as an appropriate control

group. Detailed information regarding participants, recruitment, eligibility criteria, assessment protocol and ethical approval for 'PROP' is described in detail in Chapter 4.

7.2.4 Outcome Measures

7.2.4.1 Sociodemographic outcomes

Participants completed general health questionnaires. Information such as age, race, income, highest level of education and number of years participating in their sport was gathered from each participant using the Retired Professional Athlete Questionnaire (RPAQ) [See Chapter 4; Section 4.7.1]. Participants were then administered the Michigan Traumatic Brain Injury (TBI) Identification Method in order to gain an estimate of lifetime concussions sustained [See Chapter 4; Section 4.7.2]. A list of validated mental health questionnaires was then administered to address the aims of the study. The questionnaires took approximately 30 minutes to complete.

The following health-related questionnaires, previously described in Chapter 4 (See Section 4.8), were completed:

- The Pain and Disability Index (PDI) (See Section 4.8.1)
- The Alcohol Use Disorders Identification Test (AUDIT) (see Section 4.8.2)
- The Godin Leisure-Time Exercise Questionnaire (see Section 4.8.3.1)
- The Pittsburgh Sleep Quality Index (PSQI) (see Section 4.8.4)
- Neuro-QOL-Cognition Function-Short Form (see Section 4.8.5)

The following sports-related self-reported questionnaire, previously described in Chapter 4, was completed:

- The Athletic Identity Measurement Scale (AIMS) (see Section 4.8.6.1)

The following mental health-related questionnaires, previously described in Chapter 4 [See Section 4.9], were completed:

- The Brief Symptom Inventory-18 (BSI-18) (See Section 4.9.1)
- The Patient Health Questionnaire-9 (PHQ-9) (See Section 4.9.2)
- The 12-Item Short Form Health Survey (SF-12) (See Section 4.9.3)
- The Connor-Davidson Resilience Scale-25 (CD-RISC-25) (See Section 4.9.4)
- The Satisfaction with Life Scale (SWLS) (See Section 5.9.6)

7.3 Statistical Analysis

Statistical analyses were performed with SPSS for Windows version 26 (IBM, Armonk, New York, USA). Descriptive statistics of participant characteristics for continuous data were reported as mean (SD) or median (IQR), as appropriate. The Shapiro-Wilk normality test was used to analyse distributions for normality using (with a $p > .05$ indicative of normal distribution). Histograms and normal Q-Q plots of residuals were also visually evaluated. Group differences were examined by independent samples t-tests for normally distributed variables. Mann-Whitney U tests were used to assess non-parametric continuous variables. For all analyses, $p < .05$ (two-tailed) was taken as statistically significant. Correlational analyses and regression were used to investigate associations between variables of interest. Correlations between outcomes of interest such as depression indicators and concussion history were examined using Pearson Product Moment correlations or Spearman's rho correlations, as appropriate. Multiple linear regression analysis was used as an extension of simple linear regression analysis, to assess the association between independent variables of

interest (predictor variables) and the mental health indicators investigated. For all analyses, $p < .05$ (two-tailed) was taken as statistically significant.

7.4 Results

7.4.1 Recruitment & participant characteristics

A total of 95 retired athletes took part in this study; 67 retired professional rugby players (58 males and 9 females) and 28 retired international rowers (21 males and 7 females). The age of the retired rugby players (Mean 39.16 SD (5.65); Range: 27-52 years) was significantly younger than the rowers (Mean 43.89 SD (9.18); Range:28-58 years; $p = .016$). The mean duration of engagement in professional rugby (RUG: 9.14 SD (4.44) years) was not significantly different to the mean participation in international rowing among the controls (ROW: 7.62 SD (5.44) years). In terms of mean number of years participation at any level, rugby players (RUG: 23.13 SD (7.49) years), were not statistically different to the control group (ROW: 22.14 SD (9.36) years). Rugby players had a significantly greater number of self-reported concussions (RUG: 6.55 SD (10.13), ROW: 0.54 SD (1.14); $p < .001$).

7.4.2 Mental Health Results

7.4.2.1 Depression and Anxiety

Mental health scores are displayed in Table 7.1. All mental health outcome measures revealed worse mean scores in the rugby group compared with the rowers. Depression and anxiety were investigated using the BSI-18 [Figure 7-1]. Scores on the BSI-18 revealed no between group difference in the BSI Anxiety (ANX), Depression (DEP) and Global Severity (GSI) items. However, the Somatization Dimension (SOM) revealed a significantly greater physical manifestation of psychological concerns among the rugby players (Mean 1.70 SD (2.84)) compared to the rowers (Mean 1.00 SD (2.55); $p = .049$) [Table 7-2]. On the PHQ-9

measure of depression, 27.9% of rugby players (95% CI: 17.7-40.1) reported some level of depression (i.e. a PHQ-9 score of 5 or above) compared to 10.7% of rowers (95% CI: 2.3-28.2) [Table 7-3]. The mean score for the RUG group was 3.27 SD (3.79), while the rowers had a mean score of 2.21 SD (3.10) [Figure 7-3], though these differences were not significant. The SF-12 was used to investigate mental and physical functioning and overall health-related-quality of life. The rugby players reported greater mental health issues on the Mental Component Score (MCS) of the SF-12. Lower scores represent poorer mental health on the MCS. However, no significant between group differences were found.

Table 7-1 Prevalence of Symptoms of Mental Health Disorders among the RUG and ROW groups.

	RUG (n=67)		**ROW (n=28)**		
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	p-value
BSI-18	6.74 (8.78) $^{+}$	4.00 [63.00]	5.21 (7.95)	2.50 [36.00]	.083
PHQ-9	3.27 (3.79) *	2.00 [25.00]	2.21 (3.10)	1.50 [15.00]	.074
SF-12 MCS	21.22 (6.97	23.50 [28.00]	23.36 (2.60)	24.00 [11.00]	.250

***n-1 $^{+}$ n-2**

Table 7-2 Brief Symptom Inventory-18 Symptom Dimensions List for RUG and ROW groups (Mean ± SD; Median, IQR in parentheses).

	RUG (N=67)	ROW (N=28)	p-value
Somatization Dimension Item (SOM)	1.70 ± 2.84	1.00 ± (2.55)	**.049**
• Faintness or dizziness • Pains in heart or chest • Nausea or upset stomach • Trouble getting your breath • Numbness or tingling in parts of your body • Feeling weak in parts of your body	1.00 [19.00]	0.00 [13.00]	

Depression Item (DEP)	2.52 ± (3.54)	1.89 ± (2.53)	.515
• Feeling no interest in things • Feeling lonely • Feeling blue • Feelings of worthlessness • Feeling hopeless about the future • Thoughts of ending your life	1.50 [22.00]	1.00 [9.00]	
Anxiety dimension (ANX)	2.56 ± (3.27)	2.32 ± (3.50)	.277
• Nervousness or shakiness inside • Feeling tense or keyed up • Suddenly scared for no reason • Spells of terror or panic • Feeling so restless you couldn't sit still • Feeling fearful	2.00 [22.00]	0.00 [14.00]	

Table 7-3 Point Prevalence of Depression, Alcohol Misuse, Pain and Disability and Sleep Disturbance among the RUG and ROW groups (95% confidence interval in parentheses).

	RUG (N=67)	**ROW (N=28)**
Depression	27.9 [17.7-40.1]	10.7 [2.3-28.2]
Alcohol Misuse	45.5 [33.1-58.2]	35.7 [18.6-55.9]
Pain and Disability	16.7 [8.6-27.9]	3.6 [1.0-18.3]
Sleep Disturbance	55.9 [42.4-68.8]	35.7 [18.6-55.9]

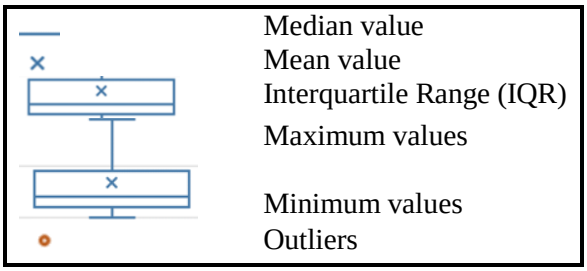


Figure 7-1 *Box and Whisker Plot Key.*

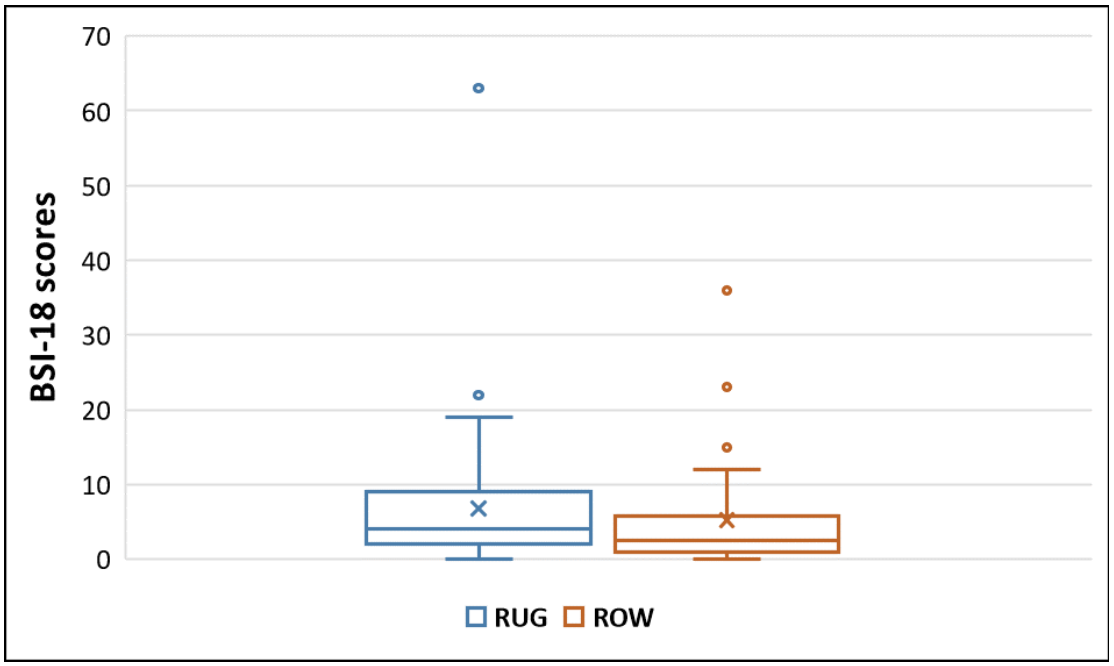


Figure 7-2 *Depression/Anxiety/Somatization; Box and Whisker Plots for RUG and ROW groups.*

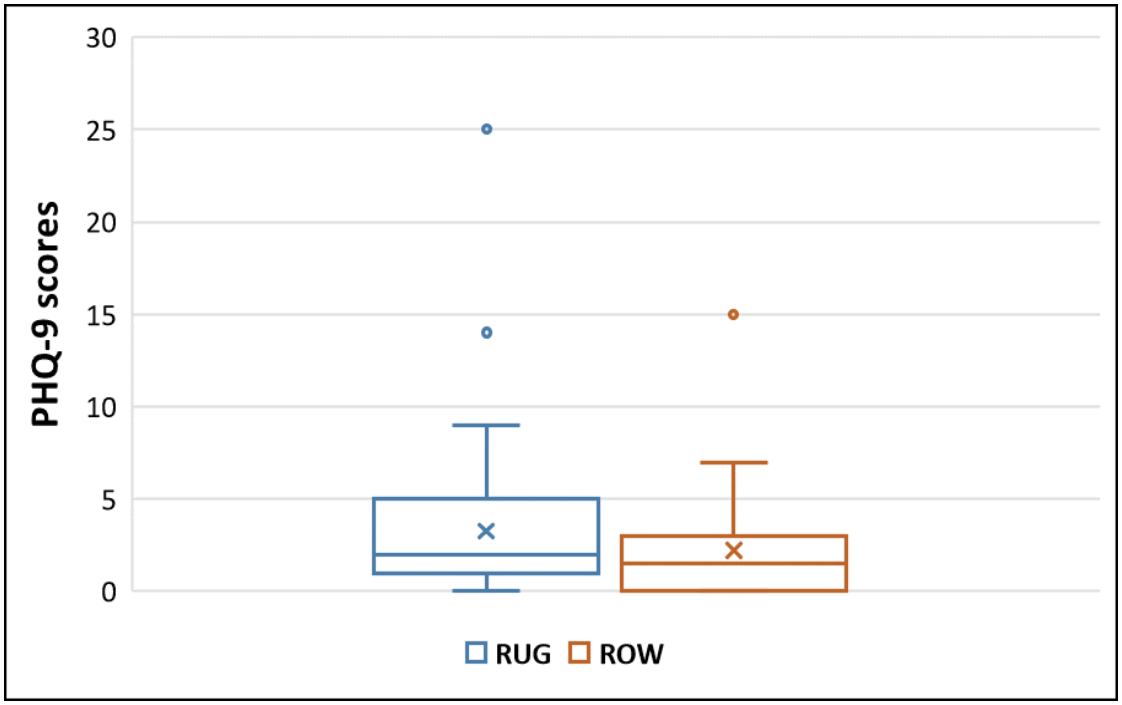


Figure 7-3 *Depression; Box and Whisker Plots for RUG and ROW groups.*

7.4.2.2 Symptoms related to mental health

Various mental health related symptoms were explored. A summary of these results across the two groups is provided in Figure 7-4. Results are displayed in Table 7-4. The level of self-reported pain and disability was significantly higher among the rugby players (Mean 6.88 SD (9.01)) in comparison to the rowers (Mean 3.61 SD (5.58); p = .045). Present level of alcohol consumption was explored using the AUDIT. Hazardous alcohol use is defined by a score of ≥ 8 on the AUDIT. The rugby group reported significantly higher alcohol usage (Mean 8.50 SD (4.91)) compared to the rowing group (Mean 6.26 SD (5.08); p = .006). There was a point prevalence of hazardous or harmful alcohol of 45.5% (95% CI: 33.1-58.2) among the rugby group, while the rowers had a point prevalence of 35.7% and 95% CI: 18.6-55.9. The PSQI revealed no significant between group differences in terms of sleep disturbance. The point prevalence of sleep disturbance among the RUG group was 55.9% [95% CI 42.4-68.8] compared to 35.7% [95% CI 18.6-55.9] among the ROW group. The rugby group also had a significantly greater sense of athletic identity when compared to the rowers (p = .046).

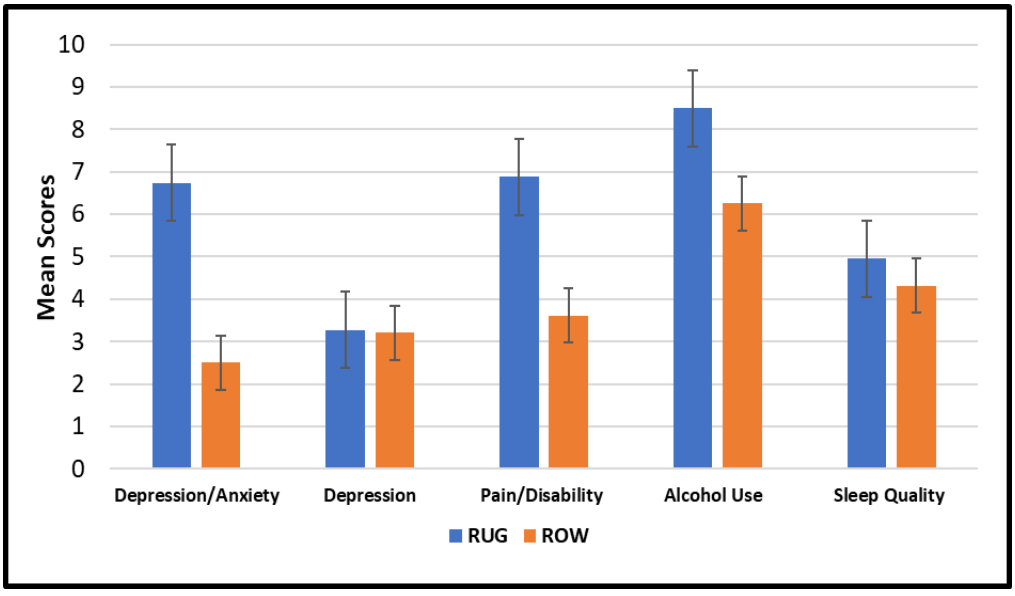


Figure 7-4 *Mental Health-related Symptoms by group (mean, error bars equal ± 1 standard error).*

Table 7-4 Factors Relating to Mental Health among the RUG and ROW groups (Median, IQR parentheses).

	RUG (n=67)		ROW (n=28)		
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	p-value
General					
Pain/Disability	6.88 (9.01) **	5.00 [51.00]	3.61 (5.58)	2.00 [24.00]	**.045**
Alcohol Use	8.50 (4.91) **	7.00 [26.00]	6.26 (5.08)	5.00 [24.00]	**.006**
Sleep Quality	4.95 (2.77) +	5.00 [14.00]	4.32 (2.42)	3.00 [11.00]	.289
Cognition	32.66 (6.23) +	34.00 [24.00]	33.64 (5.22)	35.50 [23.00]	.659
Resilience	74.77(12.88) **	77.00 [78.00]	75.29 (10.93)	75.00 [46.00]	.924
Satisfaction with Life	25.94 (5.76) *	28.00 [24.00]	26.74 (4.06) *	27.00 [18.00]	.957
Sports Specific					
Athletic Identity	39.47(10.61) ++	40.00 [42.00]	44.10 (9.01)	41.00 [27.00]	**.046**

*n-1, ** n-2, + n-3, ++ n-6

7.4.3 Association between symptoms of common mental problems

Associations between symptoms of common mental problems and mental health indicators were explored. Bivariate non-parametric correlational analysis revealed no significant association between depression and anxiety indicators and self-reported concussion history estimates among the rugby players [Table 7-5]. Number of years played professional rugby was also not significantly correlated with symptoms of anxiety and depression. Various factors unique to an athletic population such as athletic identity and non-unique to an athletic population such as satisfaction with life, resilience, pain and disability etc. were also

investigated among the entire cohort of rugby players and rowers [Table 7-6]. Among both cohorts, higher levels of depression were associated with higher levels of pain and disability, poorer self-reporting cognitive functioning, decreased satisfaction with life and resilience and greater athletic identity and alcohol usage (all p <.05). Multiple regression analysis revealed decreased satisfaction with life and resilience, and higher levels of athletic identity and pain and disability were significant predictors of depression among the rugby cohort [Figure 7-7].

Table 7-5 Bivariate Correlations (Spearman's rho) between Mental Health Indicators and Concussion Estimates and Exposure to Contact Sport (years professional and years total) among the RUG group.

	Years Professional	**Years Total**	**Concussion Estimates**
Years Professional			
Years Total	**.000****		
Concussion Estimates	**.017***	**.011***	
Depression (PHQ-9)	.382	.268	.753
Depression/Anxiety (BSI)	.097	.395	.995

* Correlation is significant at the 0.05 level (2-tailed).

Table 7-6 Bivariate Correlations (Spearman's rho) between Mental Health Indicators and Unique and Non-unique Factors to an Athletic Population for combined RUG and ROW groups.

		DEP (PHQ-9)	DEP/ANX (BSI)	SWLS	Resilience	Cognitive Function	Pain/ Disability	Alcohol Usage
DEP (PHQ-9)	Spearman's rho							
	p-value							
DEP/ANX (BSI)	Spearman's rho	**.665****						
	p-value	**.000****						
SWLS	Spearman's rho	**-.535****	**-.416****					
	p-value	**.000****	**.000****					
Resilience	Spearman's rho	**-.418****	**-.278****	**.458****				
	p-value	**.000****	**.007****	**.000****				
Cognitive Health	Spearman's rho	**-.559****	**-.342****	**.297****	**.396****			
	p-value	**.000****	**.001****	**.004****	**.000****			
Pain/Disability	Spearman's rho	.127	**.214***	-.090	**-.208***	-.187		
	p-value	.224	**.040***	.392	**.045***	.073		
Alcohol Usage	Spearman's rho	**.231***	**.254***	-.186	-.094	**-.228***	.198	
	p-value	**.025***	**.014***	.074	372	**.028***	.056	
Athletic Identity	Spearman's rho	**-.220***	**-.318****	.133	-.171	.132	-.057	**-.277****
	p-value	**.039***	**.003****	.219	.114	.223	.597	**.009**

*Correlation is significant at the 0.05 level (2-tailed).
**Correlation is significant at the 0.01 level (2-tailed).
$^{+}$ Approaching statistical significance

DEP: depression, ANX: anxiety, SWLS: satisfaction with life scale

Model	Unstandardized coefficients	Standardized Coefficients		t	Sig.	Lower Bound	Upper Bound
1	**B**	**Std. Error**	**Beta**				
Constant	21.007	2.646		7.938	.000	15.701	26.313
Pain/Disability	.091	.039	.213	2.322	.024	.012	.170
Resilience	-.129	.030	-.432	-4.320	.000	-.189	-.069
Satisfaction with Life	-.223	.062	-.333	-3.606	.001	-.347	-.099
Athletic Identity	-.073	.032	-.197	-2.299	.025	-.137	-.009

***Dependent Variable**: Depression (PHQ-9)*

Model Summary [b]

Model	R	R Square	Adjusted R square	Std Error of the Estimate
1	.817[a]	.668	.643	2.36224

***a Predictors:** (Constant), Athletic Identity, Resilience, Pain and Disability, Satisfaction with Life*
***b** Dependent Variable*

***Figure 7-5** Multiple Linear Regression Model illustrating Predictors of Depression among the RUG group.*

7.5 Discussion

This explorative cross-sectional study provides the first insight into the mental health burden among retired professional rugby players compared to a non-contact control group. A variety of self-reported questionnaires regarding symptoms associated with mental health disorders were used. Areas such as anxiety, depression, pain and disability, sleep disturbance and alcohol misuse were examined. Results demonstrated that the prevalence of mental health symptoms and disorders among former rugby players was 10% higher for alcohol misuse, 17% higher for depression, 13% higher for pain and disability and 20% higher for sleep disturbance compared to rowers. The prevalence of mental health symptoms and disorders found in former rugby players appears to be higher than in the general population. Various systematic reviews and meta-analyses indicated that prevalence of anxiety, depression among the general population was found to range from 13% to 25% (Steel et al., 2014, Korten and Henderson, 2000, Bultmann et al., 2002, Lynge et al., 2004).

A prevalence rate of 9.2% of a current PHQ-9 depressive disorder has been cited in the general population (Martin et al., 2006). Rugby players had a higher point prevalence of depression on the PHQ-9 (27.9%) compared to the rowers (10.7%) who were closer to the expected normal prevalence. This finding was not associated with concussion estimates or number of years of exposure to professional rugby. Former rugby players had a significantly stronger sense of athletic identity, higher alcohol use and higher levels of pain and disability than rowers (all $p<.05$) [Table 7-4]. Findings suggest that these may be among factors contributing to the overall higher depression prevalence among rugby players compared to rowers. Multiple regression analysis revealed decreased satisfaction with life, decreased resilience, greater athletic identity and higher levels of pain and disability were significant predictors of depression among the rugby cohort. These factors were found to account for 67% of the variation in the chance of former rugby players having depression as per the PHQ-9 [Figure 7-5].

The former rugby players also reported significantly greater somatic symptoms than the rowers [Table 7-2]. The manifestation of psychological distress by the presentation of physical symptoms has been previously described as a defence against the awareness or expression of psychological distress (Katon et al., 1982). While there is a gradual move towards speaking about mental health, stigma particularly in male elite athletes still exists (Souter et al., 2018, Bauman, 2016). Greater scores on indexes of somatization among the rugby players may also be influenced by actual physical symptoms, stemming from longstanding musculoskeletal injuries which are poorly managed, as suggested by the significantly higher levels of pain and disability reported by the rugby group. It has been demonstrated that one of the most recognised risk factors for psychological distress amongst male athletes is sports injury (Wolanin et al., 2015). Pain and disability due to osteoarthritis in the general population is known to be associated with depression (Parmelee et al., 2012, Sharma et al., 2016, Nazarinasab et al., 2017).

Aside from the risk of concussion associated with rugby union, the prevalence of musculoskeletal injuries are high among rugby union players (Brooks and Kemp, 2008) and should not be discounted when discussing long-term mental health in this group or other former contact collision sport athletes. This is unsurprising given the nature of the game involving high-impact body contact being commonplace due to multiple physical collisions and tackles which occur at high speed, along with regular twisting and manoeuvring (Brazier et al., 2019). Furthermore, a large proportion (89%) of the former rugby players reported having undergone at least one general anaesthetic associated with their sporting injury. Therefore, musculoskeletal injuries and multiple surgeries leading to secondary osteoarthritis and chronic pain in former players may increase overall risk of experiencing mental health symptoms and disorders in retirement. This is of particular concern given the young mean age of the rugby cohort, who are self-reporting significantly greater levels of pain and disability than their rowing counterparts. It is important that mental health interventions with

this cohort take account of these physical factors. Evidence suggests that this may influence their management as noted by The National Institute of Clinical Health and Excellence (NICE, 2011), which outlines differentiated mental health support pathways for adults with depression with or without chronic physical health problems.

Concussion history and repetitive head impacts have been previously linked to depression in former athletes (Manley et al., 2017a). A systematic review demonstrated a frequency–response relationship between sport-related concussion (SRC) history or head impact exposure and symptoms of depression in retired NFL players and collegiate athletes (Montenigro et al., 2016, Kerr et al., 2014a, Didehbani et al., 2013, Guskiewicz et al., 2007). Decq et al. (2016) reported that PHQ-9 scores increased with the number of reported concussions among former rugby players and other sportsmen ($p = .026$). In the current study number of years playing professional or amateur rugby were used as a proxy for head impact exposure, neither of which were associated with depression. Therefore, contrary to previous studies, we found no association between concussion history estimates and depression scores among the rugby players [Table 7-5]. Self-perceived higher cognitive difficulties were significantly associated with higher levels of depression among both cohorts and depression in absence of concussion history is known to negatively influence cognitive function (Zuckerman et al., 2018, Rock et al., 2014). For the former rugby players this could potentially be explained due to anxiety regarding past concussions and future health, driven by social media and perception among the general public regarding concussion. However, a similar association was found among the rowers. Therefore, it may be that perceived poorer cognitive health affects overall brain health including mental health.

The greater athletic identity in retirement among the rugby players compared to rowers could suggest that rowers were more likely to prepare for their future beyond their athletic careers. This is perhaps not surprising given that while the rowers had participated at an elite level, they were not compensated to an extent that this could be their sole profession. Therefore, rowers would have been obliged to maintain a working job while being on the national team.

This would arguably make the transition from elite sport less difficult for rowers. On the contrary, unlike the rowers, retired rugby players must transition into a new career following retirement which has been shown to be psychologically challenging, particularly for athletes with high athletic identity (Park et al., 2013). This study's finding of links between greater athletic identity and higher depression scores corroborates previous work in other sports suggesting that athletes who have a strong athletic identity may be more vulnerable to mental health difficulties such as depression (Souter et al., 2018). Our study suggests maintaining a strong athletic identity beyond the point of retirement may increase risk of experiencing mental health problems, likely exacerbated by career transitioning difficulties (Grove et al., 1997, Brown et al., 2018).

The number of years participating in sport at a professional/international level was found to correlate with anxiety and depression among the combined rowers and rugby groups ($p = .022$). A sense of athletic identity presumably would increase with the number of years participating at sport among both cohorts. Therefore, the greater number of years solely in the environment of professional sport may leave retired elite sports people at an increased risk for mental health problems. Although many of the challenges of transition from elite sport are present for rowers too, the shift required for rugby players in terms of factors such as identity and source of income may be greater. Given the association between mental health issues and athletic identity found in this study, the rugby players may have been assessed at a particularly vulnerable time, due to their young age and relatively recent retirement from the professional game. It could be postulated that over time, player's strong athletic identity may be replaced with a new sense of identity associated with changes in life stage and career status. Furthermore, forced retirement in rugby has been linked to greater symptoms of distress (Brown et al., 2017). It is probable that rowers would have greater control over when they retire, unlike rugby players who may be forced to retire due to unforeseeable injuries. Given that rugby players are more solely financially dependent on their professional rugby career, unlike rowers, this may add to the stress burden.

The prevalence of depression was higher in the former rugby players compared to the rowers and the general population. However, mean scores between the two groups for the PHQ-9 were not significantly different indicating that there may be a substantial risk of poorer mental health following retirement across various sports and that this is not unique to rugby. Presence of mental health issues prior to involvement in sport may become amplified by stressors that are associated with the aftermath of career in professional sport. Reasons for the reported prevalence of depression among former rugby players in this study may be due to a combination of factors. Among both cohorts, higher levels of depression were associated with higher levels of pain and disability, poorer self-reporting cognitive functioning, decreased satisfaction with life and resilience and greater athletic identity and alcohol usage (all $p < .05$). As demonstrated rugby players reported significantly greater levels of the majority of these symptoms. However, prevalence of alcohol misuse using the AUDIT screening tool among the general population is estimated at 18% (Bergman and Källmén, 2002). Therefore, both groups (RUG: 46%, ROW: 36%) reported a high level of alcohol misuse and dependency. Therefore, many potential contributory factors to poorer mental health were not unique to the rugby cohort.

The intense mental and physical demands placed on professional athletes are unique and inescapable aspects of an elite sporting career. Such pressures may increase their vulnerability to mental health problems (Hughes and Leavey, 2012). The elite athlete faces unique physical and mental pressures and challenges associated with their chosen career. The psychological challenges include public scrutiny, stigma, isolation, injury, fear of failure and the perception of seeking help as a sign of weakness (Rice et al., 2016, Gulliver et al., 2012, Reardon and Factor, 2010). Other reasons for potential psychological issues in retired elite athletes are plentiful and may include involuntary retirement (Wolanin et al., 2015), life events (Gouttebarge et al., 2016), disordered eating (McArdle et al., 2016), substance abuse (Dietze et al., 2008) and transition into retirement (Martin et al., 2014). The issue of retirement from competitive sport is an important factor in former professional rugby union

players which may pose a difficult transitioning period, including challenges regarding lack of structure, changes to social support systems and identity, finances, change of occupation and the dwindling of public and media interest (Wylleman et al., 2015). This study highlights sports-specific stressors which impact former players, alongside common stressors which affect the general population at large such as sleep disturbance, alcohol misuse and pain. There is also some evidence to demonstrate that forced retirement from rugby union due to injury is associated with increased symptoms of distress (Brown et al., 2017). This suggests that physical sequelae of playing and retiring from professional sport may contribute to depression burden in former athletes regardless of sport.

Various 'exit from elite sport' interventions and strategies have been suggested and piloted in professional football players to address issues such as mental health and transitioning from elite sport (Gouttebarge et al., 2018). Such interventions are increasingly being put in place for retired elite rugby players, often incorporating preventative aspects (e.g. supporting players to expand their identity beyond sport whilst still playing) as well as reactive mental health supports. This study evidences the need for these interventions. Alcohol misuse in former retired professional rugby union players requires further investigation. Reasons for this adverse lifestyle behaviour may include difficulty in transitioning from a career in professional rugby, loss of identity and pain and disability burden. The literature suggests that the prevalence of symptoms of distress, sleep disturbance, anxiety and depression may be higher in current athletes than in former athletes due to sport-specific pressure during an elite sporting career (Gouttebarge et al., 2019). Therefore, results from this study are likely not generalizable to current players who should be evaluated under a different context. Investigation into potential factors associated with increased risk for symptoms of mental health disorders may allow rugby union player's associations identify and monitor players at risk and encourage early engagement in support and transitioning programmes.

7.6 Limitations

The main limitation of this study is the reliance on self-reported cross-sectional data. Therefore, findings indicate the need for further investigation and are not clinically diagnostic of mental health disorders. Mental health disorders are diagnosed according to strict criteria, such as in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (Regier et al., 2013). Mental health symptoms are more common and may not meet specific diagnostic criteria or necessarily cause significant distress or functional impairment. Furthermore, the majority of scales used in this study were originally developed and validated in general populations other than elite athletes. Additionally, this study largely focused on former male rugby union players and former male international rowers. All efforts were made to include females in the current study. However, there was limited uptake, possibly due to smaller population and the relatively recent upsurge in women's rugby. This should be considered for future studies. Measures of depression used in this study were formed on populations who experience average levels of pain and disability. Given the higher incidence of physical injury for the rugby playing cohort and the higher reported levels of pain it may be that depression scales that acknowledge these factors may be more suited (e.g. the Hospital Anxiety and Depression scale).

7.7 Conclusion

This study found that retired professional rugby players are an at-risk demographic for experiencing mental health issues due to a combination of factors, including those which are unique to the elite athlete. These sport-specific stressors, alongside common stressors which affect the general population, make former professional rugby players vulnerable to substantial prevalence of mental health symptoms and disorders.

Chapter 8 An assessment of neurocognitive functioning in retired professional rugby union players with a history of concussion; a cross-sectional study.

8.1 Introduction

Rugby union is a popular international collision sport, with an estimated over eight million people participating in rugby worldwide at varying levels including junior, amateur, elite and professional (King et al., 2019). The incidence of concussion in rugby is high, with recent rates of 15.8 concussions per 1000 contact hours among professional rugby reported by the English Rugby Football Union (RFU, 2017). Rafferty et al. (2019) reported that on average, a professional rugby union player is more likely than not to sustain a concussion after 25 matches. These estimates are higher than previously reported (Hollis et al., 2009, Hootman et al., 2007, Kemp et al., 2008) and are recognised as one of the highest rates of concussion of all full-contact sports (Gardner et al., 2014b). Furthermore, given that rugby is a high-intensity collision sport, repetitive head impacts are commonplace (King et al., 2017). Exposure to multiple concussions or cumulative head impacts associated with contact sports may increase the risk of subsequent development of neurocognitive impairment or neurodegenerative disorders in some athletes later in life (Manley et al., 2017a, McAllister and McCrea, 2017).

Despite the burden of concussion in rugby being high (Gardner et al., 2014b, Roberts et al., 2016), there is a dearth of research regarding the long-term cognitive effects of repeated concussion or repeated head injuries in rugby, with the evidence to date being mixed (Cunningham et al., 2018). Self-reported cognitive issues such as memory complaints associated with concussion exposure have been reported among retired rugby players

(Thornton et al., 2008). Hume et al. (2017) reported decreased processing speed and cognitive flexibility in former rugby players (elite and community) compared to non-contact sport athletes. However, few studies have objectively investigated long-term cognitive health beyond standard psychometric assessments in retired rugby players with a history of concussion (Pearce et al., 2018). Further, there is limited exploration of the long-term cognitive functioning of former rugby players across the variety of cognitive domains. The majority of studies have focussed on tests of self-reported memory (Decq et al., 2016, Thornton et al., 2008, Gardner et al., 2017, Lewis et al., 2017), to the exclusion of domains such as attention, perception and visuospatial and psychomotor function.

Therefore, the primary aim of this study was to

i) investigate cognitive functioning in the domains of attention, psychomotor speed, memory and executive function using the standardized tasks from the Cambridge Neuropsychological Test Automated Battery in retired professional rugby players (RUG) compared to a non-contact sport control group (ROW).

The secondary aim of the study was to

i) investigate whether concussion history estimates or exposure to head impacts among the rugby players may influence performance on the CANTAB.

8.2 Methods

The current cross-sectional explorative study was conducted as part of the 'PROP' project and was conducted between August 2018 and June 2019 [See chapter 4; Section 4.5] for detailed methodology and details of ethical approval). The 'Strengthening the Reporting of Observational studies in Epidemiology' (STROBE) guidelines for reporting observational studies were used as a template in shaping this chapter (von Elm et al., 2007). Detailed

information regarding participants, recruitment, eligibility criteria, assessment protocol and ethical approval for 'PROP' is described in detail in Chapter 4.

8.2.1 Stimuli and Apparatus

8.2.1.1 Demographics, Medical and Sporting History

Organized professional sport history, medical, occupational and demographic information such as age, sex, marital status and highest level of education, were obtained using the Retired Professional Athletes Questionnaire (RPAQ) specifically designed for the PROP study [See Chapter 4; Section 4.7.1].

8.2.1.2 Concussion History

Concussion history was gained form each participant using the Michigan Traumatic Brain Injury Identification Method [See Chapter 4; Section 4.7.2] (Broglio et al., 2018). Prior to completing the Michigan TBI Identification Method questionnaire, participants were supplied with a written copy of the definition of concussion based on the most up to date guidelines; the 5th Consensus Statement on Concussion in Sport (McCrory et al., 2017). Estimation of concussion history was then used to explore the relationship between sports-related concussion and performance on the CANTAB and SIFI tests.

8.2.1.3 Pre-Morbid Intelligence (IQ)

An estimate of premorbid intelligence was gained from all participants using the full-scale intelligence quotients obtained by the National Adult Reading Test (Nelson, 1991) [See Chapter 4; Section 4.13]. This was deemed necessary to rule out any statistical between group differences in estimated intellectual functioning which may account for differences in

cognitive or perceptual ability. Full-scale intelligence quotient (FSIQ) was calculated by testing reading ability of phonetically irregular words (Nelson, 1991).

8.2.1.4 The Cambridge Neuropsychological Test Automated Battery (CANTAB)

Cognitive health was examined using the Cambridge Neuropsychological Test Automated Battery (CANTAB); a nonverbal visuospatial stimulus battery that employs touchscreen technology to obtain nonverbal responses from participants. Six subtests were selected in line with Cambridge Cognition Consultancy recommendations for mild traumatic brain injury [Table 8-1]. Descriptions on each subtest scoring is provided in Table 8-2. These subtests are described in detail in Chapter 4, Section 4.11.

The battery of tests employed included assessments of:

i) Psychomotor function: Motor Screening Task (MOT)

ii) Processing speed: Reaction Time (RTI)

iii) Sustained attentional processes: Rapid Visual Information Processing (RVP)

iv) Episodic memory: Paired Associates Learning (PAL)

v) Spatial working memory and executive function: Spatial Working Memory (SWM)

vi) Visuospatial working memory capacity and executive function: Spatial Span (SSP)

Table 8-1 CANTAB Test and Corresponding Cognitive Domain.

CANTAB Test	Cognitive Domain
Motor Screening Task (MOT)	Psychomotor Function
Reaction Time (RTI)	Attention
Paired Associates Learning (PAL)	Memory
Spatial Working Memory (SWM)	Memory
Spatial Span (SSP)	Executive Function
Rapid Visual Information Processing (RVP)	Attention

Table 8-2 CANTAB Subtest Descriptions.

CANTAB subtests	Description
MOT Mean Latency (MOTML)	Mean latency to correctly respond to the stimulus on screen, measured in milliseconds[*].
RTI Median Five Choice (RTIFMDRT)	Median duration to release a response button after the presentation of a target stimulus. Measured in milliseconds. A higher score indicates poorer performance on the task. [*]
RTI Median Five Choice Movement Time (RTIFMDMT)	Median time taken to release a response button and select a target stimulus after it flashes yellow on screen. Measured in milliseconds. [*]
PAL First Attempt Memory Score (PALFAMS)	The number of times the correct box is chosen on first attempt when recalling the pattern locations. [+]
PAL Total Errors Adjusted (PALTEA)	The number of times the incorrect box is chosen for a stimulus. [*]
SWM Between Errors BE468 (SWMB468, SWMBE4, SWMBE6, SWMBE8)	The number of times a box is incorrectly revisited in which a token has previously been found. Calculated across all assessed four, six and eight token trials. [*]
SWM Strategy (6-8 Boxes)	The number of times a new search pattern is begun from the same box started with previously. [*]
SSP Forward Span Length (SSPFL)	The longest sequence of boxes successfully recalled. [+]
RVP A Prime (RVPA)	The signal detection measure of sensitivity to the target sequence. [+]

RVP Probability of False Alarm (RVPPFA)	The number of sequence presentations that were false alarms divided by the number of sequence presentations that were false alarms plus the number of sequence presentations that were correct rejections. *
RVP Median Response Latency (RVPMDL)	Median response latency on trials where the subject responded correctly. *

*A higher score indicates poorer performance on the task.

+ A higher score indicates a better performance.

8.3 Statistical Analysis

Statistical analyses were performed with SPSS for Windows version 26 (IBM, Armonk, New York, USA) statistic software package and R version 3.6.0 with package lme4. For all analyses, $p < .05$ (two-tailed) was taken as statistically significant. Distributions were analysed for violation of the assumptions of normality using the Shapiro-Wilk normality test (with a $p > .05$ indicative of normal distribution). Visual inspection of Q-Q plots and histograms was performed. Descriptive statistics of participant characteristics were reported as mean (SD) or median (IQR), as appropriate. For the analysis, between-group differences between RUG and ROW were analysed. Group differences were examined by independent samples t-tests for normally distributed variables. Independent samples Mann-Whitney U tests were used to assess non-parametric continuous variables. Further exploration of the data was performed in the form of a Principal Components model-based clustering analysis. CANTAB scores were analysed in multivariate model. This analysis grouped the CANTAB scores into similar groups. Pearson product-moment correlation coefficient (r) and Spearman Rank Order Correlation (rho) were used as appropriate to identify whether cognitive performance on the CANTAB was associated with concussion history estimates or concussion exposure estimates in addition to visual evaluations of histograms and normal Q-Q plots of residuals. Regression analyses were used to explore the associations and predict the relationship between cognitive performance and function and concussion estimates and concussion exposure estimates.

8.4 Results

8.4.1 Participant Characteristics

Twenty-eight retired international rowers (21 male, 7 female) and 68 retired professional rugby union players (59 male, 8 male) volunteered to take part in the study. Descriptive statistics are provided in Table 8-3. The mean age of the control sample (ROW: 43.89, SD (9.18)) was significantly older than the rugby mean age (RUG: 39.13 SD (5.61); p = .015). Control measure analyses revealed that there was no significant difference in Full Scale Intelligence Quotient (FSIQ) between the two groups (RUG: 114.08, SD (4.74)) and the control sample (ROW: 113.21, SD (8.05); p = .883). Estimates of premorbid intelligence were found to be within the average domain (Nelson, 1991). The mean duration of engagement in professional rugby (RUG: 9.23 years SD (4.46)) was not statistically different to the mean duration of participation in international rowing among the controls (ROW: 7.62, SD (5.46); p = .080). In terms of concussion history, the control group had significantly less self-reported concussions (Mean 0.54, SD (1.14)) than the rugby group (Mean 6.79, SD (10.23)); p <.001.

Table 8-3 Characteristics of RUG and ROW groups across Age, Estimates of Pre-Morbid Intelligence, Number of Years in Sport and Concussion History (mean, standard deviation in parenthesis).

	RUG (n=68)	**ROW (n=28)**	**p-value**
Age	39.13 (5.61)	43.89 (9.18)	**.015**
No. of lifetime concussions[+]	6.79 (10.23)	0.54 (1.14)	**<.001**
No. of years participating professionally/internationally	9.23 (4.46)	7.62 (5.46) [**]	.080
No. of years participating at any level	23.27 (7.51)	22.14 (9.36) [*]	.545
NART FSIQ	114.08 (4.74) [*]	113.21 (8.05) [**]	.883

[*] Two players missing, [**] Four players missing, [+] diagnosed/non-diagnosed concussions included

8.4.2.1 Neurocognitive Performance on the CANTAB

Principal Components model-based clustering analysis did not reveal any correlation between concussion history and performance on any of the CANTAB subtests. Number of years played professional rugby (exposure to contact-sport) which was used as a proxy for head impact exposure was not associated with performance. Analyses revealed group differences in the domains of attention, psychomotor speed and executive function. Retired rugby players performed significantly better across motor speed, reaction time, rapid visual processing task and spatial span tasks. Results are displayed in Table 8-4. The rugby players had significantly quicker motor skills than the rowers ($p = .012$); measured as the mean latency to correctly respond to the stimulus on the screen. Visuomotor reaction times showed that rugby players were significantly quicker in both reaction time to the stimulus ($p = .010$), and movement time ($p = .012$) to the stimulus [Figure 8-1-2 and 8-1-3]. Performance on the rapid visual processing task also revealed significant between group differences on one test. Former rugby group were significantly better at detecting the correct target sequence on the RVPA task ($p = .019$) [Figure 8-1-6]. On the Spatial Span task, rugby players were significantly better than the controls at recalling longer sequences of boxes successfully ($p = .003$) [Figure 8-1-14]. All of the remaining CANTAB cognitive measures revealed no significantly difference between groups in performance.

Table 8-4 Cognitive Performance on the CANTAB across RUG and ROW groups (mean, standard deviations in parenthesis).

CANTAB Subtests	**RUG (n=68)**		**ROW (n=28)**		**p-value**
	Mean (SD)	Median (95% [CI])	Mean (SD)	Median (95% [CI])	
Motor Screening Task (MOT)					
MOT Latency (ms)	724.11 (156.19)	675.8 [686.30, 761.91]	867.43 (275.37)	819.65 [760.65, 974.20]	**.012**
Reaction Time Task (RTI)					
RT Selection Latency (ms)	227.69 (55.44)	227.25 [214.27, 241.11]	264.14 (73.94)	263.5 [235.47, 292.81]	**.010**
RT Release Latency (ms)	348.80 (30.28)	343.25 [340.01, 354.85]	365.11 (31.50)	365 [352.89, 377.32]	**.012**
Paired Associates Learning (PAL)					
PAL Total Errors (adjusted)	9.49 (8.00)	8.5 [7.55, 11.42]	10.89 (8.81)	9 [7.48, 14.31]	.513
PAL Total Attempts	14.12 (3.48)	14.00 [13.27, 14.96]	13.93 (2.85)	14.00 [12.82, 15.04]	.805
Spatial Working Memory (SWM)					

SWM Strategy	6.54 (2.64)	7.00 [5.91, 7.18]	6.79 (3.16)	7.00 [5.56, 8.01]	.629
SWM Between Errors 4 Boxes	0.47 (1.01)	0.00 [0.23, 0.72]	0.61 (1.10)	0.00 [0.18, 1.03]	.449
SWM Between Errors 6 Boxes	2.57 (3.19)	1.00 [1.80, 3.35]	3.00 (3.44)	2.00 [1.67, 4.34]	.614
SWM Between Errors 8 Boxes	6.19 (6.09)	6.00 [4.72, 7.66]	6.54 (6.05)	7.50 [4.19, 8.88]	.780
SWM Between Errors	8.84 (8.37)	9.00 [6.81, 10.86]	8.71 (8.00)	7.50 [5.61, 11.82]	.909
Rapid Visual Processing (RVP)					
RVP Median Response Latency (ms)	431.93 (58.50) **	420.00 [417.44, 446.43]	458.48 (118.87)	432.50 [412.39, 504.58]	.253
RVP Probability of False Alarm	0.00 (0.01) *	0.00 [0.00, 0.01]	0.01 (0.01)	0.00 [0.00, 0.01]	.596
RVP A' A' (A prime)	0.94 (0.037) **	0.95[0.93, 0.95]	0.92 (0.05)	0.92 [0.90, 0.94]	**.019**
Spatial Span (SSP)					
SSP Forward Span Length	7.28 (1.34)	7.00 [6.96, 7.60]	6.43 (1.20)	6.00 [5.96, 6.89]	**.003**

* 2 players missing, ** 3 players missing.

8.4.2.2 Box and Whisker plots for the retired rugby (RUG) and retired rowing (ROW) groups across CANTAB measures.

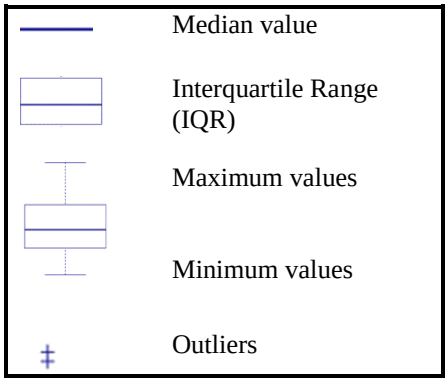


Figure 8-1 *Box and Whisker Plot Key.*

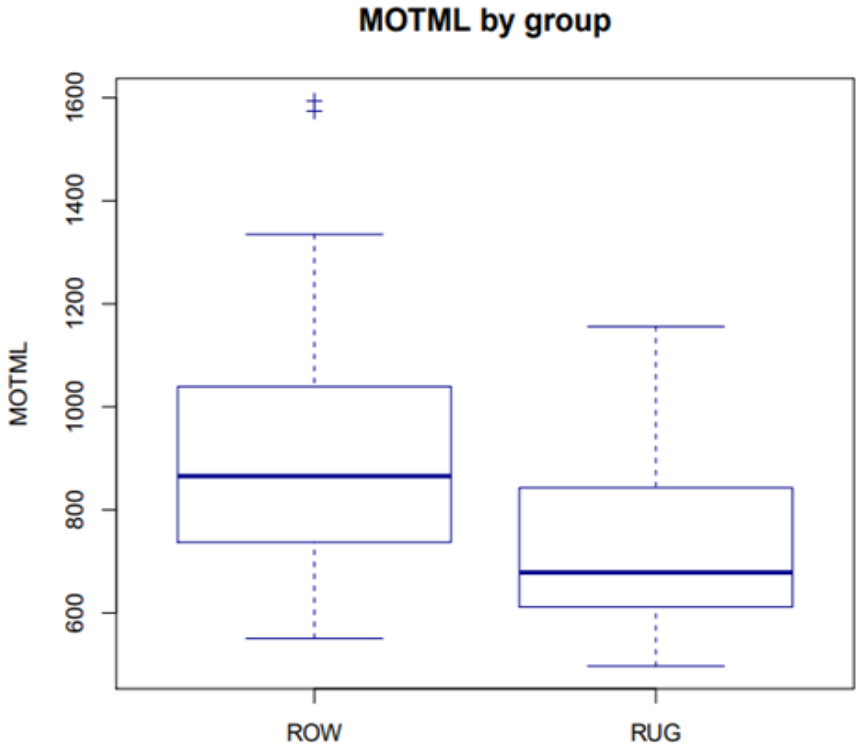


Figure 8-1-1 *Motor Screening Task Mean Latency: MOTML.*

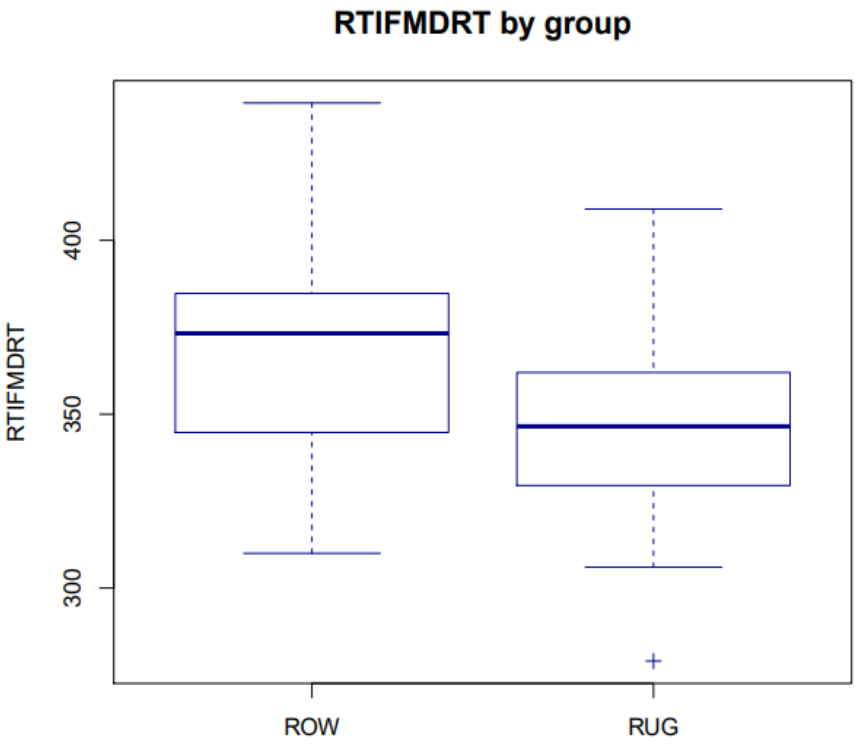


Figure 8-1-2 *Reaction Time Median Five Choice Reaction Time: RTIFMDRT.*

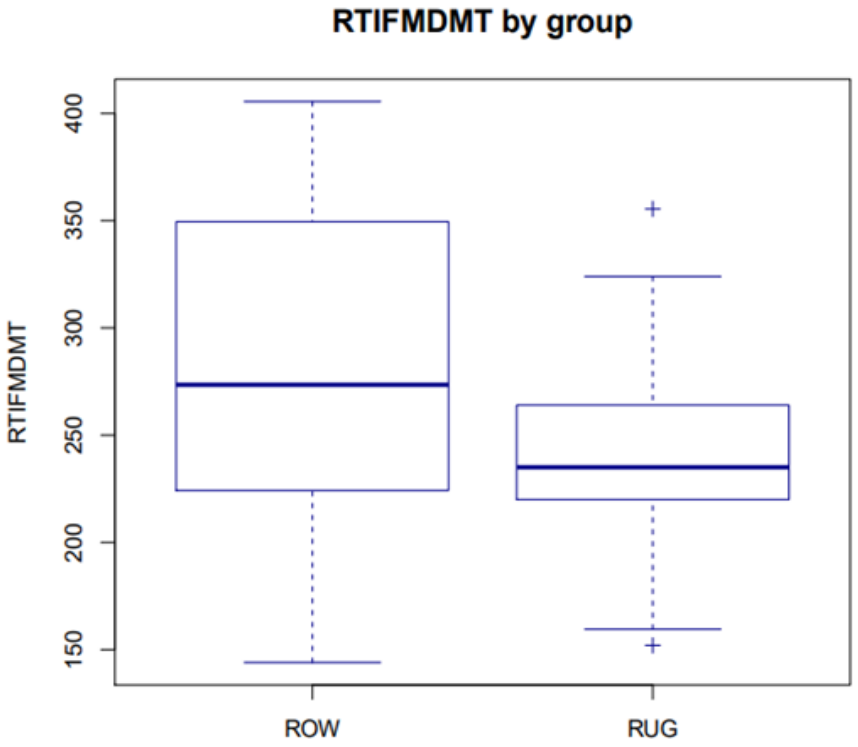


Figure 8-1-3 *Reaction Time Median Five Choice Movement Time: RTIFMDMT.*

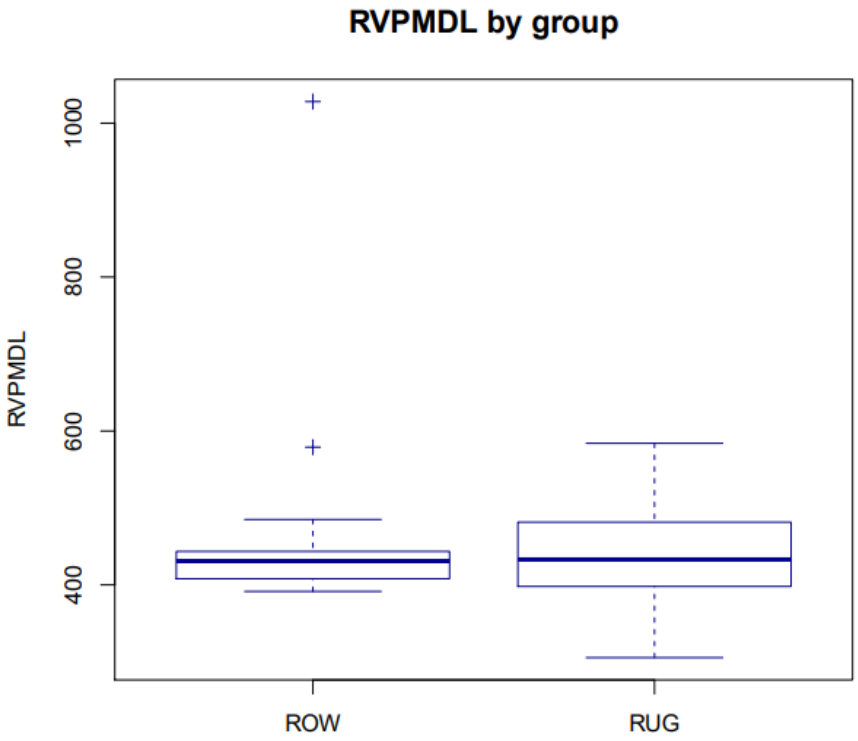


Figure 8-1-4 *Rapid Visual Processing Median Response Latency: RVPMDL.*

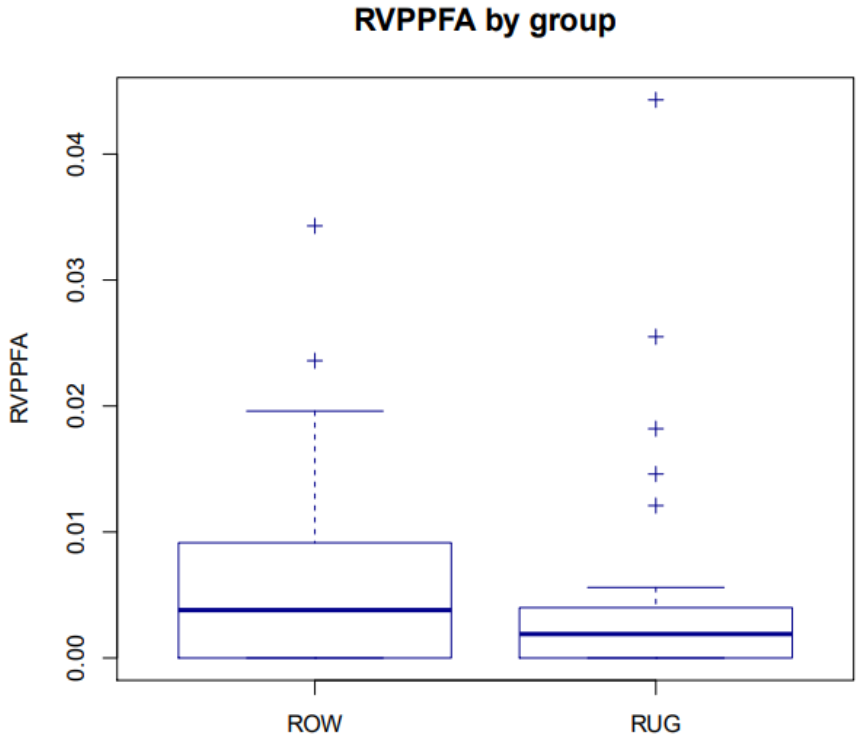


Figure 8-1-5 *Rapid Visual Processing Probability of False Alarm: RVPPFA.*

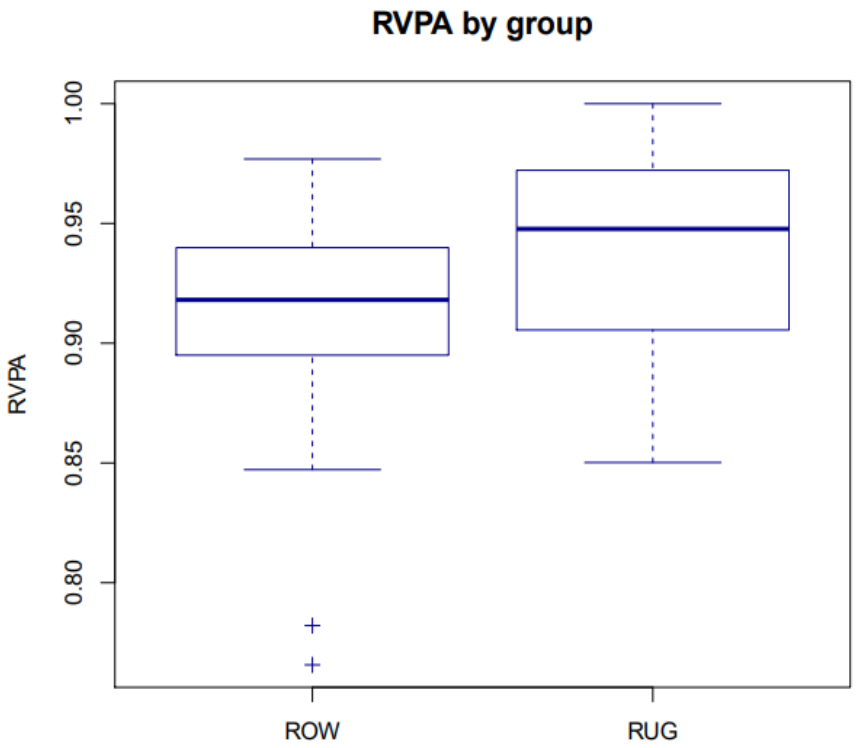


Figure 8-1-6 *Rapid Visual Processing A' (A prime): RVPA.*

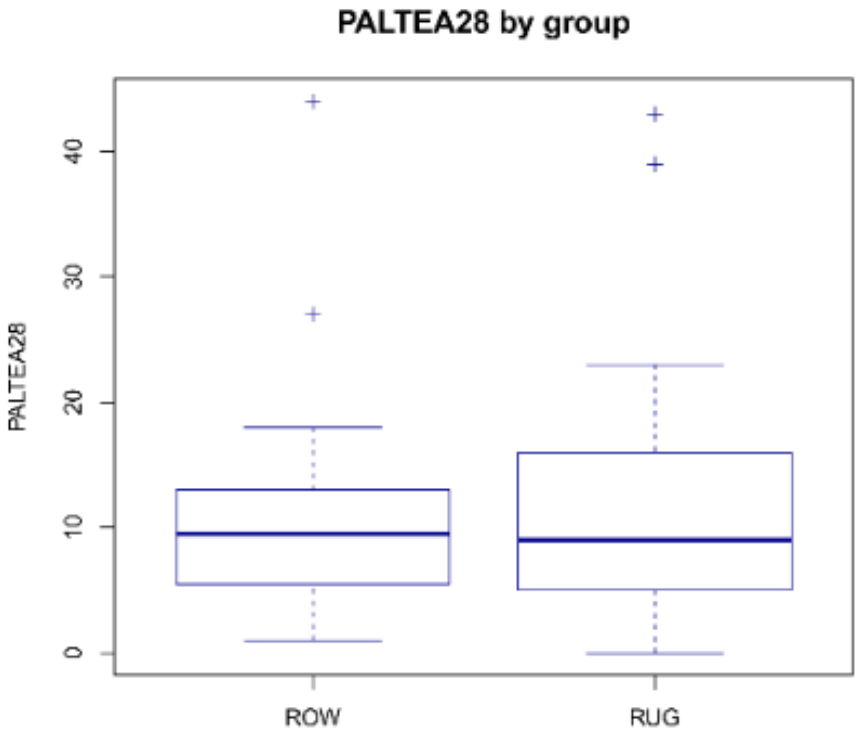


Figure 8-1-7 *Paired Associates Learning Total Errors (adjusted): PALTEA28.*

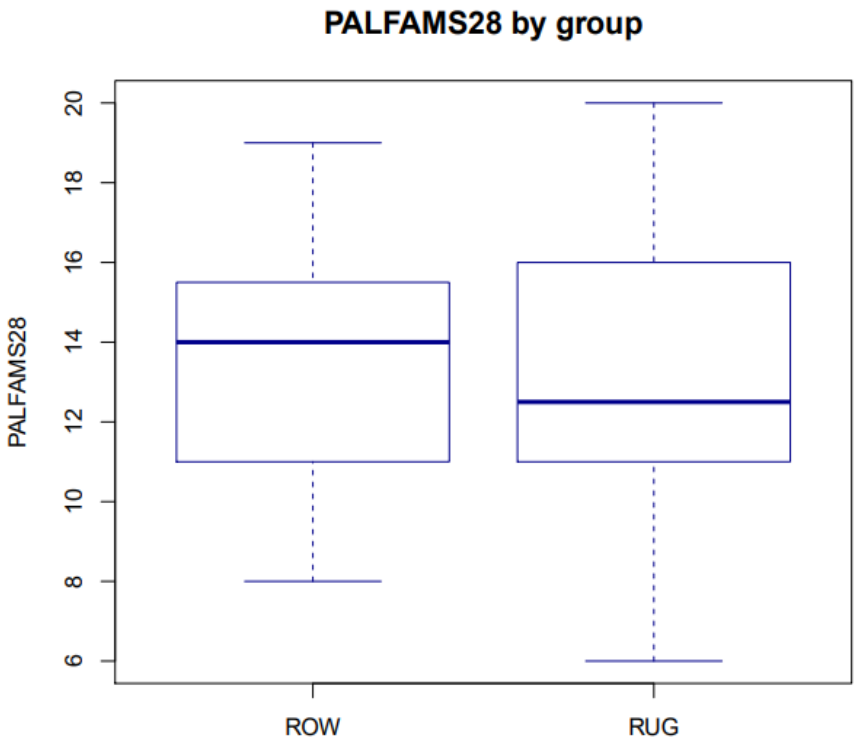


Figure 8-1-8 *Paired Associates Learning First Attempt Memory Score: PALFAMS.*

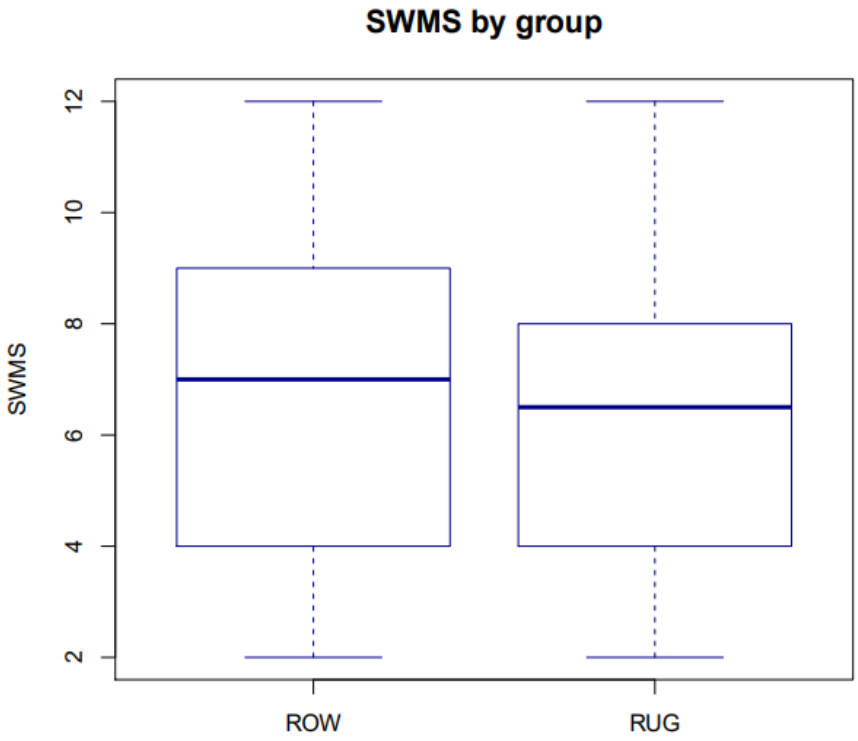


Figure 8-1-9 *Spatial Working Memory Strategy: SWMS.*

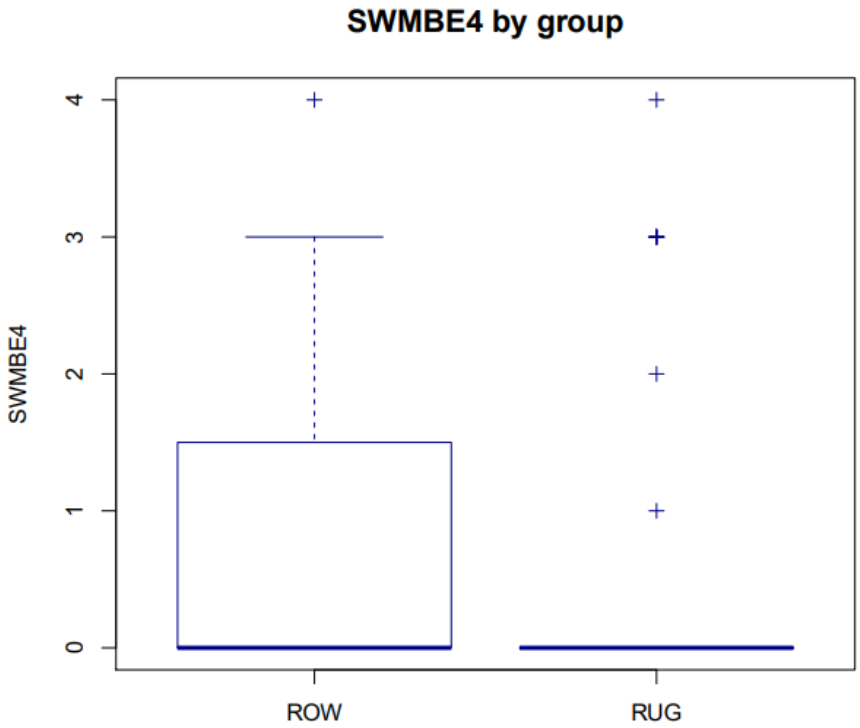


Figure 8-1-10 *Spatial Working Memory Between Errors 4 Boxes: SWMBE4.*

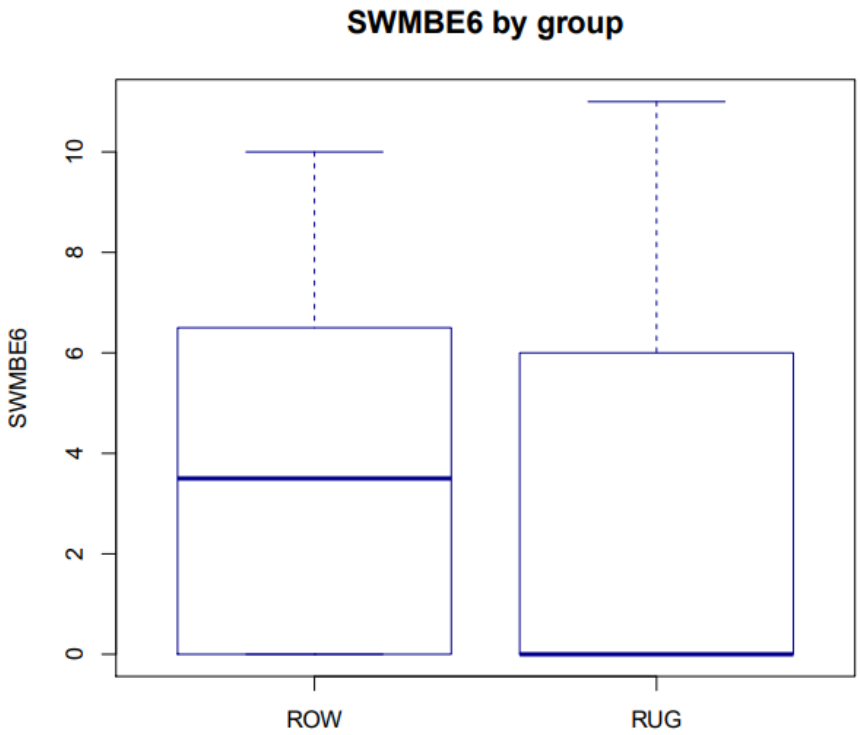


Figure 8-1-11 *Spatial Working Memory Between Errors 6 Boxes: SWMBE6.*

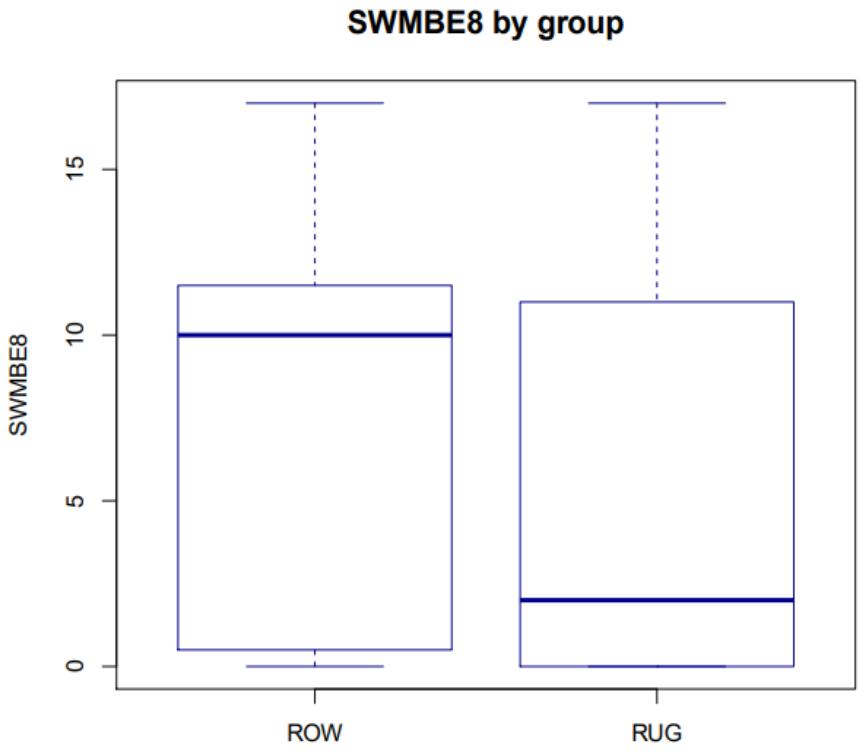


Figure 8-1-12 *Spatial Working Memory Between Errors 8 Boxes (SWMBE8).*

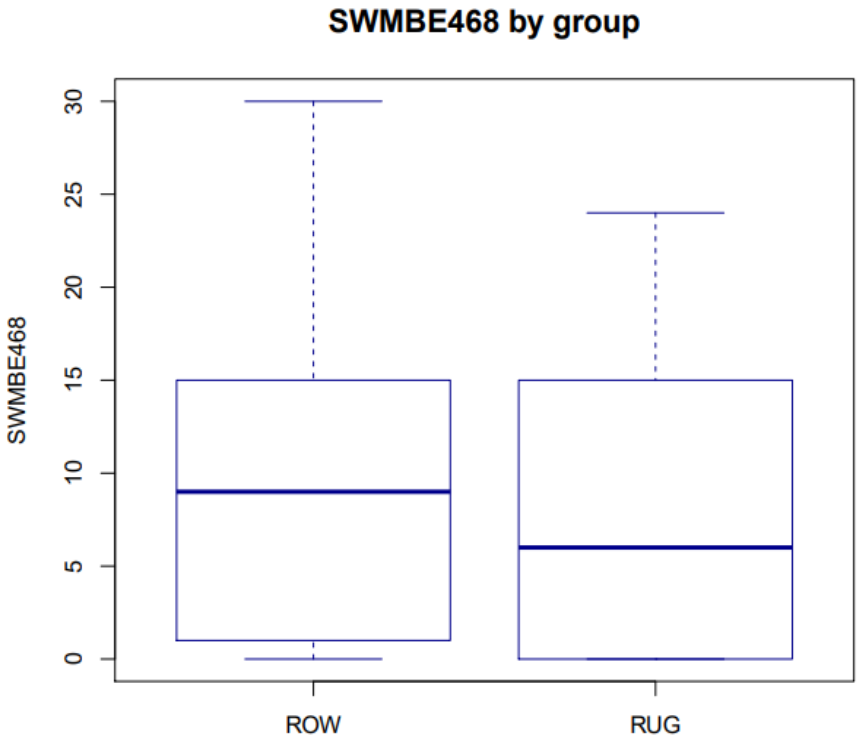


Figure 8-1-13 *Spatial Working Memory Between Errors (SWMBE468).*

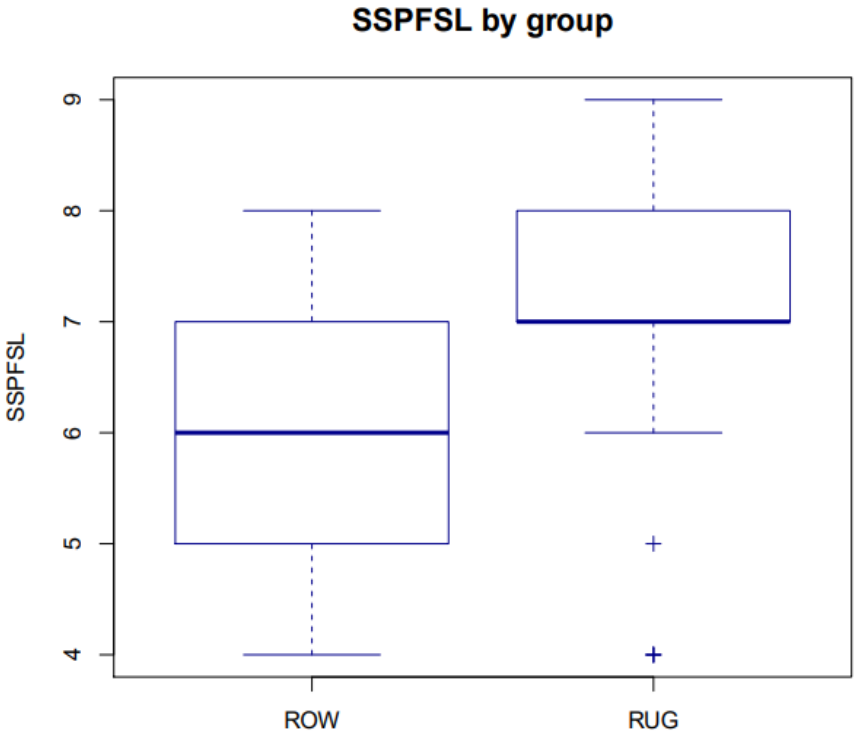


Figure 8-1-14 *Spatial Span Forward Span Length: SSPFL.*

8.4.2.2 Retired professional rugby players (RUG) and control group (ROW) compared to Normative data

As part of the CANTAB software, normative data in the form of z-scores and percentiles were available for selected subtests of different aspects of cognition including; Paired Associates Learning, Spatial Working Memory, Rapid Visual Processing and Spatial Span tests. Measurements were normalized to z-scores which controlled for age and highest level of education. Box and whisker plots are reported below. Normative data for rapid visual processing revealed that rugby players were significantly better at detecting the target sequence on the RVPA task in comparison to the rowers ($p = .006$). Rugby players also performed better than the general population on the RVPA task, whereas rowers performed slightly worse than the general population [Figure 8-2-1]. While there was no significant

between group differences at rejecting incorrect sequences on the RVPPFA task, both cohorts performed better than the general population [Figure 8-2-2]. Paired Associates Learning tasks including the PALTEA and the PALFAMS revealed no significant difference between the rugby and rowing groups on the. In terms of the number of errors on the PALTEA task, rugby players performed better than the general population, while the rowers were in line with the general population [Figure 8-2-3]. However, rugby players were worse than the general population at recalling where the pattern was located and hence choosing the correct box on their first attempt on the PALFAM task [Figure 8-2-4]. Rowers were on par with the general population on the same task. With regard the Spatial Working Memory task there was no significant difference between the two groups based on z-scores. However, rugby players performed worse than the general population on both tasks in terms of number of errors (SWMBE468) and strategy (SWMS) [Figure 8-2-5 and Figure 8-2-6 respectively]. While the rowers performed worse than the general population in the SWMBE468 task only. The Spatial Span task revealed rugby players were better at detecting longer sequences of boxes on the (SSPFL task) compared to the rowers (p = .005). Rugby players also performed better than the general population on this task, while the rowers performed worse than the general population [Figure 8-2-7].

8.4.2.3 Box and Whisker plots for RUG and ROW Z-scores across selected CANTAB measures

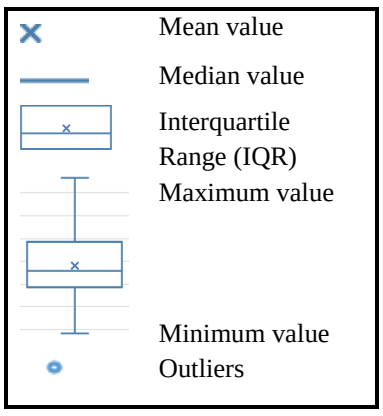


Figure 8-2 Box and Whisker Plot Key.

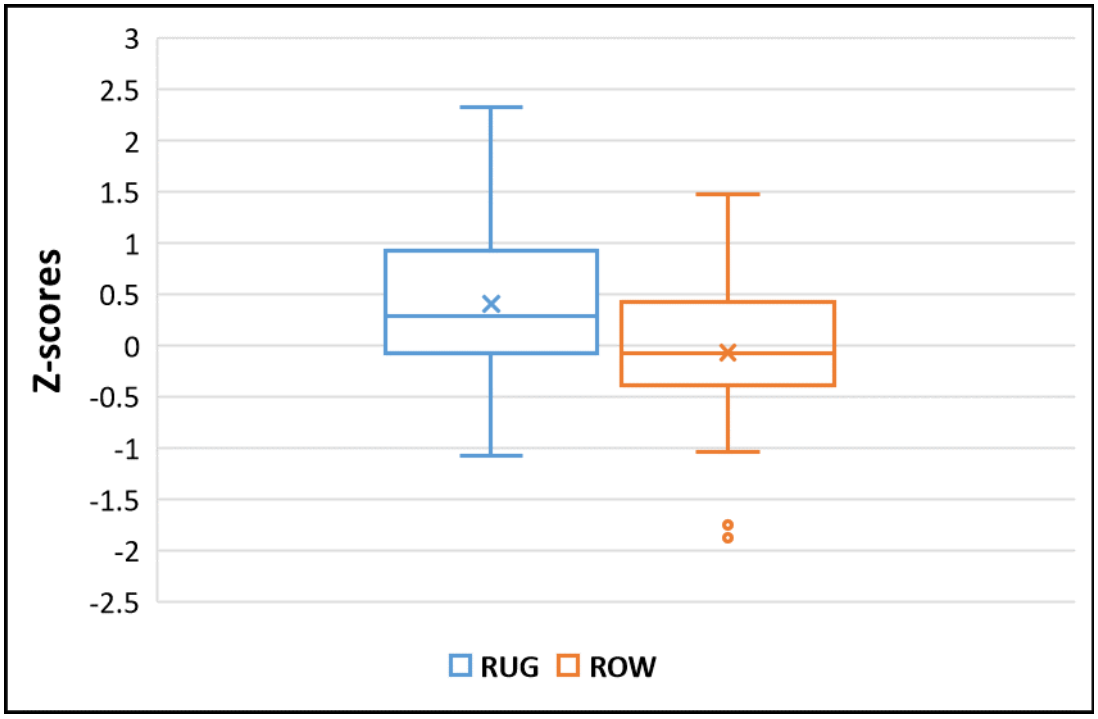


Figure 8-2-1 *Rapid Visual Processing A' (A prime): RVPA.*

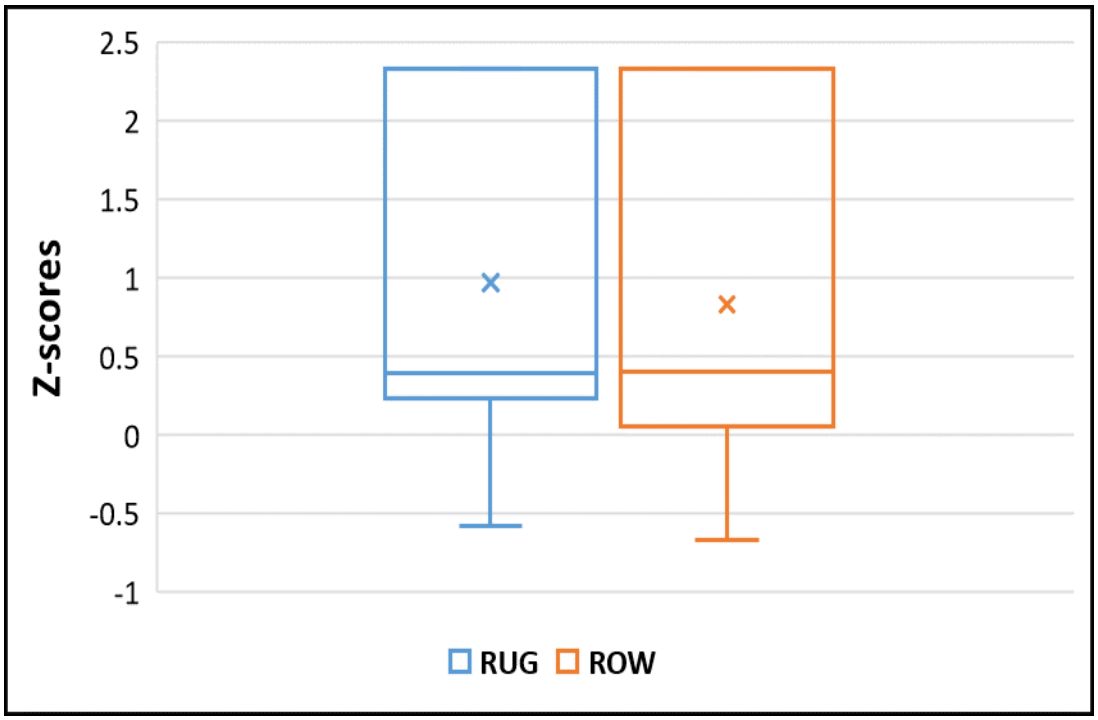


Figure 8-2-2 *Rapid Visual Processing Probability of False Alarm: RVPPFA.*

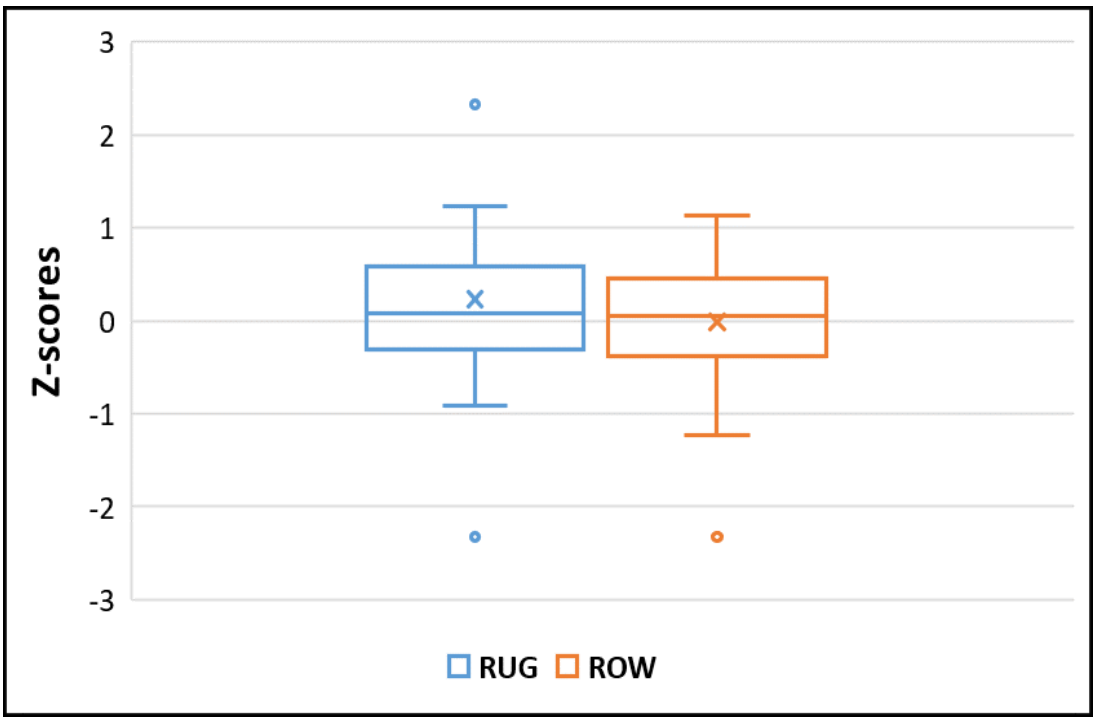


Figure 8-2-3 *Paired Associates Learning Total Errors (adjusted): PALTEA28.*

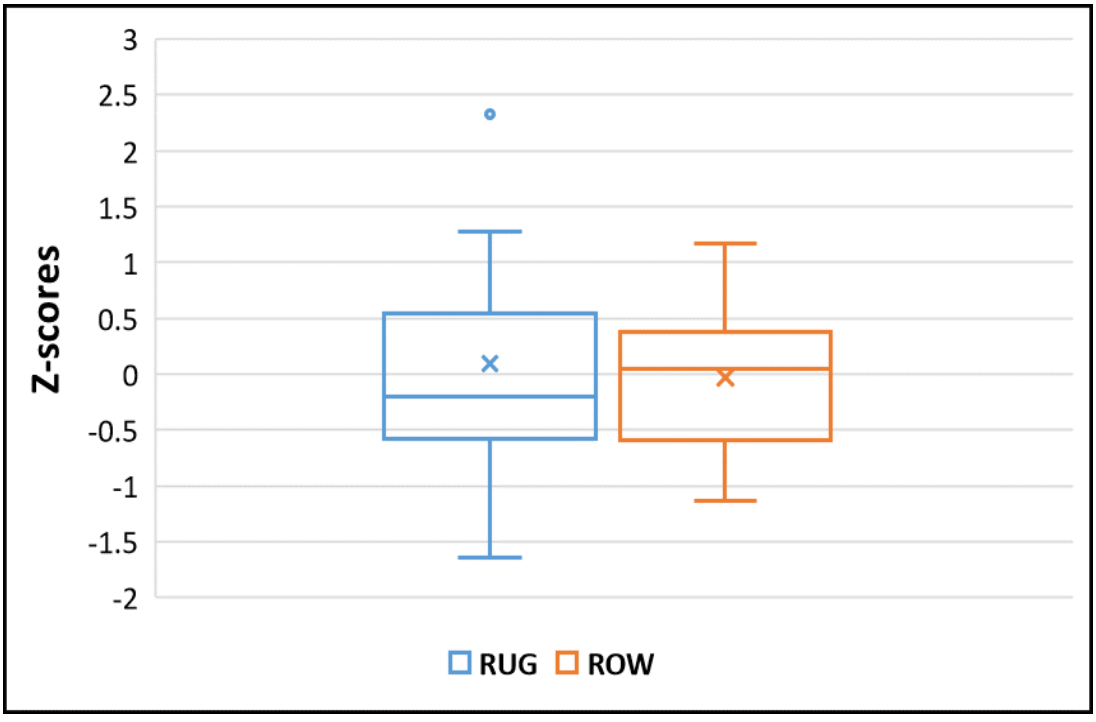


Figure 8-2-4 *Paired Associates Learning First Attempt Memory Score: PALFAMS.*

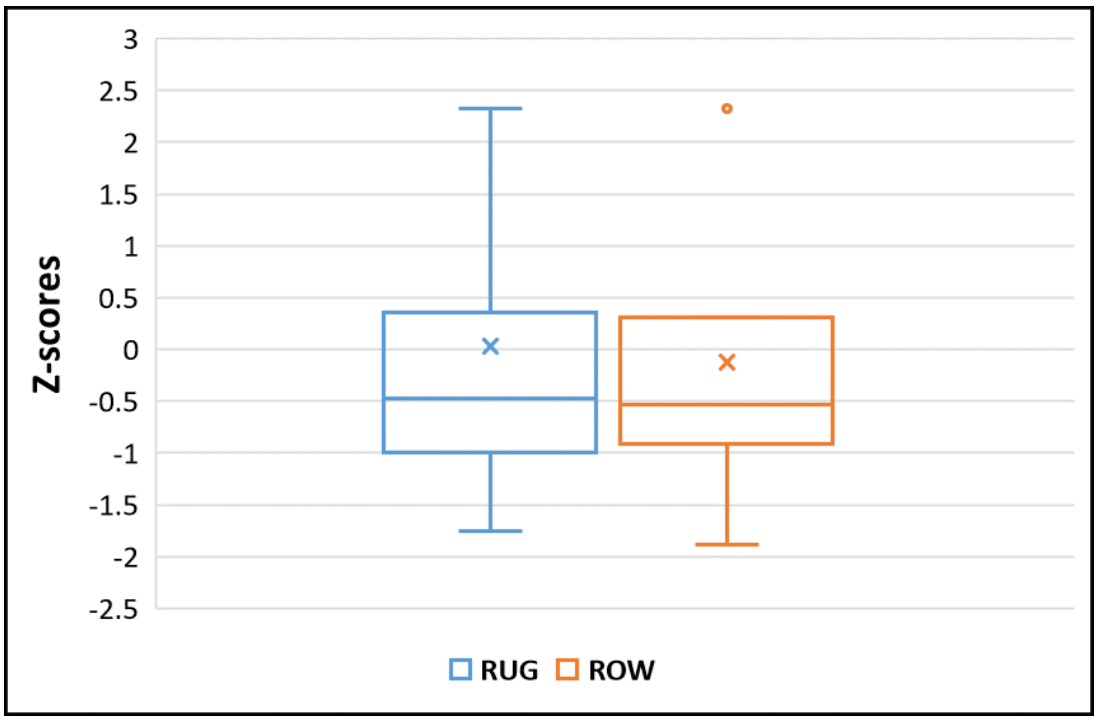


Figure 8-2-5 *Spatial Working Memory Between Errors: SWMBE468.*

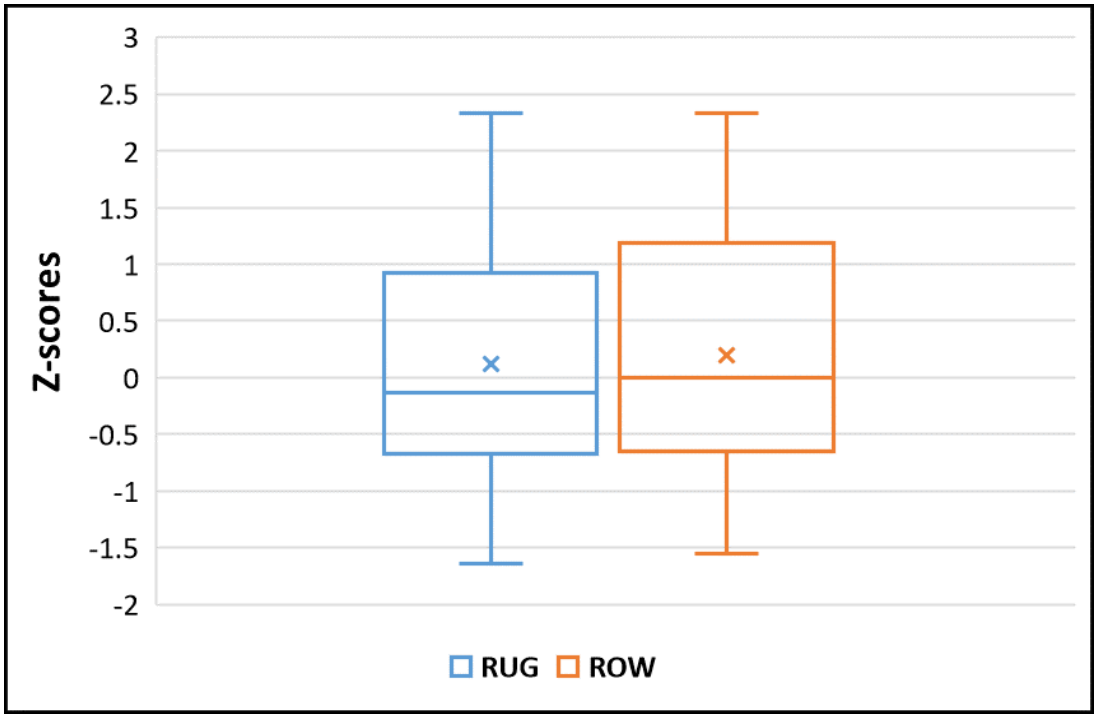


Figure 8-2-6 *Spatial Working Memory Strategy: SWMS.*

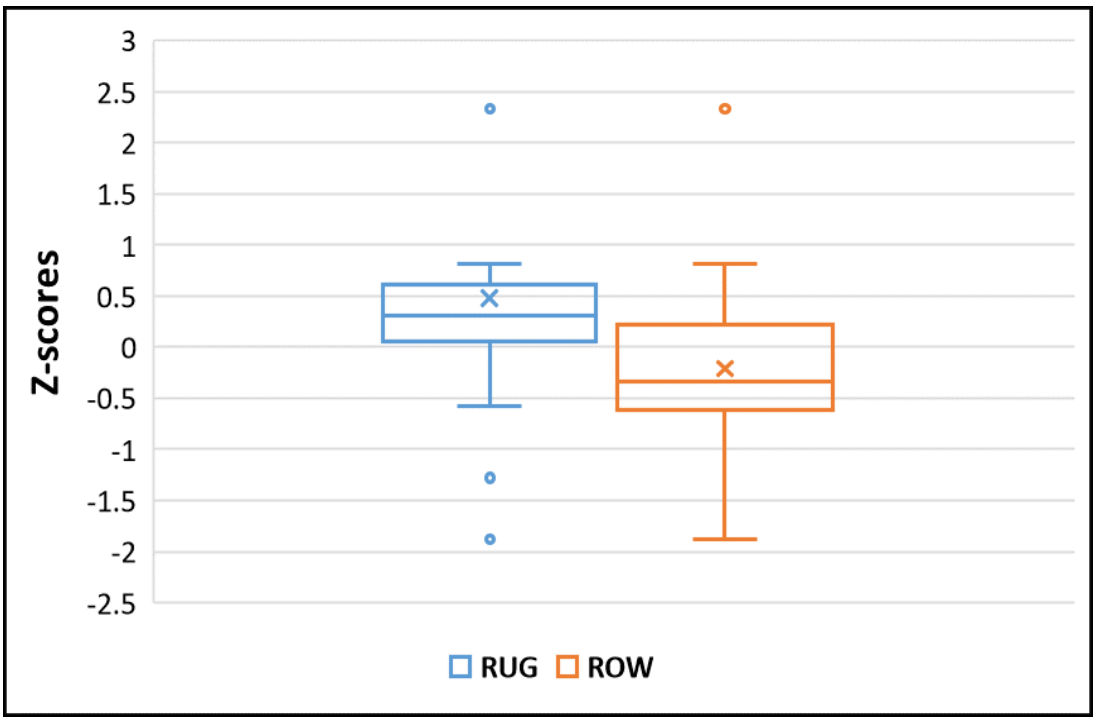


Figure 8-2-7 *Spatial Span Forward Span Length: SSPFL.*

8.9 Discussion

This study provides an insight into neurocognitive functioning among former professional rugby players compared to non-contact controls, (all of whom were in the early stages of retirement from play) by using a standardized battery of neuropsychological measures. The CANTAB provided a variety of assessments across multiple neurocognitive domains (Clark et al., 2012). Our findings suggest that past participation in rugby and related concussion and head impact exposure is not associated with any overt decline in neurocognitive performance. Rugby players outperformed rowers in tests of visuomotor reaction time, motor speed, processing speed and visuospatial working memory. Furthermore, concussion history or number of years playing rugby were not correlated with performance. Alterations to the corticomotor system have been described as one of the earliest clinical manifestation of chronic repetitive head impacts which precedes cognitive decline, therefore psychomotor

tests may be important early indicators of long-term effects of concussion (Rabadi and Jordan, 2001). The current findings conflict that of Pearce et al. (2018) who reported decreased dexterity and slower visuomotor reaction time among former rugby players compared to controls.

Execution of the skills required in the game of rugby, particularly at the professional level, necessitate highly developed and finely-tuned psychomotor skills particularly in certain playing positions. It is therefore perhaps unsurprising that the rugby group displayed significantly quicker reactions when compared to rowers given the fast-paced competitive environment in which the game of rugby is played. Hence between group differences observed may be attributable to this. Quicker visuomotor reaction time has been demonstrated in athletes compared to non-athletes (Nakata et al., 2010, Yarrow et al., 2009). This has been postulated to be due to functional and structural neuroplastic adaptations in the central nervous system (Hülsdünker et al., 2018), which may occur due to the acquisition and repetition of motor-related skills and higher cognitive processing such as decision making and reaction to stimuli (Power and Schlaggar, 2017, Nakata et al., 2010, Sekiguchi et al., 2011). Rugby players are required to be highly efficient in motor response and inhibition throughout a training or match period. Automatic cognitive activation or suppression of motor actions could have knock on effects on future tackles, kicking or scores. Thus, sustained attention, processing speed, reaction times are arguably critical to the game. Further, such complex cognitive demands are placed on rugby players in a fast-paced competitive environment and require processing of information, reactions and physical execution of goals in an extremely time-dependent manner.

The enhanced performance on rapid visual processing among the former rugby players supports a previously described strategy among rugby players of taking a 'bird's eye view' (Sekiguchi et al., 2011). When controlling for age and highest level of education, results revealed that rugby players performed better than the general population on the rapid visual processing speed tasks, while the rowers also performed better than the general population

on one of the rapid visual processing tasks; the RVPPFA task, but not the RVPA task. This may suggest that participation in sport at an elite level, regardless of whether it is contact or not, may enhance motor, reaction and processing speed to some extent. However, given that the rugby players performed significantly better than the rowers on one of task (RVPA) and outperformed the general population on both tasks it is likely that this adaptation is influenced by the unique training regimes specific to the two sports. These findings are contrary to results from Hume et al. (2017), in which former elite rugby players were reported to have performed worse on tests of processing speed when compared to a non-contact-sport. Rugby players also performed significantly better than the rowers and the general population on the spatial span task. While the rowers performed worse than general population on this task. This may be explained when comparing the sport of rowing and rugby. During play, rugby players are consistently required to be aware of and retain knowledge of the visuospatial conditions around them, which then enables them to tactically manipulate their current environmental conditions for the advancement of themselves and their team (Furley and Memmert, 2012). Rowers on the other hand, require much less developed visuospatial skills to perform. Hence, better visuospatial skills on the spatial span task may be derived from years of training in these cognitive environments. The spatial span task results also suggest that contact sports may enhance visuospatial skills more so than non-contact sports.

While there was no significant between group differences found on tests of memory, both groups performed poorly on certain subtests; namely the Paired Associates Learning; First Attempt Memory Score and the Spatial Working Memory; Strategy and Between Errors Tasks. The rugby groups' performance on all three tasks was below the general population. Despite the poorer results in the memory domain among the rugby players, the study failed to yield significant deviations among the rugby group from the non-contact control sample. Further performance on the memory tasks was not associated with player self-reported concussion history estimates or number of years played professional/at any level. The lack of any between group significant differences does not implicate concussion history or

cumulative head impact exposure in this poor memory performance. The current study is positive with regards long-term cognitive effects of concussion, with rugby players outperforming the rowers and the general population on certain CANTAB tests. However, we cannot rule out the potential long-term implications of multiple sports-related concussion on the domains assessed in the CANTAB. There is the possibility that damage from concussions and/or repetitive head impacts may exist, but is masked by the ability to compensate, hence manifestation of previous concussive injury could potentially emerge in older age and accelerate the rate of age-related decline (Broglio et al., 2012). The rugby players were performing below the general population on all three tests of memory. Therefore, this domain would presumably be the most vulnerable to a further decline with an accelerated reduction in cognitive reserve associated with history of concussion.

Superior performance on tests of psychomotor speed, reaction time and spatial span among the rugby players may suggest that cognitive reserve may differentially protect some cognitive domains such as psychomotor speed and visuospatial skills against neuropathology more so than others such as memory. An alternative hypothesis could be that former rugby players are genetically predisposed to a career in sport due to innate superior motor, reaction and visuospatial skills. Hence, they have a greater cognitive reserve in this area to begin with and therefore, potential effects of concussion would be less likely to manifest themselves due to this high starting point. This research particularly regarding the positive findings indicating enhanced functioning in psychomotor and visuospatial function among the rugby players could in turn be used as a basis to explore potential neuroprotective factors associated with engagement in professional rugby. Cognition is known to decrease with advancing age and the onset of decline is associated with cognitive aging over the age of 50 (Stern, 2002). The sample of retired professional rugby players in the current research was significantly younger than the majority of study cohorts on retired athletes who have retired from an active career, the majority of whom are over the age of 50 (Cunningham et al., 2018). This study is therefore informative regarding early onset implications of rmTBI in early retirement. However,

longitudinal follow-up of players would be required as it may be premature to elicit potential long-term effects of a career in professional rugby union in this cohort, on the CANTAB.

8.10 Limitations

Given the retrospective nature of this study, the main limitation was the historical self-reporting of concussion history, which is open to recall bias, hence reducing the reliability of the number of concussions scale. Our method of gaining self-reported concussions which involved a number per player was consistent with previous studies (Pearce et al., 2018). However, the number of self-reported concussions should be viewed with caution and head impact exposure should be considered more in future studies. In the current study we included an up to date definition of concussion based on the latest Concussion Consensus Statement (McCrory et al., 2017). Anecdotally many players found it difficult to recall their concussions. Given the lack of awareness and adequate concussion diagnosis at the time when they played, they struggled to distinguish between concussion and impacts below the concussion threshold. Many players reported below concussion threshold impacts to be a regular feature of every game. Further the non-specific nature of concussion symptomology such as depression, headache, nausea and dizziness were difficult to account for. Given the lack of adequate concussion assessment at the time of the injury, many players reported that concussive injuries were generally overlooked and that they continued to play unless an episode of loss of consciousness occurred. Therefore, it was difficult for the recruited players in this study to provide an accurate diagnostic report and list of their concussion history.

This study benefited from inclusion of a comparison group of athletes which aimed to control for factors that may be associated with competitive team sport. The lack of a sporting control group has been cited as a limitation of many studies to date (McMillan et al., 2017). By

comparing contact and non-contact sport populations, the current study investigated two sporting populations both of which participated at a high level in their respective sports. There is ample evidence to demonstrate that physical exercise affects brain plasticity in turn influencing cognition (Mandolesi et al., 2018, Fernandes et al., 2017). Therefore, it would be interesting to compare these groups to a normative more 'sedentary' non-sporting population. The significant difference in age between the two groups was also a limitation, however, this was largely overcome by the availability of normative data in CANTAB subtests. Variability within the study cohort across numerous factors such as sex distribution, concussion history, lower exposure to training and play, shorter career span in professional rugby and age could have produced potential covarying factors that could not be controlled for in the current research. Given that there was a limited number of females included in the current study, sex differences were difficult to discern. Future studies should encompass investigations into the repercussions of concussions in female players, as sex differences within working memory capacity and other domains have been documented (Dick, 2009, Robert and Savoie, 2006). Further follow-up is required in former rugby players to explore the effects of repetitive head impacts on long-term neurocognitive outcomes.

8.11 Conclusion

Our findings, particularly in the context of the normative data, suggest that among retired rugby players, cognitive processes such as attention; including tests of selective and sustained attention and tests of psychomotor speed; including reaction time, motor release, selection speed and rapid visual processing and visuospatial skills, remain intact despite a career in rugby and exposure to head trauma. While rugby players were worse than the general population on the majority of memory tasks, performance was not associated with concussion history or exposure to contact sport. Therefore, history of concussion does not appear to have had a deleterious effect on the neurocognitive functioning of the professional rugby union players in the early stages of retirement.

Chapter 9 Assessment of multisensory processing in retired professional rugby union players with a history of concussion; a cross-sectional study.

9.1 Introduction

The long-term cumulative effects of sports-related concussion (SRC) are an ongoing concern in contact sports such as rugby. Forwards have been shown consistently to have a higher injury incidence including greater head impact exposure than backs owing to their position (Gissane et al., 1997, Gabbett, 2005, Carey et al., 2019). Failure to accurately diagnose concussion can lead to repeat concussions, increased symptom burden, worsening of the injury and prolonged recovery (Asken et al., 2018, Asken et al., 2016a, Elbin et al., 2016a, Howell et al., 2018). There is evidence of increased risk of long-term consequences including cognitive, neuropsychiatric, and neurodegenerative disorders associated with repeated SRCs (McAllister and McCrea, 2017, Manley et al., 2017b). The Sport Concussion Assessment Tool 5 (SCAT-5), recommended by the Concussion in Sport Group consensus statement, relies on cognitive, balance and symptom evaluation for concussion identification (McCrory et al., 2017). Despite increased awareness and availability of side-line medical assessments, detection and diagnosis remains challenging due to the absence of an objective diagnostic marker of concussion (Broglio et al., 2017a) and limited availability of validation of assessment tools (Harmon et al., 2013b). Diagnosis and assessment of concussion remains guided by a self-reported symptom checklist, which is limited by the intrinsic subjective nature of such tools and the diverse and non-specific nature of concussion symptoms (McCrory et al., 2017). Based on the current clinical evaluation and available tests, a concussed individual typically has a full restoration of clinical functioning within 10-14 days of the concussive injury (McCrory et al., 2017). However, emerging research using more sensitive techniques such as advanced imaging, electroencephalography and event-related

potentials (ERPs) have illustrated subtle persisting deficits associated with concussion, indicating potential chronic cognitive deficits and nervous system dysfunction (Broglio et al., 2011, Bernstein, 2002, De Beaumont et al., 2011, Bazarian et al., 2012, Manley et al., 2017b). Studies employing standard cognitive assessments have largely failed to reproduce findings of cognitive decline across multiple full contact sports populations (Manley et al., 2017b, Cunningham et al., 2020). Therefore, the current battery of tests may be insensitive to persistent subtle deficits associated with concussions. Early detection of a suspected concussion and removal from play is paramount in minimising potential prolonged post-concussion syndrome and long-term sequalae (Elbin et al., 2016b). Therefore, more sensitive clinical tools are required for the diagnosis of acute SRC and monitoring of the concussion recovery time-line and long-term effects (McKeithan et al., 2019). The current battery of tests for concussion does not include an assessment of perception, specifically the ability to process and integrate sensory information, which is essential to execute activities of daily life.

There is a need for investigation into potential early onset precursors of neurocognitive decline and their relationship to cognitive functioning in later life (Thornton et al., 2008). Investigation beyond standard psychometric assessments of higher cognitive functioning is scarce particularly regarding sensory integration within the early processing stream (Shams et al., 2002). Decreased efficiency with age in processing information from different sensory systems can affect perception, behaviours and decision-making (Stein et al., 2009, McGovern et al., 2014). In order to execute activities of daily life, humans have evolved to become adept at processing relevant information in a timely and efficient fashion (Deroy et al., 2016). Multisensory processing involves the integration of information from two or more sensory modalities in the brain (Deroy et al., 2016). Therefore, successful cognitive integration of multimodal stimuli requires combining relevant and inhibiting irrelevant information (Ernst and Bülthoff, 2004, Shams et al., 2002). Although vision is often shown to influence the perception of sound (Bertelson, 1999, Keil, 2020), auditory information is known to have the

ability to alter visual perception (Shimojo and Shams). The Sound Induced Flash Illusion (SIFI) is a fission illusion which enlists both of these sensory domains to induce the illusion, whereby a single visual flash is erroneously perceived as two flashes when paired with two brief auditory tones (beeps) [Figure 9-1] (Shams et al., 2002, Shams et al., 2000b, Hirst et al., 2020). The SIFI is increasingly recognised as a potential tool for measuring multisensory processing efficiency (Keil, 2020) and the fission illusion is thought to have its own temporal integration window, a limited time span to rapidly integrate discrete perceptual events, which is derived from distinct neural processes .

Advancing age is associated with a decline in cognitive functioning (Murman, 2015),and cumulative head impacts are proposed to expedite decline in cognitive functions associated with the normal aging process and hence increase risk of cognitive impairment in some individuals (Broglio et al., 2012). Along with age-related neurocognitive decline, the SIFI task (Shams et al., 2002), has revealed an age-related decline in multisensory integration among older adults (McGovern et al., 2014). Such age-related declines can affect motor and cognitive abilities such as movement, gait, perception, memory and decision-making (Stein et al., 2009, McGovern et al., 2014). Older adults have been shown to be more susceptible to the SIFI even across wide ranges of temporal asynchronies, i.e. manipulation of various timing between onset of stimuli, whereas younger adults have been found to be susceptible only at shorter time intervals (Stapleton et al., 2014, McGovern et al., 2014, Diederich et al., 2008). Multisensory perception has also been shown to be influenced by both traumatic and mild brain injury (Hirst et al., 2020). Among university students, it was revealed that those with a recent history of concussion were less efficient at determining whether multisensory audio-visual events corresponded with the same event, with the temporal binding window being widest in those with recent concussions (Wise and Barnett-Cowan, 2018). Furthermore, another study found that measurement of perceptual-cognitive ability revealed a negative impact of acute concussion on processing and learning on a 3D-Multiple-object tracking task (Chermann et al., 2018). Long-term impairments to visual processing and

higher-level cognitive function associated with concussion have also been reported (Moore et al., 2014). It is suggested that the SIFI illusion arises from processes occurring at least as early as primary visual cortical processing regions (Bolognini et al., 2016), whereby auditory inputs influence early visual representations (Hirst et al., 2020). Therefore, damage to these regions induced by concussion made reduce multisensory integration efficiency.

Accurate depiction of reality by cross-modal integration can fail specifically when two separate perceptual modalities compete due to close temporal proximity in stimulus onsets (Setti et al., 2011). The temporal range of susceptibility to lapses in successful integration has been shown to become greater across age-related neurocognitive decline and in acute concussion as discussed (McGovern et al., 2014, Wise and Barnett-Cowan, 2018). Thus, multisensory sensory processing efficiency might be similarly affected by repetitive mTBI (Broglio et al., 2011). It is unknown whether concussion history and/ or head impact exposure associated with a career in professional rugby may hasten the age-associated decline in long-term multisensory efficiency. We hypothesized that cumulative head impact exposure may speed up the normal age-related decline in multisensory efficiency observed in the general population and hence, estimated concussion history or playing position may influence performance on the SIFI task resulting in retired rugby players performing worse (i.e. more susceptible to the illusion) than non-contact sport athlete controls. This is the first study to present data on multisensory processing efficiency among former professional rugby union players with a history of exposure to concussion or repeated head impacts during their career.

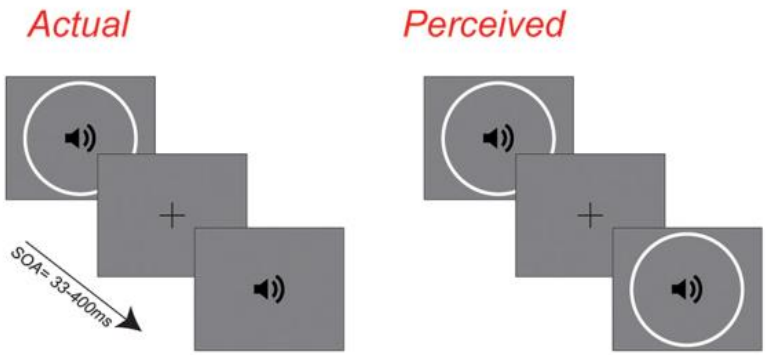


Figure 9-1 *Schematic illustration of the sound-induced fission illusion. The fission illusion refers to incidents whereby a single visual flash accompanied by two auditory tones is perceived as two flashes. Figure adapted from (McGovern et al., 2014).*

The primary aim of this study was to

i) investigate multisensory integration efficiency using the SIFI task in retired professional rugby players (RUG) compared to a non-contact sport control group (ROW).

The secondary aim of this study was to

ii) investigate whether a history of concussion or history of exposure to contact sport among rugby players may increase susceptibility to the sound induced flash illusion.

9.2 Methods

The current cross-sectional explorative study was conducted as part of the 'PROP' project as above. See Chapter 4 for detailed methods.

9.2.1 Concussion History

Concussion history was gained from each participant using the Michigan Traumatic Brain Injury (TBI) Identification Method [Chapter 4; Section 4.7.2] (Broglio et al., 2018). Prior to completing the Michigan TBI Identification Method questionnaire, participants were supplied with a written copy of the definition of concussion based on the most up to date guidelines; the 5th Consensus Statement on Concussion in Sport (McCrory et al., 2017). Estimation of concussion history was then used to explore the relationship between sports-related concussion and performance on the SIFI task.

9.2.2 Pre-Morbid Intelligence (IQ)

An estimate of premorbid intelligence was gained from all participants using the full-scale intelligence quotients obtained by the National Adult Reading Test (Nelson, 1991) [Chapter 4; Section 4.13]. This was deemed necessary to rule out any statistical between group difference in estimated intellectual functioning which may account for differences in cognitive or perceptual ability. Full-scale intelligence quotient (FSIQ) was calculated by testing reading ability of phonetically irregular words (Nelson, 1991).

9.2.3 The Sound-Induced Flash Illusion Task (SIFI)

The Sound Induced Flash Illusion Task was administered to investigate cross-modal multisensory integration efficiency, i.e. how information from two sensory modalities are integrated and processed. The SIFI measures multisensory integration through the susceptibility to the audio-visual fission illusion (a single flash being perceived as two flashes due to two rapid auditory beeps presented concurrently) (Setti et al., 2011, Shams et al., 2002, Shams et al., 2005). Each trial incorporates unisensory visual (V) and auditory (A) conditions introduced to control for visualauditory (V/A) deviations from the norm, i.e. any visual or

hearing impairment. The ‘congruent trials’ involve either one or two flashes or beeps presented in synchrony. Whereas, during the multisensory incongruent trials, the onset of the secondary auditory beep either precedes or succeeds the first auditory beep across different time delays of 230ms, 150ms and 70ms pre (A-V/A) and post (V/A-A) visual flash. These time delays are referred to as negative and positive ‘stimulus onset asynchronies’ (SOAs) respectively. These incongruent trials are also referred to as the ‘illusory trials.’ The SIFI experiment is described in detail in Chapter 4; Section 4.12.

9.3 Statistical Analysis

Statistical analyses were performed with SPSS for Windows version 26 (IBM, Armonk, New York, USA) statistic software package and R version 3.6.0 with package lme4. Distributions were analysed for normality using the Shapiro-Wilk normality test (with a $p > .05$ indicative of normal distribution). Visual inspection of Q-Q plot (to look for systematic deviations) and histogram was performed (to examine skew). Descriptive statistics of participant characteristics were reported as mean (SD) or median (IQR), as appropriate. Between-group differences for RUG and ROW were analysed. Group differences were examined by independent samples t-tests for normally distributed variables. Independent samples, Mann-Whitney U tests were used to assess non-parametric continuous variables. For all analyses, $p < .05$ (two-tailed) was taken as statistically significant. Further analysis was performed to investigate whether there was a difference in correct response rate in each SIFI illusory condition (6 SOA's) between rugby players and rowers. Logistic Regression was used to model the number of correct responses in each condition for each individual, allowing the probability of a correct response to vary according to group and condition. If there are n repetitions of the condition for each individual i, the number of correct responses y is binomial with success probability pi:

$$y_i \sim \text{Binomial}(n, p_i)$$

where p_i is modelled via

$$\log\left(\frac{p_i}{1-p_i}\right) = \alpha + \gamma_i + \beta_i$$

with γi the group effect for individual i (RUG or ROW) and βi is the effect for condition. A grouped logistic regression was used. In order to investigate concussion history and whether this was a predictor of performance on the SIFI, a Logistic Regression Model including number of concussions was then devised.

9.4 Results

9.4.1 Participant Characteristics

Twenty-eight retired international rowers (21 male, 7 female) and 62 retired professional rugby union players (54 male, 8 female) underwent the SIFI testing. Descriptive statistics are provided in Table 9-1. The control sample (ROW: 43.89 SD (9.18) years) was significantly older than the rugby cohort (RUG: 39.03 SD (5.65) years; p = .016). Control measure analyses revealed that there was no significant difference in Full Scale Intelligence Quotient (FSIQ) between rugby players (Mean 114.24 SD (4.55)) and the rowers (Mean 113.75 SD (7.26)); p = .795), both of which were within the average domain (Nelson, 1991). The mean duration of engagement in professional rugby (RUG: 9.14 SD (4.39) years), which was not statistically significantly different to the mean duration of participation in international rowing among the controls (ROW: 7.62 SD (5.46) years; p = .133). In terms of concussion history, the control group had significantly less self-reported concussions (Mean 0.5 SD (1.1)) than the rugby group (Mean 6.9 SD (10.4); p <.001) [Table 9-1]. In terms of self-reported cognitive functioning in the Neuro-QoL, there was no statistical difference between the two groups.

Table 9-1 Characteristics of the RUG and ROW groups across Age, Estimates of Pre-Morbid Intelligence, Number of Years in Sport and Concussion History (mean, standard deviation in parenthesis).

	RUG (n=62)	ROW (n=28)	p-value
Age	39.03 (5.65) *	43.89 (9.18) *	**.016**
No. of lifetime concussions	6.92 (10.43)	0.54 (1.14)	**<.001**
No. of years participating professionally	9.14 (4.39)	7.62 (5.46) *	.088
No. of years participating at any level	23.21 (7.36) **	22.14 (9.36) *	.909
NART FSIQ	114.24 (4.55)	113.75 (7.26) +	.795
Neuro-QoL	32.48 (6.37) *	33.64 (5.23)	.574

* One player missing, ** Two players missing, +Four players missing

9.4.2 Multisensory Integration Efficiency

SIFI scores are reported for 62 rugby players and 28 rowers over the six multisensory incongruent SIFI conditions. The score for each individual in each condition is reported as a proportion (0,0.25,0.5,0.75,1), giving the proportion of correct responses in four repetitions of the condition. Negative SOAs indicate a sequence of stimuli A–V/A, while positive SOAs indicate V/A–A. A high score means that participants responded correctly, i.e. they perceived one flash even when presented with two beeps. A low score indicates that participants experienced a high number of illusions. The mean percentage of correct trials across unisensory and multisensory conditions for each participant was calculated. Coding of responses was consistent with previous research (Setti et al., 2011, Andersen et al., 2004). In experimental conditions when two or more stimuli were presented (e.g. 2 beeps or 2 flashes or 2 flashes/2 beeps), a correct response was one in which the participant indicated that two or more flashes (or beeps when flashes were not present) occurred. Both study groups

demonstrated significant reduction in accuracy with decreasing SOA pairing latencies. However, both groups also displayed low accuracy on unisensory trials when two visual stimuli were presented [Table 9-2].

Mann Whitney U tests revealed a significant between group difference in the unisensory two auditory beeps with a 230ms stimulus onset asynchrony (Two Beeps SOA 230), with the RUG group performing significantly worse (Mean 93.55, SD (19.09)) than the ROW group (Mean 100.00, SD (0.00)), p = .035. Exploratory analysis revealed that the rugby group appear to have lower response proportion for the negative or pre (A-V/A) trials, SOA conditions (i.e. SOA-230, -150, -70), while the positive or post (V/A-A) SOA conditions did not appear to show as clear a pattern [Figure9.2]. Both groups displayed decline in accuracy across shortening of SOAs and both samples showed a reduction across auditory stimulus onsets across pre and post flash presentations. This is in line with previous studies which demonstrated increasing susceptibility to the SIFI with decreasing SOAs (Shams et al., 2002). Rugby players were further explored according to position. No significant difference on the illusory trials was found between backs and forwards [Figure 9-3].

A Logistic Regression Model including the rugby group as an explanatory variable demonstrated significance at the 10% level as the rugby having a lower proportion of correct responses (p = 0.06) [Table 9.3]. It can be seen that the odds of being either a rugby player or rower getting the correct response is .9914, i.e. 99%. The odds-ratio table displays the fold change in the odds of having a correct response for each of the effects relative to SOA −230. [Table 9.4]. The 95% confidence interval for this odds ratio is between 0.68 and 1.01. Therefore, we are 95% confident that the true odds ratio of a rugby player getting the correct response compared to the rower lies between 0.68 and 1.01. While 1 is just narrowly included in this interval (implying no difference), the interval is wide and there appears to be a trend indicated by the 10% significance indicating that ‘rugby group indicator’ reduces the odds of a correct response (i.e. increases susceptibility to illusion).

Table 9-2 Percentage of Correct Responses in RUG and ROW groups across each of the Unisensory and Multisensory Conditions in the Experiment (including standard deviations in parenthesis).

SIFI Task Experimental Conditions	**RUG (N=62)**		**ROW (n=28)**		
	Mean	**SD**	**Mean**	**SD**	**p-value**
Unisensory Conditions					
1 Beep	96.77	14.66	97.32	7.87	.523
1 Flash	91.94	19.09	90.18	24.85	.944
Two Beeps SOA 230	93.55	18.63	100.00	0.00	**.035**
Two Beeps SOA 150	96.77	14.66	99.11	4.73	.568
Two Beeps SOA 70	54.44	38.82	52.68	40.45	.833
Two Flashes SOA 70	26.21	31.83	23.21	26.29	.738
Multisensory Conditions					
Congruent					
One Beep One flash	95.16	13.46	94.64	15.75	.989
Two beeps Two flashes SOA 230	49.19	29.33	57.14	31.07	.267
Two beeps Two flashes SOA 150	45.56	36.36	51.79	40.21	.518
Two beeps Two flashes SOA 70	46.77	33.41	43.75	27.74	.874

Incongruent

SOA-230	68.95	35.26	7321	32.58	.617
SOA-150	62.50	36.71	73.21	37.84	.136
SOA-70	44.76	36.81	50.00	39.68	.596
SOA70	36.29	37.51	38.39	41.10	.513
SOA150	66.53	36.48	68.75	33.07	.931
SOA230	81.85	29.40	81.25	23.20	.906

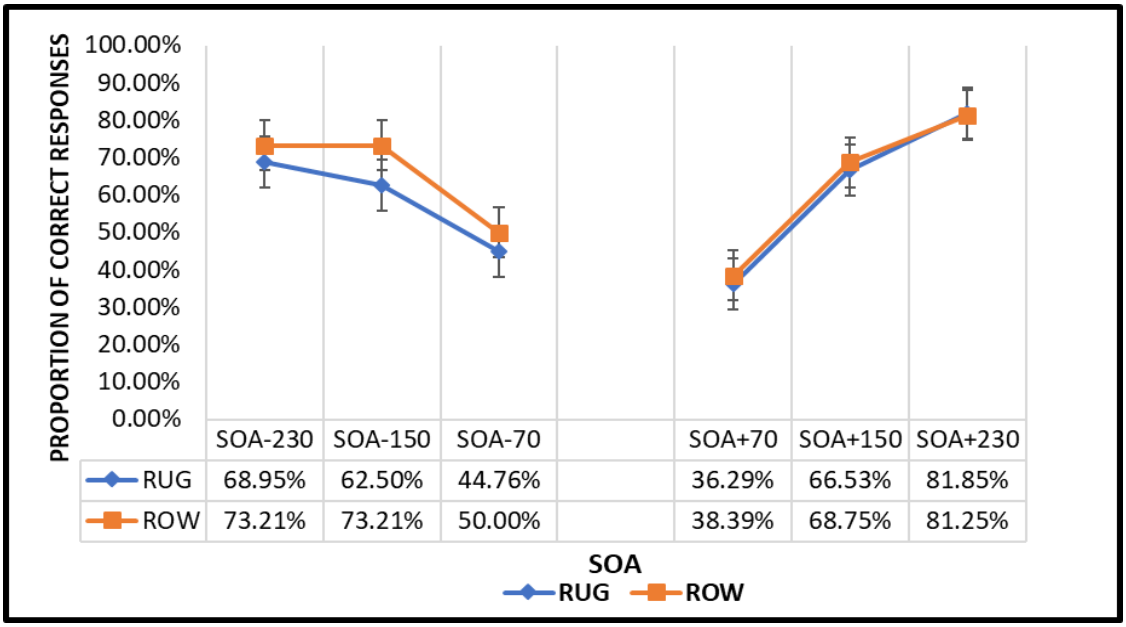


Figure 9-2 *Proportion of correct responses across the different SOAs in the incongruent conditions for the retired rugby (RUG) and retired rowing (ROW) groups (Negative (A-V/A) and Positive (V/A-A) Stimulus Onset Asynchronies (SOA)); mean, error bars equal +/- 1 standard error of the mean.*

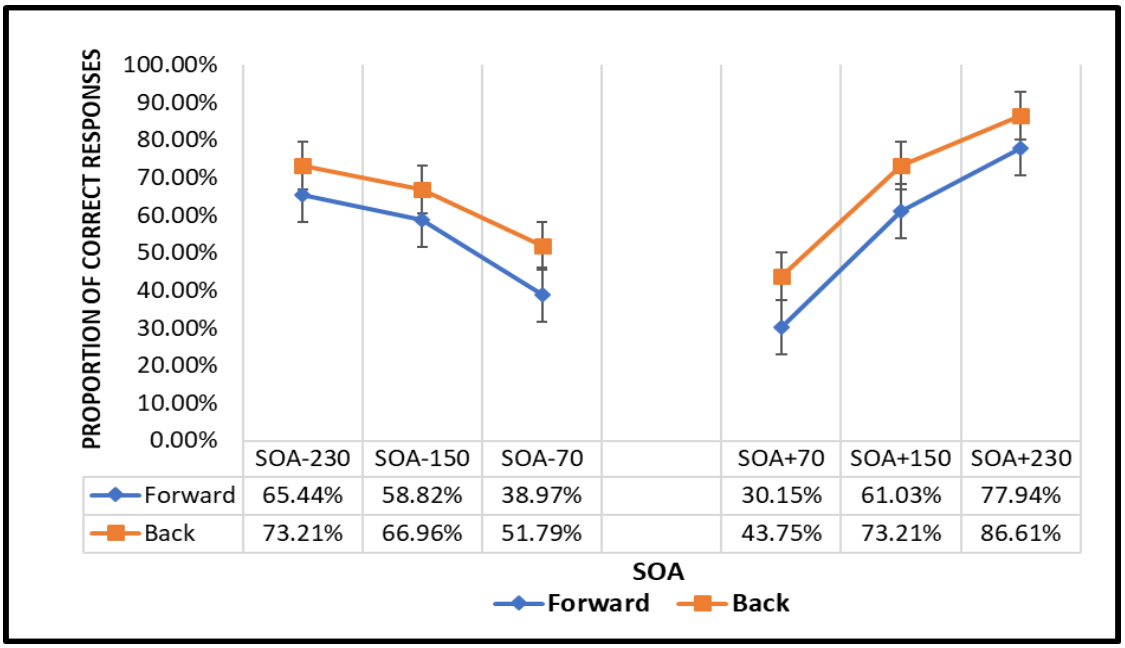


Figure 9-3 *Proportion of correct responses across the different SOAs in the incongruent conditions for the retired rugby players (Negative (A-V/A) and Positive (V/A-A) Stimulus Onset Asynchronies (SOA)); mean, error bars equal +/- 1 standard error of the mean.*

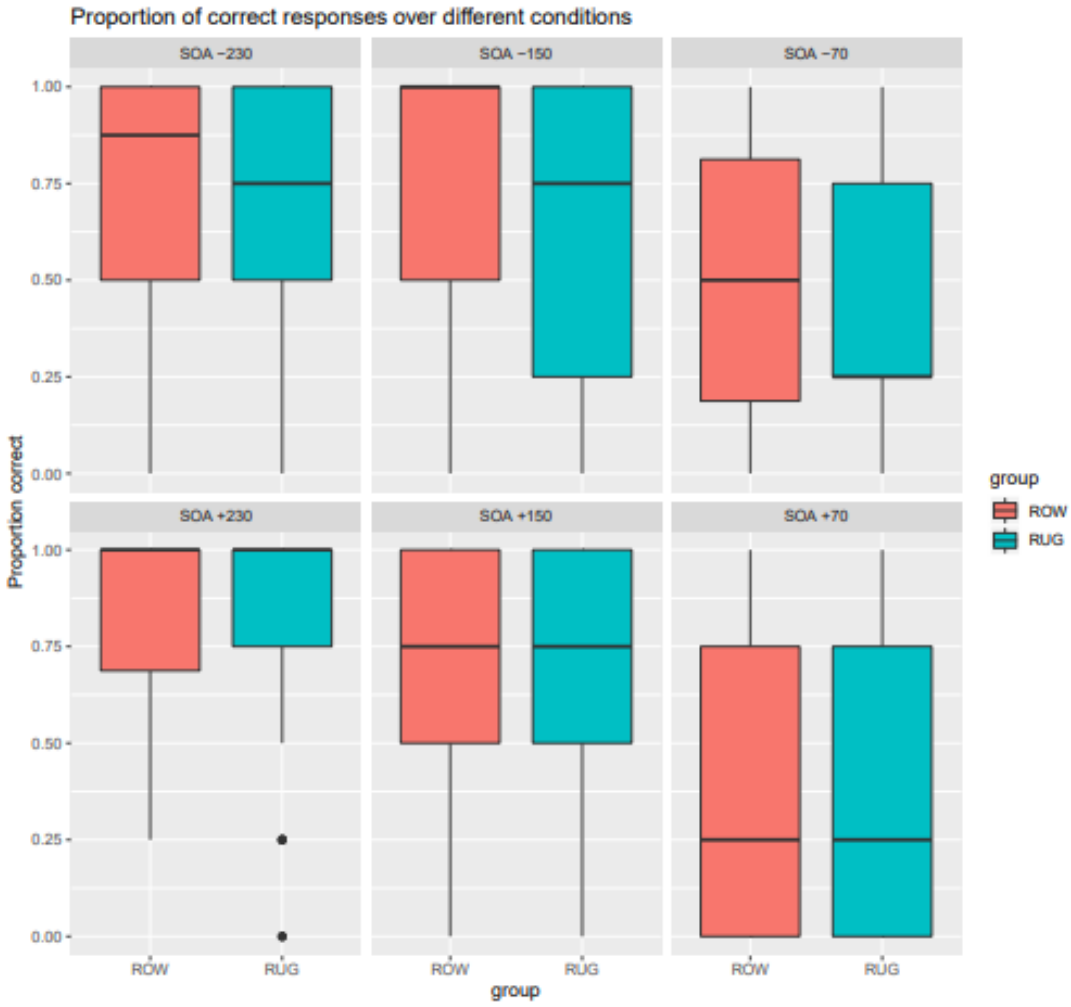


Figure 9-4 *Boxplot illustrating proportions of correct responses over the six SIFI incongruent conditions (Negative (A-V/A) and Positive (V/A-A) Stimulus Onset Asynchronies (SOA)) across the RUG and ROW groups.*

Table 9-3 Table including RUG group as an Explanatory Variable in the Model. Effect estimates and significance are displayed (Effects are relative to SOA −230).

	Estimate	Std. Error	z value	p-value
Intercept	0.9914	0.1357	7.30	0.0000
RUG	-0.1877	0.1013	-1.85	0.0639
SOA -150	-0.2050	0.1603	-1.28	0.2009
SOA -70	-1.0070	0.1566	-6.43	0.0000
SOA +230	0.6342	0.1786	3.55	0.0004
SOA +150	-0.1425	0.1611	-0.88	0.3762
SOA +70	-1.3977	0.1590	-8.79	0.0000

Table 9-4 Odds-ratio Table illustrating 95% Confidence Intervals for Odds-ratios associated with the Model Estimates.

	2.5 %	97.5 %
RUG	0.68	1.01
SOA -150	0.59	1.11
SOA -70	0.27	0.50
SOA +230	1.33	2.68
SOA +150	0.63	1.19
SOA +70	0.18	0.34

9.4.3 Concussion History and SIFI Performance

In order to explore whether there was an effect of concussion history on SIFI performance, the number of concussions was incorporated as an explanatory variable into the Logistic Regression Model described above. Figure 9-5 illustrates the estimated number of concussions per group. The inclusion of concussion history estimates resulted in the rugby indicator becoming redundant as the number of concussions were more informative than the player grouping by sport [Table 9-5]. A model was then fitted with only number of concussions included as an explanatory variable. The p-value for number of concussions as a predictor of correct response on the SIFI illusory trials was <0.05. A table of odds-ratios is shown illustrating the odds-ratio interval for number of concussions, this refers to the change in odds of getting the correct response for one extra concussion. A reduction in the ability to

get the correct result when the number of concussions increases is observed [Table 9-6]. The odds-ratio table displays the fold change in the odds of having a correct response for each of the effects relative to SOA −230 as before [Table 9-7]. The 95% confidence interval for this odds ratio is between 0.97 and 0.99. Therefore, we are 95% confident that the true odds ratio of a player with one concussion getting the correct response lies between 0.97 and 0.99. This is significant at the 5% level; p <.001. Therefore, we can say that for every one concussion, the probability of a participant getting the correct response on the illusory trails decreases by 1%.

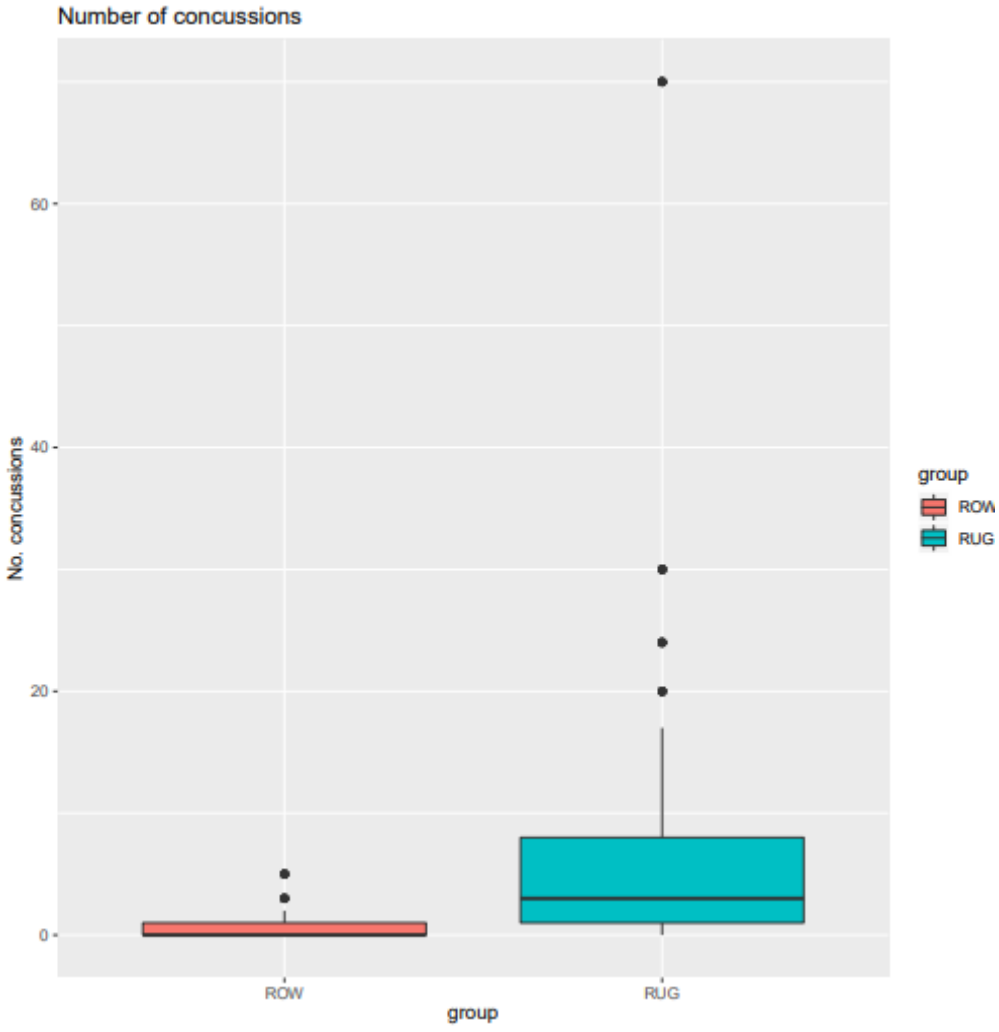


Figure 9-5 *Estimated number of concussions per group.*

Table 9-5 Table including RUG group and Concussion History as Explanatory Variables in the Model. Effect estimates and significance are displayed (Effects are relative to SOA −230).

	Estimate	Std. Error	z value	p-value
Intercept	1.0457	0.1392	7.51	0.0000
RUG	0.0148	0.1088	0.14	0.8917
SOA -150	-0.2330	0.1658	-1.40	0.1600
SOA -70	-1.0624	0.1613	-6.59	0.0000
SOA +230	0.5990	0.1850	3.24	0.0012
SOA +150	-0.1933	0.1664	-1.16	0.2453
SOA +70	-1.4674	0.1636	-8.97	0.0000
number concussions	-0.0232	0.0057	-4.10	0.0000

Table 9-6 Table including Number of Concussions only as an Explanatory Variable in the Model (concuss= (concussions).

	Estimate	Std. Error	z value	p-value
Intercept	1.0545	0.1231	8.57	0.0000
SOA -150	-0.2330	0.1658	-1.40	0.1600
SOA -70	-1.0624	0.1613	-6.59	0.0000
SOA +230	0.5990	0.1850	3.24	0.0012
SOA +150	-0.1933	0.1664	-1.16	0.2453
SOA +70	-1.4675	0.1636	-8.97	0.0000
number concuss	-0.0230	0.0053	-4.31	0.0000

Table 9-7 Odds-ratio Table illustrating 95% Confidence Intervals for Odds-ratios associated with the Model Estimates.

	2.5 %	97.5 %
SOA -150	0.57	1.10
SOA -70	0.25	0.47
SOA +230	1.27	2.62
SOA +150	0.59	1.14
SOA +70	0.17	0.32
number concussions	0.97	0.99

9.8.4 Model with outliers removed

Due to the lack of normative data and the novelty of the assessment, further exploration of the data was performed. This resulted in four players who had more than 17 concussions (95% quantile of number of concussions in the cohort) being removed from the analysis. These players were extreme outliers and hence the analysis was redone with these players removed from the sample to explore whether this would impact upon the findings. With these removals the significance level changes [see Tables 9-8 and 9-9 below]. It can be seen that the significance was no longer observable, however the trend remained that rugby players performed worse than rowers.

Table 9-8 Table including RUG group as an Explanatory Variable in the Model (outliers removed). Effect estimates and significance are displayed (Effects are relative to SOA −230).

	Estimate	Std. Error	z value	p-value
Intercept	0.9970	0.1282	7.78	0.0000
SOA -150	-0.2283	0.1692	-1.35	0.1773
SOA -70	-1.0415	0.1645	-6.33	0.0000
SOA +230	0.6304	0.1901	3.32	0.0009
SOA +150	-0.2008	0.1696	-1.18	0.2364
SOA +70	-1.4756	0.1670	-8.84	0.0000
concuss	-0.0156	0.0111	-1.41	0.1599

Table 9-9 Odds-ratio Table illustrating 95% Confidence Intervals for Odds-ratios associated with the Model Estimates (outliers removed).

	2.5 %	97.5 %
Intercept	2.12	3.50
SOA -150	0.57	1.11
SOA -70	0.25	0.49
SOA +230	1.30	2.74
SOA +150	0.59	1.14
SOA +70	0.16	0.32
concuss	0.96	1.01

Table 9-10 Bivariate Correlations (Spearman's rho) between SIFI incongruent trials and Self-reported Cognitive Health on the Neuro-QoL among the RUG group.

Spearman's Rho		**SOA -230**	**SOA -150**	**SOA -70**	**SOA +230**	**SOA +150**	**SOA +70**
Neuro-QoL	r	.187	.107	.395*	.011	.187	.333*
	p-value	.149	.411	.002*	.935	.148	.009*

**Correlation is significant at the 0.01 level (2-tailed).

9.4.5 Cognitive-Perceptual Correlates

Based on the outcomes obtained from between group analyses, the individual A-V/A and V/A-A SOAs were employed to explore potential relationships with self-reported cognitive functioning on the Neuro-QoL using Spearman's Rho (r). Within the RUG group, outcomes demonstrated a significant positive correlation between accuracy on SOA-70 and Neuro-QoL results (r = .395; p = .002). The SOA+70 was also positively correlated with Neuro-QoL results (r = .333; p = .009). Therefore, better self-reported cognitive functioning was correlated with greater accuracy on the SIFI across the shortest SOA conditions. This correlation was not present among the rower group.

9.5 Discussion

This study provides an insight into perceptual performance among former professional rugby players compared to non-contact controls, all of whom were in the early stages of retirement from play by using a novel assessment of multisensory integration; the Sound Induced Flash Illusion (SIFI). The SIFI Task contrasts sensory processing and acuity and so investigates investigating multisensory integration efficiency (Setti et al., 2011). Former rugby players had sustained a significantly greater number of self-reported concussions when compared to

the non-contact sport control group ($p < .001$), therefore potential associations between concussion history estimates and perceptual performance were explored. This is the first study to investigate multisensory integration in former rugby players with a history of concussion. The temporal onset (i.e. stimulus onset asynchrony, SOA) was manipulated between the auditory beeps in order to measure the susceptibility to the double flash illusion across the two groups as in Shams et al. (2002). By manipulating the SOAs, we indirectly measured differences in the temporal window of integration across the rugby and rowing groups.

During play, rugby players are consistently required to process the visuospatial conditions around them and react appropriately. This includes information processing across multiple senses, stimulus discrimination and prioritisation in a hierarchy of importance, referred to as 'multisensory reweighting' (Setti et al., 2011). Therefore, it was hypothesized that fewer errors in the illusory trials of the SIFI task may be detected in former rugby players which could be associated with years of training and adaptation. In other words, we expected that rugby players would be less susceptible to the sound induced flash illusion across longer delays between the auditory beeps than the rowers. In contrast to this view, rugby players were more susceptible to the erroneous illusion of two visual flashes across the multiple incongruent stimulus onset asynchronies (SOAs). This was particularly true for the negative (A-V/A) pairings. Although the two groups overall did not statistically differ in the number of illusions experienced, regression analysis revealed a trend that being a rugby player increased the odds of experiencing the illusion ($p=0.06$); that is, responding incorrectly. Further, for every concussion reported, the odds of experiencing the illusion were significantly increased. Similar to previous work (Shams et al., 2002, Setti et al., 2011), we found that susceptibility to the double flash illusion increased as the onset delay decreased. Previous research has also found that susceptibility to the SIFI increases with age (McGovern et al., 2014). Therefore, given that rugby players were significantly younger than the rowers, our results contradict what would be expected. Findings from this study suggest that the

rugby players' cognitive ability to omit erroneous responses was consistently poorer than the rowers (p-value of 0.06 was approaching statistical significance). While it was expected that a career in a dynamic contact sport environment may equip former rugby players with a greater ability to integrate and process multiple sensory stream, this does not appear to be the case as revealed by the incongruent multisensory condition results.

The current findings suggest that multisensory integration efficiency may be adversely affected in the current rugby population and is associated with concussion history. The SIFI results indicate that this audio-visual integration task may be sensitive to past concussion history and detecting subtle changes in perceptual ability. The probability of getting the correct response on the SIFI task was reduced for every concussion. This implies that the SIFI may hold potential as an early predictor of onset of deterioration in cognitive and perceptual performance associated with past concussions. Given the variability in the sample and the explorative nature of this research, all participants were included in the initial analysis. However, due to the lack of normative data and the novelty of the assessment, further exploration of the data was performed. Four rugby players reported greater than 17 concussions. These players were extreme outliers and hence the analysis was redone with these players removed to explore whether this would impact upon the findings. Results revealed that a small subsample of the cohort, with large numbers of estimated concussions had a large influence on the initial analysis. When these outliers were removed from the sample, the significance was no longer observable, however the trend remained that rugby players performed worse than rowers. These findings are more favourable towards rugby players with history of concussion as when a small sample with a large number of concussions were removed, concussion was no longer a significant predictor of performance. Figure 9-2 illustrates performance on the illusory trials based on position among the former rugby players. While there is no statistical difference observable, it can be observed that forwards are consistently performing worse than the backs. In the literature, forwards have consistently been shown to have a higher injury incidence including greater head impact

exposure than backs owing to their position (Gissane et al., 1997, Gabbett, 2005, Carey et al., 2019). This supports the hypothesis that concussion history or head impact exposure may influence long-term multisensory integration.

Wise and Barnett-Cowan (2018) found a correlation between the time elapsed since last concussion and a delay in discriminating the temporal order of audio-visual stimuli which suggested that perception was impaired following concussion but improved with time since last concussion. However, given that our findings suggest that the SIFI task may be sensitive to past concussions in former rugby players, a long-lasting effect may persist that can be detected on the SIFI task. The current standard battery of tests for assessing and diagnosing concussions does not include a perceptual task such as the Sound Induced Flash Illusion. However, this study along with Wise and Barnett-Cowan (2018) indicate that audio-visual perceptual tasks may be a potential sensitive marker for detecting changes in the Central Nervous System (CNS) and hence to neural function induced by concussions. Further reduced efficiency at integrating multisensory events may have a sequential effect on decision-making and behaviour, which are characteristics of well described long-term complications of repetitive head trauma such as Chronic Traumatic Encephalopathy (CTE) (Fesharaki-Zadeh, 2019).

As previously stated, cognitive changes associated with advancing age are well documented (Harada et al., 2013). There is a body of research suggesting that repeated exposure to head trauma may expedite the normal cognitive aging process; often referred to as the cognitive reserve hypothesis in mild traumatic brain injury (Stern, 2017, Steward et al., 2018, Leary et al., 2018, Broglio et al., 2012). The role of cognitive reserve and age are therefore are thought to inform cognitive recovery and long-term prognosis (Steward et al., 2018). While the literature is contradictory regarding multisensory integration efficiency in the elderly, there is consensus that the way in which inputs from several senses are combined is influenced by age (Hirst et al., 2019). Some studies have demonstrated increased multisensory integration in older adults (Laurienti et al., 2006, Peiffer et al., 2007, Diederich et al., 2008). However,

this has largely been attributed to compensatory mechanisms which are thought to counteract age-related unisensory decline with aging. In contrast, other studies have shown decreased integration in older adults which is likely to reflect a decrease in multisensory processing (Stephen et al., 2010, Roudaia et al., 2013). More recently, it has been demonstrated that older people are more susceptible to the fission illusion, while this was not the case for the fusion illusion (McGovern et al., 2014). Older individuals have been shown to be more susceptible to the Sound Induced Flash Illusion across a wider range of temporal asynchronies when compared to younger adults (Setti et al., 2011). This supports the idea that this illusion is mediated by neural mechanisms (McGovern et al., 2014). However, the underlying neural mechanism for decreased multisensory efficiency in older age is unclear (Freiherr et al., 2013, Laurienti et al., 2006) (Freiherr et al., 2013, Laurienti et al., 2006).

Functional Magnetic Resonance Imaging (fMRI) studies have illustrated that older individuals may have a reduced ability to inhibit irrelevant cross-modal information in multisensory tasks (Stevens et al., 2008, Persson et al., 2007, Andres et al., 2006, Hasher and Zacks, 1988). An explanation for this is that all available sensory information is processed more extensively which leads to less discrimination and a decline in efficient processing (Poliakoff et al., 2006). This is thought to negatively influence performance when information from various sensory domains is incongruent, while congruent information processing may actually be enhanced for the same reason (Peiffer et al., 2007). Andres et al. (2006) demonstrated that older adults were more vulnerable to distraction by irrelevant auditory information on an auditory-visual oddball task which indicated a decreased ability to filter out task-irrelevant auditory noise. Suppression of the Default Mode Network (DMN) is purportedly less efficient during external tasks in older adults as in the young (Persson et al., 2007, Stevens et al., 2008, Anticevic et al., 2012, Sambataro et al., 2010). Stevens et al. (2008) linked increased background activity in the auditory cortex in older adults to age-related increased DMN activity. This has been described as ‘increased noise’ which may lead

to increased errors while integrating sensory stimuli and delays in processing sensory information (Mozolic et al., 2012) (Mozolic et al., 2012).

An age-related loss of the inhibitory neurotransmitter GABA has been proposed as an explanation for decreased multisensory integration efficiency in older adults which may also link poorer multisensory integration to concussion (Wise and Barnett-Cowan, 2018, Bedard and Barnett-Cowan, 2016). Loss of GABA producing cells is known to occur following a concussion which disrupts the balance of excitation and inhibition leading and can further cell injury or death (Giza and Hovda, 2014). GABA modulates the excitation of cortical and thalamocortical networks relaying visual and auditory stimuli along with other sensory information (Castro-Alamancos and Connors, 1997, Qin et al., 2012). GABA is also responsible for inhibitory signalling in the CNS, therefore reduced ability to inhibit irrelevant sensory stimuli also demonstrated in the elderly may also occur following a concussion (Caspary et al., 2005). Alterations in neurotransmitter level release are hypothesized to increase noise in the system, therefore increasing distractibility and resulting in slower processing of sensory information (Wise and Barnett-Cowan, 2018). There is emerging evidence that an imbalance between inhibition and excitation may underlie the mechanism of long-term neurological consequences of concussion (Guerriero et al., 2015), this may in turn explain the increased errors among the former rugby players with concussion history in the current study. These neurophysiological changes may add noise to signal processing in the CNS. Therefore, the neurophysiology of concussion should be explored further in the context of the Sound Induced Flash Illusion.

Other work has demonstrated that structural differences in brain regions involved in the illusion namely local grey matter volume in early retinotopic visual cortex was correlated with susceptibility to the sound-induced flash illusion. Those with smaller early visual cortices were more prone to the illusion (Haas et al., 2012). Evidence from neuroimaging studies suggest potential alterations in brain structure such as reduced white and grey matter volume associated with mild traumatic brain injury (mTBI) (Sussman et al., 2017).

Multisensory integration efficiency in the presence of neuropathological diseases has also been explored. Research have shown that people with Mild Cognitive Impairment (MCI) and Alzheimer's Disease (AD) exhibit a delayed ability to integrate audio-visual information compared to a healthy population (Wu et al., 2012). Wise and Barnett-Cowan (2018) demonstrated a similar finding in students who had recently sustained a concussion. Given that similar audio-visual sensory integration impairments have been demonstrated in those with MCI or AD and those with concussion history, Wise and Barnett-Cowan (2018) suggest that impaired integration may hold potential as a predictor factor of an individual's susceptibility to increased risk of earlier onset of cognitive impairment. In the context of our findings this makes sense as the ability to integrate information from different sources is pivotal for perception and for higher order cognitive functions. This has been described as an important 'intermediary role' (McGovern et al., 2014), therefore impairment in multisensory integration may precede cognitive decline. If greater susceptibility to the illusion reflects inefficient audio–visual processing in the central nervous system due to lasting effects of concussion, the Sound Induced Flash Illusion may have important implications for the diagnosis of concussion. These findings add weight to the hypothesis that impaired audio–visual integration could constitute an early biomarker for long-term effects of concussion. The finding that self-reported poorer cognitive health among the rugby players was correlated with susceptibility to the illusory flash across the shortest temporal asynchrony (70ms) also suggests that the SIFI may be sensitive to subtle declines in cognitive functioning. However, further research is required.

In the context of current literature regarding long-term effects of concussion and head impact exposure in retired contact sports people, these results may suggest that a small subsample of individuals may be at risk of decreased multisensory processing and integration. Research into long-term neurodegenerative diseases associated with repetitive head trauma such as Chronic Traumatic Encephalopathy (CTE) among former National Football League players suggests that the incidence and prevalence of CTE is unknown. However, the large number

of athletes participating in contact sports and the relatively low number of documented CTE cases indicates that it is rare and there are likely a myriad of factors involved (Concannon et al., 2014, McCrory et al., 2017). Given that our findings demonstrated that a small number of players with the greatest number of concussions influenced the overall findings, it also suggests that a small minority of the sample may be vulnerable to long-term effects of concussion associated with rugby.

9.6 Limitations

There is ample evidence to demonstrate that physical exercise affects brain plasticity in turn influencing cognition (Mandolesi et al., 2018, Fernandes et al., 2017). By comparing contact and non-contact sport populations, the current study investigated two sporting populations both

of which participated at a high level in their respective sports. Therefore, it would be interesting to compare these groups to a normative more 'sedentary' non-sporting population. Self-reported concussion history is open to recall bias, hence reducing the reliability of the number of concussions scale. Both groups performed poorly on the pairing of two unisensory visual stimuli presentations over short temporal periods, which is in line with what would be expected from the literature. However, the rugby players performed significantly worse on the two unisensory auditory stimuli presentation at the SOA 230ms. Therefore, the trend towards significantly poorer accuracy on illusory conditions within the rugby population may be related to differences in sensory acuity rather than susceptibility to the fission illusion (Setti et al., 2011). Hence, results may not be due to a lack of audio–visual integration due to concussion but to a reduced ability to perceive a distinction between the beeps among the rugby players. However, given that there was no statistical between group difference on the two unisensory auditory stimuli presentation at SOAs of 150ms and 70ms, it seems unlikely. It was deemed unnecessary to assess hearing among the participants given their age.

However, future studies may need to consider this possibility among former rugby players. It is possible that poorer performance is related to head impacts which have affected hearing acuity.

Furthermore, some reduction in accuracy in the multisensory trials from SOA230 to 70ms suggests that significant differences could potentially be accurately depicted by further shortening of SOAs. Variability within the study cohort across numerous factors such as sex distribution, concussion history, lower exposure to training and play, shorter career span in professional rugby and age could have produced potential covarying factors that could not be controlled for in the current research. Given that there was a limited number of females included in the current study, sex differences were difficult to discern. Future studies should encompass investigations into the repercussions of concussions in female players, as sex differences have been documented on the SIFI task, which have suggested that females may be more susceptible to the fission illusion (Hernández et al., 2019).

9.7 Conclusion

Similar to other cognitive functions, multisensory integration efficiency changes with age. Compromised audio–visual integration or increased susceptibility to the sound induced flash illusion was found among former rugby players compared to the rowers. Concussion history estimates significantly predicted the odds of a correct response suggesting that history of concussion may have a deleterious effect on multisensory integration efficiency. Visual illusions induced by sound may represent a valuable tool to explore the effects of concussion on aging rugby players. However, associations between susceptibility to the sound induced flash illusion and implications of repetitive sports related concussion need to be further investigated using large-scale comparisons.

Chapter 10 Discussion

10.1 Introduction

Historically sports related traumatic brain injuries may have been thought to be restricted to sports such as boxing (Bernick and Banks, 2013). However, evidence regarding long-term neurological effects of head trauma in contact or collision sports is now believed to extend to contact and collision sports with high levels of head trauma exposure such as football, soccer and rugby. A growing body of research from American NFL players suggest that certain former sportspeople may be at risk of poorer neurological health than the general population due to repetitive head impact exposure (McAllister and McCrea, 2017). Mackay et al. (2019) recently reported a higher mortality rate due to neurodegenerative disease among former professional soccer players compared to the general population. Further, the association between exposure to repeated head injury and increased risk of neurodegenerative diseases such as Chronic Traumatic Encephalopathy (CTE), Amyotrophic Lateral Sclerosis (ALS), Alzheimer's Disease and Parkinson's Disease among former American NFL player's risk has been recognized (Graham and Sharp, 2019, Lehman et al., 2012). Stewart et al. (2016) have suggested the potential for CTE to be an under-recognised late consequence of rugby, with one documented case in a former professional rugby player to date. However, as a corollary to the findings of increased risk of neurodegenerative disease by Mackay et al. (2019), mortality from other common diseases such as cancers and ischaemic heart disease was found to be lower among former Scottish professional soccer players than the matched controls. Similarly, there is evidence suggesting that former American NFL players have decreased overall mortality when compared to the general population (Baron et al., 2012, Lincoln et al., 2018). Therefore, the risks and benefits to long-term health associated with a sporting career must be weighed in order to make an informed decision regarding participation in elite level sport. While there is evidence for poorer

neurological health in former boxers (Lincoln et al., 2018, Martland, 1928) and American NFL players (Maroon et al., 2015), rugby is not directly comparable with sports such as American NFL football. Research is warranted on rugby players specifically, as they are a unique cohort.

The studies contained within this thesis are timely, given the concerns around brain health in rugby. The nature of rugby has changed over time and continues to evolve. With the introduction of professionalism in 1995 (Garraway et al., 2000), an increase in injuries at both amateur and professional level have been reported in epidemiological studies (Fuller et al., 2009, Garraway et al., 2000, Targett, 1998). Since 1955, trends of increasing injuries and injury severity in rugby has coincided with increases in average body mass of rugby players by an estimated 25%, as player weights increased from 85kg to 105kg (Hill et al., 2018). Hence the modern game has larger, faster, stronger players with greater body mass, experiencing greater impact forces (Hume et al., 2017). Coupled with increasing male player size, there has been a global increase in rugby participation, with women's rugby growing rapidly in popularity (King et al., 2019). The number of women participating in rugby in Ireland has grown exponentially over the past decade (Gilmartin and Ryan, 2019). With this upsurge in participation in rugby among males and females, there is a concern regarding the inherent risk of injury in rugby union (Chalmers et al., 2012). There has been a focus on brain health, given the high incidence of concussion in rugby; recognised as one of the highest rates of concussion of all full contact sports (Gardner et al., 2014b).

Strides in the awareness of sports-related concussion (SRC), availability of side-line medical assessment and treatment of players has been evident across the board and specifically within the sport of rugby in Ireland and internationally. The rigour with which concussion is identified and return to play management strategies implemented have greatly improved (McMillan et al., 2017). International governing bodies have attempted to address the issue of head trauma in rugby by implementing stricter guidelines on high tackles, education in tackling skills and stricter head injury management protocols (McCrory et al., 2017). The

Irish Rugby Football Union (IRFU) have launched multiple initiatives, in line with the 5th International Consensus Conference on Concussion in Sport, in an effort to increase awareness of concussion and to put in place appropriate management procedures to safeguard players. Despite this move towards improving the safety of the game, there still remains calls for bans by some and concerns regarding the level of head impact exposure in rugby which remains high. Due to the relatively recent introduction of the professional game of rugby in Ireland, the opportunity to investigate the effects of a career in professional rugby on brain health is now arising. A number of gaps within the research remain pertaining to long-term brain health of retired professional rugby players. The studies within this thesis aimed to fill knowledge gaps relating to understanding the influence of a career in professional rugby on brain health in retirement. Given that the implications of individual results have been discussed in each chapter preceding the current one, the present section will provide a succinct analysis of the key points.

10.2 Overview of studies

The studies described within this thesis investigated the effect of a career in professional rugby on brain health in retirement. Studies were designed to allow for a robust exploration of brain health in a sample of former elite Irish rugby players with varying estimates of concussion and career duration. Concussion history estimates were explored in relation to mental health indicators (depression, anxiety and somatization), neurocognitive performance (attention, psychomotor speed, memory, executive function and memory) and multisensory integration in the former professional rugby union players. Within the literature, there is a small number of studies assessing objective neurocognitive performance in former professional rugby union players, indicating the importance of this topic. To our knowledge the SIFI task has never been assessed in former rugby players to investigate perceptual ability. Therefore, this is a novel and unique contribution to knowledge in this area, which

should prompt further investigation into multisensory processing and perceptual functioning in former professional rugby players with a history of SRC or head impact exposure.

None of the participants included had any diagnosed neurological or neurodegenerative condition. Hence, the studies were designed to investigate for any early subtle signs of decreased neurocognitive or perceptual ability associated with concussion history which may predict further future decline. Throughout studies II-V (Chapters 6-9) retired international rowers were included as a non-contact control group. The lack of elite sportspeople control groups in studies investigating the effects of concussion has been noted as a limitation in the literature to date (McMillan et al., 2017). The inclusion of a comparison group of athletes allowed us to control for health factors that may be associated with participation in elite sport due to certain exposures during an athlete's career such as high levels of physical fitness, musculoskeletal injuries and opioid use throughout their career (McMillan et al., 2017). The overall aim of this thesis was to explore brain health in former professional rugby union players in Ireland and to provide meaningful data on health and specifically brain health among retired rugby players. In pursuing this aim, two systematic reviews of the existing literature and five original studies were completed. Within this thesis, studies addressed the following areas:

The validity of concussion history recall using the Michigan Traumatic Brain Injury (TBI) Identification Method was investigated in Study I:

- Athlete concussion history recall is underestimated: a validation study of self-reported concussion history among current professional rugby union players (Chapter 5).

The effect of a career in professional rugby union on general health was investigated in Study II:

- Lifestyle factors and general health status among former professional rugby union players in retirement: a cross-sectional study (Chapter 6).

The effect of a career in professional rugby union on brain health was investigated in Studies III-V:

- An investigation into the mental health status of retired professional rugby union players and its association with a history of concussion: a cross-sectional study (Chapter 7).
- An assessment of neurocognitive functioning in retired professional rugby union players with a history of concussion; a cross-sectional study (Chapter 8).
- Assessment of multisensory processing in retired professional rugby union players with a history of concussion; a cross-sectional study (Chapter 9).

10.2.1 Summary of Systematic Reviews

Systematic Review I (presented in Chapter 2), aimed to investigate long-term brain health in retired rugby players. The search strategy yielded nine studies that met the inclusion criteria. This review illustrated the lack of research to date into the potential cause-and-effect relationships between concussions in rugby and long-term brain health. There was some evidence of reduced cognitive function among former rugby players, particularly in tests of fine motor control, processing speed, and memory (McMillan et al., 2017, Hume et al., 2017). However, the results were mixed and were often not significantly lower than population norms. Cautious interpretation of findings was needed as some study findings were biased towards positive findings when only self-reported measures of cognition were used. Evidence of decreased fine motor control in retired players was found. A limited number of studies that have investigated symptoms of common mental health disorders in retired rugby players provided an insight into the potential depression burden on this population. Further

investigation was warranted into the prevalence of common mental health problems and factors associated with the psychological and physical sequelae of playing and retiring from professional rugby union. Therefore, despite some evidence of poorer long-term brain health in former rugby players with a lifetime history of playing rugby, the literature was found to be limited. Furthermore, the majority of studies focussed on male rugby players, research on female rugby players was found to be lacking. It was concluded from this review that large gaps persist in the research into the potential cause-and-effect relationships between concussions, repetitive head impact exposure and long-term brain health among rugby players.

Given the sparse number of studies investigating the long-term effects of a career in rugby on living retired professional rugby players, systematic review II (presented in Chapter 3) synthesized and appraised the evidence base regarding cognitive health in living retired athletes with a history of head-impact exposure or sports-related concussion. The search strategy yielded 46 studies, which was found to be largely dominated by investigations of retired American NFL players, who are a unique cohort. While others included professional, university, high school, and amateur retired athletes participating in a range of sports. Aspects of cognitive health including domains of memory, executive function, psychomotor speed, attention, language, intelligence and perception among retired athletes with a history of concussion and head-impact exposure were reported. The results suggested that a history of concussion may more greatly affect the cognitive domains of memory, executive function, and fine motor functioning. Retired athletes also appeared to have increased self-reported cognitive difficulties in retirement. Twenty-eight percent of the studies reported a frequency–response relationship, with poorer cognitive outcomes in athletes with greater levels of exposure to head impacts or concussions. However, similar to the previous systematic review, limitations of the included studies included biased recruitment, convenience sampling, lack of methodologic rigour and self-reported outcome measures open to bias. It was found that certain key cognitive domains, such as visuospatial processing, psychomotor

function, language and reaction time are underassessed. Given the methodologic biases, confounding variables, and lack of control groups in a substantial number of studies, it was difficult to extrapolate findings from this review.

A range of cognitive health outcomes, as well as premorbid ability, in diverse samples of athletes with and without a history of concussion or head-impact exposure was recommended to delineate long-term effects of sport participation on cognitive functioning. Reliability of player self-reported concussion and the evidence of increased self-reported cognitive difficulties among some retired rugby players requires further investigation. The paucity of high-quality, prospective studies limited the conclusions that could be drawn regarding a cause-and-effect relationship between concussion and long-term health. A significant limitation noted in both systematic reviews was regarding the validity of self-reported concussion history. Hence, a validation study of a concussion history tool was undertaken (Study I, Chapter 5). In light of the lack of research to date on the influence of a career in professional rugby on brain health observed in Systematic Review 1, the large cross-sectional studies II-V- (Chapter 6-9) were conducted to explore (1) physical health (2) mental health (3) neurocognitive functioning (4) and multisensory processing/ perceptual functioning among former professional rugby players.

10.3 Analysis of key findings

10.3.1 Study I

Athlete concussion history recall is underestimated: a validation study of self-reported concussion history among current professional rugby union players.

This cross-sectional study was the first of its kind among rugby players in assessing the validity of self-reported concussion histories, by comparing the agreement between retrospective player self-reported and clinically diagnosed concussion histories. Despite

improved diagnosis and documentation of concussive injuries, clinicians routinely rely on athlete recall as part of patient care. The accuracy and reliability within and between these sources are poorly quantified, but of growing concern with an increased focus on potential long term declines. Due to greater awareness, diagnosis and documentation of concussions, there is increasing opportunity to estimate the agreement between player-recalled and clinically diagnosed concussion histories. Despite greater detection and awareness of concussion, the ability to gain an accurate concussion history from current or past rugby players is frustrated by many issues. The lack of universal consensus regarding a concussion definition means that ambiguity and uncertainty persist in recognising and diagnosing concussion. Given that concussion is a syndrome, signs and symptoms can be vague and often non-specific. A further difficulty in gaining concussion history from rugby players is the issue of recall bias.

The Michigan TBI Identification Method was used to obtain self-reported concussion histories from 62 professional rugby players. This tool is a National Institutes of Health (NIH) Common Data Element which has been implemented in large scale concussion studies (Broglio et al., 2018). Therefore, research on its validity compared to the recognised gold standard of clinical documentation of concussion history is required. Self-reported concussion information was compared to medically recorded data captured between 2008 and 2017. A total of 38 players encountered 99 total concussions. The mean number of clinically diagnosed (medically documented) concussions per player was 30% more than the mean number of self-reported concussions per player. Overall, player self-reported and clinically diagnosed concussion histories was found to have a ‘fair’ level of agreement, while the test re-test reliability of the tool was ‘moderately strong’. This study highlights that caution is needed in interpreting concussion histories from self-reported measures with rugby players. The retired professional rugby players played in an era in which concussion was often trivialised due to lack of awareness and diagnosis and when documentation of concussion was not the norm. Therefore, the lack of gold-standard clinical documentation of

concussion renders self-reported history the sole means of gaining an estimate of concussion history. This study preceded the large cross-sectional study which used the Michigan TBI Identification Method to gain an estimate of concussion history among former rugby players across studies II-V. Despite the mixed validity and reliability results regarding the Michigan TBI Identification, it was used throughout the 'PROP' studies. It was still deemed the most appropriate tool when compared to various other tools used in the literature which are more suitable to moderate/severe TBI and have reported similar reliability on other athletes (Corrigan and Bogner, 2007, Kerr et al., 2011). The current study using the Michigan TBI Identification Method is the first to investigate the validity of self-reported concussion history among rugby players specifically. The moderately strong test re-test reliability indicates preliminary support for use of this tool in a professional rugby population.

10.3.2 Studies II-V

In order to empirically establish the extent of the potential long-term consequences of a career in professional rugby, undoubtedly large-scale longitudinal prospective studies are required. Hoverer, cross-sectional studies such as the one described in this thesis investigating the influence of a career in rugby on long-term brain health, serve to provide information in the interim.

10.3.2.1 General Health Status

Lifestyle factors and general health status among former professional rugby union players in retirement: a cross-sectional study.

The sociodemographic and health characteristics of both groups were detailed in Chapter 6. Sociodemographic factors such as level of education and income and health-related factors such as medical history have been linked to cognitive health in previous studies (Wu et al.,

2011). This chapter raises a number of factors including exercise, pain and disability and alcohol consumption, all of which are known to influence long-term brain health (Hogan, 2005, Bernardin et al., 2014, Moriarty et al., 2017). Alcohol use was significantly higher among the rugby players when compared to the rowers. The point prevalence of alcohol misuse was very high among the rugby players at 45%, while 36% of rowers reported misuse of alcohol. Both groups had a higher prevalence of alcohol misuse than the general population. While this was a once off questionnaire and hence is open to bias, this finding warrants further investigation. Long-term alcohol abuse is known to impact upon brain health (Welch, 2017). Further alcohol related brain damage (ARBD) accounts for possibly 10% of early onset dementia (Harvey et al., 2003). Therefore, future studies investigating long-term brain health in professional rugby players should consider the impact of alcohol use and the potential for alcohol abuse in this cohort.

The level of pain and disability was significantly higher among the former rugby players when compared to the rowers. Prevalence of pain and disability was 17% among rugby players, compared to 4% among rowers. Exercise levels were also significantly lower in rugby players than among rowers, with pain and disability correlating with exercise levels among the rugby players. These findings indicate that there are many factors associated with the aftermath of a career in elite rugby which may influence long-term brain health. Exercise has a known neuroprotective effect during aging and hence should be continued throughout the lifespan (Vecchio et al., 2018). Therefore, functional barriers to exercise among former professional rugby may players pose a concern for aging retired professional rugby players and should be considered in future studies.

Factors such as pain and disability, lack of exercise and alcohol abuse may have detrimental knock on effects on overall brain health among former professional rugby players. Therefore, need to be addressed. Health related factors assessed such as body mass index, body and visceral fat percentage and blood pressure may indicate poor future cardiovascular health in retired rugby players. Results from Study II revealed that 68% of rugby players were in the

hypertensive category. Investigations in the current study were not diagnostic but suggest that non-cognitive factors may be influencing brain function. Alcohol consumption is known to influence blood pressure in a dose-response manner (Roerecke et al., 2017). Therefore, the high levels of alcohol consumption among the rugby players puts them at risk of hypertension, which particularly in midlife is linked with cognitive impairment and dementia (Elias et al., 2004, Walker et al., 2017, Walker et al., 2019). The presence of BMI categorised as overweight and obese among the former rugby players was commonplace and was significantly higher among rugby players when compared to rowers. Population based evidence indicates that being in the overweight or obese range in midlife is a risk factor for dementia later in life (Albanese et al., 2017a). Higher visceral fat levels found among rowers compared to rowers is also a known risk factor for cardiovascular disease (Despres, 2007, Lee et al., 2016). Therefore, these factors need to be taken into account when investigating brain heath in aging retired rugby players.

These findings suggest that programmes to aid players with the transition into retirement should be considered. These could serve to support rugby players particularly during the initial transitioning period. A transitioning program from professional rugby for example could help protect players from the potential adverse consequences of abrupt physical, social and lifestyle changes associated with retirement, particularly forced retirement from professional rugby. Issues such as pain and disability associated with the physicality of professional rugby could be addressed and players supported in continuing to exercise. The game of rugby is becoming more physical and players are required to have a larger body mass. Therefore, body composition changes which occur in retirement should be viewed in the context of known cardiovascular risk profiles among the general population. Upon retirement, linemen in American NFL have been shown to have a higher prevalence of metabolic risk factors along with increased left ventricular mass and left atrial area compared with non-linemen (Selden et al., 2009, Kim et al., 2018), and a comparable or increased risk for metabolic syndrome when compared to the general population (McHugh et al., 2019). In

light of this emerging research, findings from the current study may be particularly important for forwards in rugby. The average body mass of rugby players is on the rise highlighting the growing trend of so called ‘supersizing’ rugby players (Hill et al., 2018). Visceral adipose tissue which was found to be higher among rugby players and correlated with BMI, is associated with low grade inflammation, and chronic diseases such as cardiovascular disease (Wang and Nakayama, 2010). Therefore, supersizing players in rugby coupled with a lack of detraining strategies may lead to not only increased cardiovascular risk among former professional rugby players but also increased risk of poorer brain health including cognitive impairment and vascular dementia (Feinkohl et al., 2018).

Appropriate medical professional help should be provided to players to cope with the delayed impact of musculoskeletal injuries and multiple surgeries on subsequent functional disability, secondary arthritis and chronic pain associated with a career in professional rugby. Rugby players reported undertaking significantly less exercise than their rowing counterparts. This is of particular importance given the young mean age of the rugby cohort and that higher pain and disability was associated with lower levels of exercise among the rugby players. Therefore, barriers to exercise in retirement needs to be addressed in this cohort to prevent the negative long-term consequences of sedentary lifestyle due to chronic pain. Unlike rowing, continuation of rugby playing is often not feasible post retirement and as the player ages. This is largely due to the physicality of rugby and the collisions involved. Rugby players could however consider transitioning to field team sports such as tag rugby involving less physical contact.

10.3.2.2 Mental Health

An investigation into the mental health status of retired professional rugby union players and its association with a history of concussion: a cross-sectional study.

This study provides an insight into the mental health of retired professional rugby players, all of whom were in the early stages of retirement from play. A variety of self-reported questionnaires regarding symptoms associated with mental health disorders such as anxiety, depression, pain and disability, sleep disturbance and alcohol misuse were examined. It was found that retired professional rugby players have a higher prevalence of mental health issues such as depression and anxiety compared to rowers and the general population. Concussion history was not found to be associated with mental health indicators. However, regression analysis revealed predictors of depression included lower levels of satisfaction with life and resilience and higher levels of pain and disability and athletic identity. Therefore, future studies investigating brain health among former professional rugby union players, should consider these factors.

Retirement from elite rugby or any elite sport is a unique period of change in a rugby player's life. For players this transition from professional rugby occurs early in life and can sometimes be sudden and involuntary, therefore, posing various challenges of adjusting and adapting to a non-elite sport lifestyle. A big change which occurs is the shift in self-identity and a re-direction of goals and aspirations. We found that retired rugby players had a significantly higher sense of athletic identity than the rowers. As discussed in Chapter 7, this may be due to a number of reasons, including the fact the majority of rowers had a working job alongside their rowing career, therefore perhaps making the transition to retirement smoother. Further, rugby players are better known among the general population and are more likely to be identified solely as a professional rugby player. Forced retirement from rugby has been shown to be associated with increased distress (Brown et al., 2017). If transitions are foreseeable and anticipated, a period of time facilitates preparation and planning which may lessen the difficulties associated with the transitional period. While pain and disability are prevalent in the general population, history of musculoskeletal injuries among the former rugby players may place them at an increased risk of poorer mental health associated with chronic pain.

Preparation for career transition for post sporting career life interventions and strategies could be useful. They could reduce the risk of the occurrence of mental health symptoms and disorders among former rugby union players. Thorough preparation for career transition is recommended for professional rugby union players. The association between the pain disability index and depression indicators suggests that interdisciplinary medical care and support for rugby players should be incorporated into the overall management of the transitioning player. Timely mental health diagnoses and management strategies are required which are specific to this population. Mental health symptoms and disorders in former professional rugby players must be addressed by national and international stakeholders, with prioritisation on the physical and psychological sequelae of retirement from professional rugby union. The mental health burden among rugby players was due to a combination of factors including those which are unique to the elite athlete. These sport-specific stressors alongside common stressors which affect the general population, make former professional rugby players vulnerable to substantial prevalence of mental health symptoms and disorders.

10.3.2.3 Cognitive and Perceptual Functioning

i) An assessment of neurocognitive functioning in retired professional rugby players with a history of concussion; a cross-sectional study.

ii) Assessment of multisensory processing in retired professional rugby players with a history of concussion; a cross-sectional study.

Findings in the CANTAB tests of neurocognitive functioning revealed no negative impact of a concussion or years of exposure to rugby on performance. Relative to rowers, rugby players performed better in the domains of attention and psychomotor speed assessed by the CANTAB which revealed that the rugby players performed significantly better on tests of reaction time, motor speed, processing speed and visuospatial ability. Cluster-based analysis

revealed no association between concussion history estimates and performance on any tests on the CANTAB. Our cognitive-motor results do not support previous data on retired professional athletes with a history of concussions (Hume et al., 2017, De Beaumont et al., 2009, De Beaumont et al., 2007, McMillan et al., 2017, Pearce et al., 2018). Pearce et al. (2018) found that professional rugby players (Mean age: 48.4, 95% CI (45.8, 51.0)) had slower visuomotor reaction time compared to controls using a similar methodology (Pearce et al., 2018). Whereas, Hume et al. (2017) found that concussion history was associated with small to moderate neurocognitive deficits in retired rugby players (Mean age: 43.3 ± SD (8.2) years) in areas such as cognitive flexibility, complex attention and executive function. It is of note that the mean rugby player age in the current study was younger than the above studies. Therefore, findings in the current study could be significantly influenced by the age of participants, variation in number of concussions and severity of acute concussion. Neuroplasticity, cognitive reserve and effective compensatory recruitment of brain-structural domains which are unaffected by concussion history could account for the intactness of neurocognitive health in our retired elite rugby sample (Stern, 2009). Furthermore, we cannot rule out the potential for future long-term negative consequences of concussion on cognitive functioning in our sample.

While it was expected that a career in a dynamic contact sport environment might equip former rugby players with a greater ability to integrate and process information from the senses, this does not appear to be the case as revealed by the sound induced flash illusion results. This study is the first to report alterations in multisensory integration in retired professional rugby union players with a history of concussions during their careers. The novel finding of our study was the observation that performance on the SIFI task was associated with concussion history in the former rugby population. This finding is not in keeping with results from the CANTAB, which suggested that cognitive performance on all tests was not associated with concussion history or years playing (exposure to contact sport). This may suggest that concussion may have a selective negative effect on the domain of perception. It

could also be hypothesized that the rugby players' younger age and relatively recent retirement enabled them to capitalize on cognitive reserve. This could have resulted in resilience in neurocognitive performance and account for intact neurocognitive health among the rugby players with a history of repetitive head impacts in the CANTAB tests (Stern, 2002, Satz, 1993, Stern, 2009, De Beaumont et al., 2009). However, the SIFI task may be more sensitive to concussion history and better at detecting subtle changes in perceptual ability. Multisensory integration is essential in facilitating higher order cognitive processes such as attention and executive function (Talsma and Woldorff, 2005). Susceptibility to the sound induced flash illusion has been shown to increase with age (McGovern et al., 2014) and can increase following concussion (Wise and Barnett-Cowan, 2018). Long-term damage to the nervous system associated with concussion history may result in expediated decline in efficiency at coordinating the processing and integration of sensory information. It could be hypothesized that concussion history may adversely affect multisensory processing ability and potential early onset cognitive deterioration may be reflected by reduction in performance on the SIFI Task. Cognitive reserve and neuroplasticity may provide an explanation regarding the relationship between potential perceptual and subsequent neurocognitive decline and history of SRC among the former rugby players. Therefore, meaningful relationships between incongruent SIFI experiments and past concussions could provide a basis for further investigation into potential perceptual correlates of SRC in rugby players and other contact sport populations.

10.4 Findings in the context of previous work

Recent studies have highlighted the insufficient number of longitudinal studies with a high-quality design in discerning the long-term effects of a career in professional rugby on brain health. There has been a surge in research reporting significant risks of adverse neurocognitive health implications of concussion and head impact exposure in contact sports. Findings reflected in a limited rugby population research have demonstrated neurocognitive

deficits in retired rugby players in areas such as cognitive flexibility, complex attention and executive function, dexterity and visuomotor reaction time relative to non-contact control groups (Hume et al., 2017, Pearce et al., 2018). There is growing international attention towards understanding the relationship between repetitive concussions experienced in sport and the development of chronic neurological impairment later in life. To date, the majority of data has stemmed from North America in sports such as football, soccer and ice hockey. In retired athletes with a history of concussions, studies have reported ongoing neurological symptoms, neurophysiological abnormalities, and/or cognitive impairments (Zhang et al., 2019). Previous studies have varied in terms of definition of concussion, reporting of the incidence of concussions, exposure period and characteristics of controls groups. A study on retired national/international rugby players in France found depression and mild cognitive impairment to be more common than in controls; with depression associated with a higher frequency of self-reported concussion (Decq et al., 2016). Of interest the number of concussions (Mean: 3.1 SD (5.01)) was lower than in the present study (Mean: 6.92 SD (10.43)). In a study on retired NFL players an association between risk of depression and number of concussions was also reported although evidence for this was not found in the present study.

10.4 Overview

Healthy brain aging is known to be influenced by multiple factors both inert and environmental (Mora, 2013, Kramer et al., 2004). The overall benefits of physical activity associated with sports participation in the prevention of chronic diseases are well established (Reiner et al., 2013). Long-term health benefits attributed to certain elite sports include lower all-cause mortality and lower risk of cardiovascular disease than the general population have been attributed to certain elite sports (Lehman et al., 2012, Mackay et al., 2019, McMillan et al., 2017). Observational studies have shown that exercise reduces the risk of cognitive decline in aging (Livingston et al., 2017). However, increased risk of neurodegenerative

disease compared to the general population has been demonstrated in former soccer and football players (Mackay et al., 2019, Lehman et al., 2012), suggesting that concussion history may offset potential neuroprotective benefits of exercise accrued throughout a sporting career. The combined long-term effects of concussion on the brain health of aging rugby players in the context of neuroplastic adaptation due to exercise is unclear (Tremblay et al., 2018). However, in order to gain continued and optimal brain health benefits from exercise, it should be continued throughout the lifespan. Higher cardiovascular fitness in midlife has been associated with decreased risk of dementia (Horder et al., 2018, Hansson et al., 2019). Unhealthy lifestyle behaviours and negative health-related factors in retirement, including; excessive alcohol, physical inactivity, sleep disturbance and pain and disability are known to adversely affect mental and cognitive health and increase the risk of neurodegeneration (Kempermann, 2019, Livingston et al., 2017).

10.5 Critical Analysis

This thesis contained a number of studies that were designed to examine brain health in retired professional rugby players. Analysis of limitations of the studies contained in this thesis is important. A summary of common limitations across all studies will be summarised below.

10.5.1 Potential Bias

The cross-sectional study design employed enabled us to provide a large body of information in a short period of time on the burden of mental, physical and brain health among retired professional rugby players. However, the main limitation of this study is the cross-sectional design, which does not eliminate the potential for recall and selection bias. The self-reported concussion history and health outcome data were all collected at one time point which may introduce recall bias. In common with many similar retrospective studies (Hume et al., 2017,

McMillan et al., 2017), the current study is limited by an absence of objective information about concussions in terms of number and severity. As demonstrated in Study I (Chapter 5), concordance between recorded incidence of concussion in rugby and self-report may be poor. The impact of retrospective recall bias on concussion reporting is unknown in the current study of former professional rugby players. Also, relying on player self-report for a number of characteristics of their rugby playing history (i.e. number of years professional and number of years playing at any level (amateur and professional)) was also subject to bias. Furthermore, players with a poorer perception of their general health may attribute this to their playing career and concussion history, leading them to overestimate concussion history. This could also be fuelled by heightened media interest in concussion and public perceptions.

10.5.2 Study sample

Given the exploratory nature of this study, an a priori sample size calculation was not conducted for the outcomes discussed. This may result in the study being underpowered. A consequence of the cross-sectional design is the risk of selection bias. A further limitation of the study is recruitment. While the governing sporting bodies facilitated mass recruitment strategies via email, talks, advertisement on websites and so forth, we cannot eliminate the possibility of convenience sampling and selection bias. Participants were recruited from advertisements self-selected into the study, potentially introducing inherent bias into the sample. A self-selecting population in a study of this nature may be biased towards well-educated, motivated and cognitively well volunteers. For example, a player who has developed serious cognitive impairment or a neurodegenerative disease since retirement from professional rugby may be less likely or even able to participate in the current study. Therefore, our sample may be biased towards inclusion of healthier able bodied retired rugby players. A corollary to this may be that players who are anxious and experiencing cognitive symptoms may be more likely to put themselves forward for inclusion in the study. As they may want to be examined and to seek reassurance. While every effort was made to gain a

representative sample of retried professional rugby players, the current study is limited by the response from the potential alumni pool of an estimated 400 players. We do not have any data available on the non-respondents. Therefore, whether the sample presented in the studies in this thesis are representative of the population is largely unknown. Our study benefited from the inclusion of a retired non-contact elite sporting comparison group. The control group were similar in terms of sociodemographic factors. However, a limitation in the studies was the significant between group differences in age. The cross-sectional nature of the studies contained in the thesis allow for the exploration of associations. However, they do not allow for determination of causality. One strength of studies within this work was that a unique population, a cohort of retired professional rugby players with history of concussion and head impact exposure and hence considered as a potential high risk group for future cognitive decline were recruited. Research into female rugby players is lagging when compared to its men's counterpart in terms of medical research. There is a dearth of research on women's rugby injuries including concussion (Peck et al., 2013). While every effort was made to recruit female international rugby players, the uptake of female athletes to the current study was small. However, there was a smaller pool to draw from when compared to the male rugby alumni.

10.5.3 Cognitive testing

In the current thesis, the CANTAB battery of validated neuropsychological tests were chosen in collaboration with a neuropsychologist and based on sound theoretical justification. Furthermore, many of the assessments used were designed to detect gross cognitive impairments and may have failed to uncover subtle changes in cognitive function. However, there is the possibility that the chosen tests were insensitive to the long-term differential effects of varying levels of concussion. Previous studies have used variations in definitions of concussion and a variety of offering neuropsychological tests.

10.5.4 Future Directions

10.5.4.1 Ethics and dissemination

As previously stated, the cross-sectional study design enabled us to provide meaningful data on the brain health of a young cohort of retired professional rugby players. The main advantage of the cross-sectional nature was the ability to collect a large amount of data in a short space of time. Depending on the availability of funding, the current study could inform a more detailed longitudinal prospective study assessing the association between concussion in rugby players and long-term brain health. The current study was designed to detect subtle preclinical changes that might be associated with concussion history in the former rugby players. A novel aspect of this project was the assessment of multisensory processing and perceptual ability among the players using the Sound Induced Flash Illusion task. Our findings on the SIFI task are a basis to prompt further exploration into multisensory processing and integration in individuals with a history of concussion. Future research is required to investigate the clinical significance of this finding. Furthermore, while we did not find any overt signs of adverse effects of concussion based on the performance on the CANTAB, future longitudinal follow-up of the players is required. The dataset collected electronically throughout this project would provide a useful basis for comparison with future follow-up. As discussed, cognitive reserve owing to the young age of players may have influence current results. Long-term follow-up would be required to delineate any negative impacts of concussion in this cohort as they age.

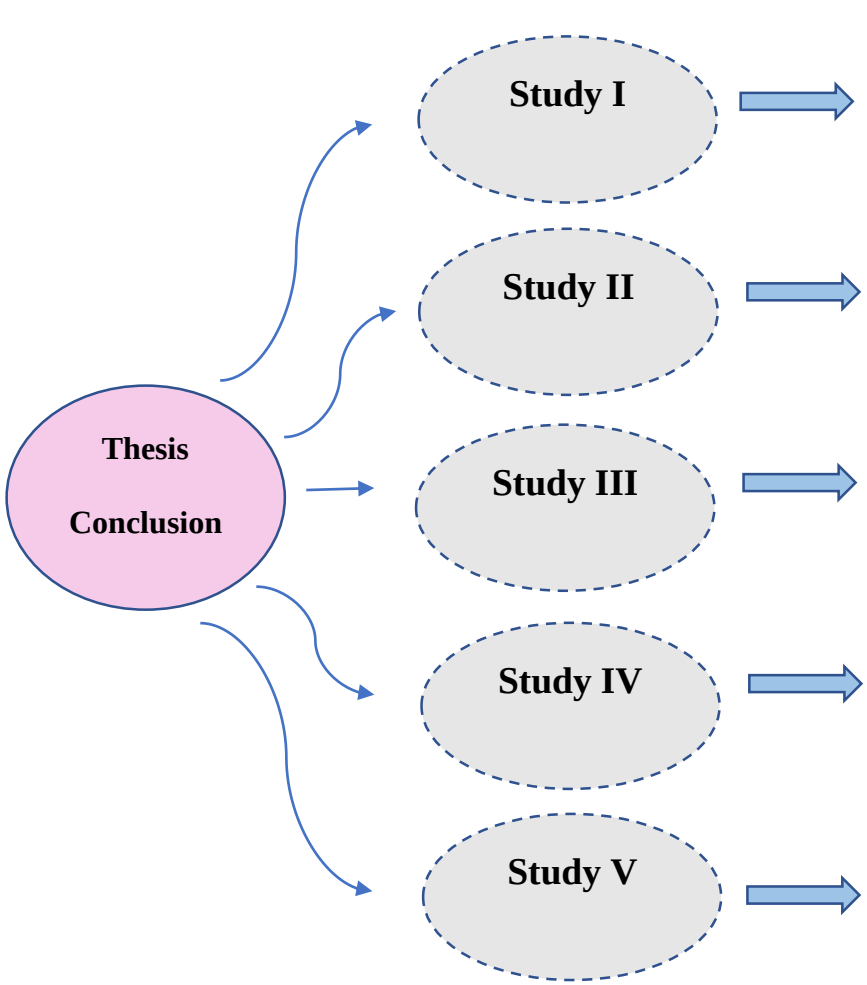
The current study provides a basis for future prospective studies to investigate the extent to which the susceptibility to the illusion may be associated with concussion history and future risk of developing cognitive decline in retired professional rugby players. Data from this project will firstly be disseminated to players and the aforementioned sports governing bodies involved in the study. Dissemination of this body of work will then take place through peer-

reviewed publication and conference presentation, in order to add to the evidence based literature investigating association between exposure concussion in rugby, and brain health in retirement. The study focussed on subclinical problems (i.e. performance below average on cognitive tests or compared to controls). However, none of the tests were diagnostic. A protocol was put in place to manage any signs of adverse health among the players and this was highlighted in the consent form to players, prior to them participating in the study. The questionnaires used to screen for depression did identify participants with significant mental health problems who were at potential risk. In cases where this arose, players were given information regarding emergency services, advised to return to their primary care physician and were referred to our project clinical psychologist who contacted the individuals and provided expert advice and counselling. Throughout testing, participants were identified as having varying extents of hypertension. As previously noted, the scope of our study did not enable us to investigate these initial signs of high blood pressure further. However, the participants were counselled on the lifestyle and behavioural factors associated with high blood pressure. They were also urged to attend their primary care physician for further investigation.

10.6 Conclusion

The studies contained in this thesis provide valuable insights into the burden of physical, mental and cognitive health among retired professional rugby players following a career in professional rugby playing. The players in the current study are the first cohort retiring from the professional era of rugby in Ireland. Results may not be immediately generalisable to current players as playing rules and conditions continue to evolve. This is particularly true with regards the rigour with which concussion is identified and return to play managed, which has improved substantially since the playing era of many players in the current study. Therefore, this may positively influence the long-term brain health of current rugby players and minimise any potential adverse long-term effects of rugby on brain functioning. The long-term risks associated with professional rugby are likely to change over time, however. Large-scale, prospective longitudinal studies with a high level of control of confounding factors are required to confirm the effects of aging with a history of concussion on brain health in the aging former professional rugby player. The transitional implications of retiring from professional rugby on brain health need to be explored further. There is a need for identifying opportunities for interventions and implementing pro-active strategies to encourage positive transition into post-sports life for rugby players. Particularly given the abrupt physical and social transformations that may elicit feelings of poor mental health, adverse alcohol use and sleep disturbance.

Table 10-1 Thesis Conclusion



- Number of player self-reported and diagnosed concussions had a 'fair' level of agreement. Lifetime concussion history was found to be significantly negatively correlated with player self-report accuracy, with recall worsening as the number of lifetime concussions increased.
- The test re-test reliability of concussion history was moderately strong.

- Significantly greater BMI and visceral fat among RUG compared to ROW group. Increased prevalence of hypertension among RUG group.
- Significantly decreased exercise levels and increased pain and disability and alcohol usage among RUG compared to ROW group.

- Higher depression prevalence among RUG group.
- Significantly higher somatization among RUG compared to ROW group.
- Significantly greater sense of athletic identity among RUG compared to ROW group.
- Decreased satisfaction with life, decreased resilience, greater athletic identity and higher levels of pain and disability significantly predicted depression among the RUG group.

- Significantly better performance on tests of attention, psychomotor speed, rapid visual processing and visuospatial skills among RUG compared to ROW group.
- RUG group performed worse than the general population on the majority of memory tasks. Concussion history or number of years playing rugby were not correlated with performance on any CANTAB tests.

- Compromised audio–visual integration was found among RUG compared to ROW group.
- Concussion history estimates significantly predicted the odds of an accurate response on the SIFI.

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Appendix A: Publications Resulting from this Thesis

Full-text Publications

Appendix A.1 Cunningham J., Broglio S., and Wilson F. (2018). Influence of playing rugby on long-term brain health following retirement: a systematic review and narrative synthesis. *BMJ open sport & exercise medicine.* 4(1), e000356.

Appendix A.2 Cunningham J., Broglio S., O'Grady M and Wilson F. (2020). History of Sport-Related Concussion and Long-Term Clinical Cognitive Health Outcomes in Retired Athletes: A Systematic Review. *Journal of Athletic Training.*

Abstract Publications

Abstracts from the 37th Annual National Neurotrauma Symposium Pittsburgh, Pennsylvania.

Appendix A.3 Cunningham J., Broglio S., Wyse J., Farrell G., Denver K., Wilson F. Reliability of self-reported concussion history in current professional rugby union players (2019*). Journal of Neurotrauma. Vol. 36, No. 13.*

Appendix A.4 Cunningham J., Broglio S., Mc Cabe E., Wilson F. Depression indicators in former professional rugby players are related to number of playing years and not concussion history. *Journal of Neurotrauma. Vol. 36, No. 13.*

Appendix B.1 PROSPERO Registration for Systematic Review I**.**

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PROSPERO
International prospective register of systematic reviews

The influence of rugby on later life cognitive functioning: a systematic review

Fiona Wilson, Steven Broglio

Citation

Fiona Wilson, Steven Broglio. The influence of rugby on later life cognitive functioning: a systematic review. PROSPERO 2017 CRD42017081586 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42017081586

Review question

Objectives The aim of this review was to systematically evaluate the available evidence for long-term cognitive deficits in retired rugby players.

Searches

EMBASE, PsycINFO, Web of Science, CINAHL, Cochrane Library and MEDLINE.

No restrictions will be placed on dates or language. Search strategy will be restricted to humans.

1. 'cognitive defect'/exp
2. 'depression'/exp

3. ((Cogniti* OR neuropsychological OR neurocognitive OR executive OR brain) NEAR/3 (impairment OR defect* OR function* OR dysfuntion* OR process* OR symptom* OR factor* OR Deficit* OR disorder*)):ti,ab

4. (Neuropsychological NEAR/3 test*):ti,ab

5. Depressi*:ti,ab

6. #1 OR #2 OR #3 OR #4 OR #5

7. 'athlete'/exp

8. 'rugby'/exp

9. ((Athlete* OR 'sports person' OR sportswomen OR sportswoman OR sportsman OR sportmen OR rugby OR player* OR 'contact-sport') NEAR/5 (retire* OR former)):ti,ab

Types of study to be included

Observational cross-sectional studies.

Condition or domain being studied

Cognitive Functioning - key domains including learning and memory, executive function and complex attention, language and visuospatial abilities.

Participants/population

Inclusion Criteria/Exclusion Criteria For the purpose of this review, studies were required to include living retired male or female rugby players. The studies were required to include at least one form of cognitive testing as an outcome measure. Studies were excluded if they explored only athletes still actively involved in sport. Studies with case studies with five or fewer participants were excluded.

Intervention(s), exposure(s)

Mild traumatic brain injury/concussion/head impact exposure.

Comparator(s)/control

Inclusion Criteria/Exclusion Criteria: For the purpose of this review, studies were required to include living

retired male or female rugby players. The studies were required to include at least one form of cognitive testing as an outcome measure. Studies were excluded if they explored only athletes still actively involved in sport. Studies with case studies with five or fewer participants were excluded.

Controls - ideally include retired non-contact sport athletes

Context

Main outcome(s)
The primary outcomes of interest to this review are key domains of cognitive functioning including learning and memory, executive function, visuospatial abilities, language and complex attention.

Additional outcome(s)
Secondary outcome of interest is a history of sports-related concussion (mTBI)/ head impact exposure.

Data extraction (selection and coding)
A data extraction template will be used as a checklist of items which should be included in reports of cross-sectional observational studies, based on STROBE guidelines. One reviewer will record participant characteristics; details of concussion history; outcome measures used and relevant outcome data (group means and standard deviations.

Risk of bias (quality) assessment
A modified Downs and Black Methodological Assessment will be performed.The checklist will be modified to a maximum of 17 applicable questions which address the following methodological components: reporting, external validity, internal validity (bias and confounding) and power. Seventeen items will be rated either as yes (=1) or no/unable to determine (=0), and one item will be rated on a 3-point scale (yes=2, partial=1 and no=0). The maximum achievable score is 18, with higher scores indicating a better methodological quality of the study. Results will be interpreted as follows: strong quality (?14) representing the top 75%; moderate quality (scores 9-13) representing 50-74%; limited quality representing (5-8) represented 25-49%; poor quality (<5) represented <25%). This will inform the data synthesis stage, depending on methodological quality of studies and whether absolute values are provided for quantitative synthesis.

Strategy for data synthesis
This review will likely be narrative; depending on homogeneity of data quantitative synthesis may be undertaken.

Analysis of subgroups or subsets
Undetermined as of yet-planned systematic review and descriptive synthesis

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Organisational affiliation of the review
Trinity College Dublin

Review team members and their organisational affiliations
Assistant/Associate Professor Fiona Wilson. Department of Physiotherapy, School of Medicine, Trinity College Dublin
Assistant/Associate Professor Steven Broglio. Department of Kinesiology, University of Michigan

Type and method of review
Meta-analysis, Systematic review

Anticipated or actual start date
15 November 2017

Anticipated completion date
15 December 2017

Funding sources/sponsors
Trinity College Dublin

Conflicts of interest

Language
(there is not an English language summary)

Country
Ireland

Stage of review
Review Completed not published

Details of final report/publication(s)

Cunningham J, Broglio S, Wilson F. Influence of playing rugby on long-term brain health following retirement: a systematic review and narrative synthesis. BMJ Open Sport & Exercise Medicine 2018;4:e000356. doi: 10.1136/bmjsem-2018-000356
https://bmjopensem.bmj.com/content/4/1/e000356

Subject index terms status
Subject indexing assigned by CRD

Subject index terms
Cognition; Football; Humans; Life

Date of registration in PROSPERO
15 December 2017

Date of publication of this version
21 January 2019

Details of any existing review of the same topic by the same authors

Stage of review at time of this submission

Stage	Started	Completed
Preliminary searches	Yes	Yes
Piloting of the study selection process	Yes	Yes
Formal screening of search results against eligibility criteria	Yes	Yes
Data extraction	Yes	Yes
Risk of bias (quality) assessment	Yes	Yes
Data analysis	Yes	Yes

Versions
15 December 2017
21 January 2019

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PROSPERO
International prospective register of systematic reviews

Appendix B.2 Electronic Databases Search Strategy for Systematic Review I.

Brain health in retired rugby union players

EMBASE	1. 'cognitive defect'/exp 2. 'depression'/exp 3. ((Cogniti* OR neuropsychological OR neurocognitive OR executive OR brain) NEAR/3 (impairment OR defect* OR function* OR dysfuntion* OR process* OR symptom* OR factor* OR Deficit* OR disorder*)):ti,ab 4. (Neuropsychological NEAR/3 test*):ti,ab 5. Depressi*:ti,ab 6. #1 OR #2 OR #3 OR #4 OR #5 7. 'athlete'/exp 8. 'rugby'/exp 9. ((Athlete* OR 'sports person' OR sportswomen OR sportswoman OR sportsman OR sportmen OR rugby OR player* OR 'contact-sport') NEAR/5 (retire* OR former)):ti,ab 10. #7 OR #8 OR #9 11. #6 AND #10	1760
PsycINFO	1. DE "Cognitive Impairment" OR DE "Depression (Emotion)" OR DE "Executive Function" 2. TI ((Cogniti* OR neuropsychological OR neurocognitive OR executive OR brain) N3 (impairment OR defect* OR function* OR dysfuntion* OR process* OR symptom* OR factor* OR Deficit* OR disorder*)) OR AB ((Cogniti* OR neuropsychological OR neurocognitive OR executive OR brain) N3 (impairment OR defect* OR function* OR dysfuntion* OR process* OR symptom* OR factor* OR Deficit* OR disorder)) 3. TI (Neuropsychological N3 test*) OR AB (Neuropsychological N3 test*) 4. TI Depressi* OR AB Depressi* 5. S1 OR S2 OR S3 OR S4 6. DE "Athletes" 7. DE "Rugby" 8. TI ((Athlete* OR 'sports person' OR sportswomen OR sportswoman OR sportsman OR sportsmen OR rugby OR player* OR 'contact-sport') N5 (retire* OR former)) OR AB ((Athlete* OR 'sports person' OR sportswomen OR sportswoman OR sportsman OR sportsmen OR rugby OR player* OR 'contact-sport') N5 (retire* OR former)) 9. S6 OR S7 OR S8 10. S5 AND S9	756
Medline	1. (MH "Cognition Disorders+") OR (MH "Neurocognitive Disorders+") OR (MH "Mild Cognitive Impairment") OR (MH "Depression") OR (MH "Depressive Disorder+") 2. TI ((Cogniti* OR neuropsychological OR neurocognitive OR executive OR brain) N3 (impairment OR defect* OR function* OR dysfuntion* OR process* OR symptom* OR factor* OR Deficit* OR disorder*)) OR AB ((Cogniti* OR neuropsychological OR neurocognitive OR executive OR brain) N3 (impairment OR defect* OR function* OR dysfuntion* OR process* OR symptom* OR factor* OR Deficit* OR disorder)) 3. TI (Neuropsychological N3 test*) OR AB (Neuropsychological N3 test*) 4. TI Depressi* OR AB Depressi* 5. S1 OR S2 OR S3 OR S4 6. (MH "Athletes") 7. (MH "Rugby") 8. TI ((Athlete* OR 'sports person' OR sportswomen OR sportswoman OR sportsman OR sportsmen OR rugby OR player* OR 'contact-sport') N5 (retire*	1004

	OR former)) OR AB ((Athlete* OR 'sports person' OR sportswomen OR sportswoman OR sportsman OR sportsmen OR rugby OR player* OR 'contact-sport') N5 (retire* OR former)) 9. S6 OR S7 OR S8 10. S5 AND S9	
CINAHL	1. (MH "Cognition Disorders+") OR (MH "Depression+") 2. TI ((Cogniti* OR neuropsychological OR neurocognitive OR executive OR brain) N3 (impairment OR defect* OR function* OR dysfuntion* OR process* OR symptom* OR factor* OR Deficit* OR disorder*)) OR AB ((Cogniti* OR neuropsychological OR neurocognitive OR executive OR brain) N3 (impairment OR defect* OR function* OR dysfuntion* OR process* OR symptom* OR factor* OR Deficit* OR disorder)) 3. TI (Neuropsychological N3 test*) OR AB (Neuropsychological N3 test*) 4. TI Depressi* OR AB Depressi* 5. S1 OR S2 OR S3 OR S4 6. (MH "Athletes") 7. (MH "Rugby") 8. TI ((Athlete* OR 'sports person' OR sportswomen OR sportswoman OR sportsman OR sportsmen OR rugby OR player* OR 'contact-sport') N5 (retire* OR former)) OR AB ((Athlete* OR 'sports person' OR sportswomen OR sportswoman OR sportsman OR sportsmen OR rugby OR player* OR 'contact-sport') N5 (retire* OR former)) 9. S6 OR S7 OR S8 10. S5 AND S9	214
Cochrane Library	1. [mh "Cognition Disorders"] OR [mh "Neurocognitive Disorders"] OR [mh "Mild Cognitive Impairment"] OR [mh "Depression"] OR [mh "Depressive Disorder"] 2. ((Cogniti* or neuropsychological or neurocognitive or executive or brain) near/3 (impairment or defect* or function* or dysfuntion* or process* or symptom* or factor* or Deficit* or disorder*)):ti,ab,kw 3. (Neuropsychological NEAR/3 test*):ti,ab,kw 4. Depressi*:ti,ab,kw 5. {OR #1-#4} 6. [mh "Athletes"] 7. [mh "Rugby"] 8. ((Athlete* OR 'sports person' OR sportswomen OR sportswoman OR sportsman OR sportmen OR rugby OR player* OR 'contact-sport') NEAR/5 (retire* OR former)):ti,ab,kw 9. {OR #6-#8} 10. {AND #5,#9}	18
Web of Science	1. TS=((Cogniti* or neuropsychological or neurocognitive or executive or brain) NEAR/3 (impairment or defect* or function* or dysfunction* or process* or symptom* or factor* or Deficit* or disorder*)) OR TS=((Neuropsychological NEAR/3 test*)) OR TS=(Depressi*) 2. TS=((Athlete* OR "sports person" OR sportswomen OR sportswoman OR sportsman OR sportsmen OR rugby OR player* OR 'contact-sport') NEAR/5 (retire* OR former)) 3. #2 AND #1	146

Appendix B.3 Modified Downs and Black Checklist.

Modified Downs and Black checklist for the assessment of the methodological quality of both randomized and non-randomized studies[1]

Item	Criteria	Possible Answers
Reporting		
1	*Is the hypothesis/aim/objective of the study clearly described?*	Yes = 1 No = 0
2	*Are the main outcomes to be measured clearly described in the Introduction or Methods section?* If the main outcomes are first mentioned in the Results section, the question should be answered no.	Yes = 1 No = 0
3	*Are the characteristics of the patients included in the study clearly described?* In cohort studies and trials, inclusion and/or exclusion criteria should be given. In case-control studies, a case-definition and the source for controls should be given.	Yes = 1 No = 0
4	*Are the distributions of principal confounders in each group of subjects to be compared clearly described?* A list of principal confounders is provided.	Yes = 2 Partially = 1 No = 0
5	*Are the main findings of the study clearly described?* Simple outcome data (including denominators and numerators) should be reported for all major findings so that the reader can check the major analyses and conclusions. (This question does not cover statistical tests which are considered below).	Yes = 1 No = 0
6	*Does the study provide estimates of the random variability in the data for the main outcomes?* In non-normally distributed data the interquartile range of results should be reported. In normally distributed data the standard error, standard deviation or confidence intervals should be reported. If the distribution of the data is not described, it must be assumed that the estimates used were appropriate and the question should be answered yes.	Yes = 1 No = 0

7	*Have actual probability values been reported (e.g. 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?*	Yes = 1 No = 0
External validity		
8	*Were the subjects asked to participate in the study representative of the entire population from which they were recruited?* The study must identify the source population for patients and describe how the patients were selected. Patients would be representative if they comprised the entire source population, an unselected sample of consecutive patients, or a random sample. Random sampling is only feasible where a list of all members of the relevant population exists. Where a study does not report the proportion of the source population from which the patients are derived, the question should be answered as unable to determine.	Yes = 1 No = 0 Unable to determine = 0
9	*Were those subjects who were prepared to participate representative of the entire population from which they were recruited?* The proportion of those asked who agreed should be stated. Validation that the sample was representative would include demonstrating that the distribution of the main confounding factors was the same in the study sample and the source population.	Yes = 1 No = 0 Unable to determine = 0

Appendix to: Trac MH, McArthur E, Jandoc R, et al. Macrolide antibiotics and the risk of ventricular arrhythmia in older adults. *CMAJ* 2016. DOI:10.1503/cmaj.150901.

Internal validity - bias		
10	*If any of the results of the study were based on "data dredging", was this made clear?* Any analyses that had not been planned at the outset of the study should be clearly indicated. If no retrospective unplanned subgroup analyses were reported, then answer yes.	Yes = 1 No = 0 Unable to determine = 0
11	*In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls?* Where follow-up was the same for all study patients the answer should be yes. If different lengths of follow-up were adjusted for by, for example, survival analysis the answer should be yes. Studies where differences in follow-up are ignored should be answered no.	Yes = 1 No = 0 Unable to determine = 0
12	*Were the statistical tests used to assess the main outcomes appropriate?* The statistical techniques used must be appropriate to the data. For example nonparametric methods should be used for small sample sizes. Where little statistical analysis has been undertaken but where there is no evidence of bias, the question should be answered yes. If the distribution of the data (normal or not) is not described it must be assumed that the estimates used were appropriate and the question should be answered yes.	Yes = 1 No = 0 Unable to determine = 0
13	*Were the main outcome measures used accurate (valid and reliable)?* For studies where the outcome measures are clearly described, the question should be answered yes. For studies which refer to other work or that demonstrates the outcome measures are accurate, the question should be answered as yes.	Yes = 1 No = 0 Unable to determine = 0
Internal validity - confounding (selection bias)		

14	*Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?* For example, patients for all comparison groups should be selected from the same hospital. The question should be answered unable to determine for cohort and case-control studies where there is no information concerning the source of patients included in the study.	Yes = 1 No = 0 Unable to determine = 0
15	*Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?* For a study which does not specify the time period over which patients were recruited, the question should be answered as unable to determine.	Yes = 1 No = 0 Unable to determine = 0
16	*Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?* This question should be answered no for trials if: the main conclusions of the study were based on analyses of treatment rather than intention to treat; the distribution of known confounders in the different treatment groups was not described; or the distribution of known confounders differed between the treatment groups but was not taken into account in the analyses. In non-randomized studies if the effect of the main confounders was not investigated or confounding was demonstrated but no adjustment was made in the final analyses the question should be answered as no.	Yes = 1 No = 0 Unable to determine = 0
Power		
17*	*Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%?* Sample sizes have been calculated to detect a difference of x% and y%.	Yes = 1 No = 0 Unable to determine = 0

*Item has been modified.

Reference

1. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *J Epidemiol Community Health* 1998; 52:377-84.

Appendix B.4 PROSPERO Registration for Systematic Review II.

NIHR | National Institute for Health Research

PROSPERO
International prospective register of systematic reviews

A systematic review on the evidence for cognitive health deficits in retired professional athletes with a history of mild traumatic brain injury/concussion

Joice Cunningham, Fiona Wilson, Steve Broglio

Citation

Joice Cunningham, Fiona Wilson, Steve Broglio. A systematic review on the evidence for cognitive health deficits in retired professional athletes with a history of mild traumatic brain injury/concussion. PROSPERO 2016 CRD42016050750 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42016050750

Review question

Is there evidence for long-term cognitive health issues in retired professional athletes with a history of sports-related mild traumatic brain injury/concussion?

Searches

We will search the following bibliographic databases: Cochrane Central Register of Controlled Trials (CENTRAL), EMBASE, MEDLINE/PubMed, AMED, CINAHL with medical subject headings and keywords including mild traumatic brain injury, concussion, sport-related, professional athlete, retired.

Types of study to be included

We will include observational studies which explore the association of history of concussion and cognitive health issues in retired former professional athletes.

Condition or domain being studied

Sports related mild traumatic brain injury/concussion.

Participants/population

Retired former professional athletes with a history of reported mild traumatic brain injury/concussion.

Intervention(s), exposure(s)

The association of cognitive health deficits with previous exposure to sports-related mild traumatic brain injury/concussion will be reviewed in retired professional athletes.
Concussion is a subset of traumatic brain injury and it is defined as a complex pathophysiological process affecting the brain, induced by biomechanical forces.

Comparator(s)/control

Inclusion Criteria: Retired professional non-contact athletes without a history of concussion.
Exclusion Criteria: Active Professional Athletes, history of non sports related concussion/traumatic brain injury.

Context

Retired professional athlete associations.

Main outcome(s)

To investigate cognitive function in retired professional athletes with a history of sports-related mild traumatic brain injury/concussion.

Additional outcome(s)

To investigate reported concussion history in retired professional athletes.

Data extraction (selection and coding)

A data extraction template will be used as a checklist of items which should be included in reports of cross-sectional studies, based on STROBE guidelines.One reviewer will record study aim, participant characteristics, details of concussion history, outcome measures used and relevant outcome data (group means and standard deviations

Risk of bias (quality) assessment
Two review authors will independently assess the risk of bias in included studies using standard tools.

Strategy for data synthesis
We will provide a narrative synthesis of the findings from the included studies, structured around the target population characteristics, type of outcome and outcome measures used and the reported concussion events. We will provide summaries of exposure of sports-related mild traumatic brain injury/concussion effects for each study.
We anticipate that there will be limited scope for meta-analysis because of the range of different outcomes measured across the small number of existing trials.

Analysis of subgroups or subsets
None planned.

Contact details for further information
Joice Cunningham
cunninj1@tcd.ie

Organisational affiliation of the review
Department of Physiotherapy, Trinity College Dublin
physio@tcd.ie

Review team members and their organisational affiliations
Miss Joice Cunningham. PhD Candidate, Department of Physiotherapy
Dr Fiona Wilson. Department of Physiotherapy, Trinity College Dublin
Dr Steve Broglio. Department of Kiniesiology, University of Michigan,

Type and method of review
Systematic review

Anticipated or actual start date
04 November 2016

Anticipated completion date
16 January 2017

Funding sources/sponsors
Trinity College Dublin

Conflicts of interest
None known

Language
English

Country
Ireland

Stage of review
Review Completed not published

Subject index terms status
Subject indexing assigned by CRD

Subject index terms
Athletes; Brain Concussion; Brain Injuries; Cognition; Cognition Disorders; Humans; Retirement

Date of registration in PROSPERO
03 November 2016

Date of publication of this version
21 January 2019

Details of any existing review of the same topic by the same authors

Stage of review at time of this submission

Stage	Started	Completed
Preliminary searches	Yes	Yes
Piloting of the study selection process	Yes	Yes
Formal screening of search results against eligibility criteria	Yes	Yes
Data extraction	Yes	Yes
Risk of bias (quality) assessment	Yes	Yes
Data analysis	Yes	Yes

Versions
03 November 2016
21 January 2019

Appendix B. 5 Electronic Databases Search Strategy for Systematic Review II.

DATABASE	SEARCH STRATEGY	RESULTS
EMBASE	1. 'cognitive defect'/exp 2. 'depression'/exp 3. ((Cogniti* OR neuropsychological OR neurocognitive OR executive OR brain) NEAR/3 (impairment OR defect* OR function* OR dysfuntion* OR process* OR symptom* OR factor* OR Deficit* OR disorder*)):ti,ab 4. (Neuropsychological NEAR/3 test*):ti,ab 5. Depressi*:ti,ab 6. #1 OR#2 OR #3 OR #4 OR #5 7. 'athlete'/exp 8. ((Athlete* OR 'sports person' OR sportswomen OR sportswoman OR sportsman OR sportmen OR rugby OR player* OR box* OR 'contact-sport') NEAR/5 (retire* OR former)):ti,ab 9. #7 OR #8 10. #6 AND #9	1792
PYSCINFO	1. DE "Cognitive Impairment" OR DE "Depression (Emotion)" OR DE "Executive Function" 2. TI ((Cogniti* OR neuropsychological OR neurocognitive OR executive OR brain) N3 (impairment OR defect* OR function* OR dysfuntion* OR process* OR symptom* OR factor* OR Deficit* OR disorder*)) OR AB ((Cogniti* OR neuropsychological OR neurocognitive OR executive OR brain) N3 (impairment OR defect* OR function* OR dysfuntion* OR process* OR symptom* OR factor* OR Deficit* OR disorder)) 3. TI (Neuropsychological N3 test*) OR AB (Neuropsychological N3 test*) 4. TI Depressi* OR AB Depressi* 5. S1 OR S2 OR S3 OR S4 6. DE "Athletes" 7. TI ((Athlete* OR 'sports person' OR sportswomen OR sportswoman OR sportsman OR sportsmen OR rugby OR player* OR box* OR 'contact-sport') N5 (retire* OR former)) OR AB ((Athlete* OR 'sports person' OR sportswomen OR sportswoman OR sportsman OR sportsmen OR rugby OR player* OR box* OR 'contact-sport') N5 (retire* OR former)) 8. S6 OR S7 S5 AND S8	783
MEDLINE	1. (MH "Cognition Disorders+") OR (MH "Neurocognitive Disorders+") OR (MH "Mild Cognitive Impairment") OR (MH "Depression") OR (MH "Depressive Disorder+") 2. TI ((Cogniti* OR neuropsychological OR neurocognitive OR executive OR brain) N3 (impairment OR defect* OR function* OR dysfuntion* OR process* OR symptom* OR factor* OR Deficit* OR disorder*)) OR AB ((Cogniti* OR neuropsychological OR neurocognitive OR executive OR brain) N3 (impairment OR defect* OR function* OR dysfuntion* OR process* OR symptom* OR factor* OR Deficit* OR disorder)) 3. TI (Neuropsychological N3 test*) OR AB (Neuropsychological N3 test*) 4. TI Depressi* OR AB Depressi* 5. S1 OR S2 OR S3 OR S4 6. (MH "Athletes") 7. TI ((Athlete* OR 'sports person' OR sportswomen OR sportswoman OR sportsman OR sportsmen OR rugby OR player* OR box* OR 'contact-sport') N5 (retire* OR former)) OR AB ((Athlete* OR 'sports person' OR sportswomen OR sportswoman OR sportsman OR sportsmen OR rugby OR player* OR box* OR 'contact-sport') N5 (retire* OR former)) 8. S6 OR S7 9. S5 AND S8	459

CINAHL	1. (MH "Cognition Disorders+") OR (MH "Depression+") 2. TI ((Cogniti* OR neuropsychological OR neurocognitive OR executive OR brain) N3 (impairment OR defect* OR function* OR dysfuntion* OR process* OR symptom* OR factor* OR Deficit* OR disorder*)) OR AB ((Cogniti* OR neuropsychological OR neurocognitive OR executive OR brain) N3 (impairment OR defect* OR function* OR dysfuntion* OR process* OR symptom* OR factor* OR Deficit* OR disorder)) 3. TI (Neuropsychological N3 test*) OR AB (Neuropsychological N3 test*) 4. TI Depressi* OR AB Depressi* 5. S1 OR S2 OR S3 OR S4 6. (MH "Athletes") 7. TI ((Athlete* OR 'sports person' OR sportswomen OR sportswoman OR sportsman OR sportsmen OR rugby OR player* OR box* OR 'contact-sport') N5 (retire* OR former)) OR AB ((Athlete* OR 'sports person' OR sportswomen OR sportswoman OR sportsman OR sportsmen OR rugby OR player* OR box* OR 'contact-sport') N5 (retire* OR former)) 8. S6 OR S7 9. S5 AND S8	239
COCHRANE LIBRARY	1. [mh "Cognition Disorders"] OR [mh "Neurocognitive Disorders"] OR [mh "Mild Cognitive Impairment"] OR [mh "Depression"] OR [mh "Depressive Disorder"] 2. ((Cogniti* or neuropsychological or neurocognitive or executive or brain) near/3 (impairment or defect* or function* or dysfuntion* or process* or symptom* or factor* or Deficit* or disorder*)):ti,ab,kw 3. (Neuropsychological NEAR/3 test*):ti,ab,kw 4. Depressi*:ti,ab,kw 5. {OR #1-#4} 6. [mh "Athletes"] 7. ((Athlete* OR 'sports person' OR sportswomen OR sportswoman OR sportsman OR sportmen OR rugby OR player* OR box* OR 'contact-sport') NEAR/5 (retire* OR former)):ti,ab,kw 8. {OR #6-#7} 9. {AND #5,#8}	14

Appendix C.1 Participant Information Leaflet for Study I.

Participant Information Leaflet

Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin

Title of Study:

An investigation into the reliability of self-reported concussion history in current Leinster rugby players.

Introduction:

Rugby has a high incidence of concussion. The majority of research on concussion is dedicated to the immediate effects of concussion and return-to-play decisions. However, the potential long-term effects of sports concussion are less understood. Recent research of retired professional athletes has found that the number of concussions sustained during professional sporting careers was associated with cognitive issues in later-life. Due to the fact that these studies are based solely on player's ability to self-report their concussion history, realistically they may be biased and/ or inaccurate. Due to these concerns of the quality of self-reported concussion history, we considered that it was important to look at the reliability of self-reported concussion history. Therefore, this study is focussing on the reliability of current Leinster rugby players self-report of concussion history, by asking each player to report their concussion history and then cross-matching player's self-report to recorded medical data.

Aims of the study:

Procedures:

In order to be eligible for this study you must:

- Be an adult of 18 years or older
- Contracted to Leinster rugby senior or academy squad
- Be able to read and understand the English language

Design:

All players who consent to take part in the study, will be pre-screened by the lead investigator (Joice Cunningham) for eligibility. Data collection will take place at Leinster Rugby training facility in UCD. We will obtain a full medical history from you at a time and date that is convenient to you. We will also get you to fill out the National Institute of Health Concussion questionnaire, which will inform us of your history of concussion. We will also seek your consent to investigate your individual documented medical data.

This process will be repeated at a later stage on a random small sample of the team, in order to test the reliability of your reported concussion. Your self-reported history of concussion will be compared to your individual medical records.

Benefits:

There are no immediate benefits. However, this study will give an indication as to the reliability of player's self-reported concussion history. By participating in this study you will facilitate further investigation into the association between player's self-reported concussion history and later-life cognitive issues. The potential long-term effects of sports concussion are poorly understood.

Risks:

There are no anticipated risks associated with participation in this study.

Exclusion from Participation:

If you have a history of non-sports related concussion/severe traumatic brain injury due to road traffic collisions etc., you will not be eligible to participate in this study.

Confidentiality:

Your identity will remain confidential. Your name will not be published and will not be disclosed to anyone outside of the research team.

Insurance:

This study is covered by insurance policies organised by the institution.

Voluntary Participation:

You have volunteered to participate in this study. You may withdraw at any time if you so wish. If you decide not to participate or if you wish to withdraw yourself from the study, you will not be penalised.

Permission:

This study has received the Faculty of Health Science Research Ethics Committee approval.

Further information:

If you require any further information on this study, your participation or your rights, please do not hesitate to contact Joice Cunningham securely and confidentially at cunninj1@tcd.ie / +353 86 2108765

Appendix C.2 Trinity College Dublin Ethical Approval for Study I.

Coláiste na Tríonóide, Baile Átha Cliath
Trinity College Dublin
Ollscoil Átha Cliath | The University of Dublin

Joice Cunningham
Department of Physiotherapy,
Trinity Centre for Health Sciences,
James's Street,
Dublin 8.

Ref: 170102

Title of Study: An investigation into the reliability of self-reported concussion history in current Leinster rugby players.

Dear Joice,

Further to a meeting of the Faculty of Health Sciences Ethics Committee held in January 2017, we are pleased to inform you that the above project has been approved without further audit.

Yours sincerely,

p.p. Brian Brown

Prof. Brian O'Connell
Chairperson
Faculty Research Ethics Committee

Dámh na nEolaíochtaí Sláinte
Foirgneamh na Ceimice,
Coláiste na Tríonóide,
Ollscoil Átha Cliath,
Baile Átha Cliath 2, Éire.

Faculty of Health Sciences
Chemistry Building,
Trinity College Dublin,
The University of Dublin,
Dublin 2, Ireland.

www.healthsciences.tcd.ie

Appendix C.3 Leinster Rugby Club Ethical Approval for Study I.

Letter of Approval from Leinster Rugby

STUDY TITLE: An Investigation into the reliability of self-reported concussion history in current Leinster rugby players.

To whom it may concern,

We, Leinster Rugby, give our consent for the above study to be carried out on our players using the Leinster Rugby facilities. We have been informed as to what the study will entail and how the processes involved in the study will be performed. We have been provided with an information leaflet and we have reviewed the consent form. We are happy for the chief investigators Joice Cunningham and Dr. Fiona Wlison to proceed with the study.

Best Wishes,

Guy Easterby
Leinster Team Manager.

"SEEING IS BELIEVING"
Leinster Rugby, Newstead Building A,
UCD, Belfield, Dublin 4
Main: 00353 1 2693224
Fax: 00353 1 2693142
e-Mail: information@leinsterrugby.ie
Website: www.leinsterrugby.ie

Appendix C.4 Informed Consent Form for Study I.

Informed Consent Form

Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin

Title of Study:

An investigation into the reliability of self-reported concussion history in current Leinster rugby players.

This study and this consent form have been explained to me. I believe I understand what will happen if I agree to take part in this study. I have read, or had read to me, this consent form. I have had the opportunity to ask questions and all my questions/queries relating to this study have been answered to my satisfaction. I freely and voluntarily agree to take part in this research study, though without prejudice to my legal and ethical rights. I have received a copy of this consent form.

Participant's name:

Participant's Signature:

Date:

Date on which the participant was first furnished with this form:

Statement of investigator's responsibility:

I have explained the nature, purpose, procedures, benefits, risks of, or alternatives to, this research study. I have offered to answer any questions and fully answered such questions. I believe that the participant understands my explanations and has freely given informed consent.

Players have been made aware that their involvement in the study will remain confidential and their identity anonymous. Only one participant will be tested at one time so their identity will only be known to the investigator. All data collected throughout the study will be confidential and secure. No-one outside the research team will have access to the data collected. Data will be retained securely for a period of five years within the Discipline of Physiotherapy, Trinity College Dublin, for the purpose of final thesis submission for an academic qualification.

Principal Investigator's signature:

Date:

(Keep the original of this form in the participant's medical record, give one copy to the participant, keep one copy in the investigator's records, and send one copy to the sponsor (if there is a sponsor).

Appendix C.5 The Michigan TBI Identification Method

Michigan TBI Identification Method

CONCUSSION HISTORY									
	Mechanism	The concussion was diagnosed or undiagnosed	Date of injury (mm/yyyy)	Age at time of injury	Did you lose consciousness (i.e. knocked out/blacked out)?	How long were you unconsciousness (seconds)?	Did/do you have difficulty remembering things before or after the injury?	How many minutes do you not remember (min)	How many days did you experience symptoms related to the injury?
Injury #1	☐ Blow to head or neck ☐ Car / vehicle accident ☐ Sport / recreation Sport: _____ ☐ Fall ☐ Fight or being hit ☐ Explosion / Blast ☐ Other	☐ Diagnosed ☐ Undiagnosed	____/____		☐Yes ☐No	_____(sec) ☐ Unknown	☐Yes ☐No	_____(min) ☐ Unknown	_____(days) ☐ Unknown
Injury #2	☐ Blow to head or neck ☐ Car / vehicle accident ☐ Sport / recreation Sport: _____ ☐ Fall ☐ Fight or being hit ☐ Explosion / Blast ☐ Other	☐ Diagnosed ☐ Undiagnosed	____/____		☐Yes ☐No	_____(sec) ☐ Unknown	☐Yes ☐No	_____(min) ☐ Unknown	_____(days) ☐ Unknown
Injury #3	☐ Blow to head or neck ☐ Car / vehicle accident ☐ Sport / recreation Sport: _____ ☐ Fall ☐ Fight or being hit ☐ Explosion / Blast ☐ Other	☐ Diagnosed ☐ Undiagnosed	____/____		☐Yes ☐No	_____(sec) ☐ Unknown	☐Yes ☐No	_____(min) ☐ Unknown	_____(days) ☐ Unknown
Injury #4	☐ Blow to head or neck ☐ Car / vehicle accident ☐ Sport / recreation Sport: _____ ☐ Fall ☐ Fight or being hit ☐ Explosion / Blast ☐ Other	☐ Diagnosed ☐ Undiagnosed	____/____		☐Yes ☐No	_____(sec) ☐ Unknown	☐Yes ☐No	_____(min) ☐ Unknown	_____(days) ☐ Unknown
Injury #5	☐ Blow to head or neck ☐ Car / vehicle accident ☐ Sport / recreation Sport: _____ ☐ Fall ☐ Fight or being hit ☐ Explosion / Blast ☐ Other	☐ Diagnosed ☐ Undiagnosed	____/____		☐Yes ☐No	_____(sec) ☐ Unknown	☐Yes ☐No	_____(min) ☐ Unknown	_____(days) ☐ Unknown

* adapted from the Ohio State University TBI Identification Method (Corrigan, J.D., Bogner, J.A. (2007). Initial reliability and validity of the OSU TBI Identification Method. *J Head Trauma Rehabil, 22*(6):318-329.

Injury #6	☐ Blow to head or neck ☐ Car / vehicle accident ☐ Sport / recreation Sport: _____ ☐ Fall ☐ Fight or being hit ☐ Explosion / Blast ☐ Other	☐ Diagnosed ☐ Undiagnosed	____/____		☐Yes ☐No	_____(sec) ☐ Unknown	☐Yes ☐No	_____(min) ☐ Unknown	_____(days) ☐ Unknown
Injury #7	☐ Blow to head or neck ☐ Car / vehicle accident ☐ Sport / recreation Sport: _____ ☐ Fall ☐ Fight or being hit ☐ Explosion / Blast ☐ Other	☐ Diagnosed ☐ Undiagnosed	____/____		☐Yes ☐No	_____(sec) ☐ Unknown	☐Yes ☐No	_____(min) ☐ Unknown	_____(days) ☐ Unknown
Injury #8	☐ Blow to head or neck ☐ Car / vehicle accident ☐ Sport / recreation Sport: _____ ☐ Fall ☐ Fight or being hit ☐ Explosion / Blast ☐ Other	☐ Diagnosed ☐ Undiagnosed	____/____		☐Yes ☐No	_____(sec) ☐ Unknown	☐Yes ☐No	_____(min) ☐ Unknown	_____(days) ☐ Unknown
Injury #9	☐ Blow to head or neck ☐ Car / vehicle accident ☐ Sport / recreation Sport: _____ ☐ Fall ☐ Fight or being hit ☐ Explosion / Blast ☐ Other	☐ Diagnosed ☐ Undiagnosed	____/____		☐Yes ☐No	_____(sec) ☐ Unknown	☐Yes ☐No	_____(min) ☐ Unknown	_____(days) ☐ Unknown
Injury #10	☐ Blow to head or neck ☐ Car / vehicle accident ☐ Sport / recreation Sport: _____ ☐ Fall ☐ Fight or being hit ☐ Explosion / Blast ☐ Other	☐ Diagnosed ☐ Undiagnosed	____/____		☐Yes ☐No	_____(sec) ☐ Unknown	☐Yes ☐No	_____(min) ☐ Unknown	_____(days) ☐ Unknown

** Additional Injury lines can be added as needed

Mechanism Prompts:

Blow to the head or neck: Have you ever been hospitalized or treated in an emergency room following an injury to your head or neck? Think about any childhood injuries you remember or were told about.

Car / vehicle accident: Have you ever injured your head or neck in a car accident or from some other moving vehicle accident (e.g. motorcycle, ATV)?

Sport / recreation: Have you ever been hit in the head or fallen on your head while participating in an organized sport or recreational activity, including on the playground? If yes, indicate the sport/recreational activity you were participating in at the time.

Fall: Have you ever injured from falling?

Fight or being hit: Have you ever injured your head or neck in a fight, from being hit by someone/something, or from being shaken violently?

Explosion / Blast: Have you ever been nearby when an explosion or a blast occurred? If you served in the military, think about any combat- or training-related incidents.

Appendix C.6 Professional Rugby Union Questionnaire

Professional Rugby Union Questionnaire

Last Name (current)_____ First Name (current)_____

Were you given a Middle Name: ☐Yes ☐No Middle Name (at birth)_____

Have you had a legal name change since birth: ☐Yes ☐No (if Yes, complete questions below)

Last Name (at birth)_____ First Name (at birth)_____

City/County of Birth_____

Date of Birth (mm/dd/yyyy)_____

Height _____Feet _____Inches

Weight _____ lbs

Handedness ☐Left ☐Right ☐Ambidextrous

Country of Birth ☐ Ireland Other_____

Current Biological Sex: ☐Male ☐Female

Primary Language: ☐English ☐ Other

If English is not your primary language, are you fluent in English: ☐Yes ☐No

Ethnicity

☐ Caucasian
☐ African American/Black
☐ Hispanic/Latino
☐ American Indian/Alaska Native
☐ Asian
☐ Native Hawaiian/Pacific Islander
☐ Unknown
☐Mixed
☐Other_____

Race

☐ White/Caucasian
☐ Black/ African American
☐ Yellow/Mongolian
☐ Unknown
☐ Other

ORGANIZED SPORT HISTORY - *Primary Sport*

Primary Sport for the 2017-2018: ☐ Rugby ☐ Other_____

What is your *Primary Position* in this sport? _____

Your *Secondary Position* within this sport? _____

From birth, how many years have you participated in *Primary Sport* above___? (Only count years you registered to participate)

Of the years you participated in your *Primary Sport*, how many were you a starter? ____ years

Do you expect to be a starter this year?
☐Yes ☐No ☐Unknown

ORGANIZED SPORT HISTORY - *Secondary Sport(s)*

Other than your primary sport

From birth, indicate if you have participated in any of the following organized sports (check all that apply).

Also indicate the number of years participation for each sport.

☐ I have not participated in any other/secondary sports

☐ GAA _____yrs
☐ Soccer _____yrs
☐ Basketball _____yrs
☐ Skiing _____yrs
☐ Golf _____yrs
☐ Rowing _____yrs
☐ Swimming _____yrs
☐ Tennis _____yrs
☐ Other ____yrs

From birth, total combined years you were a starter in Other Sport(s) [do not include your Primary Sport] _____ years

ACADEMIC HISTORY

Current Education Status:

☐ University Student:
- ☐ Freshman
- ☐ Sophomore

☐ Secondary School Graduate
☐ University Graduate
☐ Masters/PhD Graduate
☐ Other_____

Completed formal education to date? /What is your highest level of education?

☐ No schooling
☐ Primary Education only
☐ Some Secondary Education but left school before 16
(Junior Certificate Completed ☐Yes ☐No)

☐ Secondary School only (completed Leaving Certificate)
☐ At least one year of university but no degree (years completed_____)
☐ University Graduate (BA or BSc)
☐ Master's Degree (MA or MSc)
☐ Higher Degree (Ph.D, M.D, or other)

Name of secondary school graduated from:
_____

Year of secondary school graduation_____

Secondary school town_____
County_____

Type of school student: ☐ Above Average
☐ Average
☐ Below Average

Secondary School Leaving Certificate Points _____ Scale: ☐ 100-200 ☐ 200-300 ☐ 300-400 ☐ 400-500 ☐ 500-600 ☐ N/A ☐
Name of university graduated from: _____ Year of university graduation: _____ University Degree Scale: ☐ NG Fail < 40% ☐ Pass 40-44% ☐ 3 45-49% ☐ 2.2 50-59% ☐ 2.1 60-69% ☐ 1.1 70% +

Have you ever skipped a year/grade of school? ☐Yes ☐No If Yes, what year(s)? _____	Have you ever repeated a year of school? ☐Yes ☐No If Yes, what year(s)? _____
Prior to college, have you ever received school mandated academic assistance (e.g. tutoring or extended test time)? ☐Yes ☐No	Prior to college, have you had required resource/ other assistance? ☐Yes ☐No If Yes to any, in what areas: ☐ Reading ☐ Writing ☐ Math ☐ Other_____

MEDICAL HISTORY		
For **every** condition below, have **you** ever been diagnosed by a Physician/MD with: [if you are unsure of the meaning of a condition, please ask the test administrator]		
Meningitis:	You: ☐Yes ☐No	
Seizure Disorder:	You: ☐Yes ☐No	
Diabetes:	You: ☐Yes ☐No	
Sleep Disorder:	You: ☐Yes ☐No	
Balance Disorder	You: ☐Yes ☐No	
If yes, what was/is the diagnosis	☐ Vestibular Disorder ☐ Vertigo ☐ Motion Sickness ☐ Meniere's Disease ☐ Other_____	
Psychiatric Disorder:	You: ☐Yes ☐No	
If yes, what was/is the diagnosis	☐Unknown ☐Mood Disorder (Excluding depression and bipolar disorder) ☐Anxiety Disorder ☐PTSD ☐Somatoform Disorder ☐Alcohol Abuse ☐Drug Abuse ☐ Gambling Disorder ☐Personality Disorder ☐Psychotic Disorder (Excluding schizophrenia) ☐ Other	
Learning Disorder (e.g. dyslexia):	You: ☐Yes ☐No	
Attention Deficit-Hyperactivity Disorder (ADD/ADHD):	You: ☐Yes ☐No	
Autism Spectrum Disorder:	You: ☐Yes ☐No	
Depression:	You: ☐Yes ☐No	
Bipolar Disorder:	You: ☐Yes ☐No	
Schizophrenia:	You: ☐Yes ☐No	
Moderate/Severe Traumatic Brain Injury:	You: ☐Yes ☐No	
Brain Surgery:	You: ☐Yes ☐No	
Vision Problems (other than glasses/contacts):	You: ☐Yes ☐No	
Hearing Problems:	You: ☐Yes ☐No	
Stroke:	You: ☐Yes ☐No	
For **every** condition below have **you or a family member** ever been diagnosed by a Physician/MD with: [if you are unsure of the meaning of a condition, please ask the test administrator]		
	YOU	**FAMILY MEMBER (if applicable)**
Headaches Disorder (non-migraine):	☐Yes ☐No	☐ Mother/Father ☐Sister/Brother ☐Grandparent
Migraine Headaches:	☐Yes ☐No	☐ Mother/Father ☐Sister/Brother ☐Grandparent
Parkinson's Disease:	☐Yes ☐No	☐ Mother/Father ☐Sister/Brother ☐Grandparent
Memory Disorder:	☐Yes ☐No	☐ Mother/Father ☐Sister/Brother ☐Grandparent
If yes, was/is it Alzheimer's Disease:	☐Yes ☐No	☐ Mother/Father ☐Sister/Brother ☐Grandparent
If yes, was/is it Other non-Alzheimer's dementia:	☐Yes ☐No	☐ Mother/Father ☐Sister/Brother ☐Grandparent
If yes, was/is it -Mild Cognitive Impairment:	☐Yes ☐No	☐ Mother/Father ☐Sister/Brother ☐Grandparent
Have you ever been under general anesthesia? ☐Yes ☐No If yes, how many times? _____		
Average hours of sleep each night for the past week: Sunday to Thursday? _____	Average hours of sleep each night for the past week: Friday and Saturday? _____	

MEDICATIONS

Are you currently taking prescription medications? ☐Yes ☐ No

If Yes, check all that apply: ☐ Antidepressants ☐ Anti-anxiety ☐ Anti-psychotic ☐ Narcotic pain medication ☐ Non-narcotic pain medication ☐ Sleep aid/sedative ☐ Psychostimulant (e.g. ADD/ADHD medications)

☐ Birth Control ☐ Allergy ☐ Asthma ☐ Acid Reflux/heart burn

☐ Other(s)_____

If you indicated yes to any of the above, please provide the name(s): _____

_____

_____

Are you taking over-the-counter medications (e.g. Ibuprofen, Paracetamol, Zyrtec etc.)? ☐Yes ☐No

If yes, check all that apply: ☐ Ibuprofen ☐ Paracetamol ☐ Zyrtec/ Allergy medication ☐ Other_____

Are you taking over-the-counter supplements (e.g. protein or vitamins)? ☐Yes ☐No

If yes, check all that apply: ☐ Protein ☐Creatine ☐ DHEA (Dehydroepiandrosterone) ☐Chromium ☐ Androstenedione ☐Vitamins ☐Weight loss ☐

Other_____

Have you used tobacco (e.g. smoked) in the past month ☐Yes ☐No

If yes, how many cigarettes/cigars per week?_____

Have you used alcohol in the past month? ☐Yes ☐No

If yes, how many days per week over the last month did you drink? _____

On those days, what is the average number of drinks you consumed? _____

Appendix C.7 Participant Information Leaflet for the 'PROP' studies.

Participant Information Leaflet

Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin

Brain Health and Wellness in Retired Professional Athletes

ROWING IRELAND

RUGBY PLAYERS IRELAND

Introduction: It is well known that there are many benefits to taking part in sport. As a former professional athlete, you have achieved high levels of physical fitness throughout your career and are unique from the majority of the general population. We know that the high levels of physical activity that you have completed has numerous health benefits. As part of sport, there is also risk of injury, including exposure to head impacts in some sports. Currently there is not enough research to inform us how the effects of a sporting career benefits your long term health. Likewise, we do not know if injury during your career has a long-term influence on your health.

This study is interested in exploring the overall general health and wellness of retired elite athletes, with a particular interest in brain health. Your participation will mean that you be provided with useful information about your current brain health and wellness.

Eligibility for the study

To be eligible to take part in this study, we require you to be:

- Male
- A retired professional rugby player (no age limited) who has played at least one season of professional rugby.
- A retired international rower (no age limited) who competed and trained full time for at least one season.

You will not be able to take part if:

- You have a history of a non-sports related moderate to severe concussion or brain injury (e.g. a motor vehicle accident).
- You have had a concussion in the last year.
- You have had treatment of chemotherapy or radiotherapy in last 12 months.

What you will be required to do:

If you consent to take part in the study, we will first confirm that you are eligible to take part by asking you some pre-screening questions.

You will be asked to attend an appointment in the Trinity Centre for Health Sciences at St James's Hospital in Dublin or if this does not suit, we can meet at a time and place that is convenient to you. Prior to this appointment you will be sent a number of general health and wellness questionnaires, to be filled out by you and brought with you to testing. At the appointment you will be asked to fill in questionnaires on demographic information, your past medical history as well as information on your sporting career. We will also ask you about any concussions which you may have sustained throughout your sporting career or your life. We will then guide you through a list of some easily administered computer tests of brain functioning.

Benefits:

Benefits to partaking in this study include, general health and wellbeing screening for each retired athlete. We will give you these results. You will also contribute to research in this field and help further understanding of the long-term benefits or potential risks in participation of sports at an elite level on overall brain health and wellness.

Risks:

There is a rare chance than some of questions in the questionnaires may identify some concerns regarding your mental health. One of the research team is a qualified Clinical Psychologist who will discuss these findings with you and help you decide how to manage these symptoms.

Confidentiality:

The information will remain completely confidential and any data that we store will only have a code number on it and not your name. This data will only be viewed by members of the research team.

Insurance:

This study is covered by insurance policies organised by the institution.

Voluntary Participation:

If you volunteer to participate in this study, you may withdraw at any time if you so wish. You will not be penalised for withdrawing at any time

Permission:

This study has received the Faculty of Health Science Research Ethics Committee approval.

Further information:

If you require any further information on this study and/or you would like to take part, please contact Joice Cunningham (the Lead investigator of the study) securely and confidentially at

cunninj1@tcd.ie / +353 86 2108765

or Dr Fiona Wilson who is the study supervisor at:

wilsonf@tcd.ie / +353874174807

Appendix C.8 Advertisement Poster for the 'PROP' studies.

As a former elite athlete, you have performed at the top level and achieved high levels of physical fitness. Would you like to find out how a career in professional sport influences your brain health and general wellness when you retire?

ROWING IRELAND

TRINITY COLLEGE DUBLIN

RUGBY PLAYERS IRELAND

---------For more information/to register---------

Please contact Joice Cunningham at cunninj1@tcd.ie

Appendix C.9 Retired Professional Athletes Questionnaire for the 'PROP' studies.

Retired Professional Athletes Questionnaire (RPAQ)

Please take as much time as need to fill out each part of this questionnaire carefully. If you have any queries regarding any of the questions, do not hesitate to ask the study investigator. Thank you for your participation.

Demographics

Athlete ID:

_____

Current Biological Sex: ☐ Male ☐ Female

_____

Marital Status: ☐ Married ☐ Never Married/Single

☐ Widowed ☐ Separated ☐ Other (please specify)_____
☐ Divorced

_____

Age:

_____

City of Birth: _____

Country of Birth: _____

_____

Handedness: ☐ Right ☐ Left ☐ Ambidextrous

Primary Language: ☐ English ☐ Spanish ☐ Other (please specify)_____

If English is not your primary language, are you fluent in English: ☐ Yes | ☐ No |

Ethnicity/Race: ☐ White ☐ Hispanic/Latino ☐ Black/African American

☐ Native American/American Indian ☐ Asian/Pacific Islander ☐ Other (please specify)_____

Organized Professional Sport History

Primary sport: ☐ Rugby ☐ Rowing ☐ Other (please specify)_____

Primary Position (if applicable): _____

Secondary Position (if applicable): _____

From Birth, how many years have you participated in the Primary Sport above?

_____

How many years, have you participated in the Primary Sport above at a professional level?

_____

How many seasons, have you participated in the Primary Sport above at a professional level?_____

Of the seasons participated in your Primary Sport above at professional level, how many years were you a starter?_____

Organized Sport History (Secondary Sport)

Other than your primary sport, from birth:

Indicate if you have participated in any of the following organized sports (please tick all that apply):

Indicate the number of years participation for each sport:

☐ Baseball _____yrs ☐ Basketball_____yrs ☐ Rowing _____yrs

☐ Rugby _____yrs ☐ Diving_____yrs ☐ Hockey_____yrs

☐ Football (GAA)_____yrs ☐ Soccer_____yrs ☐ Golf_____yrs

☐ Skiing_____yrs ☐ Tennis _____yrs ☐ Swimming_____yrs

☐ Wrestling_____yrs ☐ Other (please specify)_____ _____yrs

Academic History

Highest Level of Education: ☐ No schooling ☐ Primary education only

☐ Some secondary education, but left school before 16 (Junior Certificate/equivalent completed ☐ Yes | ☐ No)

☐ Secondary school education only (Leaving Certificate/equivalent completed ☐ Yes | ☐ No)

☐ At least one year of university completed but no degree (years completed_____)

☐ University Graduate (BA or BSc) ☐ Master's Degree (MA or MSc) ☐ Higher Degree (PhD, M.D) ☐ Other

(please specify)_____

Name of secondary school graduated from: _____

Secondary school:

Town_____ County_____

Year of secondary school graduation: _____

Type of School student: ☐ Above Average ☐ Average ☐ Below Average

Secondary School Leaving Certificate Points: ☐ 100-200 ☐ 200-300 ☐ 300-400 ☐ 400-500 ☐ 500-600 ☐ n/a

Name of university graduated from: _____

Year of university graduation: _____

University Degree Scale: ☐ NG Fail <40% ☐ Pass 40-44% ☐ 3 45-49% ☐ 2.2 50-59% ☐ 2.1 60-69% ☐ 1.1 70% +

Have you ever skipped a year/grade of school? ☐ Yes | ☐ No

If Yes, what year(s)? _____

Have you ever repeated a year of school? ☐ Yes | ☐ No

If Yes, what year(s)? _____

Prior to college, did you ever receive school mandated academic assistance (e.g. tutoring or extended test time?
☐ Yes | ☐ No |

Prior to college, did you ever require resource/other assistance? ☐ Yes | ☐ No

If yes to any, in what area(s)? ☐ Reading ☐ Writing ☐ Math ☐ Other (please specify)_____

Current Employment

Current employment status:

☐ Employed (working 40 or more hours a week) ☐ Employed (working 1-39 hours per week)
☐ Not Employed ☐ Not Employed, looking for work ☐ Not Employed, NOT looking for work

☐ Retired ☐ Other (please specify)_____ **Current Salary Band per annum:**

☐ less than €10'000 ☐ €10'000- €20'000 ☐ €20'000-€40'000 ☐ €40'000-€70'000 ☐ €70'000-€100'000
☐ €100'000-€200'000 ☐ greater than €200'000

Medical History

For every condition below, have you ever been diagnosed by a doctor with:

*If you are unsure of the meaning of a condition, please ask the test administer

Meningitis:	You ☐ Yes | ☐ No |
Seizure Disorder:	You ☐ Yes | ☐ No |
Sleep Disorder:	You ☐ Yes | ☐ No |
Balance Disorder: **If yes, what was/is the diagnosis?**	You ☐ Yes | ☐ No | ☐ Vestibular Disorder ☐ Vertigo ☐ Motion Sickness ☐ Meniere's Disease Other(please specify)_____
Moderate/Severe Traumatic Brain Injury:	You ☐ Yes | ☐ No |
Neurological Condition **If yes, what what/is the diagnosis?**	You ☐ Yes | ☐ No | Epilepsy ☐ Multiple Sclerosis ☐ Parkinson's ☐ Stroke☐ Brain/Spinal Cord Tumour ☐ Other ☐ Please Specify _____

Memory Disorder:	You ☐ Yes | ☐ No | Please Specify

Are you currently experiencing any difficulties with your memory or forgetfulness?	You ☐ Yes | ☐ No |

Are you currently experiencing any difficulties with concentrating or taking longer to think?	You ☐ Yes | ☐ No |
Are you experiencing any other cognitive difficulties? If yes please specify?	You ☐ Yes | ☐ No | Please specify _____
Psychiatric Disorder: **If yes, what what/is the diagnosis?**	☐ Depression ☐ Anxiety ☐ Addiction (alcohol, substance use or gambling disorder) ☐ Eating Disorder ☐ Bipolar Disorder ☐ Psychosis or Schizophrenia ☐ Personality Disorder ☐ Post-Traumatic Stress Disorder (PSTD) ☐ Attention Deficit Hyperactivity Disorder (ADHD / ADD) ☐ Autism Spectrum Disorder ☐ Other
Specific learning difficulty (e.g. dyslexia, dyscalculia):	You ☐ Yes | ☐ No |
Sensory or motor difficulties (e.g. dyspraxia):	You ☐ Yes | ☐ No |

Speech and language difficulty:	You ☐ Yes | ☐ No |
Intellectual disability	You ☐ Yes | ☐ No |
Hearing Problems:	You ☐ Yes | ☐ No |

Diabetes:	You ☐ Yes | ☐ No |
Heart Problems:	You ☐ Yes | ☐ No |
High Blood Pressure:	You ☐ Yes | ☐ No |
Osteoarthritis:	You ☐ Yes | ☐ No |
If yes, please specify which joints are affected?	_____
Rheumatoid Arthritis: **If yes, please specify which joints are affected?**	You ☐ Yes | ☐ No | _____
Asthma:	
Are you a current/past regular smoker? **If past, please specify for how long you were a regular smoker?**	☐ Current ☐ Past ☐ Never smoked _____
Have you ever been under a General Anesthetic If yes, please specify how many times?	☐ Yes | ☐ No | _____
Have you ever undergone a joint replacement? If yes please specify which joint:	☐ Yes | ☐ No | _____

Have you ever been treated with chemotherapy? If yes, please specify for what and when:	☐ Yes | ☐ No | _____
Have you ever been treated with radiotherapy? If yes, please specify for what and when:	☐ Yes | ☐ No | _____
Average hours of sleep each night for the past week: Sunday to Thursday	_____
Average hours of sleep each night for the past week: Friday and Saturday	_____

Medical History

For every condition below, have you OR a family member ever been diagnosed by a doctor with:

*If you are unsure of the meaning of a condition, please ask the test administer

	You	Family Member (If applicable)
Headaches Disorder (non-migraine):	☐ Yes | ☐ No |	☐ Mother | ☐ Father | ☐ Brother| ☐ Sister| ☐ Grandmother| ☐ Grandfather |
Migraine Headaches:	☐ Yes | ☐ No |	☐ Mother | ☐ Father | ☐ Brother| ☐ Sister| Grandmother| ☐ Grandfather |
Parkinson's Disease:	☐ Yes | ☐ No |	☐ Mother | ☐ Father | ☐ Brother| ☐ Sister|
		Grandmother| ☐ Grandfather |
Memory Disorder: **If yes was/is it Alzheimer's Disease** **If yes was/is it Other non-Alzheimer's Dementia** **If yes was/is it Mild Cognitive Impairment?**	☐ Yes | ☐ No | ☐ Yes | ☐ No | ☐ Yes | ☐ No | ☐ Yes | ☐ No |	☐ Mother | ☐ Father | ☐ Brother| ☐ Sister| Grandmother| ☐ Grandfather |

Medications

Are you currently taking prescription medications? ☐ Yes | ☐ No

If yes, please tick all that apply:

☐ Anti-depressants ☐ Anti-anxiety ☐ Anti-psychotic ☐ Narcotic pain medication ☐ Non-narcotic pain medication

☐ Sleep aid/sedative ☐ Psychostimulant (e.g. ADD/ADHD medications) ☐ Allergy ☐ Asthma

Acid Reflux/Heart Burn ☐ Others (please specify)_____

If you indicated yes to any of the above, please provide the name(s):

_____

Are you taking any over-the counter medication (e.g. Advil/Ibuprofen, Claritin, etc.)? ☐ Yes | ☐ No

If yes, please tick all that apply:

☒ Advil/Ibuprofen ☐ Tylenol/Acetaminophen ☐ Claritin/Allergy medication ☐ Other (please specify)_____

If you indicated yes to any of the above, please provide the name(s):

_____

Are you taking over-the counter supplements (e.g. protein or vitamins)? ☐ Yes | ☐ No

If yes, please tick all that apply:

☒ Protein ☐ Creatine ☐ DHEA ☐ Chromium ☐ Androstenedione ☐ Vitamins ☐ Weight Loss

☒ Other (please specify) _____

Have you used tobacco (e.g. smoked) in the past month? ☐ Yes ☐ No

If yes, how many cigarettes/cigars per week? _____

Have you used alcohol in the past month? ☐ Yes ☐ No

If yes, how many days per week over the last month did you drink?_____

On those days, what is the average number of drinks consumed?_____

End of Questionnaire

Thank you for taking the time to participate.

Appendix C.10 The Pain Disability Index

Pain Disability Index

Pain Disability Index: The rating scales below are designed to measure the degree to which aspects of your life are disrupted by chronic pain. In other words, we would like to know how much pain is preventing you from doing what you would normally do or from doing it as well as you normally would. Respond to each category indicating the overall impact of pain in your life, not just when pain is at its worst.

For each of the 7 categories of life activity listed, please circle the number on the scale that describes the level of disability you typically experience. A score of 0 means no disability at all, and a score of 10 signifies that all of the activities in which you would normally be involved have been totally disrupted or prevented by your pain.

Family/Home Responsibilities: This category refers to activities of the home or family. It includes chores or duties performed around the house (e.g. yard work) and errands or favors for other family members (e.g. driving the children to school).
No Disability 0__. 1__. 2__. 3__. 4__. 5__. 6__. 7 __. 8__. 9__. 10__. Worst Disability

Recreation: This disability includes hobbies, sports, and other similar leisure time activities.
No Disability 0__. 1__. 2__. 3__. 4__. 5__. 6__. 7 __. 8__. 9__. 10__. Worst Disability

Social Activity: This category refers to activities, which involve participation with friends and acquaintances other than family members. It includes parties, theater, concerts, dining out, and other social functions.
No Disability 0__. 1__. 2__. 3__. 4__. 5__. 6__. 7 __. 8__. 9__. 10__. Worst Disability

Occupation: This category refers to activities that are part of or directly related to one's job. This includes non-paying jobs as well, such as that of a housewife or volunteer.
No Disability 0__. 1__. 2__. 3__. 4__. 5__. 6__. 7 __. 8__. 9__. 10__. Worst Disability

Sexual Behavior: This category refers to the frequency and quality of one's sex life.
No Disability 0__. 1__. 2__. 3__. 4__. 5__. 6__. 7 __. 8__. 9__. 10__. Worst Disability

Self Care: This category includes activities, which involve personal maintenance and independent daily living (e.g. taking a shower, driving, getting dressed, etc.)
No Disability 0__. 1__. 2__. 3__. 4__. 5__. 6__. 7 __. 8__. 9__. 10__. Worst Disability

Life-Support Activities: This category refers to basic life supporting behaviors such as eating, sleeping and breathing.
No Disability 0__. 1__. 2__. 3__. 4__. 5__. 6__. 7 __. 8__. 9__. 10__. Worst Disability

Signature_____ **Please Print**_____

Date _____

The Pain Disability Index (PDI)

Overview: The Pain Disability Index (PDI) a simple and rapid instrument for measuring the impact that pain has on the ability of a person to participate in essential life activities. This can be used to evaluate patients initially to monitor them over time and to judge the effectiveness of interventions. The index was developed at St. Louis University Medical Center.

Measures of disability related to pain:

(1) family and home responsibilities: activities related to home and family

(2) recreation: hobbies sports and other leisure time activities

(3) social activity: participation with friends and acquaintances other than family members

(4) occupation: activities partly or directly related to working including housework or volunteering

(5) sexual behavior: frequency and quality of sex life

(6) self care: personal maintenance and independent daily living (bathing dressing etc.)

(7) life-support activity: basic life-supporting behaviors (eating sleeping breathing etc.)

Level of Disability	Points	My Terms (not from paper)
none	0	
	1	
	2	mild
	3	
	4	
	5	moderate
	6	
	7	
	8	severe
	9	
total	10	

pain disability index =

= SUM(points for all 7 parameters)

Interpretation:

• minimal index: 0

• maximal index: 70

• The higher the index the greater the person's disability due to pain.

Performance:

• modest test-retest reliability

• discriminates between patients with low and high levels of disability

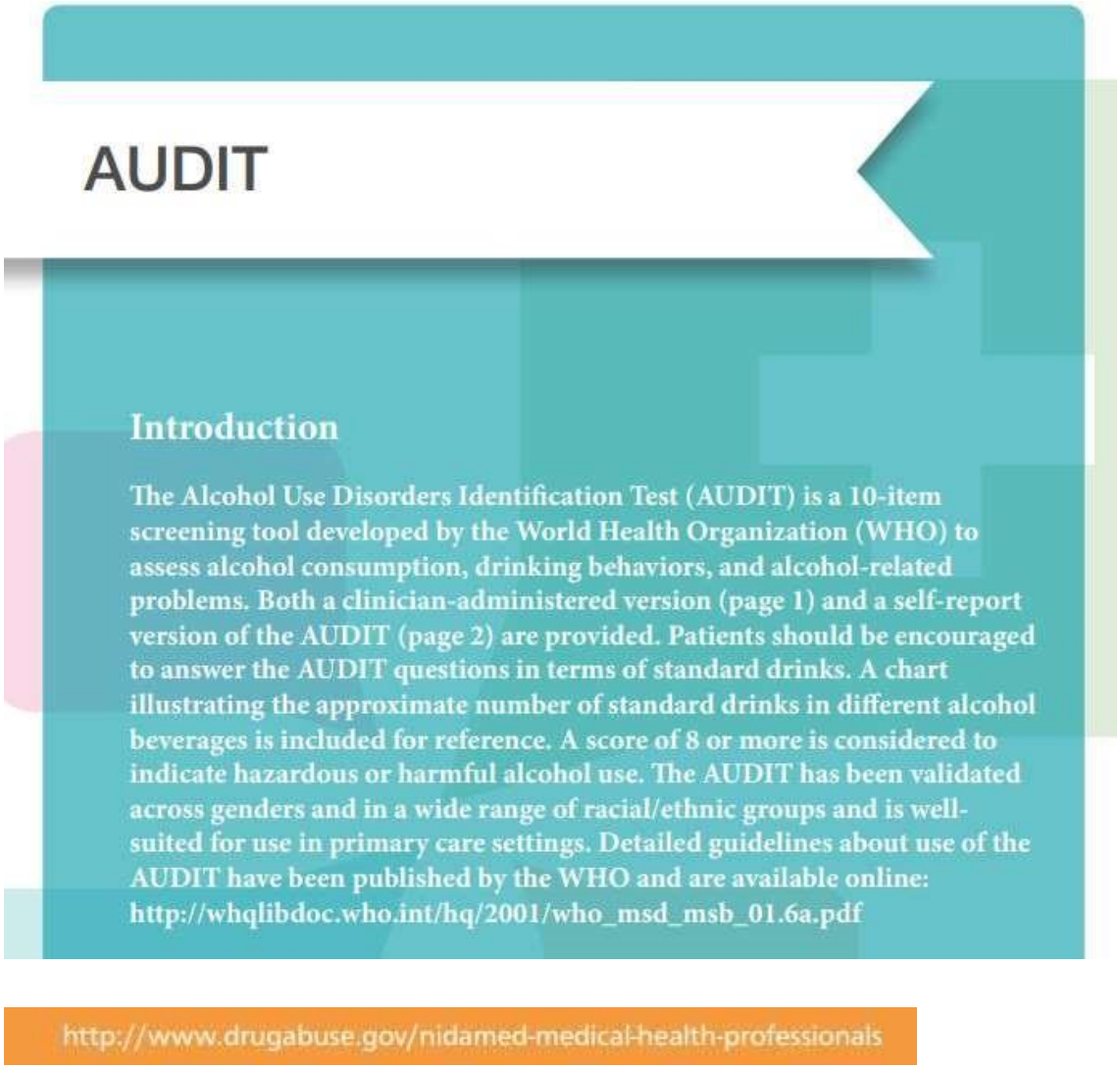
References:

Chibnall JT Tait RC. The Pain Disability Index: Factor Structure and Normative Data. Arch Phys Med Rehabil. 1994; 75: 1082-1086.

Pollard CA. Preliminary validity study of the pain disability index. Perceptual and Motor Skills. 1984; 59: 974.

Tait RC Chibnall JT Krause S. The pain disability index: psychometric properties. Pain. 1990; 40: 171-182.

Appendix C.11 The Alcohol Use Disorders Identification Test



The Alcohol Use Disorders Identification Test: Interview Version

Read questions as written. Record answers carefully. Begin the AUDIT by saying "Now I am going to ask you some questions about your use of alcoholic beverages during this past year." Explain what is meant by "alcoholic beverages" by using local examples of beer, wine, vodka, etc. Code answers in terms of "standard drinks". Place the correct answer number in the box at the right.

1. How often do you have a drink containing alcohol?
   (0) Never [Skip to Qs 9-10]
   (1) Monthly or less
   (2) 2 to 4 times a month
   (3) 2 to 3 times a week
   (4) 4 or more times a week

2. How many drinks containing alcohol do you have on a typical day when you are drinking?
   (0) 1 or 2
   (1) 3 or 4
   (2) 5 or 6
   (3) 7, 8, or 9
   (4) 10 or more

3. How often do you have six or more drinks on one occasion?
   (0) Never
   (1) Less than monthly
   (2) Monthly
   (3) Weekly
   (4) Daily or almost daily
   Skip to Questions 9 and 10 if Total Score for Questions 2 and 3 = 0

4. How often during the last year have you found that you were not able to stop drinking once you had started?
   (0) Never
   (1) Less than monthly
   (2) Monthly
   (3) Weekly
   (4) Daily or almost daily

5. How often during the last year have you failed to do what was normally expected from you because of drinking?
   (0) Never
   (1) Less than monthly
   (2) Monthly
   (3) Weekly
   (4) Daily or almost daily

6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?
   (0) Never
   (1) Less than monthly
   (2) Monthly
   (3) Weekly
   (4) Daily or almost daily

7. How often during the last year have you had a feeling of guilt or remorse after drinking?
   (0) Never
   (1) Less than monthly
   (2) Monthly
   (3) Weekly
   (4) Daily or almost daily

8. How often during the last year have you been unable to remember what happened the night before because you had been drinking?
   (0) Never
   (1) Less than monthly
   (2) Monthly
   (3) Weekly
   (4) Daily or almost daily

9. Have you or someone else been injured as a result of your drinking?
   (0) No
   (2) Yes, but not in the last year
   (4) Yes, during the last year

10. Has a relative or friend or a doctor or another health worker been concerned about your drinking or suggested you cut down?
    (0) No
    (2) Yes, but not in the last year
    (4) Yes, during the last year

Record total of specific items here

If total is greater than recommended cut-off, consult User's Manual.

The Alcohol Use Disorders Identification Test: Self-Report Version

PATIENT: Because alcohol use can affect your health and can interfere with certain medications and treatments, it is important that we ask some questions about your use of alcohol. Your answers will remain confidential so please be honest. Place an X in one box that best describes your answer to each question.

Questions	0	1	2	3	4	
1. How often do you have a drink containing alcohol?	Never	Monthly or less	2-4 times a month	2-3 times a week	4 or more times a week	
2. How many drinks containing alcohol do you have on a typical day when you are drinking?	1 or 2	3 or 4	5 or 6	7 to 9	10 or more	
3. How often do you have six or more drinks on one occasion?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
4. How often during the last year have you found that you were not able to stop drinking once you had started?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
5. How often during the last year have you failed to do what was normally expected of you because of drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
7. How often during the last year have you had a feeling of guilt or remorse after drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
8. How often during the last year have you been unable to remember what happened the night before because of your drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
9. Have you or someone else been injured because of your drinking?	No		Yes, but not in the last year		Yes, during the last year	
10. Has a relative, friend, doctor, or other health care worker been concerned about your drinking or suggested you cut down?	No		Yes, but not in the last year		Yes, during the last year	
					Total	

STANDARD DRINK EQUIVALENTS	APPROXIMATE NUMBER OF STANDARD DRINKS IN:
BEER or COOLER	
12 oz.  **~5% alcohol**	12 oz. = 1 16 oz. = 1.3 22 oz. = 2 40 oz. = 3.3
MALT LIQUOR	
8-9 oz.  **~7% alcohol**	12 oz. = 1.5 16 oz. = 2 22 oz. = 2.5 40 oz. = 4.5
TABLE WINE	
5 oz.  **~12% alcohol**	a 750 mL (25 oz.) bottle = 5
80-proof SPIRITS (hard liquor)	
1.5 oz.  **~40% alcohol**	a mixed drink = 1 or more* a pint (16 oz.) = 11 a fifth (25 oz.) = 17 1.75 L (59 oz.) = 39 *Note: Depending on factors such as the type of spirits and the recipe, one mixed drink can contain from one to three or more standard drinks.

http://pubs.niaaa.nih.gov/publications/Practitioner/pocketguide/pocket_guide2.htm

Appendix C.12 The International Physical Activity Questionnaire-Short Form

Evaluation Measures

International Physical Activity Questionnaire - Short Form

OVERVIEW

- This measure assesses the types of intensity of physical activity and sitting time that people do as part of their daily lives are considered to estimate total physical activity in MET-min/week and time spent sitting.

SUBSCALES

- None
- Sample items from the scale:
  - During the last 7 days, on how many days did you do vigorous physical activities like heavy lifting, digging, aerobics, or fast bicycling?

STEPPING UP THEME(S) & OUTCOME(S)

- **Health & Wellness**
  - Youth are physically healthy

TARGET POPULATION

- Youth 15 years of age and older

LENGTH & HOW IT IS MEASURED

- 7 items
- Open-ended questions surrounding individuals' last 7-day recall of physical activity
- Self-report, paper-pencil version or orally
- Available in: English and many other languages

DEVELOPER

- International Physical Activity Questionnaire, 1998

GOOD TO KNOW

- Used by the Ontario Trillium Foundation
- Click here for Guidelines for Data Processing and Analysis of the International Physical Activity Questionnaire (IPAQ) - Short Form

PSYCHOMETRICS

- **Reliability**

  Test-rest reliability indicated good stability

  High reliability (α <.80)

- **Validity**

  Predictive validity

  Concurrent validity

  Convergent validity

  Criterion validity

  Discriminant validity

LEARN MORE

- International Physical Activity Questionnaire. (2016). Home. Retrieved from https://sites.google.com/site/theipaq/
- C.L. Craig, A. Marshall, M. Sjostrom, A. Bauman, M. Booth, B. Ainsworth, *et al.* International Physical Activity Questionnaire: 12-country reliability and validity. Med Sci Sports Exerc, 35 (2003), pp. 1381–1395
- Lee, P.H., Macfarlane, D.J., Lam, T.H., Stewart, S.M. (2011). *Validity of the international physical activity questionnaire short form (IPAQ-SF): A systematic review.* International Journal of Behavioral Nutrition and Physical Activity. 8:115.
- van Poppel MNM, Chinapaw MJM, Mokkink LB, van Mechelen W, Terwee CB: Physical activity questionnaires for adults: A systematic review of measurement properties. Sports Medicine. 2010, 40: 565-600. 10.2165/11531930-000000000-00000.

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE (August 2002)

SHORT LAST 7 DAYS SELF-ADMINISTERED FORMAT

FOR USE WITH YOUNG AND MIDDLE-AGED ADULTS (15-69 years)

The International Physical Activity Questionnaires (IPAQ) comprises a set of 4 questionnaires. Long (5 activity domains asked independently) and short (4 generic items) versions for use by either telephone or self-administered methods are available. The purpose of the questionnaires is to provide common instruments that can be used to obtain internationally comparable data on health–related physical activity.

Background on IPAQ

The development of an international measure for physical activity commenced in Geneva in 1998 and was followed by extensive reliability and validity testing undertaken across 12 countries (14 sites) during 2000. The final results suggest that these measures have acceptable measurement properties for use in many settings and in different languages, and are suitable for national population-based prevalence studies of participation in physical activity.

Using IPAQ

Use of the IPAQ instruments for monitoring and research purposes is encouraged. It is recommended that no changes be made to the order or wording of the questions as this will affect the psychometric properties of the instruments.

Translation from English and Cultural Adaptation

Translation from English is supported to facilitate worldwide use of IPAQ. Information on the availability of IPAQ in different languages can be obtained at www.ipaq.ki.se. If a new translation is undertaken we highly recommend using the prescribed back translation methods available on the IPAQ website. If possible please consider making your translated version of IPAQ available to others by contributing it to the IPAQ website. Further details on translation and cultural adaptation can be downloaded from the website.

Further Developments of IPAQ

International collaboration on IPAQ is on-going and an ***International Physical Activity Prevalence Study*** is in progress. For further information see the IPAQ website.

More Information

More detailed information on the IPAQ process and the research methods used in the development of IPAQ instruments is available at www.ipaq.ki.se and Booth, M.L. (2000). *Assessment of Physical Activity: An International Perspective*. Research Quarterly for Exercise and Sport, 71 (2): s114-20. Other scientific publications and presentations on the use of IPAQ are summarized on the website.

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Think *only* about those physical activities that you did for at least 10 minutes at a time.

1. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, aerobics, or fast bicycling?

   _____ **days per week**

   ☐ No vigorous physical activities → ***Skip to question 3***

2. How much time did you usually spend doing **vigorous** physical activities on one of those days?

   _____ **hours per day**

   _____ **minutes per day**

   ☐ Don't know/Not sure

Think about all the **moderate** activities that you did in the **last 7 days**. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.

3. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.

   _____ **days per week**

   ☐ No moderate physical activities → ***Skip to question 5***

SHORT LAST 7 DAYS SELF-ADMINISTERED version of the IPAQ. Revised August 2002.

4. How much time did you usually spend doing **moderate** physical activities on one of those days?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

Think about the time you spent **walking** in the **last 7 days**. This includes at work and at home, walking to travel from place to place, and any other walking that you have done solely for recreation, sport, exercise, or leisure.

5. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time?

_____ **days per week**

☐ No walking → ***Skip to question 7***

6. How much time did you usually spend **walking** on one of those days?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

The last question is about the time you spent **sitting** on weekdays during the **last 7 days**. Include time spent at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading, or sitting or lying down to watch television.

7. During the **last 7 days**, how much time did you spend **sitting** on a **week day**?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

This is the end of the questionnaire, thank you for participating.

SHORT LAST 7 DAYS SELF-ADMINISTERED version of the IPAQ. Revised August 2002.

Appendix C.

Appendix C.13 The Godin Leisure-Time Exercise Questionnaire

Godin Leisure-Time Exercise Questionnaire

INSTRUCTIONS

In this excerpt from the Godin Leisure-Time Exercise Questionnaire, the individual is asked to complete a self-explanatory, brief four-item query of usual leisure-time exercise habits.

CALCULATIONS

For the first question, weekly frequencies of strenuous, moderate, and light activities are multiplied by nine, five, and three, respectively. Total weekly leisure activity is calculated in arbitrary units by summing the products of the separate components, as shown in the following formula:

Weekly leisure activity score = (9 × Strenuous) + (5 × Moderate) + (3 × Light)

The second question is used to calculate the frequency of weekly leisure-time activities pursued "long enough to work up a sweat" (see questionnaire).

EXAMPLE

Strenuous = 3 times/wk

Moderate = 6 times/wk

Light = 14 times/wk

Total leisure activity score = (9 × 3) + (5 × 6) + (3 × 14) = 27 + 30 + 42 = 99

Godin, G., Shephard, R. J.. (1997) Godin Leisure-Time Exercise Questionnaire. Medicine and Science in Sports and Exercise. 29 June Supplement: S36-S38.

Godin Leisure-Time Exercise Questionnaire

1. During a typical **7-Day period** (a week), how many times on the average do you do the following kinds of exercise for **more than 15 minutes** during your free time (write on each line the appropriate number).

	Times Per Week
a) **STRENUOUS EXERCISE** **(HEART BEATS RAPIDLY)** (e.g., running, jogging, hockey, football, soccer, squash, basketball, cross country skiing, judo, roller skating, vigorous swimming, vigorous long distance bicycling)	_____
b) **MODERATE EXERCISE** **(NOT EXHAUSTING)** (e.g., fast walking, baseball, tennis, easy bicycling, volleyball, badminton, easy swimming, alpine skiing, popular and folk dancing)	_____
c) **MILD EXERCISE** **(MINIMAL EFFORT)** (e.g., yoga, archery, fishing from river bank, bowling, horseshoes, golf, snow-mobiling, easy walking)	_____

2. During a typical **7-Day period** (a week), in your leisure time, how often do you engage in any regular activity **long enough to work up a sweat** (heart beats rapidly)?

OFTEN	SOMETIMES	NEVER/RARELY
1. ☐	2. ☐	3. ☐

Appendix C.14 The Pittsburgh Sleep Quality Index

Name_____ Date_____

Sleep Quality Assessment (PSQI)

What is PSQI, and what is it measuring?

The Pittsburgh Sleep Quality Index (PSQI) is an effective instrument used to measure the quality and patterns of sleep in adults. It differentiates "poor" from "good" sleep quality by measuring seven areas (components): subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medications, and daytime dysfunction over the last month.

INSTRUCTIONS:

The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. Please answer all questions.

During the past month,

1. When have you usually gone to bed? _____
2. How long (in minutes) has it taken you to fall asleep each night? _____
3. What time have you usually gotten up in the morning? _____
4. A. How many hours of actual sleep did you get at night? _____
   B. How many hours were you in bed? _____

5. During the past month, how often have you had trouble sleeping because you	Not during the past month (0)	Less than once a week (1)	Once or twice a week (2)	Three or more times a week (3)
A. Cannot get to sleep within 30 minutes				
B. Wake up in the middle of the night or early morning				
C. Have to get up to use the bathroom				
D. Cannot breathe comfortably				
E. Cough or snore loudly				
F. Feel too cold				
G. Feel too hot				
H. Have bad dreams				
I. Have pain				
J. Other reason (s), please describe, including how often you have had trouble sleeping because of this reason (s)				
6. During the past month, how often have you taken medicine (prescribed or "over the counter") to help you sleep?				
7. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?				
8. During the past month, how much of a problem has it been for you to keep up enthusiasm to get things done?				
9. During the past month, how would you rate your sleep quality overall?	Very good (0)	Fairly good (1)	Fairly bad (2)	Very bad (3)

Scoring

Component 1	#9 Score	C1 _____
Component 2	#2 Score (<15min (0), 16-30min (1), 31-60 min (2), >60min (3)) + #5a Score (if sum is equal 0=0; 1-2=1; 3-4=2; 5-6=3)	C2 _____
Component 3	#4 Score (>7(0), 6-7 (1), 5-6 (2), <5 (3)	C3 _____
Component 4	(total # of hours asleep) / (total # of hours in bed) x 100 >85%=0, 75%-84%=!, 65%-74%=2, <65%=3	C4 _____
Component 5	# sum of scores 5b to 5j (0=0; 1-9=1; 10-18=2; 19-27=3)	C5 _____
Component 6	#6 Score	C6 _____
Component 7	#7 Score + #8 score (0=0; 1-2=1; 3-4=2; 5-6=3)	C7 _____

*Add the seven component scores together*_____ *Global PSQI* _____

A total score of "5" or greater is indicative of poor sleep quality.
If you scored "5" or more it is suggested that you discuss your sleep habits with a healthcare provider

Appendix C.15 The Neuro-QoL-Short Form

Cognition Function– Short Form

Please respond to each question or statement by marking one box per row.

	In the past 7 days…	Never	Rarely (once)	Sometimes (2-3 times)	Often (once a day)	Very often (several times a day)
NQCOG64v1	I had to read something several times to understand it……	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
NQCOG75v1	My thinking was slow……	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
NQCOG77v1	I had to work really hard to pay attention or I would make a mistake……	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
NQCOG80v1	I had trouble concentrating……	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1

	How much DIFFICULTY do you currently have…	None	A little	Somewhat	A lot	Cannot do
NQCOG22v1	reading and following complex instructions (e.g., directions for a new medication)?.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
NQCOG24v1	planning for and keeping appointments that are not part of your weekly routine, (e.g., a therapy or doctor appointment, or a social gathering with friends and family)?.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
NQCOG25v1	managing your time to do most of your daily activities?.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
NQCOG46v1	learning new tasks or instructions?.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1

Appendix C.16 Satisfaction with Rugby Playing Career Questionnaire

Satisfaction with Rugby Playing Career Questionnaire:

	1. Strongly agree	2. Agree	3.Undecided	4. Disagree	5. Strongly disagree
Considering the benefits and risks of my previous participation in rugby, I would do the same again					
	1. Strongly agree	2. Agree	3.Undecided	4. Disagree	5. Strongly disagree
Considering the benefits and risks of my previous participation in rugby, I would recommend this to my children, relatives or close friends					
	1.Dramatically	2. Somewhat	3. Undecided	4. Not really	5. Not at all
Did your rugby career enrich your life?					

Do you believe that your rugby career has impacted on your long-term cognitive functioning in anyway? *Yes* *No*

If yes, please detail how

Appendix C.17 Athletic Identity Measurement Scale

Athletic Identity Measurement Scale

Likert Scale	1 Entirely Agree	2 Mostly Agree	3 Somewhat Agree	4 Neither Agree nor Disagree	5 Somewhat Disagree	6 Mostly Disagree	7 Entirely Disagree
I consider myself an athlete							
I have many goals related to sport							
Most of my friends are athletes							
Sport is the most important part of my life							
I spend more time thinking about sport than anything else							
I need to participate in sport to feel good about myself							
Other people see me mainly as an athlete							
I feel bad about myself when I do poorly in sport							
Sport is the only important thing in my life							
I would be very depressed if I were injured and could not compete in sport							

Appendix C.18 Informed Consent Form for the 'PROP' studies.

Informed Consent Form

Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin

Title of Study:

An investigation into Brain Health and Wellness in Retired Professional Athletes.

As a former professional athlete, you have achieved high levels of physical fitness throughout your career. We know that the high levels of physical activity that you have completed has numerous health benefits. This study is interested in exploring the overall general health and wellness of retired elite athletes, with a particular interest in brain health. Your participation will mean that you will be provided with useful information about your current brain health and wellness.

This study and this consent form have been explained to me. I understand fully what will happen if I agree to take part in this study. I have read, or had read to me, this consent form. I have had the opportunity to ask questions and all my questions/queries relating to this study have been answered to my satisfaction. I freely and voluntarily agree to take part in this research study, though without prejudice to my legal and ethical rights. I have received a copy of this consent form.

Confidentiality Statement

I understand that all the information I provide as part of this study is confidential and anonymous. However, I also understand that if I report harm to myself or another (e.g. unreported concussion while still playing rugby, self-harm, suicidal intent, or child abuse) while responding to questions as part of this study, the investigator has a responsibility and a duty of care to respond to this appropriately. This may result in a need to break confidentiality in order to ensure my safety.

Participant's name:

Participant's Signature:

Date:

Date on which the participant was first furnished with this form:

Statement of investigator's responsibility:

I have explained the nature, purpose, procedures, benefits, risks of, or alternatives to, this research study. I have offered to answer any questions and fully answered such questions. I believe that the participant understands my explanations and has freely given informed consent.

Players have been made aware that their involvement in the study will remain confidential and their identity anonymous. Only one participant will be tested at one time so their identity will only be known to the investigator. All data collected throughout the study will be confidential and secure. No-one outside the research team will have access to the data collected. Data will be retained securely for a period of five years within the Discipline of Physiotherapy, Trinity College Dublin, for the purpose of final thesis submission for an academic qualification.

Principal Investigator's signature:

Date:

(Keep the original of this form in the participant's medical record, give one copy to the participant, keep one copy in the investigator's records, and send one copy to the sponsor (if there is a sponsor).

Appendix C.19 Trinity College Dublin Ethical Approval for the 'PROP' studies.

Coláiste na Tríonóide, Baile Átha Cliath
Trinity College Dublin
Ollscoil Átha Cliath | The University of Dublin

Joice Cunningham
Discipline of Physiotherapy,
Trinity Centre for Health Sciences,
St James's Hospital,
Dublin 8.

25th September 2018

Ref: 171213

Title of Study: An Investigation into Brain Health and Wellness in Retired Professional Athletes

Dear Joice,

Further to a meeting of the Faculty of Health Sciences Ethics Committee held in September 2018, we are pleased to inform you that the above project (as amended with the following changes) has ethical approval to proceed.

1) Inclusion of a Healthy Non-Sports Population
Since the first ethics application and approved amendments we now have the opportunity to include a healthy non-sports population to explore the statistical relationship between cognitive measures and to obtain baseline cognitive ability of a normative control sample for comparison with professional retired rugby players and rowers. The subset of healthy adults of both genders will be added to the pool of an estimated total sample size of 100-150 participants.

Inclusion criteria for this specific subset are:

- *Participants are between the ages of 18-65.*
- *Subjects have given informed consent and are willing to participate in the study.*

Exclusion criteria for this specific subset are:

- *Active prior engagement in either high impact or low impact sports above recreational level.*
- *A history of moderate to severe concussion or brain injury.*

Recruitment, research design, testing and briefing protocols, data storage and informed consent form and administration as per first ethics application and approved amendments. The control sample participants will complete the National Adult Reading Test, the Cambridge Neuropsychological Test Battery and the Sound Induced Flash Illusion Task only. No self-report data, health screenings or blood samples will be obtained from this subset population.

As a researcher you must ensure that you comply with other relevant regulations, including DATA PROTECTION and HEALTH AND SAFETY.

Yours sincerely,
pp Gloria Brown
Prof. Brian O'Connell
Chairperson
Faculty Research Ethics Committee

Dámh na nEolaíochtaí Sláinte
Foirgneamh na Ceimice,
Coláiste na Tríonóide,
Ollscoil Átha Cliath,
Baile Átha Cliath 2, Éire.

Faculty of Health Sciences
Chemistry Building,
Trinity College Dublin,
The University of Dublin,
Dublin 2, Ireland.

www.healthsciences.tcd.ie

Appendix C.20 Rugby Players Ireland Ethical Approval for the 'PROP' studies.

RUGBY PLAYERS
IRELAND

30th November 2017

Study Title: Brain Health and Wellness in Retired Professional Athletes

To whom it may concern,

Rugby Players Ireland gives its consent for the above study to be carried out on our retired athlete cohort.

I can confirm that all in Rugby Players Ireland have been informed as to what the study will entail and how the processes involved in the study will be performed.

We have been provided with an information leaflet and we have reviewed the consent form.

All at Rugby Players Ireland are happy for the chief investigators Joice Cunningham and Dr. Fiona Wilson to proceed with the study.

Kind regards,

Simon Keogh
CEO
simon@rugbyplayersireland.ie

Appendix C.21 Rowing Ireland Ethical Approval for the 'PROP' studies.

Rowing Ireland,
National Rowing Centre
Farran Wood
Co. Cork.

T: +353 21 743 4044
F: +353 21 743 4045
E: info@rowingireland.ie
W: www.rowingireland.ie

29th November 2017

Study Title: Brain Health and Wellness in Retired Professional Athletes

To whom it may concern,

We Rowing Ireland give our consent for the above study to be carried out on our retired athlete cohort.

We have been informed as to what the study will entail and how the processes involved in the study will be performed.

We have been provided with an information leaflet and we have reviewed the consent form.

We are happy for the chief investigators Joice Cunningham and Dr. Fiona Wilson to proceed with the study.

Yours sincerely

Hamish Adams

Hamish Adams
Chief Executive Officer

hamish.adams@rowingireland.ie

Mobile +353 86 350 2552

Appendix C.22 The Brief Symptom Inventory-18

BSI© 18

DIRECTIONS: Below is a list of problems people sometimes have. Read each one carefully and circle the number that best describes HOW MUCH THAT PROBLEM HAS DISTRESSED OR BOTHERED YOU DURING THE PAST 7 DAYS INCLUDING TODAY. Do not skip any items. If you change your mind, erase your first mark carefully and then fill in your new choice.

HOW MUCH WERE YOU DISTRESSED BY:	NOT AT ALL	A LITTLE BIT	MODERATELY	QUITE A BIT	EXTREMELY
1. Faintness or dizziness	0	1	2	3	4
2. Feeling no interest in things	0	1	2	3	4
3. Nervousness or shakiness inside	0	1	2	3	4
4. Pains in heart or chest	0	1	2	3	4
5. Feeling lonely	0	1	2	3	4
6. Feeling tense or keyed up	0	1	2	3	4
7. Nausea or upset stomach	0	1	2	3	4
8. Feeling blue	0	1	2	3	4
9. Suddenly scared for no reason	0	1	2	3	4
10. Trouble getting your breath	0	1	2	3	4
11. Feelings of worthlessness	0	1	2	3	4
12. Spells of terror or panic	0	1	2	3	4
13. Numbness or tingling in parts of your body	0	1	2	3	4
14. Feeling hopelessness about the future	0	1	2	3	4
15. Feeling so restless you couldn't sit still	0	1	2	3	4
16. Feeling weak in parts of your body	0	1	2	3	4
17. Thoughts of ending your life	0	1	2	3	4
18. Feeling fearful	0	1	2	3	4

Appendix C.23 The Patient Health Questionnaire-9

Patient Health Questionnaire (PHQ-9)

Patient name: _____ Date: _____

1. Over the last 2 weeks, how often have you been bothered by any of the following problems?

	Not at all (0)	Several days (1)	More than half the days (2)	Nearly every day (3)
a. Little interest or pleasure in doing things.	☐	☐	☐	☐
b. Feeling down, depressed, or hopeless.	☐	☐	☐	☐
c. Trouble falling/staying asleep, sleeping too much.	☐	☐	☐	☐
d. Feeling tired or having little energy.	☐	☐	☐	☐
e. Poor appetite or overeating.	☐	☐	☐	☐
f. Feeling bad about yourself, or that you are a failure, or have let yourself or your family down.	☐	☐	☐	☐
g. Trouble concentrating on things, such as reading the newspaper or watching TV.	☐	☐	☐	☐
h. Moving or speaking so slowly that other people could have noticed. Or the opposite; being so fidgety or restless that you have been moving around more than usual.	☐	☐	☐	☐
i. Thoughts that you would be better off dead or of hurting yourself in some way.	☐	☐	☐	☐

2. If you checked off any problem on this questionnaire so far, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

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

TOTAL SCORE _____

Instructions – How to Score the PHQ-9

Major depressive disorder is suggested if:

- Of the 9 items, 5 or more are checked as at least 'more than half the days'
- Either item a. or b. is positive, that is, at least 'more than half the days'

Other depressive syndrome is suggested if:

- Of the 9 items, a., b. or c. is checked as at least 'more than half the days'
- Either item a. or b. is positive, that is, at least 'more than half the days'

Also, PHQ-9 scores can be used to plan and monitor treatment. To score the instrument, tally each response by the number value under the answer headings, (not at all=0, several days=1, more than half the days=2, and nearly every day=3). Add the numbers together to total the score on the bottom of the questionnaire. Interpret the score by using the guide listed below.

Guide for Interpreting PHQ-9 Scores

Score	Recommended Actions
0-4	Normal range or full remission. The score suggests the patient may not need depression treatment.
5-9	Minimal depressive symptoms. Support, educate, call if worse, return in 1 month.
10-14	Major depression, mild severity. Use clinical judgment about treatment, based on patient's duration of symptoms and functional impairment. Treat with antidepressant or psychotherapy.
15-19	Major depression, moderate severity. Warrants treatment for depression, using antidepressant, psychotherapy or a combination of treatment.
20 or higher	Major depression, severe severity. Warrants treatment with antidepressant and psychotherapy, especially if not improved on monotherapy; follow frequently.

Functional Health Assessment

The instrument also includes a functional health assessment. This asks the patient how emotional difficulties or problems impact work, things at home, or relationships with other people. Patient responses can be one of four: Not difficult at all, Somewhat difficult, Very difficult, Extremely difficult. The last two responses suggest that the patient's functionality is impaired. After treatment begins, functional status and number score can be measured to assess patient improvement.

For more information on using the PHQ-9, visit www.depression-primarycare.org

Appendix C.24 The 12 item short form health survey

Your Health and Well-Being

This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. ***Thank you for completing this survey!***

For each of the following questions, please mark an ☒ in the one box that best describes your answer.

1. In general, would you say your health is:

Excellent	Very good	Good	Fair	Poor
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

2. The following questions are about activities you might do during a typical day. Does <u>your health now limit you</u> in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
a Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐ 1	☐ 2	☐ 3
b Climbing several flights of stairs	☐ 1	☐ 2	☐ 3

3. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Accomplished less than you would like	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b Were limited in the kind of work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

4. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Accomplished less than you would like	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b Did work or other activities less carefully than usual	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

5. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

6. **These questions are about how you feel and how things have been with you <u>during the past 4 weeks</u>. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the <u>past 4 weeks</u>…**

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Have you felt calm and peaceful?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b. Did you have a lot of energy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c. Have you felt downhearted and depressed?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

7. **During the <u>past 4 weeks</u>, how much of the time has your <u>physical health or emotional problems</u> interfered with your social activities (like visiting with friends, relatives, etc.)?**

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Thank you for completing these questions!

Appendix C.25 The Connor-Davidson Resilience Scale 25

Connor-Davidson Resilience Scale 25 (CD-RISC-25) ©

*For each item, please mark an "**x**" in the box below that best indicates how much you agree with the following statements as they apply to you over the last **month**. If a particular situation has not occurred recently, answer according to how you think you would have felt.*

		not true at all (0)	rarely true (1)	sometimes true (2)	often true (3)	true nearly all the time (4)
1.	I am able to adapt when changes occur.	☐	☐	☐	☐	☐
2.	I have at least one close and secure relationship that helps me when I am stressed.	☐	☐	☐	☐	☐
3.	When there are no clear solutions to my problems, sometimes fate or God can help.	☐	☐	☐	☐	☐
4.	I can deal with whatever comes my way.	☐	☐	☐	☐	☐
5.	Past successes give me confidence in dealing with new challenges and difficulties.	☐	☐	☐	☐	☐
6.	I try to see the humorous side of things when I am faced with problems.	☐	☐	☐	☐	☐
7.	Having to cope with stress can make me stronger.	☐	☐	☐	☐	☐
8.	I tend to bounce back after illness, injury, or other hardships.	☐	☐	☐	☐	☐
9.	Good or bad, I believe that most things happen for a reason.	☐	☐	☐	☐	☐
10.	I give my best effort no matter what the outcome may be.	☐	☐	☐	☐	☐
11.	I believe I can achieve my goals, even if there are obstacles.	☐	☐	☐	☐	☐
12.	Even when things look hopeless, I don't give up.	☐	☐	☐	☐	☐
13.	During times of stress/crisis, I know where to turn for help.	☐	☐	☐	☐	☐
14.	Under pressure, I stay focused and think clearly.	☐	☐	☐	☐	☐
15.	I prefer to take the lead in solving problems rather than letting others make all the decisions.	☐	☐	☐	☐	☐
16.	I am not easily discouraged by failure.	☐	☐	☐	☐	☐
17.	I think of myself as a strong person when dealing with life's challenges and difficulties.	☐	☐	☐	☐	☐
18.	I can make unpopular or difficult decisions that affect other people, if it is necessary.	☐	☐	☐	☐	☐
19.	I am able to handle unpleasant or painful feelings like sadness, fear, and anger.	☐	☐	☐	☐	☐
20.	In dealing with life's problems, sometimes you have to act on a hunch without knowing why.	☐	☐	☐	☐	☐
21.	I have a strong sense of purpose in life.	☐	☐	☐	☐	☐
22.	I feel in control of my life.	☐	☐	☐	☐	☐
23.	I like challenges.	☐	☐	☐	☐	☐
24.	I work to attain my goals no matter what roadblocks I encounter along the way.	☐	☐	☐	☐	☐
25.	I take pride in my achievements.	☐	☐	☐	☐	☐
Add up your score for each column		0	+ ____	+ ____	+ ____	+ ____

Add each of the column totals to obtain CD-RISC score = _____

01-01-17

Appendix C.26 The Life Events Checklist

LIFE EVENTS CHECKLIST (LEC)

Listed below are a number of difficult or stressful things that sometimes happen to people. For each event check one or more of the boxes to the right to indicate that: (a) it *happened to you* personally, (b) you *witnessed it* happen to someone else, (c) you *learned about it* happening to someone close to you, (d) you're *not sure* if it fits, or (e) it *doesn't apply* to you.

Be sure to consider your *entire life* (growing up as well as adulthood) as you go through the list of events.

Event	Happened to me	Witnessed it	Learned about it	Not Sure	Doesn't apply
1. Natural disaster (for example, flood, hurricane, tornado, earthquake)					
2. Fire or explosion					
3. Transportation accident (for example, car accident, boat accident, train wreck, plane crash)					
4. Serious accident at work, home, or during recreational activity					
5. Exposure to toxic substance (for example, dangerous chemicals, radiation)					
6. Physical assault (for example, being attacked, hit, slapped, kicked, beaten up)					
7. Assault with a weapon (for example, being shot, stabbed, threatened with a knife, gun, bomb)					
8. Sexual assault (rape, attempted rape, made to perform any type of sexual act through force or threat of harm)					
9. Other unwanted or uncomfortable sexual experience					
10. Combat or exposure to a war-zone (in the military or as a civilian)					
11. Captivity (for example, being kidnapped, abducted, held hostage, prisoner of war)					
12. Life-threatening illness or injury					
13. Severe human suffering					
14. Sudden, violent death (for example, homicide, suicide)					
15. Sudden, unexpected death of someone close to you					
16. Serious injury, harm, or death you caused to someone else					
17. Any other very stressful event or experience					

Blake, Weathers, Nagy, Kaloupek, Charney, & Keane, 1995 1

Appendix C.27 Satisfaction with Life Scale

SATISFACTION WITH LIFE SCALE

Reference:

Diener, E., Emmons, R. A., Larsen, R. J., & Griffin, S. (1985). The Satisfaction with Life Scale. *Journal of Personality Assessment, 49*, 71-75.

Description of Measure:

A 5-item scale designed to measure global cognitive judgments of one's life satisfaction (not a measure of either positive or negative affect).

Participants indicate how much they agree or disagree with each of the 5 items using a 7-point scale that ranges from 7 strongly agree to 1 strongly disagree.

Abstracts of Selected Related Articles:

Pavot, W. G., Diener, E., Colvin, C. R., & Sandvik, E. (1991). Further validation of the Satisfaction with Life Scale: Evidence for the cross-method convergence of well-being measures. Journal of Personality Assessment, 57, 149-161.

The structure of subjective well-being has been conceptualized as consisting of two major components: the emotional or affective component and the judgmental or cognitive component (Diener, 1984; Veenhoven, 1984). The judgmental component has also been conceptualized as life satisfaction (Andrews & Withey, 1976). Although the affective component of subjective well-being has received considerable attention from researchers, the judgmental component has been relatively neglected. The Satisfaction With Life Scale (SWLS; Diener, Emmnos, Larsen, & Griffin, 1985) was developed as a measure of the judgmental component of subjective well-being (SWB). Two studies designed to validate further the SWLS are reported. Peer reports, a memory measure, and clinical ratings are used as external criteria for validation. Evidence for the reliability and predictive validity of the SWLS is presented, and its performance is compared to other related scales. The SWLS is shown to be a valid and reliable measure of life satisfaction, suited for use with a wide range of age groups and applications, which makes possible the savings of interview time and resources compared to many measures of life satisfaction. In addition, the high convergence of self- and peer-reported measures of subjective well-being and life satisfaction provide strong evidence that subjective well-being is a relatively global and stable phenomenon, not simply a momentary judgment based on fleeting influences.

Pavot, W. G., & Diener, E. (1993). Review of the Satisfaction with Life Scale. *Psychological Assessment, 5*, 164-172.

The Satisfaction With Life Scale (SWLS) was developed to assess satisfaction with the respondent's life as a whole. The scale does not assess satisfaction with life domains such as health or finances but allows subjects to integrate and weight these domains in whatever way they choose. Normative data are presented for the scale,

which shows good convergent validity with other scales and with other types of assessments of subjective well-being. Life satisfaction as assessed by the SWLS shows a degree of temporal stability (e.g., .54 for 4 years), yet the SWLS has shown sufficient sensitivity to be potentially valuable to detect change in life satisfaction during the course of clinical intervention. Further, the scale shows discriminant validity from emotional well-being measures. The SWLS is recommended as a complement to scales that focus on psychopathology or emotional well-being because it assesses an individuals' conscious evaluative judgment of his or her life by using the person's own criteria.

Diener, E., Sandvik, E., Seidlitz L., Diener, M. (1993). The relationship between income subjective well-being: Relative or absolute? *Social Indicators Research, 28*, 195-223.

Although it appears that income and subjective well-being correlate in within-country studies (Diener, 1984), a debate has focused on whether this relationship is relative (Easterlin, 1974) or absolute (Veenhoven, 1988, 1991). The absolute argument advanced by Veenhoven states that income helps individuals meet certain universal needs and therefore that income, at least at lower levels, is a cause of subjective well-being. The relativity argument is based on the idea that the impact of income or other resources depends on changeable standards such as those derived from expectancies, habituation levels, and social comparisons. Two studies which empirically examine these positions are presented: one based on 18 032 college studies in 39 countries, and one based on 10 year longitudinal data in a probability sample of 4 942 American adults. Modest but significant correlations were found in the U.S. between income and well-being, but the cross-country correlations were larger. No evidence for the influence of relative standards on income was found: (1) Income *change* did not produce effects beyond the effect of income level per se, (2) African-Americans and the poorly educated did not derive greater happiness from specific levels of income, (3) Income produced the same levels of happiness in poorer and richer areas of the U.S., and (4) Affluence correlated with subjective well-being both across countries and within the U.S. Income appeared to produce lesser increases in subjective well-being at higher income levels in the U.S., but this pattern was not evident across countries. Conceptual and empirical questions about the universal needs position are noted. Suggestions for further explorations of the relativistic position are offered.

Scale:

Instructions: Below are five statements that you may agree or disagree with. Using the 1 - 7 scale below, indicate your agreement with each item by placing the appropriate number on the line preceding that item. Please be open and honest in your responding.

- 7 - Strongly agree
- 6 - Agree
- 5 - Slightly agree
- 4 - Neither agree nor disagree
- 3 - Slightly disagree
- 2 - Disagree
- 1 - Strongly disagree

____ In most ways my life is close to my ideal.

____ The conditions of my life are excellent.

____ I am satisfied with my life.

____ So far I have gotten the important things I want in life.

____ If I could live my life over, I would change almost nothing.

Scoring:

Though scoring should be kept continuous (sum up scores on each item), here are some cut-offs to be used as benchmarks.

- 31 - 35 Extremely satisfied
- 26 - 30 Satisfied
- 21 - 25 Slightly satisfied
- 20 Neutral
- 15 - 19 Slightly dissatisfied
- 10 - 14 Dissatisfied
- 5 - 9 Extremely dissatisfied