

THE RELIABILITY FINDINGS OF A NOVEL  
COMPUTERIZED NEUROCOGNITIVE ASSESSMENT  
WITH THE POTENTIAL TO BE USED TO IDENTIFY  
MILD TRAUMATIC BRAIN INJURIES

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## **Abstract**

Computerized neurocognitive tests (CNT) are quick objective assessments used to assess an individual's recovery from a concussion. However, CNT are not presently used during a pitch-side diagnosis of a concussion. Instead, paper-and-pencil assessments are administered which can lead to a subjective interpretation of a concussion and can vary between clinicians. Thus, this study looked to explore whether a new computerized neurocognitive assessment (RESET) could be used pitch-side to establish a more objective diagnosis. However, in order to do this, the reliability of RESET was firstly explored.

To determine the test-retest reliability of RESET, 44 University students completed a baseline neurocognitive assessment, and further tests 45 and 50 days after. Whilst to assess the effect of fatigue and therefore RESET's potential to be used pitch-side, a shortened RESET battery was administered to 24 University Students whom completed a the RESET battery at baseline before once again completing three further RESET assessments under the influence of fatigue.

Between baseline and day 45, RESET's reliability ranged from 0.64 to 0.78 resembling good to strong reliability and ranged from 0.47 to 0.88 between day 45 and 50 displaying moderate to strong reliability. Whilst the analysis of the exercise-induced fatigue study found that compared to baseline, neurocognitive performance post-fatigue significantly increased in three out of the six assessments administered.

The test-retest reliability of RESET over a 45 day interval was higher than previous reliability values on other computerized neurocognitive tests, currently used to assess concussion. Further, due to no assessments being negatively influenced by fatigue, it is plausible that RESET could be an effective test administered pitch-side. However, it is essential that more assessments are conducted on the reliability and also the sensitivity of RESET before it can be definitively used to assess concussion.

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## **Chapter 1 - Introduction**

### **1.1. The Problem**

Concussion is a complex mild Traumatic Brain Injury (mTBI), in which the signs and symptoms often differ between individuals, making it difficult for clinicians to make clear and objective assessments. As a result of no single sign or symptom being able to define a concussion, currently a multifaceted approach is applied to assess a group of signs and symptoms, along with neurocognitive assessments and changes in balance and emotions, in order to make a more accurate diagnosis. However, the current tools used to aid a clinician in the diagnosis of a concussion pitch-side are subjective, thus these current clinical tools used are coming under increasing scrutiny. Consequently, it is becoming ever more important to form a robust, objective tool to aid the diagnosis of concussion and also to create a more effective post-diagnosis treatment protocol.

However, there is a continuous desire by athletes to continue participating in sport even when they are experiencing a potential concussion. Therefore, athletes often underreport their signs and symptoms (Fraas et al., 2014) and consequently corrupt the diagnosis of the clinician in order to remain on the pitch. Equally, there is a constant pressure on the physicians from background staff to allow athletes to continue participating in the sport. This is best illustrated by the case of Florian Fritz, whom sustained a concussion whilst playing Rugby for Toulouse in May 2014, and was seen having extreme difficulties in exiting the pitch on his own and needed assistance from medical staff. Whilst being examined in the changing rooms, the manager of the team was seen demanding the medical staff to hurry up in treating a blood wound so that he could continue playing, regardless of the concussion that he had just sustained. Thus, the medical staff themselves are often fighting a constant battle against both

coaches and players who are keen to expedite their return to play post-concussion. However, in doing so they are putting the athlete at greater risk of subsequent injury. Therefore, to aid the clinicians in the pitch-side diagnosis of a concussion, the current subjective interpretation needs to be developed into a more objective diagnosis.

The lack of objectivity in the diagnosis of a concussion has come into question more recently due to the direct result of long-term consequences. One of which is the findings of several former National Football League Players suffering from a neurodegenerative condition found to be instigated by concussion (McKee et al., 2009), which can result in conditions such as dementia and also slow muscle movements along with resulting in suicidality. Thus, sparking various inquests into the current procedures used within sport to identify, diagnose and treat a concussion, subsequently leading to elevated media attention.

This increase in attention has been due to the direct result of several lawsuits being carried out against the National Football League, FIFA and the United States Soccer Federation. As a result, a settlement was accomplished between the NFL and former American Football Players that could cost up to \$1 billion (£770 million) over the next 65 years. Alongside this, the NFL have put forward a further \$10 million (£7.7 million) into education and medical research on concussion and a further \$75 million (£57.7 million) into developing more objective tests for concussion. Equally, a lawsuit was carried out within soccer on the United States Soccer Federation in regards to addressing head injuries. This lawsuit had no financial incentive, however looked to pursue a change in the rules and regulations of the sport itself. Subsequently, new guidelines were created in America which prohibited soccer players under the age of 10 from heading a soccer ball, whilst reducing the number of headers completed during training between the ages of 11 to 13.

This upsurge in media attention and the subsequent law suits in America, has led to an examination of how concussion is assessed within sports in the United Kingdom. The first sport of which to make any notable change to their rules and regulations, due to this inquest in America, was Rugby. The Rugby Football Union (RFU) and the Rugby Players Association came together to form new rules, where players must now pass online concussion modules to develop their own awareness of a concussion. More significantly, the RFU altered the Head Injury Assessment (HIA) process used to assess for a suspected concussion. The new rules and regulations now permit the physicians to conduct all their pitch-side assessments on concussion within a ten minute period (twice as long as previously) along with using an improved memory test and an altered balance assessment. In addition, any player with a confirmed or suspected concussion will be removed from the game. These alterations to the pitch-side HIA used in Rugby have been enforced to ultimately improve the identification of a concussion and where possible prevent further damage to players through removing them from play.

This adjustment to the HIA period provided within Rugby is just an example of how sports are altering protocols in order to allow for a more thorough and accurate pitch-side assessment of concussion. The current procedure incorporates assessments that allow for subjective interpretation, thus there should be a strong focus to integrate objective assessments to help diagnose a concussion pitch-side.

Nevertheless, even with this growing media attention and subsequent lawsuits on sport-related concussion, there is still an ever-growing cohort participating in contact sports. Further to this growing participation, there has been a fourfold increase in concussion rates over the past ten years (Lincoln et al., 2011). In all, there is an estimated 1.6-3.8 million concussions that occur annually in the United States alone (Langlois et al., 2006). However, this is widely believed to

be a pronounced underestimation due to a lack of education on, and poor identification of, concussions. Alongside this, due to the recent increased awareness of concussions there is a growing number of identified/diagnosed concussions. Therefore, it is very likely that there are significantly more concussions obtained annually than previous reports.

The escalating incidence of concussion rates is now equally becoming more evident within professional sports also. Concussion rates in Rugby have more than doubled between 2002 and 2014, where concussions have risen from 4.1 per 1000 hours of exposure (Kemp et al. 2008) to 8.9 per 1000 hours (Cross et al., 2016). However, during the 2013/14 season alone concussion rates spiked to 11 per 1000 hours, resembling a 268% increase in concussion diagnosis rates in Rugby within the last ten years.

This increasing rate of concussions within professional sports can be attributed to a growing public concern over concussion due to the mounting evidence associating sports-related concussion to neurologic diseases. This elevated attention has subsequently led to an enhanced concern over athletes suffering from a concussion and thus a more thorough examination into individuals that have sustained a potential concussive impact has been carried out, increasing the diagnosed concussion rates. Nevertheless, there still remains evidence of underreported concussions within sport (Fraas et al., 2014). Further, it could be argued that there could potentially be a cultural problem within some contact sports, where athletes will mask any signs and symptoms of a concussion in order to remain on the pitch. Therefore, these concussion rates identified within Rugby are still likely to be a major underestimation of the true value.

In addition, the effect of concussion on further injuries has equally been assessed. Cross et al., (2016) examined concussions over the course of two seasons. Interestingly, they found that

Rugby players who had sustained a concussion were 60% more likely to sustain an additional injury during that season compared to a non-concussed individual, after they had followed the current return to play protocol. Further, it was found that those players who had suffered from a concussion had a significantly shorter time interval until their next injury (53 days) compared to players who had sustained another injury (114 days).

These results clearly demonstrate how a concussion could severely effect an athlete's season through increasing their susceptibility to further injuries. Subsequently, this reinforces the importance in improving the current procedure used for concussion diagnosis and also outlines the current necessity for an objective assessment to aid concussion diagnosis pitch-side.

## **1.2. What is a concussion**

Concussion is a form of mTBI and is defined as a “complex pathophysiological process affecting the brain, induced by biomechanical forces.” (McCrory et al., 2013). It is known to occur through a direct blow to the head, face, neck or body resulting in neurological impairment which can become present within minutes to hours after the impact.

Concussion occurs through acceleration/deceleration forces which can leave axons vulnerable to injury as they become brittle after being exposed to such rapid forces, and also due to the structure of white matter tracts. Subsequently, this prompt force can damage the axonal cytoskeleton, leading to impaired transmission. Further, the axon can swell due to this damage, resulting in calcium entering the damaged axons leading to enhanced neurological dysfunction and thus leading to functional impairments (Smith & Meaney, 2000).

The recovery period from a concussion is very subjective, although 80-90% of concussions are believed to resolve within a 7-10 day period (McCrory et al., 2005). Thus, initiating the foundation of the return to play (RTP) protocol (Section 1.4.), in which diagnosed concussed athletes are required to complete a stepwise programme which takes approximately 7 days to complete all stages, prior to competing competitively within their respective sport again.

### **1.3. How is a Concussion Recognised**

Concussion is a complex mTBI and therefore can be identified through a variety of aspects such as; diminished neurocognitive performance, balance problems, emotional changes and a variety of signs and symptoms. Thus, when a clinician is looking to establish a diagnosis of a concussion it is essential that this broad spectrum of potential deficits are analysed.

#### **1.3.1 Signs and Symptoms**

Historically, concussion was defined by a loss of consciousness. However, as research has progressed, concussion is now known to be formed of a variety of signs and symptoms which differ between each diagnosis. There are various characteristics of concussion. Thus, during the diagnosis of a concussion, clinician's should assess both physical signs and symptoms along with cognitive deficits, balance difficulties and also emotional changes of the athlete.

The physical symptoms of an athlete can vary, but indicators are; headache, nausea, vomiting, balance issues, dizziness, sensitivity to light and noise, visual problems, numbness or tingling and any neck pain. Other symptoms could also include feelings of fatigue, drowsiness, sleeping less/more than usual, trouble falling or staying asleep, change in appetite or a change in energy levels.

The physicians should also look for signs of the athlete being; dazed, confused about an instruction or position on the pitch, the athlete forgetting certain tactical plays, signs of them

feeling unsure about the game, the score or the opponent. If the athlete is moving clumsily, or their responses to questions are slow, they may also display changes in their behaviour or personality and may also struggle recalling events prior to the impact along with if they lose consciousness at any point post-impact, then these are all signs of concussion.

Upon further assessment the physician should also examine the athletes for any cognitive symptoms, these account for any neurological alterations such as a feeling of foggy or “slowed down”. Along with this, if the athlete has trouble concentrating or displays issues with their memory then this could also be a sign of concussion. Completing cognitive tests or questions during the examination of a concussion is therefore an essential component of diagnosis. Further if the athletes report a change in their smell or taste along with hearing a constant “ringing” in their ear, then these are equally all possible symptoms of concussion.

Balance difficulties can equally occur as a physiological consequence of concussion and is therefore an effective way of accurately diagnosing a concussion. One way in which you can identify a concussion through balance is through using the Balance Error Scoring System (BESS).

Emotional symptoms is a further sign that an athlete is suffering from a concussion. If the athlete is feeling irritable, sad, nervous or anxious, in general this is determined by their emotions being “different” from usual, then these are all possible signs and symptoms that they are suffering from a concussion.

Subsequently, a range of these signs and symptoms, cognitive deficits, balance difficulties and emotional symptoms need to be examined by the clinician during the diagnostic procedure for a concussion. Using this multi-faceted approach will increase the accuracy of the diagnosis of a concussion. However, all of the above components contain subjective

interpretations, be that from the athlete themselves about their symptoms or the clinician. Thus, making the distinctions of a diagnosed concussion vary between clinicians.

### **1.3.2 Pathophysiology of a Concussion**

A concussive impact creates diffuse axonal stretching, initiating the release of glutamate. Glutamate is a neurotransmitter which can bind to the N-Methyl-D-Aspartate (NMDA) receptor, creating an ionic efflux of potassium and influx of calcium out of the cell (Giza & Hovda et al., 2014). This increased quantity of extracellular potassium activates the energy-dependent sodium-potassium pump, which is forced to work excessively in order to regain ionic homeostasis (Giza & Hovda, 2001). Alongside energy being needed to maintain activation of the sodium-potassium pump, the influx of calcium into the cell results in mitochondria being impaired in their ability to create energy through Adenosine Triphosphate (ATP). Coinciding with this impairment in production of ATP is also a reduction in cerebral blood flow, creating an “energy-crisis”. Thus, the brain resorts to glycolysis in an effort to produce sufficient quantities of ATP.

However a by-product of glycolysis is lactate, which has been hypothesised to further heighten the vulnerability of the brain to a secondary injury (Becker et al., 1987). Though neurometabolic changes after a single concussion can last up to a week, if a second concussive impact occurs during this time it can potentially exaggerate this impaired neurotransmission and cause further cognitive dysfunction (Giza & Hovda, 2014). This reinforces the importance of an athlete not returning to play prematurely, before they have fully recovered from the first concussive impact.

Overall, a concussive impact can result in damage to neurons through the stretching of axons which can lead to microtubule disruption. Thus, inhibiting normal neurotransmission and possibly cause axonal disconnection resulting in cognitive impairment (Giza & Hovda, 2014). Further, studies have shown that repeated mTBI results in damage to white matter, which was equally found to be associated with cognitive impairment (Prins et al., 2010). Therefore, the cognitive deficits that are often assessed during the diagnosis of a concussion have been associated with the pathophysiology of a concussion itself. Subsequently, knowledge of the neurological cascade that occurs post-concussion can be essential to help us assess and diagnose an individual for concussion.

### **1.3.3. Pathophysiology behind the Symptoms of a Concussion**

The association between the signs and symptoms experienced by the athlete and the pathophysiology of a concussion have not been definitively addressed as of yet, although through animal models we are able to make strong associative theories as to the occurrence of these symptoms.

One symptom of concussion is headaches, which are evident in 81% of concussion cases (Cross et al., 2016), whilst other symptoms such as vomiting and feeling nauseous can also outline a concussion. All these symptoms of concussion are also evident in individuals experiencing migraines. Therefore, it has been hypothesised that the same neurological processes that outlines a migraine are also evident shortly after a concussion resulting in symptoms such as headaches. Migraines have been hypothesised to occur from a 'spreading depression-like' phenomenon (Lauritzen et al., 1994). This occurs through an increase in extracellular potassium elevating excitatory amino acids (EAA), which opens EAA channels and increases potassium efflux further. This essentially results in a brief excitation, followed by a prolonged nerve depression, resulting in a migraine. It has been hypothesised that this

prolonged nerve depression could result in loss of consciousness, amnesia, headaches or other cognitive dysfunctions which are commonly seen in concussion, as the potassium efflux after a concussion affects a wide area within the brain (Giza et al., 2001).

Studies have examined the influence of impaired energy production (the ‘energy crisis’), that occurs at the onset of concussion and in the forthcoming days on cognitive traits such as working memory. Through the use of a recognition task, rats were examined in their ability to recognise previous (familiar) objects and discriminate between these and new objects after a closed head impact injury (more time should be spent with the novel object if working memory is unaffected). However, their results showed that compared to sham, both the single and repeated concussed group displayed significant decreases in the percent of time spent with the novel object (Spear, 2004), and therefore displayed deficits in their working memory post-concussion. Further, Prins et al. (2013) equally found that a repeated TBI group displayed significant deficits in recognition to a new object during this energy crisis period. These results clearly demonstrate that after a TBI, working memory can be negatively influenced. Therefore, assessments on working memory through assessing memory recall and understanding the individual’s state of mind (confusion) can be essential indicators of an individual experiencing a concussion.

Axonal Dysfunction occurs due to a concussive impact, thus the influence of axonal dysfunction on common signs and symptoms of concussion has been assessed. Kraus et al. (2007) looked at the effects of TBI of all severities on axonal integrity and the relationship between this white matter integrity and cognition. What they found was that in mTBI, changes in white matter are likely due to axonal damage. Further, it was found that a higher amount of white matter damage was related to greater cognitive deficiency. Therefore, even

though mTBI results in less white matter damage, compared to moderate and severe TBI, it still results in cognitive deficiencies.

In all, there are multiple concepts that have been theorised to result in the signs and symptoms exhibited during a concussion. With ‘spreading like depression’ considered to cause symptoms such as headaches, nausea and vomiting whilst the energy crisis experienced during a concussion has been linked to discrepancies in learning and memory tasks. Further, axonal dysfunction through damage to white matter has been hypothesised to result in cognitive deficiency. Although, these are hypothesised concepts it still clearly displays the direct correlation between the pathophysiology of a concussion and the signs and symptoms that are assessed to form a diagnosis of concussion. Thus, increasing the importance to understanding the pathophysiology of a concussion, in order to form a more robust diagnosis.

#### **1.3.4. Second Impact Syndrome**

A secondary insult to the brain during the “energy crisis” period can further exacerbate the energy-demand crisis and enhance the vulnerability to cells. However, if an individual does experience another concussive impact during this period it is known as Second Impact Syndrome (SIS). This is when an athlete who has sustained a concussion, sustains a second concussion before the symptoms of the first concussion have cleared (Cantu et al. 1998). This can result in the athlete experiencing a range of symptoms such as collapsing, rapidly dilating pupils, loss of eye movement and respiratory failure. Although considered a rare phenomenon in sport (Weinstein et al., 2013), it emphasises the importance of removing individuals from play instantly and following a thorough return to play guideline.

Even with the knowledge of how detrimental a second concussion can be within a specific time period, there is an increasing pressure and demand on both coaches and athletes to

continue to play or to return to play as fast as possible. This emphasises the importance of creating an objective tool to help aid the clinician through accurate and reliable data when placed under these pressures. Further, the use of an objective test would allow for heightened safety of the athlete through better identification of a concussion. From here they must then complete the RTP protocol.

#### **1.4. Return to Play**

Once a player has been diagnosed with a concussion, it is highly recommended that they take both physical and cognitive rest of around 24-48 hours prior to completing the graduated return to play protocol (RTP) (McCrory et al. 2013), due to this time period being a “window of vulnerability” as the brain has not yet recovered from the neurological alterations that occur due to concussion (Section 1.3.2.). After rest has occurred, participants begin to complete the RTP protocol. This is a staggered exercise protocol in which the athlete should only progress to the next stage when they become asymptomatic in respect to the stage they are currently on. However, if they once again become symptomatic when they increase to the next stage, then they should return to the previous stage where they were asymptomatic (McCrory et al., 2013). In general, each stage takes approximately 24 hours to progress through, therefore the RTP protocol itself takes around a week to complete. In addition during return to play, athletes should not take any medication as this can potentially mask any concussive symptoms that they are expressing.

#### **1.5. Neurocognitive Tests**

Concussion directly influences a wide array of factors from symptoms to neurocognitive deficits. Subsequently, during an examination of a concussion the use of a neurocognitive

assessment is an essential diagnostic tool due to its ability to outline cognitive performance that is otherwise difficult to distinguish. Therefore, the use of neurocognitive tests during the diagnosis of a concussion have been considered to be the ‘cornerstone’ in concussion detection due to their objectivity in identifying the mental status of the athlete. Therefore, the use of neurocognitive tests can aid the clinician in diagnosing an athlete with concussion.

However, due to the large range of signs and symptoms which outline a concussion it can be difficult for some clinicians to form an accurate, robust, objective diagnosis. The most commonly used assessment for a concussion pitch-side is the Sport Concussion Assessment Tool-3 (SCAT-3) (Section 1.6.) which is formed of a variety of assessments such as the physical examination, signs and symptoms evaluation alongside a balance and neurocognitive assessment. Although, these assessments have the capability to be subjective when being administered and interpreted by individuals who are not experienced in concussion diagnosis. Nevertheless, the SCAT-3 is a multifaceted concussion assessment designed to be administered pitch-side. The use of such neurocognitive tests pitch-side makes it more difficult for the athletes to hide their cognitive deficits and thus allows the clinician to more accurately diagnose a concussion.

The SCAT-3 is administered in various levels of sports from the top leagues right through to the grassroots. However, in the absence of experienced clinicians, the subjectivity in diagnosing a potential concussion using the SCAT-3 can be high due to the difficulty in interpreting when an individual is displaying signs and symptoms outlining a concussion, along with defining when an individual has cognitive or balance deficits due to the concussion. The cognitive and balance assessments of the SCAT-3 require the clinician to have adept knowledge and experience in identifying small adjustments in which can be the result of a concussion. Therefore, when no experienced clinicians are present, such as in the

lower tiers of the sport, the issue of subjectivity in diagnosing a concussion is greatly enhanced.

Due to the growing concern of sport-related concussions, it is essential to improve the accuracy in diagnosing a concussion in all levels of sport. One way to do this is through implementing a test in which will reduce variability between all individuals conducting the assessments and that also allows for a simple, clear method of presenting the results of these assessments- making it easier for the clinician to identify any significant changes in the athlete's current ability and thus also decrease subjectivity. Subsequently, this will reduce the subjectivity that could be observed in less experienced individuals who are conducting the test through a more consistent administration of the test and forming a more accurate interpretation of results.

### **1.6. How is a Concussion Assessed Pitch-Side**

To assess for a potential concussion pitch-side the tests used need to be fast, reliable and sensitive. Due to the restricted time provided to conduct such assessments, it can potentially impose more pressure upon the physician to make an accurate judgement on the diagnosis of a concussion. This can consequently lead to a misdiagnosis and allow for the athlete to return to play immediately, potentially increasing the risk of damage to the athlete.

To counteract for this opportunity to misdiagnose athletes, a multi-faceted approach is used to provide as much meaningful and objective data to the physician as possible within the time scale given. This approach is formed through the use of the SCAT-3, which athletes ideally should also complete a baseline assessment of during pre-season. The SCAT-3 is a

standardised tool used to assess concussion and compiles scores on signs and symptoms of the athlete, the severity of the concussion itself, the athlete's cognitive performance, a neck examination, followed by assessments on the athletes balance and coordination.

The SCAT-3 begins with the examination for any signs of concussion, whereby clinicians inquire about any loss of consciousness, loss of memory, any visual balance issues or disorientation in which may propose a potential concussion. Following this, the Glasgow Coma Scale (GCS) is administered which is a neurological scale used to provide a reliable and objective way to record the conscious state of the athlete. Through examining eye, verbal and motor responses it will provide the physician to quantify the level of brain injury that the athlete has sustained.

Once physical examinations, assessment of signs and the GCS have been conducted. Assessments then begin into the mental status of the athlete. The Maddocks Score is administered which assesses the individuals on their recollection of recently acquired information, such as "Which venue are we at today?" or "Who scored last in this match?" which has been found to be sensitive to concussion (Maddocks et al., 1995). Following completion of the Maddocks Questions, a Symptom Evaluation is completed requiring athletes to state from 0 (none) to 6 (severe) their perceived feelings on twenty two symptoms ranging from Headaches to Irritability.

Following these assessments a cognitive evaluation is administered using the Standardized Assessment of Concussion (SAC) (McCrea et al., 2001). This assessment contains four categories; orientation, concentration and immediate and delayed memory. It is designed to provide information about the athlete's neurocognitive performance during a suspected concussion. The SAC has been found to identify concussed athletes through performance

scores being significantly lower post-injury compared baseline (McCrea et al., 1997; McCrea et al., 1998; Barr & McCrea, 2001; McCrea et al., 2003). Further, SAC takes a total of five minutes to administer. Due to its quick application and high sensitivity it develops the physician's knowledge about the cognitive state of the athlete in question.

After the athletes cognitive performance has been established, a neck examination is used to assess the athlete's range of motion, tenderness and upper and lower limb sensation and strength. Equally, a coordination exam is also administered which is a finger-to-nose task. The final assessment conducted within SCAT-3 is a balance examination. The participant is required to complete three stances (double leg stance, single leg – non dominant and tandem stance) with their eyes closed, physicians then assess for errors using the BESS (Guskiewicz et al., 2003). After completion, the scores obtained through each category of the SCAT-3 exam are compared to the athlete's baseline performance, identifying any deficits due to concussion.

However, there are some fundamental issues with the use of some of these tests. When examining for a concussion, it has been suggested that an array of cognitive domains should be measured (Guskiewicz et al., 2004). This would therefore allow for a broader understanding and more of an in-depth knowledge of the athletes neurocognitive performance. Although, one problem for using the SAC is that it consists of mainly verbal answers and therefore is potentially ineffective at examining an array of neurocognitive aspects (i.e. visual working memory). Through examining a limited range of cognitive domains this could potentially result in the misdiagnosis of a concussion due to limited neurocognitive performance information available to the clinician. Furthermore, concussion is a complex mTBI that we know directly affects multiple neurological aspects. Subsequently, these individuals may pass the SAC test and be identified as 'non-concussed' as the test fails

to examine a sufficient quantity of cognitive aspects. Further, from the last report published from the Concussion Consensus (McCrory et al., 2013), there is an increasing demand for both visual tests and reaction time assessments to be incorporated into the pitch-side examinations. Thus, increasing the neurocognitive domains being examined and provide a more convincing diagnosis. A secondary issue with the use of SAC as a pitch-side concussion assessment is that it is very subjective and has the potential to have high inter-rater variability, especially when it is being administered throughout lower tiers of the sports in which experienced clinicians are not present.

The administration of the balance examination is equally open to subjective interpretation. Thus, the subjectivity of these pitch-side assessments have the potential to result in variable concussion diagnosis' between clinicians. Further, as variables such as signs and symptoms may take several hours to become exhibited by the athlete (McCrory et al., 2013), physicians may still have to rely on their own interpretation of the athlete's mental state and their likelihood of sustaining a concussion. Subsequently, if the clinicians are not experienced in diagnosing a concussion then this process can suddenly become further subjective. Thus, the SCAT-3 should not be solely used to diagnose a concussion (McCrory et al., 2013). In addition, "normal" SCAT-3 values do not mean that the individual is not concussed, due to scores being individualised. Subsequently, it is fundamental that when neurocognitive assessments (such as the SCAT-3) are used, all players should complete a pre-season assessment which can then be used as their baseline neurocognitive performance level, in which future assessments can be referred to.

A current major flaw within the diagnosis of a pitch-side concussion is the subjective interpretation of the medical staff. Although, there are many varying clinically used concussion tools to help form a diagnosis of a concussion (symptom scales questionnaire,

neurocognitive assessment, balance), there is currently no single measure or multiple measures that provide objective information on a concussion. Subsequently, this results in the physician making a subjective assessment on the diagnosis which, if wrong, can have damaging consequences. Therefore, this highlights the importance of producing a more objective measure of concussion, either through the use of multiple components or a single assessment, in which would remove the subjective interpretation and increase the safety of the athlete.

One way in which a more objective measure of cognitive performance can be obtained is through the use of a computerized neurocognitive assessment. This will result in reduced variability between clinicians, higher accuracy in scoring tests and also remove subjective interpretations from the neurocognitive test pitch-side, compared to conventional paper-and-pencil assessments.

However, as computerized neurocognitive assessments are yet to be administered pitch-side, and therefore post-exercise. The influence of confounding factors such as fatigue is yet to be addressed within these computerized neurocognitive assessments.

### **1.7. Exercise and Cognition**

In order to help assist the diagnosis procedure of a concussion and reduce subjective interpretations, computerized neurocognitive tests should be examined in their ability to be used “pitch-side”. External factors such as fatigue, may influence the results of these neurocognitive tests post-exercise, and thus impede the accuracy of the diagnoses formed by clinicians. Therefore, it is important to assess the influence of fatigue on neurocognitive tests before they can be considered to be used as a “pitch-side” concussion tool.

Studies have begun to examine the influence of exercise induced fatigue on the current diagnostic tools used. Boutros et al. (2013) looked at the effect of fatigue on SCAT-2 which was administered at rest, two minutes and 25 minutes post-exercise. Results displayed that SCAT-2 scores, 2 minutes post-exercise, significantly decreased before returning to baseline 25 minutes post-exercise. Further, symptom scores and balance equally displayed deficits in performance post-exercise. In addition, Morissette et al. (2014) conducted a VO<sub>2</sub> max test upon participants and analysed SCAT-3 scores, following which performance scores were compared to baseline scores. They identified that there was no significant change on all components of the SCAT-3 apart from symptom scores, which had significantly increased once again.

Although, studies suggest that the current pitch-side concussion tools (SCAT-3) are not affected by fatigue, apart from enhancing concussion-like symptoms, there still remains a demand for more robust, objective neurocognitive assessment to be used “pitch-side”.

Computerized neurocognitive tests are simple, efficient, objective assessments. However, as of yet they are not implemented “pitch-side” to aid in the diagnostic procedure of a concussion. Nevertheless, there is one assessment (The King-Devick Test) which has been created to aid in a pitch-side concussion test. This is an assessment which can be applied on a tablet and is formed of a rapid number naming assessment, which requires athletes to read numbers along the same line aloud. The assessment requires eye saccades, attention and language function in order to be completed and has been found to have 86% sensitivity (Galletta et al., 2016). However, the King-Devick test only contains one assessment. As a concussion results in a wide variety of signs, symptoms and cognitive deficits a single assessment may be inadequate to identify a concussion due to the large variety of cognitive deficits that can occur. Further, the assessment itself is very simplistic and has also been

found to have learning effects (Galetta et al., 2016). Nevertheless, it is a good starting point to determine whether an individual should be removed from play due to a suspected concussion.

In addition to the King-Devick, studies have begun to examine computerized neurocognitive test batteries such as the Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT) to determine whether such computerized neurocognitive tests are uninfluenced by exercise and thus reliable enough to be used pitch-side. The first study to assess ImPACT and exercise-induced fatigue was conducted by Covassin et al. (2007). Through exercising individuals to their VO<sub>2</sub> max they then compared post-exercise scores immediately after exercise and four days post-exercise to the athlete's baseline results. Their results display that there was no significant differences in the visual memory, motor processing speed and reaction time composites. However, the verbal memory composite was significantly affected by fatigue, in which scores decreased immediately post-exercise before returning to baseline at day 4. In addition, like the SCAT findings reported previously, they identified that there were significant differences in self-report measures due to fatigue.

Overall, the findings of Covassin et al. (2007) seem to suggest that there may be a place for computerized neurocognitive tests "pitch-side". The only assessment that differed between the computerized tests and the conventional assessments was verbal memory. Although, this could be the direct result of exercising individuals to maximal exertion through the VO<sub>2</sub> max test, in which is unrepresentative of many sport-specific exercise activity.

McGrath et al. (2013) extended the findings of Covassin et al. (2007). They looked to examine the neurocognitive performance of athletes during the RTP who had "recovered" from a concussion and produced "normal" neurocognitive scores along with being asymptomatic at rest, however were yet to return to play. Participants completed an ImPACT

assessment at baseline and then again post-concussion, and finally when asymptomatic. When participants were asymptomatic they were required to complete a physical exertion protocol at 60-80% of their maximum heart rate for 15-25 minutes before completing the ImPACT examination again after 10 minutes of rest to examine the influence of physical exercise on both their neurocognitive performance during this RTP protocol. Their results showed that even though all individuals were asymptomatic and seemed to have fully recovered from their concussion, 28% of athletes failed at least one or more composites of ImPACT post-exercise. More specifically, there were significant differences in verbal memory and visual memory post-exertion. Thus, this re-enforces the subsequent use of computerized neurocognitive tests to be administered during the RTP in order to definitively outline the athletes cognitive performance levels and thus ensure that they do not return to play prematurely and suffer an additional, more damaging concussive impact.

In essence, the results of McGrath et al. (2013) clearly display the benefits of using a computerized neurocognitive test due to their objective nature of identifying a concussion. Therefore, the use of a neurocognitive test in diagnosing a concussion pitch-side and throughout both the pitch-side concussion assessment and the RTP protocol should be considered in order to enhance diagnosis of a concussion and improve the athlete's safety.

However, there are very few studies that have assessed the influence of exercise-induced fatigue on computerized neurocognitive tests designed to identify a concussion. The two studies that have, have assessed ImPACT. Although, ImPACT takes 20-25 minutes to administer and thus is inadequate to be used within the time scale given for a "pitch-side" assessment. Moreover, many current computerized neurocognitive test batteries lack key qualities to be used within a pitch-side environment. Many of these computerized assessments do not have the capability to select individual tests in order to both randomise and/or reduce

the total length of time of the test battery. Therefore, they are not able to be applied within the 10 minute time period provided during a HIA for concussion in Rugby. Further to this, there is also a lack of studies which have looked to identify the influence of exercise on cognitive performance during these assessments. Thus, due to the combination of the length of the test, the inability to randomise assessments and finally a lack of studies looking at the reliability of these tests under the influence of exercise, these test batteries are currently inappropriate to be used under pitch-side conditions. An additional requirement of a pitch-side assessment is its ability to be applied on a portable device and thus be administered pitch-side. The combination of these requirements outlines some of the qualities that are needed for an effective computerized neurocognitive assessment.

Further to this, there is a lack of literature examining the reliability of current computerized neurocognitive tests after exercise in multiple sessions. By examining a single session, there are many external factors that could potentially alter neurocognitive performance other than fatigue itself. Therefore through the analysis of multiple exercise sessions, conflicting variables will be eradicated. Ensuring that if one session is direct influenced by a factor such as dehydration, it is unlikely that in the next session the same factor will be present. Thus, through the use of multiple exercise sessions, overall it eradicates the influence of confounding factors on the neurocognitive performance of the participant and therefore will allow for a more accurate assessment on the influence of fatigue solely on cognitive performance and the reliability of a computerized neurocognitive assessment pitch-side.

Subsequently, many questions still remain due to the lack of studies assessing both the influence of fatigue across multiple sessions and also through no studies administering a neurocognitive test that can be applied within the given protocol for a HIA in Rugby and therefore be used as a “pitch-side” concussion assessment tool. Nevertheless, if a

computerized neurocognitive test could be implemented within this given time frame then it would significantly enhance the accuracy of diagnosing a concussion. Thus, increasing the athlete's safety and also improving the current concussion diagnosis procedure.

However, if a computerized neurocognitive test was to be used pitch-side, its reliability over a clinically relevant time period would need to be established first. A clinically relevant interval relates to a time period in which an athlete would complete a baseline neurocognitive assessment to a time period in which the athlete may sustain a suspected concussion. This time interval is generally between a month to a year after baseline, due to baseline cognitive assessments taking place during pre-season. Broglio et al. (2007) identified on average a concussion was experienced after approximately a 45 day period post-baseline. Therefore, test-retest intervals of anywhere up to a month could be considered clinically invalid. Subsequently, any computerized neurocognitive assessment that is foreseen to potentially be used pitch-side would need to have high reliability values over a clinically relevant time period to assess for a concussion first. This would essentially establish that any variance in cognitive performance between the tests are due to true cognitive deficits rather than other variables such as time.

### **1.8. RESET**

RESET is a newly developed neurocognitive computerized test designed to assess severe TBI's for neural impairments found within; ADHD, Autism, Schizophrenia along with assessing side-effects from Chemo therapy. Further, it has also been created for use in individuals who are looking to enhance their executive function skills. As RESET has been

created to assess neurocognitive performance in more severe TBI, we hypothesise that RESET may also be able to assess more subtle head traumas such as sport related concussion.

In all, the RESET battery of assessments is composed a hybrid of tests, combining both conventional and computerised neurocognitive assessments. The whole assessment battery is formed of 15 assessments which can be separated into five composite scores; Memory, Attention, Executive Function, Visual Perception and Self-report. All of which have been identified to be impaired within concussed individuals.

Further, RESET has the ability to be administered on portable devices such as Tablets. This therefore, eradicates the previous issue of applying computerized neurocognitive assessments pitch-side and thus has the potential to replace the paper-and-pencil technique currently used “pitch-side” for a more objective, robust measure. In addition, the individual’s neurocognitive performance is saved on an online database in which when accessed, clinicians are able to directly compare scores within-individuals. The neurocognitive performance is displayed both graphically and also shown in raw values, allowing the clinician to efficiently compare an athlete’s current neurocognitive performance to their previous performances (i.e. baseline) and therefore forming a more objective interpretation of a potential concussion. Combined, this all aids the clinician in making a fast and accurate, objective assessment when diagnosing a potential concussion. Thus, due to the practicality of RESET it provides a potential solution to forming an objective, computerized neurocognitive assessment that could be administered pitch-side.

Further, RESET is a complex test battery composed of multiple assessments measuring differing cognitive components and has a more game-like environment compared to the King-Devick, which is a lot more minimalistic. This could result in more attention and

concentration used within the RESET battery due to the higher cognitive demands of the test. In addition to this, as RESET is a battery of assessments it will be able to provide a more robust, accurate and comprehensive diagnosis of concussion through examining a wider range of cognitive domains. Further, like the King-Devick test, it can be applied on tablets (and therefore pitch-side) and also has the potential to be applied by all individuals, not just clinicians, and provides an easier format of determining when an individual may have sustained a concussion and thus be removed from play.

Nevertheless, as the reliability of RESET is yet to be established over a clinically relevant test-retest period (45 day) to assess for a suspected concussion, this study firstly looked to address this question. Subsequent to these findings, a further study looked to establish the reliability of RESET post-exercise when administering a shortened RESET protocol so that all assessments conducted were assessed under the influence of fatigue and therefore whether RESET is applicable pitch-side. Thus, through establishing the reliability of this potential concussion test through the preliminary study, followed by outlining its potential use to be used pitch-side under fatiguing circumstances, this thesis will therefore look identify RESET's prospective use as a reliable, objective pitch-side concussion assessment tool.

## **Chapter 2 – Reliability of RESET**

In order to deem a neurocognitive test as an effective additional concussion assessment tool, preliminary studies must evaluate the reliability of the test over a sufficient test-retest period in order to be applicable as a clinical measure. When assessing for concussion, the reliability of a neurocognitive test is essential. As a concussion may occur between a month to a year after the baseline neurocognitive assessment was completed, it is vital that the scores of these assessments do not fluctuate over time and remain stable within healthy subjects. Thus, if an individual does sustain a concussion, the neurocognitive performance of the individual will display significant deficits which are not evident within healthy subjects. Ensuring for an objective, accurate diagnosis.

### **2.1. Conventional Neurocognitive Assessments**

Neurocognitive tests have generally been divided into various domains such as attention, memory, vision, executive function and language to name a few. Further, there is evidence that these neurocognitive domains are activated in specific neurological regions of the brain, displayed through clusters of brain activity (Laird et al., 2011). In addition, when addressing the influence of mTBI's on the functional connectivity of each brain network it was found that there was abnormal brain connections for visual processing, motor, limbic and executive function (Stevens et al., 2012). Therefore, when determining what neurocognitive tests to apply when assessing for sports-related concussion it is important to use a multitude of tests. Guskiewicz et al. (2004) stated that attention and concentration, cognitive processing (speed and accuracy), learning and memory, executive functioning and verbal fluency should be applied.

### 2.1.1. Attention

Attention is a domain which contains a total of four subsets; selective, sustained, executive and divided attention. Selective attention is the ability to block out specific aspects of the environment in order to focus exclusively on one aspect. Sustained attention is the ability to concentrate on a task within the environment for a prolonged period of time. Whilst executive attention is the ability to block out irrelevant stimuli within the environment in order to focus on something important. Finally, divided attention is the ability to focus on two separate stimuli simultaneously. The ability to attend to a task originates within the frontal lobe, which is regularly effected post-TBIs.

There are many variations of assessments that look to outline performance of attention. One of which is the Stroop Colour Word Test (Stroop, 1935) which is a measure of selective attention, and considered important in evaluating the attentional function of a patient (Lamar & Raz, 2005). The Stroop Colour Word Test is constructed of three pages. The first is a word page in which different colour words are written on the page in black ink, the second page is a colour page with 'X's' in different colours. The final page is a colour-word page, this is a combination of the first two pages, although the colour and the word do not match. It therefore requires your brain to inhibit saying the word through selective attention and instead acknowledge and respond with the colour of the word itself instead. However, the participant is required to name the colour of the word as quickly as possible within a time limit, therefore increasing the complexity of the task. A further test that could be considered a conventional assessment of attention is the Trails Making Test (TMT). This is a neuropsychological test of visual attention and task switching. The test has the ability to provide information on visual search speed, scanning, processing speed, mental flexibility and executive functioning. It contains two parts, Part A and Part B. Part A consists of 25 numerical dots in which the

participant is required to connect as quickly as possible. Part B contains both numbers and letters where the participant is required to connect these alternatively, once again as quickly as possible. Both parts of the TMT examine different neurocognitive aspects, Part A tests cognitive processing speed and Part B is a test of executive functioning.

Both the Stoop Colour Word Test and the TMT have been assessed for their ability to be sensitive to TBI. Echemendia et al. (2001) analysed a battery of tests including the Stoop Test and the TMT and found that individuals suffering from mTBI had significantly impaired performance scores which was present two-days later for attention and divided attention. This deficit within concussed individuals has been seen present within other studies for both the Stroop Colour Word Test (Guskiewicz et al. 2001) and for TMT (Guskiewicz et al., 2001; Macciocchi et al., 1996). Thus, due to deficits identified within attention tasks post-concussion, it is an important neurocognitive domain to assess for a potential concussion.

#### 2.1.2. Cognitive Processing

Cognitive processing is the psychological result of perception, learning and reasoning and is the process of acquiring knowledge through our thoughts, experiences and senses. One assessment that looks to determine the performance of cognitive processing is the Wechsler Digit Symbol Test. This is an evaluation tool used to assess cognitive processing through assessing processing speed, working memory, visuospatial processing and attention. It involves a key consisting of numbers 1-9 which are paired respectively with symbols. The participant is provided 90 to 120 seconds to fill in the respective symbol for each number.

Macciocchi et al. (1996) conducted a study which examined the utility of the Wechsler Digit Symbol Test to identify concussed individuals compared to a healthy cohort. Their results revealed that cognition was significantly impaired post-concussion.

### 2.1.3. Memory

Memory contains three main subsets; sensory memory, short-term (working) memory and long-term memory. Sensory memory is the ability to retain sensory information after the stimuli has finished. It is a form of short-term memory that decays quickly, after 200-500 milliseconds. The second subset is short-term memory, this is the ability to maintain information which is readily available for a short period of time. One aspect of short-term memory is working memory which holds, processes and manipulates information for decision making and behaviour. The final form of memory is long-term memory, which is the ability to store information over a prolonged period of time from a few minutes to a lifetime. Memory can be split further into both visual and verbal memory, although all forms of memory are considered to occur within the temporal lobe.

There are a variety of conventional assessments that are used to assess memory. One of which is the Wechsler Digit Span which is a measure of working memory. The test provides the participants with a series of digits (e.g. 3, 7, 5) and requires the participant to immediately repeat these digits back. If done successfully, then the number of digits provided increases (e.g. 2, 9, 5, 6). The Wechsler Digit Span Test can be conducted either forward (numbers are repeated in the same order) or backward (numbers are repeated back by the individual in reverse order). A further assessment is the Hopkins Verbal learning Test-Revised (HVLT-R) which is a measure of verbal learning and memory. The HVLT-R is formed of a total of six different forms, each containing 12 nouns, four words of which are related to specific categories and are to be learned over the course of three learning trials. After 25 minutes, a delayed recall trial and recognition trial are completed (Belkonen et al., 2011). Both the Wechsler Digit Span and the Hopkins Verbal Learning Task have both been assessed in concussed individuals. Echemendia et al. (2001) assessed both of these memory tasks in

individuals that had suffered from a concussion and found that they had a significant deficit in both of these tasks compared to a control group. An additional test equally identified that both the Wechsler Digit Span and the Hopkins Verbal Learning Task are also significantly impaired post-concussion (Guskiewicz et al., 2001).

#### 2.1.4. Executive Function

Executive functioning is formed of a variety of cognitive processes that are all used to facilitate behaviours and also to achieve specific goals. It contains aspects such as attentional and inhibitory control, working memory, cognitive flexibility and problem solving. This domain is found within the Frontal Lobe and is often identified to have significant deficits post-TBI.

There are a multitude of assessments that are used to display performance levels in executive functioning. Two of the main ones are the TMT (Section 2.1.1.) and the Wisconsin Card Sort Test (WCST) (Grant & Berg, 1948). The WCST is a neuropsychological assessment of set-shifting. Participants are required to sort cards into four different piles based on specific rules (Colour, number or shape). The participant is not provided the rule, however is told “correct” or “incorrect” based on their placement of the card. The specific rule is applied for a set number of trials before then changing without warning, resulting in the participant having to adjust to the new rule. Performance is calculated using multiple variables; the number and percentage correct, types of error, the number of trials taken to complete the first category and failure to maintain a set to name a few (Coelho et al., 2012).

Studies have administered these assessments on concussed individuals in order to establish their sensitivity to concussion. The TMT has been established to determine the difference in cognitive performance in concussed individuals compared to healthy individuals (Echemendia

et al., 2001; Guskiewicz et al., 2001; Macciocchi et al., 1996). Equally the WCST has been assessed in a group of soccer players suspected of sustaining a concussion. Results displayed that these soccer players exhibited a significant neurocognitive deficit (Matser et al., 1999).

#### 2.1.5. Verbal Fluency

Verbal fluency is the ability to form and express words that are compatible to specific criteria (Wysokiński et al., 2010). This domain originates in the temporal lobe where language is perceived and recognised, injury to the temporal lobe can often result in language issues such as communication and understanding deficits.

One assessment of Verbal Fluency is the Controlled Oral Word Association Test (COWAT). The COWAT assessment is a verbal fluency test, which requires the participant to name as many words as possible within one minute, alternating between words beginning with the letters C, F and L (Patterson et al., 2011).

Similar to many tests previously discussed, COWAT has also been assessed in its sensitivity to identify concussed individuals. Echemendia et al. (2001) examined individuals suffering from mTBI and compared performance levels to a control group. They found that the mTBI group had significantly poorer performance scores on the COWAT examination compared to the control group. Thus, demonstrating the sensitivity of verbal fluency tests to individuals that have sustained a mTBI.

These above studies and assessments outline the deficits that are regularly observed within specific neurocognitive domains in concussed individuals. Studies have continually found them to be sensitive to individuals who have suffered from concussion. However, there still remains many drawbacks to the clinical use of conventional assessments. One of which is their vulnerability to subjective interpretation from the clinician, subsequently resulting in

varying diagnosis of concussions. Further, there is a delay in the ability to diagnose a concussion due to the clinicians having to interpret the results themselves. Overall, the conventional concussion assessments used are open to interpretation, and therefore have high physician error, they take longer to analyse and can vary between each diagnosis. Whereas, a computerized neurocognitive assessment allows for better standardization during assessments and scoring, the ability to create various forms of the test to allow for repetitive testing, more precise assessment, and increases cost efficiency (Gualtieri, 2004). Equally, the use of computerized neurocognitive tests can reduce subjective assessments, allowing for higher accuracy and less variability between examinations. Therefore making it more difficult for the athletes to sandbag and disguise their signs and symptoms.

## 2.2. Computerized Neurocognitive Tests (CNT)

The more conventional neurocognitive tests have been replaced with CNT in an effort to provide more accurate, precise testing along with better standardisation between assessments (Gualter, 2004). Therefore, applying a CNT “pitch-side” could potentially form a more accurate diagnosis of a concussion, especially when an experienced clinician may not be available (e.g. grassroots), compared to the more conventional tests. When using CNT individuals are defined as being concussed if their performance displays significant deficits compared to baseline in that respective composite score. However, athletes are known to “sandbag” their baseline tests, this is where athletes will perform worse in their baseline assessment so that when concussed their performance does not display significant deficits. Although, CNT have been found to identify 71% of individuals post-concussion who are asymptomatic, as still being concussed (Broglia et al. 2007) and therefore can provide essential information on the cognitive state of an athlete. The assessments used within these

CNT are designed to test a range of neurological components which vary depending on the assessment administered by the physician.

The reliability of these CNT are established through Intraclass Coefficient Correlation (ICC) values over a given time interval. These ICC values are determined through the use of a test-retest format and provide a measure of reliability of a given assessment, and are also used to measure inter-rater reliability (Shrout & Fleiss, 1979). The ICC value ranges between 0 and 1, with the closer the score to 1 resembling higher reliability. There are a variety of different formulas for calculating an ICC value based on how the test itself is being administered. One of which that Shrout and Fleiss (1979) outlined is an equation for when all individual scores for each participant are examined and when all examiners are fixed, classified as ICC (3,1). The equation is as follows:

$$\frac{MS_S - MS_E}{MS_S + (k - 1)MS_E}$$

Formula to calculate an ICC based from Shout and Fleiss (1979) classifications. K= number of trials,  $MS_S$  = subjects mean square,  $MS_E$  = error mean square

This equation uses the mean square of the subjects ( $MS_S$ ) along with the error mean square ( $MS_E$ ) and the number of trials (k) in order to calculate a value between 0 and 1 to determine the strength of the reliability of the test over a period of time, using the same examiners and individual subject scores. However, the “cut-off” value between 0 and 1, used to establish strong reliability, has varied in literature. Although, Nunally et al., (1994) suggested that an ICC value of over 0.80 should be used for individual interpretation, as the influence of measurement error becomes minimal and therefore the test is adequate to be used clinically. Further, Cicchetti (1994) devised a classification scale of reliability based on ICC values.

They determined that ICC values below 0.40 displayed poor reliability, between 0.40-0.59 resembled fair reliability, 0.60-0.74 demonstrated good reliability and finally between 0.75-1.00 displayed excellent reliability values. Subsequently, when determining the clinical use of these computerized tests, it is important to identify their reliability over time to ensure that they are reliable enough to be used as an additional clinical tool in the identification of concussion. In addition to being reliable, these tests also need to be sensitive to concussion, and thus be subtle enough to detect alterations in neurocognitive scores that are purely due to concussion and not external factors.

The three main neurocognitive tests currently used within sport to assess concussion are CogSport/CogState, Headminder Concussion Resolution Index (Headminder CRI) and ImPACT.

These three computerized neurocognitive tests were further analysed within this thesis due to their similarities with the RESET test battery, used within this study. Further, they are also currently used within the diagnosis/recovery of a concussion and therefore displaying their reliability values along with their validity and sensitivity rates allows for a better understanding of the standards that need to be met in order for a new computerized neurocognitive test to be considered as a potential alternative assessment. In addition, these three tests are the most commonly cited computerized concussion tests within literature and therefore there is an abundance of research into their reliability and sensitivity rates. This makes it easier to establish the current strengths and weaknesses of these computerized neurocognitive tests and thus also displays their pitfalls, outlining a potential gap in which a new computerized neurocognitive test could be used. Further, due to their constant use within literature there is a higher quantity of studies outlining their reliability over various test-retest lengths. This will therefore allow for a better comparison of the reliability of a newly

proposed computerized neurocognitive test (RESET) over a similar test-retest length through comparing its reliability to already established computerized neurocognitive tests. Therefore, due to an abundance of studies examining these three assessment's reliability through the use of ICC values, their similarity to RESET when the whole battery of tests are administered and finally studies assessing them over similar test-retest lengths, allowing for better comparison of reliability between studies, it allows for a more accurate comparison to the reliability of RESET over a similar time period to established computerized neurocognitive tests.

### **2.2.1 CogState (CogSport)**

CogState is a computerized neurocognitive test that has often been cited within literature in its ability to be used as a possible concussion assessment tool. CogState itself contains various collections of subtests which assess varying disorders such as schizophrenia, alzheimers, depression, multiple sclerosis and also brain injury. The brain injury battery of tests contains a range of measurements that provide information on psychomotor function, attention, visual learning, working memory and executive function. Thus, assessing a range of functions that are affected by concussion (Guskiewicz et al., 2004). CogState is constructed of a battery of tests that consist of; simple, complex and choice reaction time, continuous monitoring task, one back working memory task, matching task, an incidental learning task and an associative learning task.

In order to examine the validity of this computerized test, studies have analysed CogState's ability to identify cognitive change compared to conventional cognitive assessments such as the TMT, which is used to assess visual attention and task switching, and the Digit Symbol Subtest Task (DSST) used to assess information processing. During these assessments they

found that the working memory task had high correlations with DSST (Collie et al. 2003) and also that complex reaction time was significantly associated with Trials A and B (Schatz et al. 2006). Furthermore, Makdissi et al. (2001) administered the simple reaction time task of the CogState battery on concussed Aussie Rules Players alongside both the TMT and DSST, and compared post-concussion scores to baseline measurements. It was identified that the CogState computerized assessment identified that concussed players had a 45% slower reaction time compared to baseline, with the response variability being the best indicator of impairment. Whilst the DSST only identified impairment in one individual and the TMT-B found no difference in any individuals. Demonstrating CogStates high potential to be used as a concussion tool due to it having a higher sensitivity to concussion compared to conventional assessments. In addition, Eckner (2011) also examined simple reaction time of the CogState battery and compared scores to a conventional assessment of reaction time. They equally found that when assessing concussed individuals, the CogState simple reaction time test identified a greater magnitude of change and had higher variability post-concussion compared to the more conventional assessment of reaction time. These studies comparing conventional tests to computerized neurocognitive assessments clearly outline the beneficial use of computerized assessments due to higher sensitivity whilst also maintaining validity compared to these conventional tests.

Once the validity of CogState was established its test-retest reliability was examined. The length of the test-retest periods varies between each study. Collie et al. (2003) advanced preliminary findings of CogSports' ability to be used as a concussion test through assessing the reliability of CogState. Through repeated assessment on healthy individuals at test-retest intervals of one hour and one week, they concluded that CogState had "high to very high" ICC scores for speed components (*Table 1*) ranging from .69 to .90 after one hour and .69

to .82 for the one week test-retest assessment. Subsequently, they concluded that such a test is capable of being used during repetitive testing due to good reliability. Equally, authors have identified that CogSport's ICC values range from .83 to .93 and .51 to .82 respectively after a one week test-retest interval (Louey et al. 2014; Falletti et al, 2006). Subsequently, all studies conclude that the ICC values that are identified over a week are high and that CogState itself is therefore able to be used within a clinical setting. However, CogState in these studies was not measured over a clinically relevant period (Broglia et al., 2007), thus studies that are administered over a more relevant timeframe could be argued to carry more authority in the argument of CogState's reliability.

One study in which did assess a more clinically valid protocol, examined football players over consecutive years during pre-season (Straume-Naesheim et al. 2005). The ICC values gained from this study ranged from .45 to .79 (*Table 1*). Therefore, when considering a longer test-retest interval, and in many ways a much more clinically valid protocol, then the reliability coefficients are reduced, outlining CogState as less reliable. Further, when assessing healthy control subjects there has been large variability in CogState scores (Schatz et al. 2006). This presents an issue for the medical staff; if there is high variability in a healthy control cohort it becomes difficult to accurately identify concussed patients due to the results of the assessments being variable within a cohort of healthy subjects, therefore it is not known that any change in scores is due to the unreliability of the test or an actual sustained concussion. A further study analysed the reliability of CogState over a month (Cole et al. 2013), as before when conducting an assessment over a more clinically relevant time period they found a larger range of ICC values, with ICC values falling below the cut-off point for adequate reliability (.22 to .79). Furthermore, Cole et al.(2013) concluded that the test-retest reliabilities reported both within this study and within current literature are unreliable and therefore may

not be suited for clinical use. The conflicting reports within literature about the reliability of CogState as an effective neurocognitive assessment battery causes concern as it creates cautiousness when interpreting the results produced due to poor reliability.

Study	Participants	Test-Retest Length	Simple RT	Choice RT	Complex RT	Continuous monitoring task	One back working memory task	Matching	Incidental learning task	Associative learning task	Visual Memory
Cole et al. (2013)	Active Service Members	30 Days	0.78	0.77			0.74				0.22
Eckner et al. (2011)	University Athletes	1 Year	0.51								
Falleti et al. (2005)	Healthy Adults	10 Minutes	0.84	0.38	0.41	0.54	0.62	0.73	0.42	0.86	
		40 minutes	0.94	0.81	0.66	0.74	0.74	0.85	0.74	0.77	
		1 Week	0.73	0.71	0.64	0.51	0.7	0.71	0.6	0.82	
Collie et al. (2003)	Elite Athletes	1 Hour	0.9		0.69	0.83	0.76				
		1 Week	0.76		0.69	0.82	0.72				
Straume-Neisham et al. (2005)	Professional Football Players	1 Year	0.73	0.65		0.45	0.71	0.69	0.79		
Louey et al. (2014)	Professional Male Athletes	1 Week	0.85	0.86			0.83				0.93
<b>Range</b>			<b>.51 - .94</b>	<b>.38 - .86</b>	<b>.41 - .69</b>	<b>.51 - .83</b>	<b>.62 - .83</b>	<b>.71 - .85</b>	<b>.42 - .79</b>	<b>.77 - .86</b>	<b>.22 - .93</b>

**Table 1:** Outlines all the reported ICC values for CogSport reported within literature

Nevertheless, CogState has been assessed for its sensitivity in identifying a concussion. This is determined through significant changes in component scores, in which if decreased would suggest that the athlete has sustained cognitive impairment as a direct result of the concussion. The simple reaction time component, in this battery of tests, has found that concussed individuals to have a 45% increase in reaction time and found their scores to vary by 16% compared to baseline (Makdissi et al., 2001). Equally, CogState has been used to assess neurocognitive performance within concussed Rugby Union players using the baseline method, players were then reassessed if identified as being concussed 72 hours post-concussion. They identified that the concussed group performed significantly worse in reaction time, decision making, the matching task and working memory compared to a control

group (Gardner et al. 2012). Therefore, although literature provides conflicting reports on CogState's reliability values, the sensitivity of CogState in identifying concussed individuals is strong when compared to a control group. However, this is undermined due to the large range of reliability reported (*Table 1*), if the test is unreliable over a clinically relevant period of time within a healthy cohort, then it does not aid the clinician in diagnosing a concussion.

### **2.2.2 HeadMinder Concussion Resolution Index (CRI)**

Another commonly used computerized concussion assessment tool is the HeadMinder CRI. The HeadMinder concussion battery is composed of a combination of five different assessments; simple reaction time, complex reaction time, simple reaction time errors and complex reaction time errors along with processing speed. Like CogSport, this test has equally been compared to more conventional concussion assessments such as TMT and Digit Symbol Test. It has been identified that the combination of the five assessments used within HeadMinder CRI are correlated to TMT A and B and also Digit Symbol Test (Schatz et al. 2006). Therefore, providing strong validity as a concussion assessment protocol due to its association with tests that have previously been used to identify a concussion.

Studies have gone on to assess both the reliability and sensitivity of HeadMinder to be used as a clinical tool to aid the diagnosis of concussion. Erlanger et al. (2001) was one of the first to assess the reliability of HeadMinder through assessing two different populations (Adults/college athlete and high school students) over a two-week test-retest interval, results displayed high values between .72 to .90 for adults and .65 to .79 for high school students (*Table 2*).

However, these high ICC values have been disputed by a study conducted by Broglio et al. (2007) who conducted a 45 day test-retest length and also analysed 45 day to 50 day scores.

The ICC ranges that were published by Broglio et al. were between .43 and .66 for the 45 day period and .36 and .66 between day 45 and day 50 (*Table 2*). Therefore, demonstrating discrepancies in the reliability reported within the literature, creating controversy in the use of HeadMinder CRI as a clinical tool in concussion diagnosis.

Alongside assessing the reliability of HeadMinder CRI, its sensitivity in identifying a concussion has equally been examined. HeadMinder CRI has been reported to identify cognitive impairments in diagnosed concussed athletes, in both simple and complex reaction time (Sosnoff et al. 2008). This result suggests that HeadMinder CRI can be sensitive to concussions and therefore potentially a beneficial concussion tool. Conversely, Erlanger (2003) conducted a baseline assessment and provided a further follow up test on 47 concussed individuals, 1-2 days post injury. Their results revealed that only 55.3% of clinically concussed athletes were identified as being concussed using HeadMinder CRI. Equally, other studies have only reported cognitive deficits in 69.2% and 78.6% of concussed athletes respectively (Erlanger et al. 2001; Broglio et al. 2007) when using HeadMinder CRI.

Subsequently, this outlines a clear flaw in using HeadMinder CRI as a concussion tool. Firstly, there are clear discrepancies in the reported reliability of the test itself. In addition, the sensitivity of the test itself is not very high. Therefore, physicians would be strongly recommended to use a variety of tests to assist in the identification of a concussion, in order for the sensitivity value of the test to be clinically acceptable. Overall, due to conflicting research on both the reliability and the sensitivity of HeadMinder CRI, it provides more doubt during the diagnosis of a concussion rather than being a valuable additional tool.

Study	Participants	Test-Retest Length	Simple Reaction Time	Simple Reaction Time Errors	Complex Reaction Time	Complex Reaction Time Errors	Processing Speed Index	False Positive Rate (%)
Broglio et al. (2007)	University Athletes	Baseline to Day 45	0.65	0.15	0.43	0.26	0.66	19.2
		Day 45 to day 50	0.36	0.03	0.66	0.46	0.58	23.3
Eckner et al. (2015)	Contact-Sport Athletes	1 Week	0.54		0.44			
Erlanger et al. (2001)	College teams	2 Weeks	0.73		0.72		0.9	
	High School Students	2 Weeks	0.72		0.65		0.79	
<b>Range</b>			<b>.36 - .73</b>		<b>.43 - .72</b>		<b>.58 - .90</b>	<b>19.2-23.3%</b>

**Table 2:** Displays all ICC values reported within literature on the HeadMinder Concussion Resolution Index

### 2.2.3 ImPACT

ImPACT has been the most widely cited computerized neurocognitive concussion test within literature. It contains a total of six assessments (word discrimination, design memory, X's and O's, symbol matching, colour matching and three letters), which are then categorised into five different composite scores; Verbal memory, visual memory, visual motor speed, reaction time and impulse control score. Thus, incorporating a multifaceted approach to examine neurocognitive deficiencies post-concussion which has been suggested to be an effective protocol for assessing a concussion (Guskiewicz et al., 2004). The verbal memory score is formed through the combination of word discrimination, symbol matching and the three letters test. Whilst the visual memory composite is formed of the design memory and X and O's test. In addition, the visual motor speed composite incorporates the X and O's test alongside the three letters. The reaction time composite score is formed of the X's and O's, symbol match and colour match. Finally the impulse control composite uses two different assessments; X's and O's and the colour match test.

Due to the vast amounts of studies assessing the practicality of ImPACT being used as an effective concussion assessment, its validity has been repeatedly assessed through comparing scores to more conventional, pencil-and-paper concussion assessments. As a result, all composites of the ImPACT battery of tests (apart from impulse control) have been found to be significantly correlated with conventional assessments used to identify a concussion (Maerlender et al. 2010). Further, the Symbol Digit Modalities Test (SDMT), which assesses cognitive impairment, was found to be highly correlated with the visual processing speed and reaction time composite (Iverson et al. 2005) whilst the verbal memory composite correlated with the California Verbal Learning test and also the Brief Visual Memory test, Revised (Maerlender et al. 2010). Subsequently, the validity of ImPACT is unquestionable and appears to contain a strong battery of tests that can be used in the identification of concussion.

The test-retest reliability of ImPACT has been examined thoroughly. Iverson et al. (2003) was one of the first studies to examine ImPACT's reliability. When assessed over an 11 day interval ImPACT displayed high ICC values (range of .65 to .86) in all composites. ImPACT has also been assessed over a longer more clinically relevant period to further examine its reliability. Schatz et al. (2010) examined the reliability of ImPACT over a two year test-retest interval period. The ICC values recorded within this study were high in context of the time interval (*Table 3*), therefore portraying ImPACT to possess equally high reliability values over a more significant period of time. Overall, there has been a magnitude of studies that have outlined high values of ICC on the components of ImPACT (Elbin et al. 2011; Schatz et al. 2013; Register-Mihalik et al. 2012; Nelson et al. 2016 and Nakayama et al. 2014) (*Table 3*) all of which have assessed varying test-retest intervals and population. Thus, enabling ImPACT to be seen as a clinically useful concussion assessment tool. However on the other hand, there has been roughly an equal number of studies in which have challenged the

reliability of ImPACT and subsequently reported conflicting findings. Broglio et al. (2007) conducted the study that instigated an elevated assessment of ImPACT's reliability. They set out to assess ImPACT's reliability over a clinically relevant time interval (45 and 50 days) in healthy individuals using ImPACT. Their results displayed ImPACT to have extraordinarily low ICC values (range .23 to .39) and therefore opposed its use by clinicians. However, Broglio's study contained a total of four different CNT carried out after one another at each session. Therefore, some argue that these low ICC values of ImPACT were the direct result of completing multiple tests and thus, aspects such as fatigue were influencing the overall findings. Although, Resch et al. (2013) assessed the reliability of ImPACT over various time points, one of which being 45 days. Upon analysis of the reliability of ImPACT reported by Resch, the ICC values remained lower than previous findings previously reported (Range .37 to .66) and thus supported the findings of Broglio et al. (2007) that the reliability of ImPACT may not be sufficient for clinical use due to poor reliability. Equally, low reliability values have been reported by numerous other studies (Bruce et al. 2014; Cole et al. 2013; Tsushima et al. 2016; O'Brien et al. 2015 and Nelson et al. 2016), this has questioned the use of ImPACT as a potential concussion assessment tool (Table 3).

Study	Participants	Test-Retest Length	Visual Motor (Processing) Speed	Reaction Time	Verbal Memory	Visual Memory
Iverson et al. (2003)	Adolescents, Youth and amateur athletes High School	7 days	0.86	0.79	0.7	0.67
Elbin et al. (2011)	Athletes	1 year	0.85	0.76	0.61	0.7
Schatz et al. (2010)	College Athletes	2 year	0.74	0.67	0.45	0.65
Schatz et al. (2013)	University Students	1 month	0.88	0.77	0.79	0.6
Register-Mihalik et al. (2012)	College and High School Students	7 days	0.71	0.6	0.29	0.45
Nelson et al. (2016)	High School and College Athletes	7 days	0.75	0.67	0.53	0.5
		2 weeks	0.75	0.65	0.5	0.6
Nakayama et al. (2014)	College Students	Baseline to 45 Days	0.87	0.67	0.76	0.72
		Day 45 to Day 50	0.91	0.80	0.78	0.74
Broglia et al. (2007)	University Athletes	Baseline to 45 Days	0.38	0.39	0.23	0.32
		45 Days to 50 Days	0.61	0.51	0.4	0.39
Resch et al. (2013)	University Students	7 days	0.71	0.78	0.41	0.26
		14 days	0.84	0.88	0.59	0.85
	University Students	45 days	0.66	0.49	0.37	0.52
		50 days	0.76	0.71	0.45	0.55
Bruce et al. (2014)	Professional NHL Players	1 year	0.76	0.64	0.45	0.52
	Active Military					
Cole et al. (2013)	Volunteers	30 days	0.83	0.53	0.6	0.5
Tsushima et al. (2015)	High School Athletes	2 years	0.72	0.46	0.21	0.49
O'Brien et al. (2015)	Youth Athletes	2 weeks	0.74	0.48	0.6	0.48
	High School and					
Nelson et al. (2016)	College Athletes	1 month	0.66	0.6	0.54	0.54
		44 days	0.78	0.67	0.6	0.59
		198 days	0.75	0.6	0.51	0.49
<b>Range</b>			<b>.38 - .91</b>	<b>.39 - .88</b>	<b>.23 - .79</b>	<b>.26 - .85</b>

**Table 3:** Displays all of the values found within literature of studies stating the Intraclass correlation coefficient values for ImPACT. The top half of the table, in general, suggests ImPACT to contain strong reliability values whilst the bottom half of the table contradicts those findings. From the range row at the bottom of the table you see the difference in reported ICC values for each ImPACT composite domain.

Nevertheless, due to the high ICC values that have been reported in literature, the use of ImPACT has been assessed for its sensitivity in identifying a possible concussion. Iverson et al. (2003) identified that concussed individuals had a lower verbal and visual memory, slower processing speed and reaction time along with a higher quantity of symptoms reported. The results of which have been corroborated, in which studies have equally found that in the first few days post-concussion there is lower memory and more symptoms exhibited (Lovell et al.

2004) and also lower visual motor speed when compared to a control group (Gardner et al. 2012). Furthermore, when comparing symptomatic athletes to asymptomatic and to a control group, there was a clear trend reported, in which both symptomatic and asymptomatic performed significantly worse than the control group and that the symptomatic group performed even worse than the asymptomatic in all composites (Fazio et al. 2007). These studies clearly show that ImPACT is sensitive to concussion when there is a clear comparison to a control group and also in some aspects when compared to baseline scores.

A challenge that continually presents itself within literature, is that there is no consistency in terms of the population assessed and the test-retest interval between studies. This makes it difficult to directly compare aspects such as ICC values between studies as they have the potential to differ between findings due to a variety of external factors (age of participants, contact/non-contact sports, concussion history and short or long time intervals). Consequently, this could be the result of the variance that is found within literature in regards to the low/high ICC values reported on ImPACT. Nevertheless, due to ImPACT's potential susceptibility to external factors it forms a cautious outlook in terms of its use by clinicians to aid the diagnosis of a concussion.

Study	Participants	Test-Retest Length	False-Positive Rate
Resch et al. (2013)	University Students	7 Days	37%
		14 Days	46%
	Univeristy Students	45 Days	22.20%
		50 Days	28.90%
Iverson et al. (2003)	Adolescents and Young People	7 days	39.30%
		45 and 50 days	
Broglio et al. (2007)	Asymptomatic High School	7 days	38%
Van Kampen et al. (2007)	Athletes	7 days	30%
<b>Range</b>			<b>22.2-46%</b>

**Table 5:** Outlines the rate of false-positive values reported within literature on ImPACT.

When examining the validity, reliability and sensitivity rates of a possible concussion test, it is equally important to analyse the false-positive rates of the assessment. This provides a value in which the neurocognitive test will determine an individual to be concussed even when they are a healthy control. It has been found that ImPACT has a false-positive rate of 30% (Van Kampen et al. 2006), therefore studies that elicit a false-positive rate higher than 30% in at least one or more composites of ImPACT suggest that these healthy individuals assessed may be “truly” concussed. This would mean that multiple studies using ImPACT have reported the test to outline truly concussed individuals within their healthy control population, with some studies identifying a 46% false-positive rate (Resch et al. 2013) (Table 5). Moreover, due to the questionable reliability values found within literature on ImPACT and the high false-negative values presented, it could be argued that there could be an equally high false-negative rate (Randolph et al. 2011). This would suggest that ImPACT could possibly be classifying individuals as "non-concussed" or "recovered" even though they are still experiencing cognitive impairment. Possibly leading the clinician to approve the individual to return to play or continue within a match or practice and therefore dramatically increase the potential of further cognitive damage if they were to experience a second concussive injury.

Subsequently, due to the many conflicting studies within literature that report varying reliability values on ImPACT and also the high false-positive rates reported it questions ImPACT's effective use as a concussion assessment tool. In all, the three main computerized neurocognitive tests used within literature now (CogSport, HeadMinder CRI and ImPACT) have flaws that may not help aid the clinician in the process of diagnosing a concussion. Therefore, this creates a gap in which maybe a different neurocognitive test may be a more suitable assessment of concussion.

### **2.3. RESET**

RESET is a newly developed computerized neurocognitive assessment which has been designed to assess severe TBI. However, we propose that RESET could potentially be used in the assessment of more mTBI also such as concussion. Current literature on the use of RESET clinically is sparse, however internal studies have been conducted by the company, through the use of the army, in the ability of RESET to detect and help the recovery process after a TBI. RESET was applied within this current study due to various key qualities that we believed made it applicable to concussion detection. RESET is formed of a variety of conventional and computerised assessments, all of which have been examined for their sensitivity to TBI within other test batteries. In line with this, you are able to be selective in the tests you administer, it can be applied pitch-side due to its use on mobile devices such as tablets and most importantly it records a log of previous cognitive performance of each athlete and outlines in a clear and effective manner when an individual's cognitive performance has significantly differed, thus making it easier for clinicians pitch-side (in all levels of the sport) to determine when an athlete should be removed from play.

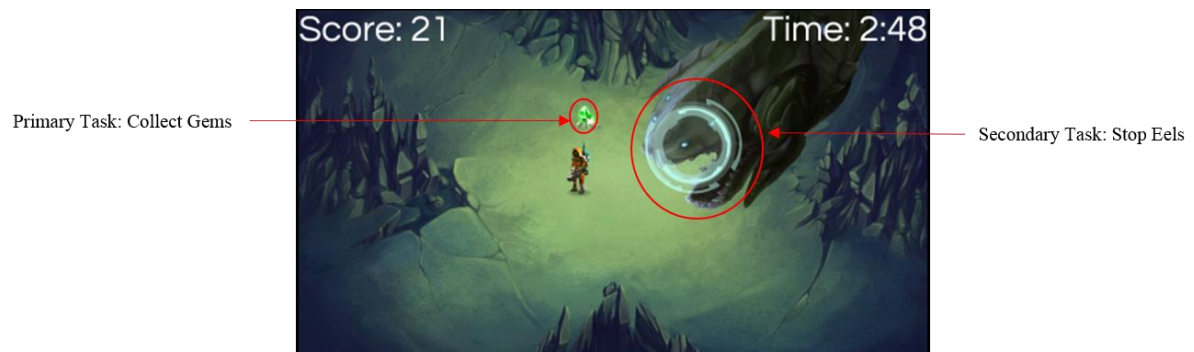
Like many of the previously discussed computerized neurocognitive assessments, RESET also incorporates previously established more conventional concussion assessments such as Card Sort and the Trials Making Test. In all, the RESET battery of assessments is composed of a hybrid of tests with a total of 15 assessments that are separated into five composite scores; Memory, Attention, Executive Function, Visual Perception and Self-report. All of which have been identified to be impaired within concussed individuals.

### 2.3.1 Attention

#### Divided Attention (Crystal Chompers)

This is a novel assessment used within RESET. The purpose of divided attention is to examine the performance of an individual in a primary task whilst simultaneously completing a secondary task. Further, in terms of concussion, divided attention has been stated to “give timely and relevant information to clinicians” (Register-Mihalik et al. 2013) and thus assist in the diagnostic procedure of a concussion.

Within RESET the divided attention task requires the participant to collect as many gems as possible (primary task) whilst dividing their attention to the secondary stimuli (*Figure 1*). If the participant’s attention from the primary task is broken as a direct result of the secondary task, then they will be penalised through a reduction in the total time available to attend to the primary task. Thus, limiting the total score that they are able to obtain.



**Figure 1:** Divided Attention assessment. The participant is required to collect as many gems as possible by clicking on them (primary task) whilst attending to a secondary stimulus (clicking on eels). This is a timed task in which the participants have a total of three minutes to collect as many gems as possible whilst still attending to the secondary task. The individuals performance increases based on the quantity of gems collected, thus how well they attain to concurrent tasks.

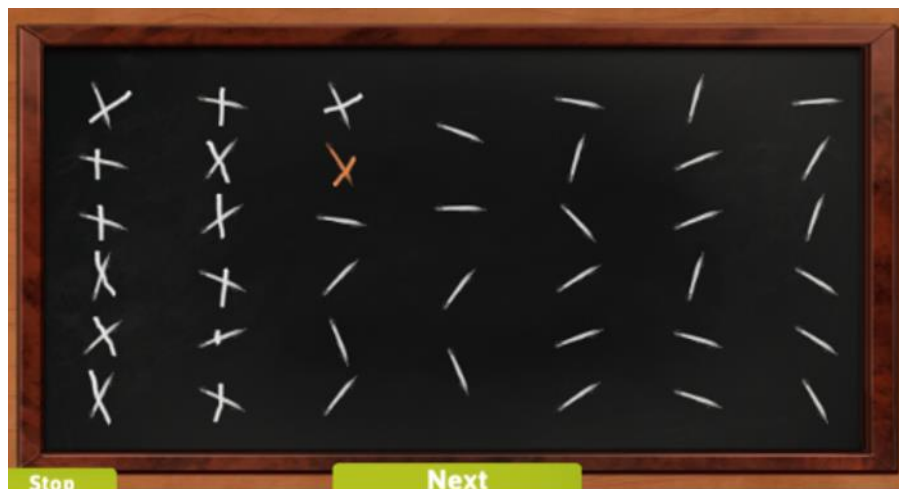
Although, the divided attention task used with RESET can be dependent on external factors such as the speed of mouse control, the sensitivity of the mouse and also the individual’s accuracy. All of which could potentially influence the cognitive performance score of the individual, regardless of them being able to attend to both stimuli. Therefore, in order to limit

the influence of these variables, participants could be refined to completing the assessment on the same computer. This would limit the influence of these external factors as much as possible and therefore cognitive performance between each session will be examined under the same circumstances and thus these external factors should not play any significant role in altering the performance score of the participant.

The Divided Attention task was administered within RESET as individuals who have sustained TBI have been found to perform significantly worse when completing concurrent assessments compared to completing these assessments separately (Park et al., 1999) and more specifically that divided attention itself is negatively affected within concussed individuals (Stuss et al., 1989). Therefore, due to divided attention being able to provide important information to clinicians and also being sensitive to concussion, it was incorporated within the RESET assessments.

#### Line Crossing (hemispatial awareness)

Line Crossing is an assessment composed of seven rows of single lines drawn at varying angles. The participant must create a cross by drawing a line through these single lines provided (*Figure 2*). The assessment finishes when the participant selects “next”. This assessment compares 3 columns from the left and right of the screen, whilst the central column of lines are not scored. If the line drawn intersects the opposing line then it remains visible, whereas if it does not intersect the line it is hidden.



**Figure 2:** Line Crossing. The participant is required to create a cross through each line as quickly as they can before progressing. Within the above screenshot the participant has crossed 12 of the lines so far. The red cross is the line that is currently being drawn by the participant.

Line crossing is an assessment which is more commonly used within more severe TBI's and is considered a test for hemispatial awareness. However, it was included within this study as it could still potentially provide further information to the clinician about the cognitive capacity of the athlete and thus form a more robust diagnosis. Although this test may not play an important role within the assessment of more mTBI's, it was included in order to understand the reliability of the RESET battery as a whole.

### 2.3.2 Memory

#### Gem Guardians (Associative Memory)

This is a computerized version of the standardized associative memory paradigm and contains three separate evaluations of memory; learning, immediate and delayed memory recall. It requires the participant to learn symbol pairs and recall these same pairs later (*Figure 3*). In the tutorial the participant learns to select the correct symbol pairing, in which 9 pairings are presented to them. During the learning phase, the participant continues pairing stimulus symbols with response symbols, through referring to the reference key provided. Whilst

during the immediate and delayed recall phases the reference key is not available to the participant, therefore the participant must select the correct response symbol to make a pairing through their memory only. The delayed recall phase is similar to the immediate recall phase where the pairing is needed to be made from memory only, however this occurs ten minutes or more after completion of the immediate recall phase. The participant is provided with visual feedback on their responses, either a green image reveals the response to be correct and a red to be the wrong response. If the player is unable to make a pairing within a given timeframe then the stimulus disappears, however this does not reduce their score it instead limits their total score due to each pairing being shown a set number of times.



**Figure 3:** Associative memory task. During the Learning Phase the participants are required to refer to the reference key in order to match the stimulus symbol to the respective response symbol, these are displayed below one another within the reference key. Although, during the immediate and delayed recall assessments, the reference key is not available. Therefore, participants must match these same pairings of symbols through their memory only.

The Associative memory assessment contains similar properties to the symbol match assessment used within the visual memory composite of ImPACT which has been found to be sensitive to concussed athletes (Iverson et al., 2003; Fazio et al., 2007; Majerske et al., 2008; Talavage et al., 2014). Therefore, through integrating a similar test within this test battery it will make the test as a whole stronger. Equally, similar immediate memory tests are being

conducted pitch-side through the SCAT-3. Thus, incorporating a memory composite within the RESET battery of tests is essential.

### **2.3.3. Self-Report**

#### **Patient Reported Outcomes (PRO):**

This assessment provides an opportunity for the participant to reveal how they are feeling through a range of 14 questions in which the participant selects the corresponding box to how they feel. The participants rate their perceived feelings on a scale of 1-7 on how well they believe they relate to that question or how well they can carry out the task that the question includes (with 7 being the highest; they fully relate to the statement or can carry out the task). There are a wide variety of questions that the participant completes which provide information to the clinician on the participant's physical and mental health alongside their cognitive performance levels during that session. This is achieved through a range of questions which are used to determine the individual's ability to complete everyday tasks, their cognitive capacity, concentration levels, along with questions situated around signs and symptoms such as headaches in addition to questions determining quantity of sleep an individual is obtaining. As RESET has been developed for more severe TBI, some of these questions may not be as relevant to concussed individuals such as their capability in completing everyday (i.e. climbing stairs). Nevertheless, the use of the PRO will provide the clinician with information on the athlete's symptoms that otherwise may not have been observed. A Similar method has been used within ImPACT through the use of a Post-Concussion Symptom Scale (PCSS) (Lovell et al., 2006). It is a form of documenting post-concussion symptoms experienced by the athlete. Similarly, the PRO also examines the individual's subjective assessment of their feelings, how they are functioning and their own

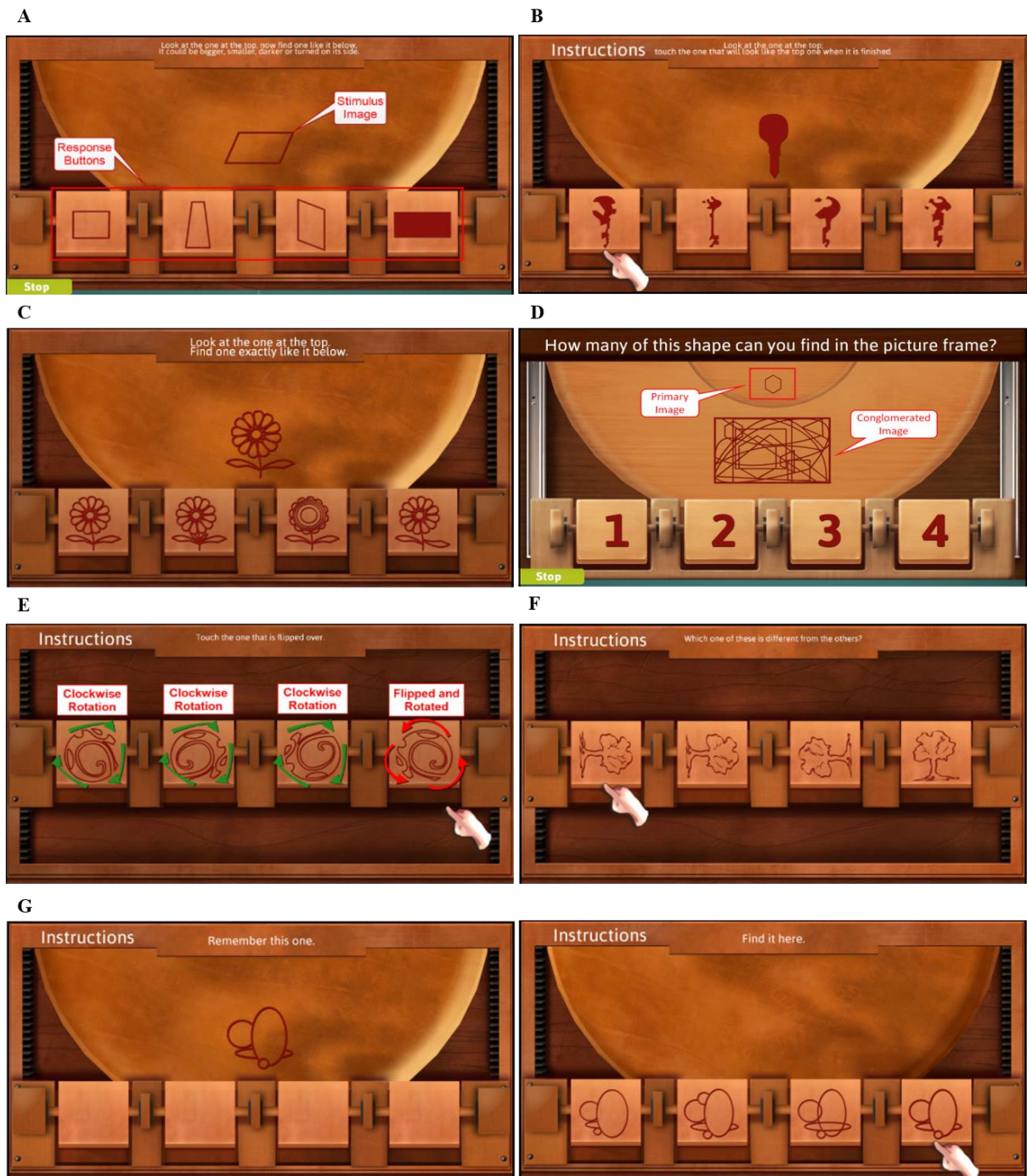
perception of a range of questions covering physical, mental and social health along with addressing the athlete's cognitive performance. Due to it being an opportunity to understand the mental state of the athlete it was also incorporated into this battery of tests.

#### **2.3.4. Visual Processing**

There are a total of seven different visual processing tasks used to form the visual processing composite within RESET; figure ground, form constancy, spatial orientation, visual discrimination, spatial orientation/visual discrimination, visual closure and visual short term memory.

The figure ground assessment requires the participant to select the number of times that a primary image appears within a conglomerated image. Whilst within the form constancy assessment the participant is required to select the response button that contains the primary stimulus image located in the centre of the screen. This primary image can be smaller, bigger, darker or flipped within the response images, however it must be the same shape. Further, the Spatial Orientation task requires the participant to select the response button that is in an opposing orientation to the other images in the corresponding response buttons (i.e. the image is flipped). In addition, within the Visual Discrimination assessment the participant views a primary stimulus image in the centre of the screen, they are required to then select the identical image from the four given response buttons. Further to this is the Spatial Orientation/Visual Discrimination task, this requires the participant to select one of the response options that is different from the other three possible responses. This test combines both spatial orientation and visual discrimination, the participant must identify the image that is in a different orientation or look for differences within the shape itself, although the participant is not told which criteria to use. In addition, the Visual closure task provides the participant with a primary stimulus image, they then are required to select an incomplete

response image that, when completed resembles the exact image of the primary stimulus. The final assessment within the Visual Processing composite is the Visual Short Term Memory assessment. Here, the participant is shown a stimulus image for five seconds before then being shown four different responses. The participant is required to select the exact same response image that resembled the primary image that was previously shown (*Figure 4*).



**Figure 4:** All assessments of the visual perception composite. **A)** Form Constancy: the participant is required to select the same stimulus image that is in the response buttons. **B)** Visual Closure: the participant must select the correct response button, that when complete, is the same as the stimulus image. **C)** Visual Discrimination: the participant is required to select the exact same image in the response buttons as the stimulus image. **D)** Figure Ground: the participant is required to select the quantity of times a primary image appears within a conglomerated image. **E)** Spatial Orientation: the participant is required to select the image that is in the opposing direction to the other images. **F)** Spatial Orientation/Visual Discrimination: the participant must select the image that is different to the other options, be that in orientation or due to differences within the shape itself. **G)** Visual Short Term Memory: the participant is displayed an image for five seconds before it disappears and they are required to select the image that is exactly the same as the previous image. Performance on these tasks were determined through the percentage correct.

Visual processing tasks have been used within other computerized neurocognitive tests such as ImPACT where they have been found to be significantly affected by concussion (Iverson et al., 2003). Further, both Form Constancy and Figure Ground are perception tasks and there has been evidence that when completing perception tasks, concussed individuals are significantly impaired (Preece et al., 2010). In addition, the Visual Short Term Memory task was applied due to immediate recall assessments being found to be directly affected by concussion (Guskiewicz et al., 2001) and that visual memory itself is found to be significantly impaired in concussed individuals (Schatz et al., 2006). Subsequently, due to literature providing evidence that visual processing is directly affected by concussion, and due to the efficiency in completing the tests, these assessments were used.

### **2.3.5 Executive Functioning**

Within the executive functioning composite, there are three subset domains; processing speed, fluid reasoning and cognitive flexibility.

#### **Processing Speed**

##### **2 Choice (Response Time):**

Reaction Time is an additional assessment administered within the RESET neurocognitive battery. The task provides a stimulus image that is either an X or an O in the centre of the screen, in which the participant has two response buttons to this image (X and O). The participant must press the same response button as the primary image shown as quickly as possible once the image appears (*Figure 5*). There is a total of 40 stimuli in which appear at random intervals between 750 and 1350ms.



**Figure 5:** Two Choice Reaction Time. The participant must hold the central button, the stimulus image will then appear as either an X or O after a 750ms to 1350ms interval, after which the participant must react and press the respective response button as quickly as possible.

Reaction time has previously been identified by multiple studies to be negatively impaired in concussed individuals (Stuss et al., 1989; Makdissi et al., 2001; Sosnoff et al., 2008; Eckner et al., 2011). Therefore, its use within this new battery of assessments used to assess concussion is inevitable as a result of its high sensitivity and fast and accurate administration.

#### Gem Grab (Go/No-Go):

This is a gamified version of the stop-signal paradigm neuropsychological assessment (Logan 1994; Verbruggen & Logan 2008). The go signal is a gem in which when appears the participant is required to collect it as soon as possible, whilst the no-go signal is a different object in which the participant must ignore (*Figure 6*). This is a response inhibition task which the participant must collect as many of the “Go” signals whilst ignore the “No/Go”. The participant completes the assessment through making binary decisions on each stimulus presented, to either collect the gem or not. The tutorial provides the participant with basic instructions on when and where to tap. Whilst the test requires the participant to make the correct decision of tapping (or not) on their own with no feedback. The difficulty is determined by the amount of time that the stimulus is on the screen, resulting in the participant needing to make a faster binary decision. The participant gains a higher score through faster responses to the gems presented, if the participant fails to respond then they do

not gain any points, this also happens if they respond to the no-go stimulus. Conversely, if they do not click on the no-go stimulus then they gain points. The higher the points obtained, then the higher the cognitive performance.



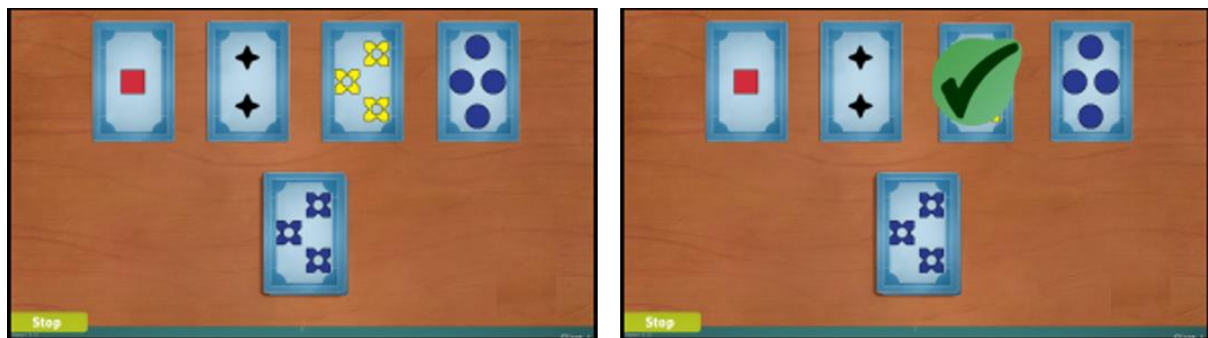
**Figure 6:** Go/No-Go task. This is a test of response inhibition. Here the participant is required to collect (click) on the floating gem as quick as possible for the Go task. Whilst they are required to ignore the idle fish within the No-Go task. The participant is given a specific amount of time to complete this task with the responses to each Go/No-Go task requiring faster responses. Enhanced performance on this task is characterized through faster responses to the stimuli.

The main outcome of the Go/No-Go task is to examine executive functioning through assessing response inhibition. Studies have used an adaptation of the stoop colour word task used to assess response inhibition, and found that those who had experienced a concussion within the previous six months performed significantly worse in terms of response inhibition and the accuracy during this test compared to a non-concussed group. Further, these concussed athletes had a 1.5 times slower response inhibition (Ellemberg et al., 2007). Similarly, within jockeys who had experienced multiple concussions, it was found that they too performed significantly worse on the Stroop Colour Word Task, suggesting that athletes with multiple concussions perform significantly worse on response initiation/inhibition tasks. (Wall et al., 2006). Thus, the use of the Go/No-Go task within RESET was to assess response inhibition which had previously been found to be effected in individuals with concussion.

## Fluid Reasoning

### Card Sort:

Card sort is a conventional neurocognitive assessment in which the objective is to sort cards into four piles based on three rules; colour, shape or number. The participant must sort the cards into one of the four piles without being told the rules, however the participants are informed about their correct/incorrect sort through visual feedback (*Figure 7*). As the participant progresses through this assessment the rules of the card sort alter between colour, shape and quantity. The rule will change without the participant knowing and will therefore examine their set-shifting ability to attain to the next rule. The rule will change if the participant completes 10 correct responses in a row. The rules and the cards are randomised.



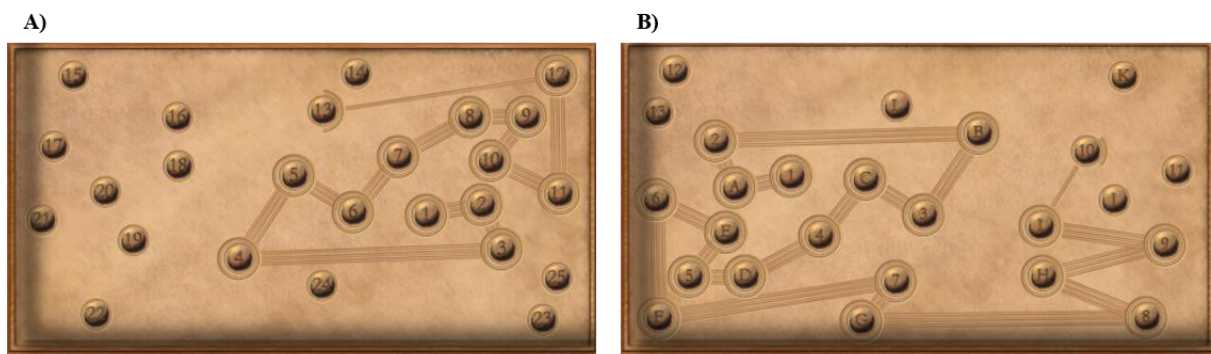
**Figure 7:** Card Sort. Here the participant is provided with a card in which they are required to sort into one of the four piles above based on three rules (colour, shape or number), they are then provided with visual feedback on whether they correctly or incorrectly categorised the card. The rule of the Card Sort test will stay the same for a set period of time before randomly altering to a different rule, the participant must then figure out the new rule and adhere to this before the rule changes again.

The Card Sort assessment used within RESET is an adaptation of the Wisconsin Card Sort Test (WCST). Literature shows that individuals that obtain a single concussion or multiple subconcussive impacts have significantly poorer performance scores on the WCST (Matser et al., 1999 & Downs et al., 2002). Therefore, as this more conventional concussion assessment is sensitive to concussion it was subsequently used within this shortened protocol.

## Cognitive Flexibility

### Trails Making Test:

The TMT contains two parts (A and B), in Part A the participant is asked to connect numbered circles sequentially. Whilst in part B they are asked to connect the scattered circles alternating between number and letters in an orderly manner. For both Part A and Part B of the TMT participants were asked to complete each section as quickly as possible (*Figure 8*).



**Figure 8:** Trails Making Test. A) In TMT-A the participant is required to connect the numbers sequentially as fast as possible. B) TMT-B the participant must alternative connect the both numbers and letters in a sequential order. Performance is judged through the time taken to complete each part of the test.

The TMT Part B has previously been found to be significantly inhibited (slower) in both severe and mild TBI patients (Stuss et al., 1989). Further, TMT-B has also been found to be associated with cognitive impairment in concussed individuals when compared to a control group (Guskiewicz et al., 2001). Therefore, as TMT is sensitive to concussion it was subsequently used within this shortened protocol.

### **2.5. Aim 1:**

Within the following study we will set out to determine the reliability of RESET over a clinically relevant test-retest interval of 45 days and 50 days (Broglia et al., 2007).

### **2.5. Hypothesis 1:**

As RESET was developed to assess other neurological disorders and also incorporates more conventional assessments, we hypothesise that RESET will have a high reliability which will be identified through ICC rates of above .80. Therefore, the general variance in performance scores between tests in healthy individuals will be low and not contain large variability.

## **2.6. Method**

### **2.6.1. Participants**

A total of 44 Participants, aged 18-24 years old, completed three sessions of RESET at baseline, 45 days and 50 days later. Prior to arrival participants were screened and excluded from the study based on the following criteria; if they had experienced a diagnosed concussion within the last 12 months, if they suffered from any learning difficulties, attention deficit disorders, cognitive deficiencies or had any visual impairments (such as having a colour vision deficiency). Finally, they were only recruited if their first language was English.

### **2.6.2. Neurocognitive Computerized Test (RESET)**

To measure each participant's neurocognitive performance, RESET version 2.2.9.0. (Blue Marble Game Co. Los Angeles, California, America) software was applied in this study. All 15 assessments of the RESET battery (Section 2.3) were used within this study. Prior to each cognitive assessment there was a tutorial which outlined the aim of the assessment and also how to complete the assessment. In addition, the experimenter also provided further

explanations of the task to ensure that the participant fully understood the task, and to reduce participant error at baseline.

### 2.6.3. Procedure

Prior to participation, all volunteers completed both a screening form and a consent form to take part in the study, used as the basis of our exclusion/inclusion criteria. In addition, all participant's height and weight measurements were taken. Following this any questions about the study were answered and the participants completed the RESET assessment.

The RESET test battery was completed on three separate occasions. Participants completed a baseline session, which was then followed by a further session approximately 45 days later (45.16 days  $\pm$  1.9) and the third session approximately 50 days (50.59 days  $\pm$  1.6) after the baseline assessment. Thus, enabling us to determine whether RESET is reliable over a clinically relevant time (Broglia et al., 2007). We effectively assessed two different time-intervals, a 45 day interval (baseline to day 45) and a 5 day interval (day 45 to day 50).

### 2.6.4. Data Analysis

All performance scores of the assessments were standardized within each composite to form a value that could be used to assess any significant change across the test-retest interval and to determine the reliability across this interval through ICC values (Section 2.2.).

In order to assess for the reliability of RESET, composite scores were formed. This created one value for each cognitive domain of RESET and provided a more stable and accurate measure of cognitive performance within that domain due to multiple assessments forming that one value, rather than multiple single assessments providing numerous values for the same cognitive area. Further, this would allow for a more practical comparison of an individual's cognitive performance between assessments, therefore allowing for any cognitive

deficiencies to be more identifiable. These composite scores were formed through unit-weighted z scores, allowing for more stable measures to be assessed (Ackerman & Cianciolo, 2000). This standardised all components of the respective sub-tests for that composite, this allowed the formation of one respective value that could be assessed between sessions. Z scores were created through taking each individual score on the assessment and subtracting this from the average of the assessment and then dividing this value by the standard deviation ( $z \text{ score} = (\text{score} - \text{mean}) / \text{standard deviation}$ ). Once this had been established the z scores for each composite were added together (or subtracted if a lower value represented a higher score, i.e. reaction time) and then divided by the quantity of assessments within the composite. This essentially created a sole value in which could be analysed between sessions to outline any improvement in scores. These composites were formed for each session.

The self-report composite was formed of the PRO assessment. Within this assessment there were six variables that were analysed to provide a reliability value between each session. The variables analysed were; global health score, global physical health raw score and t-score, global mental health raw score and t-score and their self-reported cognitive performance.

A total of two assessments were used to form a composite value for attention, these were the divided attention task (which was analysed for the overall score/total gems collected) and the line crossing/spatial awareness assessment (total time to complete the task was calculated).

In order to analyse the memory composite, the associative memory task was administered. Z scores for the learning, immediate and delayed recall assessments were created for performance on the percentage correct for each individual assessment.

A further composite was the visual processing battery which included seven assessments; figure ground, visual discrimination, visual short term memory, visual closure, spatial

orientation, spatial orientation visual discrimination and form constancy. All of these tests were analysed for percentage correct, a composite value for each respective session was then created.

The final composite formed was executive functioning, which included three sub domains of processing speed, fluid reasoning and cognitive flexibility. Processing speed included the two choice reaction time test in which the average correct reaction time was used as a score (Iverson et al., 2003). The second component of processing speed was the Go/No-Go assessment in which the correct responses, errors of omission and commission along with response speed were calculated. For fluid reasoning, card sort was the sole assessment used. However, this included a total of eight variables; percentage correct, percentage of errors, preservative errors, conceptual responses, categories completed, the number of trials taken to complete the first category and finally the number of times the participant failed to maintain a set (Heaton et al, 1993 & Coelho et al., 2012). The final component of the executive functioning battery was cognitive flexibility, which was composed of the TMT of which the difference in time taken to complete Part-B compared to Part-A (B-A Difference) was examined (Arbuthnott & Frank, 2000; Salthouse et al., 2003).

After the formation of these composites, a reliability analysis was conducted to determine ICC values between baseline and day 45 and then between day 45 and day 50. This is a useful measure of the reliability of quantitative data and is therefore a good assessment of test-retest reliability and has subsequently been used in various other neurocognitive studies. The ICC value produced is between 0 and 1. The closer the value is to 1 represents that there is little variance in performance between these two time intervals and thus has high reliability (Anastasi, 1998). Within this study a two-way mixed ICC model was created. This was due to

each time period between the sessions being fixed although the participants being random, therefore making it a two-way mixed ICC.

#### 2.6.5 Statistical Analysis

In order to analyse the difference in composite scores within RESET between baseline and day 45 and between day 45 and day 50, a One-way repeated measures ANOVA was conducted. A statistical significant difference was accepted at the  $\alpha = 0.05$  level. If Sphericity was violated then the Greenhouse-Geisser correction was used.

### 2.7. Results

44 participants (22 Males and 22 Females) completed all three sessions of the study (age: 19.4 years old ( $\pm 1.2$  years), height: 173cm ( $\pm 9.6$ cm) and weight: 69.98kg ( $\pm 9.8$ kg). The time interval between baseline and Day 45 ranged from 41-48 days (mean 45.16 days  $\pm 1.9$ ), further between baseline and day 50 there was a range of 49 to 54 days (mean 50.59 days  $\pm 1.6$ ). All participants completed the three test-retest sessions.

#### 2.7.1. Baseline and Day 45

Between baseline and day 45 there was a non-significant difference for the memory composite ( $F_{1,36} = 0.137$ ,  $p = 0.714$ ), the attention composite ( $F_{1,29} = 0.043$ ,  $p = 0.837$ ), the executive function composite ( $F_{1,41} = 0.751$ ,  $p = 0.391$ ), the visual perception composite battery ( $F_{1,39} = 0.010$ ,  $p = 0.922$ ) and finally the self-report composite ( $F_{1,42} = 0.020$ ,  $p = 0.888$ ) scores. Therefore, between baseline and day 45 there was no-significant differences throughout all five composite domains.

### 2.7.2. Day 45 to day 50

In addition, the composite values for memory, attention, executive function, self-report and the visual perception battery were assessed for any significant alterations in performance scores over a five day period. Results identified that the memory ( $F_{1,36} = 0.017$ ,  $p = 0.898$ ), attention ( $F_{1,29} = 0.001$ ,  $p = 0.979$ ), executive functioning ( $F_{1,40} = 0.036$ ,  $p = 0.850$ ) and the self-report composite ( $F_{1,43} = 0.899$ ,  $p = 0.348$ ) revealed non-significant changes over this test-retest interval. However, there was a significant difference in the visual perception battery between day 45 and day 50 ( $F_{1,38} = 49.886$ ,  $p < 0.001$ ) in which all of the assessments of the visual perception test battery improved between each session.

### 2.7.3. ICC

Upon analysis of reliability, ICC values ranged between .64-.78 for baseline to day 45 and a range of .47-.89 between day 45 and day 50 revealing moderate to good reliability values (Anastasi, 1998; Portney & Watkins, 1993). The memory composite revealed ICC values of 0.678 and 0.472 between baseline and day 45 and also between day 45 and day 50 respectively. Whilst attention had ICC values of 0.779 between baseline and day 45 and then 0.752 between day 45 and day 50. Furthermore, executive functioning provided ICC values of 0.658 between baseline and day 45 and 0.714 between day 45 and day 50. In addition, the visual perception battery had moderate reliability with 0.640 between baseline and day 45 and then 0.495 between day 45 and day 50. Finally, ICC values for the self-report composite were found to be 0.672 and 0.885 between baseline and day 45 and then between day 45 and day 50 respectively.

### Divided Attention

Divided Attention	Baseline Mean (SD)	Day 45 Mean (SD)	Day 50 Mean (SD)	Effect Size Partial Eta Squared ( $\eta^2$ )
Total Score	145.13 ( $\pm$ 15.18)	149.09 ( $\pm$ 17.54)	159.74 ( $\pm$ 16.9)	0.579

**Table 5:** Displays the Means ( $\pm$  SD) and also the Effect Size for Divided Attention

### Line Crossing

	Baseline Mean (SD)	Day 45 Mean (SD)	Day 50 Mean (SD)	Effect Size Partial Eta Squared ( $\eta^2$ )
Time to Completion	31.33 ( $\pm$ 5.89)	28.06 ( $\pm$ 4.3)	24.95 ( $\pm$ 5.61)	0.356

**Table 6:** Displays the Means ( $\pm$  SD) and also the Effect Size for Line Crossing

### Associative Memory

	Baseline Mean (SD)	Day 45 Mean (SD)	Day 50 Mean (SD)	Effect Size Partial Eta Squared ( $\eta^2$ )
Learning (% Correct)	97.13 ( $\pm$ 2.69)	96.6 ( $\pm$ 3.77)	97.29 ( $\pm$ 3.39)	0.014
Immediate (% Correct)	62.45 ( $\pm$ 30.38)	80.13 ( $\pm$ 23.81)	90.34 ( $\pm$ 17.83)	0.346
Delayed (% Correct)	66.48 ( $\pm$ 29.31)	83.36 ( $\pm$ 24.87)	92.67 ( $\pm$ 14.73)	0.324

**Table 7:** Displays the Means ( $\pm$  SD) and also the Effect Size for Associative Memory

### Visual Perception Battery

	Baseline Mean (SD)	Day 45 Mean (SD)	Day 50 Mean (SD)	Effect Size Partial Eta Squared ( $\eta^2$ )
Figure Ground (% Correct)	68.5 ( $\pm$ 16.17)	74.35 ( $\pm$ 16.75)	81.49 ( $\pm$ 15.58)	0.261
Form Constancy (% Correct)	78.73 ( $\pm$ 16.6)	86.37 ( $\pm$ 15.25)	90.69 ( $\pm$ 11.61)	0.242
Spatial Orientation (% Correct)	68.02 ( $\pm$ 30.06)	76.87 ( $\pm$ 22.29)	80.27 ( $\pm$ 23.38)	0.141
Spatial Orientation Visual Discrimination (% Correct)	74.56 ( $\pm$ 19.3)	78.39 ( $\pm$ 18.38)	75.26 ( $\pm$ 23.9)	0.015
Visual Discrimination	80.51 ( $\pm$ 23.27)	85.06 ( $\pm$ 15.99)	87.01 ( $\pm$ 16.53)	0.042
Visual Closure	88.63 ( $\pm$ 17.85)	90.9 ( $\pm$ 11.56)	92.2 ( $\pm$ 14.27)	0.02
Visual Short Term Memory (% Correct)	82.05 ( $\pm$ 12.11)	82.05 ( $\pm$ 14.65)	86.37 ( $\pm$ 12.83)	0.041

**Table 8:** Displays the Means ( $\pm$  SD) and also the Effect Size for the Visual Perception Battery

#### Reaction Time

	Baseline Mean (SD)	Day 45 Mean (SD)	Day 50 Mean (SD)	Effect Size Partial Eta Squared ( $\eta^2$ )
Average Correct Response Time	0.66 (0.05)	0.67 (0.04)	0.65 (0.03)	0.073

**Table 9:** Displays the Means ( $\pm$  SD) and also the Effect Size for Two Choice Response Time test

#### Go/No-Go

	Baseline Mean (SD)	Day 45 Mean (SD)	Day 50 Mean (SD)	Effect Size Partial Eta Squared ( $\eta^2$ )
Correct Responses	97.43 ( $\pm$ 2.64)	97.06 ( $\pm$ 3.26)	96.56 ( $\pm$ 4.17)	0.038
Errors of Commission (%)	6.36 ( $\pm$ 8.61)	8.81 ( $\pm$ 10.79)	11 ( $\pm$ 13.37)	0.101
Errors of Omission (%)	1.5 ( $\pm$ 2.07)	1.25 ( $\pm$ 1.67)	1.38 ( $\pm$ 2.37)	0.006
Correct Response Speed	0.47 ( $\pm$ 0.07)	0.46 ( $\pm$ 0.08)	0.45 ( $\pm$ 0.07)	0.034

**Table 10:** Displays the Means ( $\pm$  SD) and also the Effect Size for the Go/No-Go assessment

#### Card Sort

	Baseline Mean ( $\pm$ SD)	Day 45 Mean ( $\pm$ SD)	Day 50 Mean ( $\pm$ SD)	Effect Size Partial Eta Squared ( $\eta^2$ )
Percentage Correct	83.85 ( $\pm$ 4.89)	83.26 ( $\pm$ 9.09)	86.07 ( $\pm$ 3.29)	0.065
Percentage of Errors	16.15 ( $\pm$ 4.89)	16.73 ( $\pm$ 9.09)	13.9 ( $\pm$ 3.25)	0.066
Categories Completed	5 ( $\pm$ 0)	4.86 ( $\pm$ 0.77)	5 ( $\pm$ 0)	0.032
Conceptual Responses	53.83 ( $\pm$ 5.87)	53.37 ( $\pm$ 10.24)	53.2 ( $\pm$ 5.87)	0.002
Failure to maintain set	1.04 ( $\pm$ 1.11)	1.18 ( $\pm$ 1.31)	0.93 ( $\pm$ 1.18)	0.014
Number of trials to complete first category	15.3 ( $\pm$ 6.75)	17.6 ( $\pm$ 9.82)	13.13 ( $\pm$ 4.04)	0.098
Total number of trials	89.41 ( $\pm$ 16.03)	89.2 ( $\pm$ 17.44)	83.55 ( $\pm$ 13.86)	0.053
Preservative errors	6.9 ( $\pm$ 3.69)	7.98 ( $\pm$ 6.65)	5.91 ( $\pm$ 2.51)	0.053

**Table 11:** Displays the Means ( $\pm$  SD) and also the Effect Size for Card Sort assessment

#### Trails Making Test

	Baseline Mean (SD)	Day 45 Mean (SD)	Day 50 Mean (SD)	Effect Size Partial Eta Squared ( $\eta^2$ )
Part B-A Difference	11.36 ( $\pm$ 7.33)	8.37 ( $\pm$ 7.27)	6.72 ( $\pm$ 4.91)	0.208

**Table 12:** Displays the Means ( $\pm$  SD) and also the Effect Size for the Trails Making Test

PRO

	Baseline	Day 45	Day 50	Effect Size
	Mean (SD)	Mean (SD)	Mean (SD)	Partial Eta Squared ( $\eta^2$ )
Global Health Score	39.51 ( $\pm$ 3.31)	39.85 ( $\pm$ 3.51)	40.34 ( $\pm$ 3.54)	0.044
Global Physical Health				
Raw	16.16 ( $\pm$ 1.32)	16.16 ( $\pm$ 1.44)	16.46 ( $\pm$ 1.54)	0.033
Global Physical Health				
T-score	51.53 ( $\pm$ 4.33)	51.6 ( $\pm$ 4.8)	62.73 ( $\pm$ 5.38)	0.028
Global Mental Health				
Raw	15.46 ( $\pm$ 1.93)	15.62 ( $\pm$ 1.89)	15.79 ( $\pm$ 1.87)	0.021
Global Mental Health				
T-score	52.12 ( $\pm$ 4.95)	52.60 ( $\pm$ 5.09)	52.34 ( $\pm$ 7.78)	0.003
Cognitive Performance	15.27 ( $\pm$ 2.4)	15.44 ( $\pm$ 2.08)	16.04 ( $\pm$ 2.34)	0.08

**Table 13:** Displays the Means ( $\pm$  SD) and also the Effect Size for the Patient Reported Outcome

### **Chapter 3 – Exercise Induced Fatigue**

When a clinician is assessing for a concussion pitch-side, they generally adopt a multi-faceted approach to form a more accurate diagnosis. One such assessment that is used is the SCAT-3. However, as previously mentioned (Section 1.6.), the use of the neurocognitive assessment within SCAT-3 (the SAC) are open to subjective interpretation as to whether an individual has sustained a concussive impact. The use of such conventional paper-and-pencil assessments can effectively increase variability between clinician's scores and increase the subjectivity of diagnosis. Thus, the use of a computerized neurocognitive assessment can reduce this variability and therefore create a more objective assessment which will subsequently result in a more consistent diagnosis of a concussion.

However, regardless of the positives in implementing a computerized neurocognitive assessment, the current available computerized assessments lack numerous key characteristics that would allow them to be effective protocols used pitch-side. One major current draw-back is the amount of time that it takes to complete the battery of assessments. The most common computerized assessment used to examine for concussion is ImPACT, however this takes approximately 25 minutes to complete. The time provided within rules and regulations for many sports to assess for a concussion is around 10 minutes, this is most evident in Rugby with their HIA period. Therefore, the implementation of ImPACT within this period is inapplicable. Not only does the administration of such a test need to be completed within a ten minute interval, but during these ten minutes further tests such as balance and physical examinations must also be completed in order to form a multi-faceted and thus a more accurate approach to diagnosing a concussion.

Nevertheless, ImPACT is currently the only computerized assessment to be examined under the constraints of fatigue, and therefore in a “pitch-side” environment. However, due to completing only a single exercise session along with a lack of randomization of the ImPACT assessments and also the length of ImPACT, fatigue is likely to be non-existent by the conclusion of the ImPACT assessment. Therefore the findings of Covassin et al. (2007) could be disputed in terms of ImPACT’s reliability under fatiguing circumstances.

In essence, the lack of studies within this domain coinciding with the need for such pitch-side tests to become more objective there is a gap to assess a new computerized neurocognitive assessment that could be administered within the time interval provided. Further, a study that would take into account multiple sessions and randomization of the assessments used would only enhance the findings of the study through controlling for confounding variables by using multiple sessions and by randomizing assessments it will indisputably determine the reliability of all assessments under fatiguing circumstances.

### **3.1. RESET**

In order for a computerized neurocognitive test to firstly be administered pitch-side it must firstly adhere to a number of factors. Firstly, there is often a set limit in terms of how long an individual is allowed to be assessed for a head injury. For example within Rugby, a ten minute HIA is applied. Thus, for the purpose of this study, the RESET assessment battery was reduced so that the time to complete all tests would be achievable within the timeframe provided. Further, as a concussion is a complex injury, a wide range of neurocognitive assessments should be administered so that a more comprehensive neurocognitive assessment of the athlete can be achieved. Lastly, the computerized assessment must be both portable and reliable when used pitch-side. As RESET can be used on portable devices such as tablets,

along with being able to select specific tests and be administered within a restricted period of time it was incorporated in this study.

Subsequently, to create a computerized pitch-side concussion assessment, a shortened battery of RESET tests were formed. This enabled all assessments to be completed within a constricted period of time. In addition to this, all assessments incorporated within this shortened battery of tests varied in the cognitive domains that they are designed to assess and also were fast, simple and were previously found to be sensitive to concussion. In all, a total of six tests were administered within this protocol; Figure Ground, Form Constancy, Visual Short Term Memory, Reaction Time, Card Sort and the TMT.

#### Figure Ground:

Figure Ground is an assessment of visual processing, this test was used within this new proposed pitch-side battery due to the need for visual based tests being incorporated into pitch-side concussion assessments (McCrory et al., 2013). Further, visual perception tests such as this have been found to be sensitive to concussion (Preece et al., 2010). Thus, due to the requirement from the concussion consensus for vision tests to be incorporated “pitch-side” corresponding with Figure Grounds sensitivity to concussion, it was incorporated.

#### Form Constancy:

Like figure ground, form constancy was equally applied to this shortened battery of tests to be used pitch-side. Aforementioned, vision tests have been proposed to be a useful addition to a pitch-side concussion test however may be impractical using the current methods (McCrory et al., 2013). However, through the use of a computerized neurocognitive test pitch-side these

tests will now be able to be administered “pitch-side” and therefore provide key information about the athletes cognitive performance that otherwise would have been unexploited.

#### Visual Short Term Memory:

Visual Short Term Memory was included within the RESET assessment battery as it is a common examination within SCAT-3, which uses an immediate memory assessment (Concussion in Sport Group, 2013). In addition, post-exercise results have demonstrated that there is no visual short term-memory differences post-exercise compared to a control group (Coles & Tomporowski, 2008). Further, short term memory tasks have been used within other computerized neurocognitive tests and have identified concussed individuals (Iverson et al., 2003; Lovell et al., 2004; Gardner et al., 2012). Therefore, due to short-term memories constant use within SCAT-3, along with being sensitive to concussion we set out to assess if a new computerized short-term memory test was an equally reliable assessment post-exercise through an inability to be influenced by fatigue.

#### 2 Choice (Response Time)

The reaction time task is a very quick, accurate and efficient assessment that could be incorporated within this reduced RESET test battery. Further, studies have identified that after exercise, reaction time did not differ significantly (McMorris & Keen, 1994; Brisswalter et al., 1997; Ando et al., 2005). Equally, it has been found that varying levels of physical activation and fitness did not affect choice reaction time either (Travlos & Marisi, 1995). Thus, the reaction time task was incorporated due to its continuous ability to identify concussed individuals (Stuss et al., 1989; Makdissi et al., 2001; Sosnoff et al., 2008; Eckner et al., 2011). Equally, as a result of reaction time being a robust assessment, reaction time would

be a very effective assessment tool to be used within this shortened concussion battery test.

#### Card Sort:

Card Sort is known for its ability to analyse executive functions such as set-shifting. The influence of exercise on a set-shifting task was assessed by Coles & Tomporowski (2008) who concluded that set-shifting was not effected post-acute exercise. Therefore, when this inability to be influenced by external factors such as exercise is combined with Card Sorts ability to identify concussed individuals (Stuss et al., 1989; Matser et al., 1999; Downs et al., 2002), it creates a strong argument as to why Card Sort should be included within this battery of tests.

#### Trails Making Test:

Equally, the TMT is another assessment of executive functioning. Studies have assessed the influence of acute bouts of exercise on the performance of the TMT. They have found that after both resistance exercise (Alves et al., 2012) and aerobic exercise (Cordova et al., 2009; Alves et al., 2012) performance of the TMT has been relatively unaffected. Once again, coinciding with its ability to identify individuals suffering from mTBI (Stuss et al., 1989; Macciocchi et al., 1996; Guskiewicz et al., 2001), it is another effective test that could be used “pitch-side” in this condensed battery of tests.

In all, the six tests chosen to be used within this shorter battery of tests were selected based on their ability to not be influenced by external factors (exercise), their capability to identify concussed individuals and finally the completion time of the assessments themselves. Combined, this created the most reliable, sensitive and efficient battery of tests available that

could examine a wide range of neurocognitive features whilst also be carried out within a constricted timeframe.

### **3.2. Aim 2:**

The effect of fatigue on a shortened battery of tests within RESET will be established in order to determine whether neurocognitive scores remain stable post-fatigue compared to baseline in multiple sessions, and therefore whether a shortened RESET assessment is applicable pitch-side.

### **3.3. Hypothesis 2:**

The cognitive performance after experiencing fatigue in a smaller battery of tests will be non-significant compared to each individuals baseline performance and therefore could potentially be an adequate concussion tool to be used “pitch-side”.

## **3.4. Method**

### **3.4.1. Participants**

A total of 24 participants from the University of Birmingham completed all four sessions of exercise-induced fatigue. Participants were aged between 18-24 years old and were understood to be of a good fitness level, in whom were physically active between two to three times per week. Prior to arrival participants were screened and excluded from the study based on the following criteria; if they had experienced a diagnosed concussion within the last 12 months, if they suffered from any learning difficulties, attention deficit disorders, cognitive deficiencies or any visual impairments (such as having a colour vision deficiency). They were

also excluded on the basis of having any self-reported lower extremity pain, cardiovascular or respiratory illnesses. Finally, they were only recruited if their first language was English.

#### 3.4.2. RESET Assessments

A shortened RESET battery was applied within this study so that it could be administered within a ten minute period, relevant for a “pitch-side” concussion assessment. The assessments used within this RESET protocol were Form Constancy, Figure Ground, Visual Short Term Memory, Two Choice Reaction Time, Card Sort and the Trials Making Test. Aforementioned, these tests have both been identified to be sensitive to concussion and also relatively unaffected by conflicting factors such as fatigue. Therefore, these tests were used within this shortened, “pitch-side” assessment.

#### 3.4.3. Procedure

Prior to participation, all volunteers completed both a screening form and a consent form to take part in the study, used as the basis of our exclusion/inclusion criteria. In addition, all participant’s height and weight measurements were taken. Following this any questions about the study were answered and the participants completed the RESET assessment. Volunteers completed a total of four sessions. The first session was a baseline session in which the participant’s cognitive performance was established alongside completing a submaximal  $\text{VO}_2$  test to obtain their workload for the following sessions. Within the next three sessions the participants were exercised to fatigue and then once again completed the same RESET tests one minute after fatigue was established. There was a minimum gap of three days between all sessions to allow for any fatigue from the previous exercise to dissipate before the next exercise-induced fatigue session begun. Throughout this study, participants completed a shortened RESET protocol.

During the first session participants completed the submaximal  $\text{VO}_2$  max test on an Excalibur Sport Lode Bike (Lode B.V., Groningen, Netherlands) after completing their baseline neurocognitive assessment. During the following three sessions, participants were then exercised to a state of fatigue on the Lode Bike before once again completing the six neurocognitive RESET assessments. During which participants' heart rate was recorded via a Polar S625X Heart Rate Monitor Watch that was linked to a Polar T31 Transmitter (Polar Electro (UK), Warwick, England) which the participants wore below their sternum.

#### Baseline:

The Astrand submaximal  $\text{VO}_2$  max test was used to estimate participants  $\text{VO}_2$  max (Astrand, 1954). Participants warmed up for two minutes at 20 watts (W) before the resistance of the cycling was adjusted so that the participant's heart rate was between 130 and 160 beats per minute (bpm). Once this value had been established the participants then cycled at this identified wattage at their own preferred cadence (between 70-90 revs.min<sup>-1</sup>) for six minutes, during which their heart rate was recorded each minute (Astrand, 1954). In order to provide an accurate estimate of each participants  $\text{VO}_2$  max, their average heart rate (HR) during the six minute cycling period, the Watts cycled at during this period to cause their heart rate to be between 130-160bpm and the participants height, weight and gender were all used. These values produced an estimated  $\text{VO}_2$  max (L) for the participant, which was then entered into a HR- $\text{VO}_2$ -Power relationship model. This model used the estimated maximum HR for the participants' age along with their  $\text{VO}_2$  max (ml), which when combined established an estimated power (Watts) that could induce the individuals  $\text{VO}_2$  max. Once each individuals estimated maximal power output was established, each participant's 70% and 40% maximal power was determined through Watts. This was then used during the exercise to fatigue and warm up periods respectively.

#### Exercise-Induced Fatigue:

Participants then exercised to fatigue via cycle ergometry in the following three sessions. They warmed up at 40% of their estimated  $\text{VO}_2$  max for two minutes. Following this the power was increased to 70% and the participants were asked to remain at their preferred cadence throughout all three sessions. After each minute of exercise the participant's heart rate was recorded, equally after every 2 minutes of exercise participants identified their rate of perceived exertion (RPE) (Borg, 1970). This occurred throughout the whole session until the participant was deemed fatigued. This was established due to the following; the participants were unable to maintain the elicited revolutions per minute (RPM), they identified having a RPE of 20 or they were voluntarily fatigued and could not continue.

Once fatigue had been established, the participants then completed the six neurocognitive RESET assessments that were completed at baseline. These neurocognitive assessments were completed one minute after a state of fatigue had been reached.

#### 3.4.4. Data Analysis

A total of six assessments were administered during this study to examine for the influence of exercise-induced fatigue to determine the reliability of RESETs. In order to assess any differences between baseline and the exercise sessions, the significance between each assessment was determined to identify the reliability of these tests post-exercise. One individual was removed from the study after the first exercise-induced session due to a suspected concussion.

The Visual Perception tasks (Visual Short-Term Memory, Form Constancy and Figure Ground) were all assessed for the percentage correct. Whilst the performance of Card Sort

was assessed for the percentage correct, percentage of errors, preservative errors, conceptual responses, categories completed, the number of trials taken to complete the first category and finally the number of times the participant failed to maintain a set (Heaton et al, 1993 & Coelho et al., 2012). The TMT was assessed for the difference in time taken to complete Part-B compared to Part-A (B-A Difference) (Arbuthnott & Frank, 2000; Salthouse et al., 2003). Finally, the two choice reaction time assessment used the average correct reaction time to examine performance (Iverson et al., 2003).

#### 3.4.5. Statistical Analysis

In order to analyse the significance between each individual assessment during the exercise-induced fatigue sessions, a One-way repeated measures ANOVA was conducted. A statistical significant difference was accepted at the  $\alpha = 0.05$  level. If Sphericity was violated then the Greenhouse-Geisser correction was used.

### 3.5. Results

24 individuals took part within the exercise-induced fatigue study. Although one individual was removed from the study after the second exercise session due to experiencing a suspected concussion whilst participating in exercise external to this study. Subsequently, 23 individuals were assessed post-fatigue (13 Males and 10 Females) in which all their results were included within the analysis (age: 19.7 years old ( $\pm 1.1$  years), height: 178cm ( $\pm 9$ cm), weight: 74.3kg ( $\pm 10.4$ kg), resting HR: 83bpm ( $\pm 13$ ), 70%  $\text{VO}_2$  Max (Watts): 175W ( $\pm 38$ ) and 40%  $\text{VO}_2$  Max (Watts): 100W ( $\pm 21$ )). On average the fatigue sessions lasted 22.34 minutes, in which individuals identified themselves as being fatigued due to having an RPE of 20 thirty times, not maintaining their given RPM ten times and finally stating voluntary exhaustion twenty

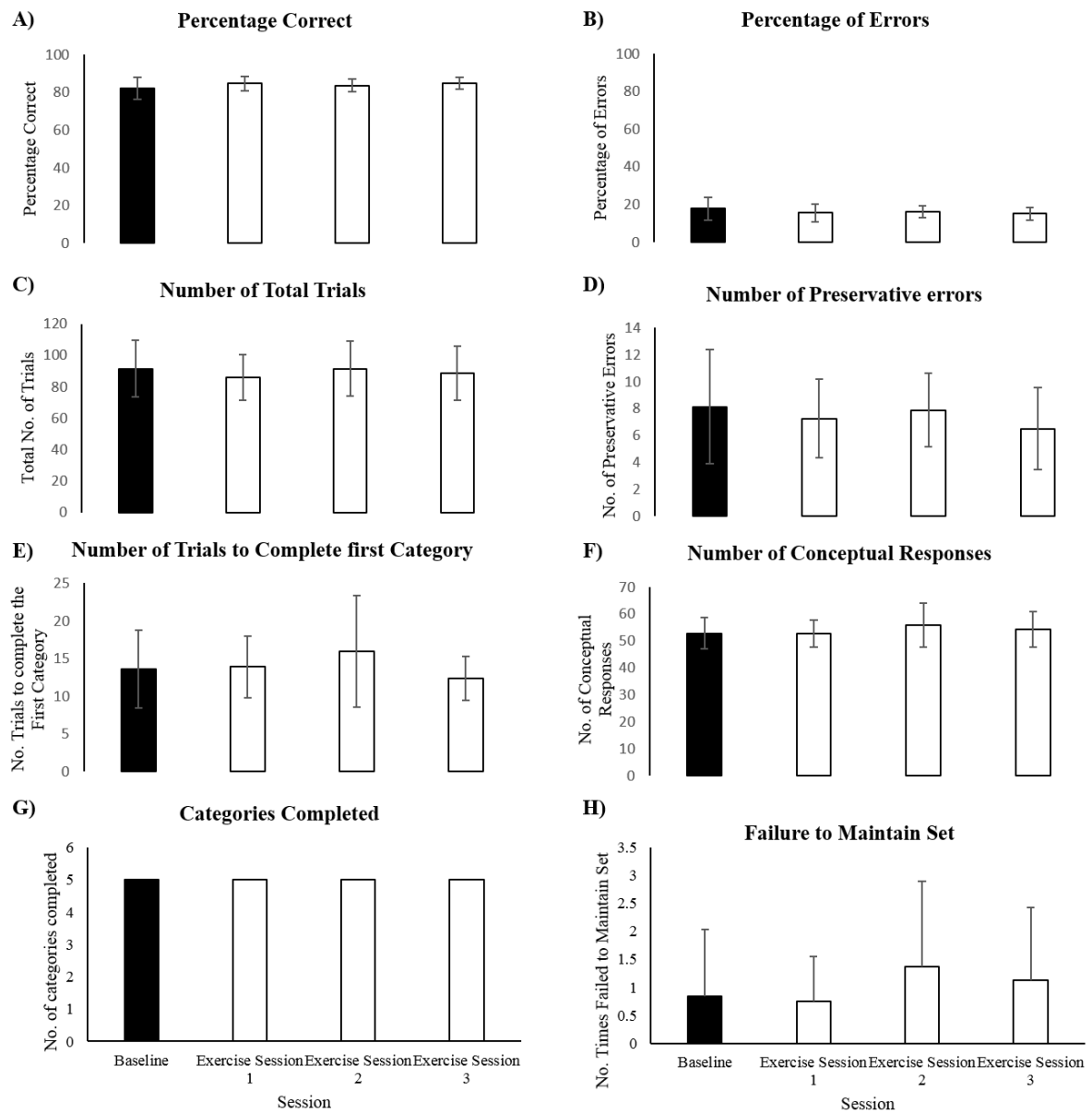
eight times. A total of three baseline assessments did not contain results for the TMT, whilst another two sessions during the second exercise session were not saved due to technical errors.

### 3.5.1. Card Sort:

Upon analysis of the eight variables examined within the Card Sort assessment there was no significant difference between the baseline evaluation and all three fatigue sessions. For the percentage correct ( $F_{3,63} = 2.239$ ,  $p=0.082$ ), percentage of errors ( $F_{3,63} = 1.693$ ,  $p=0.178$ ), conceptual responses ( $F_{3,63} = 1.885$ ,  $p=0.141$ ), failure to maintain set ( $F_{3,63} = 1.885$ ,  $p=0.101$ ), the number of trials ( $F_{3,63} = 1.051$ ,  $p=0.376$ ), preservative errors ( $F_{3,63} = 1.326$ ,  $p=0.274$ ) and the number of trials taken to complete the first category ( $F_{3,63} = 1.700$ ,  $p=0.176$ ) which all had non-significant differences between baseline and post-fatigue sessions. Whilst all participants completed all five categories during each session (*Figure 9G*).

Card Sort					
	Baseline	Session 1	Session 2	Session 3	Effect Size
	Mean ( $\pm$ SD)	Mean ( $\pm$ SD)	Mean ( $\pm$ SD)	Mean ( $\pm$ SD)	Partial Eta Squared ( $\eta^2$ )
Percentage Correct	82.3 ( $\pm$ 6.12)	85.13 ( $\pm$ 3.78)	83.71 ( $\pm$ 3.19)	84.71 ( $\pm$ 3.32)	0.1
Percentage Errors	17.69 ( $\pm$ 6.12)	15.32 ( $\pm$ 4.7)	16.28 ( $\pm$ 3.19)	15.28 ( $\pm$ 3.32)	0.075
Categories Completed	5 ( $\pm$ 0)	5 ( $\pm$ 0)	5 ( $\pm$ 0)	5 ( $\pm$ 0)	
Conceptual Responses	52.77 ( $\pm$ 5.78)	52.4 ( $\pm$ 4.87)	55.86 ( $\pm$ 8.1)	54.86 ( $\pm$ 6.65)	0.082
Failure to maintain set	0.77 ( $\pm$ 1.15)	0.68 ( $\pm$ 0.77)	1.36 ( $\pm$ 1.52)	1.22 ( $\pm$ 1.3)	0.093
Number of trials to complete first category	13.68 ( $\pm$ 5.31)	13.9 ( $\pm$ 4.27)	15.95 ( $\pm$ 7.42)	12.54 ( $\pm$ 2.98)	0.075
Total number of trials	91.36 ( $\pm$ 18.54)	84.4 ( $\pm$ 14.38)	91.59 ( $\pm$ 17.7)	89.68 ( $\pm$ 17.54)	0.048
Preservative errors	8.29 ( $\pm$ 4.39)	7.03 ( $\pm$ 2.92)	7.89 ( $\pm$ 2.75)	6.63 ( $\pm$ 3.04)	0.059

**Table 14:** Displays the Means ( $\pm$  SD) and also the Effect Size for Card Sort within the Exercise-Fatigue study



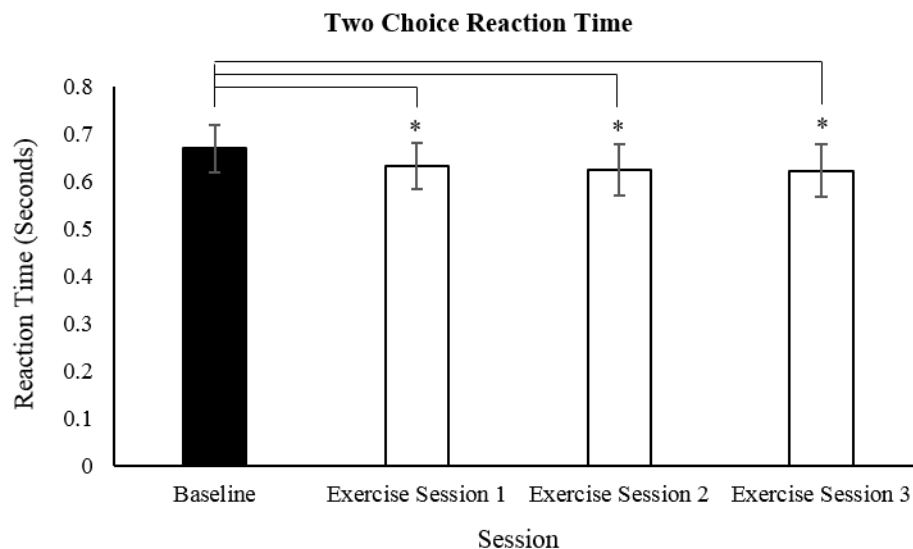
**Figure 9:** Card Sort. Above are the differences between each session for all eight variables of Card Sort. There was no significant difference in any assessment between all sessions. Error bars represent  $\pm$  SD.

### 3.5.2. Reaction Time:

There was a significant difference from baseline to each post-fatigue session in the average response time during the reaction time assessment ( $F_{2,314, 48.594} = 15.512$ ,  $p < 0.001$ ). Upon post-hoc evaluation a Bonferroni correction was applied that demonstrated a significant difference in reaction time score and all three post-fatigue sessions ( $p < .001$ ,  $p < .001$ ,  $p = .001$ ) respectively. These scores post-fatigue, decreased between each session suggesting that reaction time improved significantly between sessions compared to the baseline examination (*Figure 10*).

Reaction Time					
	Baseline	Session 1	Session 2	Session 3	Effect Size
	Mean ( $\pm$ SD)	Mean ( $\pm$ SD)	Mean ( $\pm$ SD)	Mean ( $\pm$ SD)	Partial Eta Squared ( $\eta^2$ )
Correct Response					
Time	.669 ( $\pm$ .05)	.635 ( $\pm$ .04)	.624 ( $\pm$ .05)	.625 ( $\pm$ 0.5)	0.435

**Table 15:** Displays the Means ( $\pm$  SD) and also the Effect Size for the Reaction Time assessment within the Exercise-Fatigue study



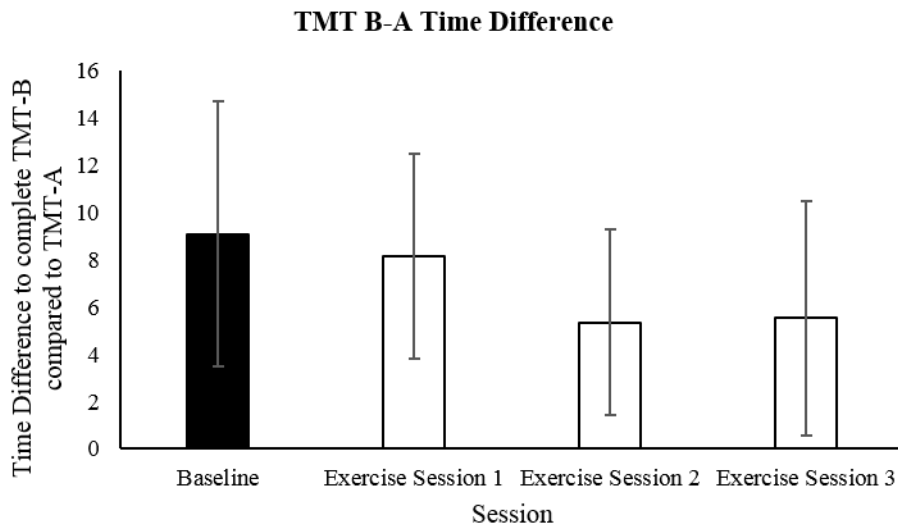
**Figure 10:** Two Choice Reaction Time. Above shows the difference between baseline and the three fatigue-induced exercise sessions. There was a significant difference ( $p < 0.05$ ) between baseline and all three exercise sessions. Error bars represent  $\pm$ SD, \* represents significance between time points

### 3.5.3. Trails Making Test:

Through the analysis of the difference in time it took to complete Part B compared to Part A, results suggested that there was no significant difference between baseline and the corresponding fatigue sessions ( $F_{2,297, 36.756} = 4.556$ ,  $p=0.074$ ). However, there was a clear trend that the TMT B-A Difference improved continually post-exercise (*Figure 11*).

Trails Making Test					
	Baseline	Session 1	Session 2	Session 3	Effect Size
	Mean ( $\pm$ SD)	Mean ( $\pm$ SD)	Mean ( $\pm$ SD)	Mean ( $\pm$ SD)	Partial Eta Squared ( $\eta^2$ )
Part B-A Difference	7.89 ( $\pm$ 4.84)	7.33 ( $\pm$ 4.07)	5.18 ( $\pm$ 4.25)	5.17 ( $\pm$ 3.75)	0.15

**Table 16:** Displays the Means ( $\pm$  SD) and also the Effect Size for the Trials Making Test within the Exercise-Fatigue study



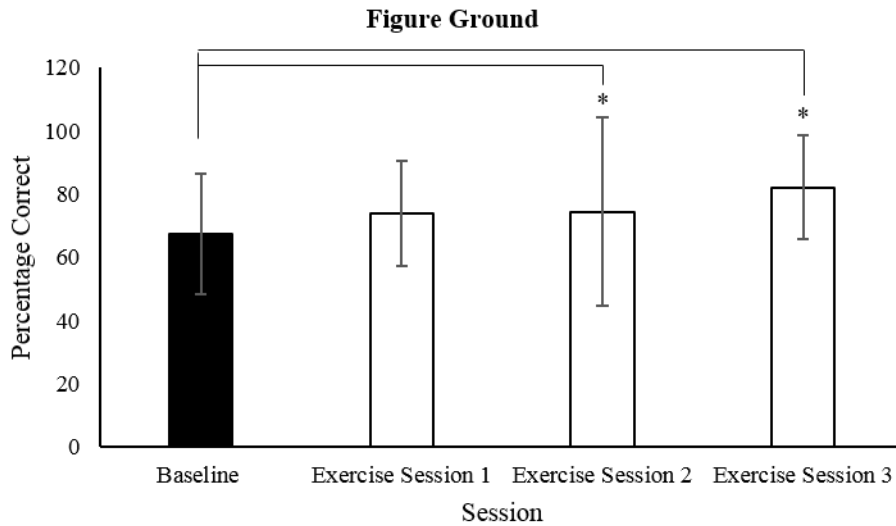
**Figure 11:** Trails Making Test. The graph above displays the difference in time to complete TMT-B compared to TMT-A between baseline and the three exercise sessions. There was a not a significant difference between baseline and any of the exercise induced fatigue sessions, although there was a clear trend in improvement in performance post-exercise. Error bars represent  $\pm$ SD.

### 3.5.4. Figure Ground:

Upon analysis of the percentage correct between baseline and the fatigue sessions, there was a significant difference in the overall percentage correct within each session ( $F_{2,169, 45.55} = 9.108$ ,  $p < 0.001$ ) Post-hoc tests revealed that there was a significant improvement in the performance of figure ground between baseline and the second fatigue induced session ( $p=0.009$ ), and also baseline and the third fatigue session ( $p=0.006$ ). Overall there was a trend in an improved performance from baseline throughout the three fatigue induced sessions (*Figure 12*).

Figure Ground					
	Baseline	Session 1	Session 2	Session 3	Effect Size
	Mean ( $\pm$ SD)	Mean ( $\pm$ SD)	Mean ( $\pm$ SD)	Mean ( $\pm$ SD)	Partial Eta Squared ( $\eta^2$ )
%	65.58	73.37	81.168	81.168	
Correct	( $\pm 18.52$ )	( $\pm 16.07$ )	( $\pm 19.9$ )	( $\pm 16.72$ )	0.303

**Table 17:** Displays the Means ( $\pm$  SD) and also the Effect Size for Figure Ground within the Exercise-Fatigue study



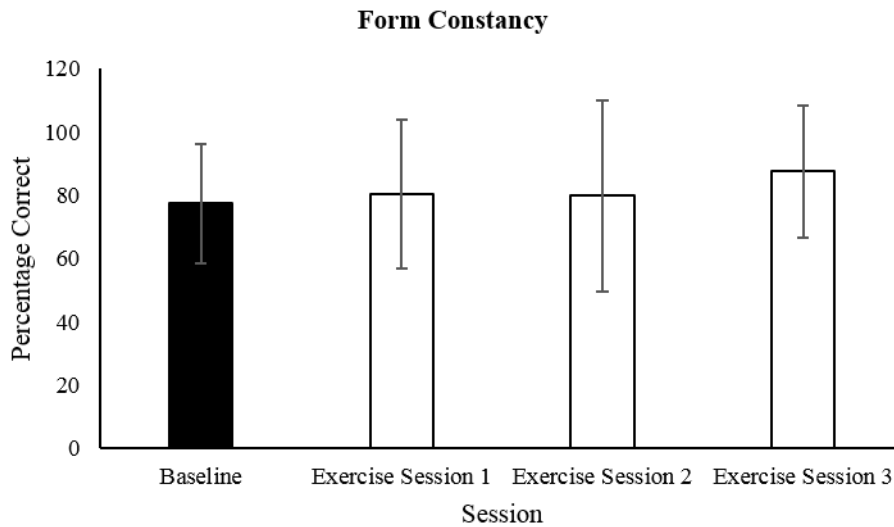
**Figure 12:** Figure Ground. The above graph displays the difference in percentage correct scores for Figure Ground between baseline and the three exercise sessions. Error bars represent  $\pm$ SD, \* represents significance between time points. There was a significant difference between baseline and session 2 and 3, where scores significantly improved.

### 3.5.5. Form Constancy:

Once again upon analysis of the percentage correct of form constancy between baseline and the following fatigue tests there was no significant difference in percentage correct between sessions ( $F_{1.741, 36.567} = 3.488$ ,  $p=0.167$ ). Although, there was a small improvement between baseline and the third fatigue session (*Figure 13*).

Form Constancy					
	Baseline	Session 1	Session 2	Session 3	Effect Size
	Mean ( $\pm$ SD)	Mean ( $\pm$ SD)	Mean ( $\pm$ SD)	Mean ( $\pm$ SD)	Partial Eta Squared ( $\eta^2$ )
Percentage Correct	82.14 ( $\pm$ 15.97)	85 ( $\pm$ 20.45)	87.85 ( $\pm$ 19.26)	89.28 ( $\pm$ 22.16)	0.094

**Table 18:** Displays the Means ( $\pm$  SD) and also the Effect Size for Form Constancy within the Exercise-Fatigue study



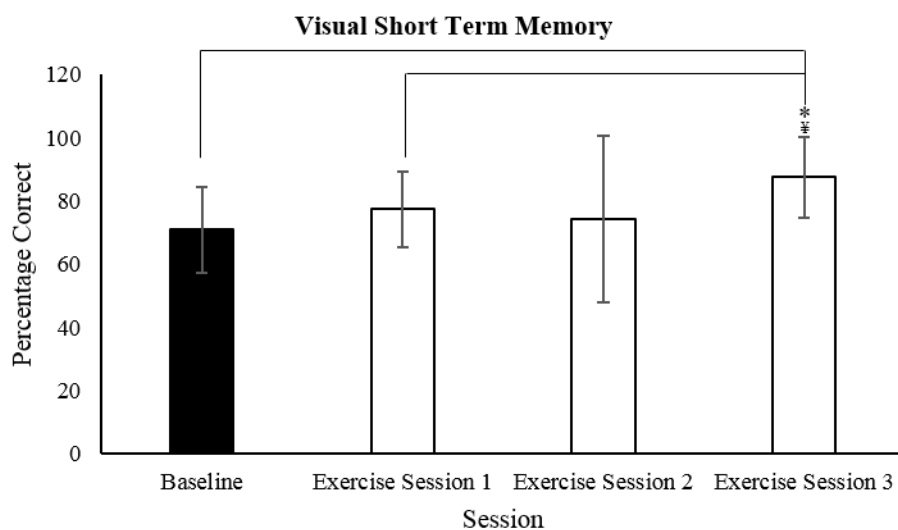
**Figure 13:** Form Constancy. The above graph displays the percentage correct scores for Form Constancy between baseline and the three exercise sessions. The error bars represent  $\pm$ SD.

### 3.5.6. Visual Short Term Memory:

Finally, upon analysis of percentage correct on the visual short term memory assessment, results revealed a significant difference in percentage correct ( $F_{2,439, 51.225} = 7.897$ ,  $p < 0.001$ ). Subsequently, a post-hoc test was conducted in which revealed that there was a significant improvement in scores between baseline and the third fatigue session ( $p=0.001$ ) and between the first fatigue session and the third fatigue session ( $p=0.009$ ) (*Figure 14*).

Visual Short Term Memory				
	Baseline	Session 1	Session 2	Session 3
	Mean ( $\pm$ SD)	Mean ( $\pm$ SD)	Mean ( $\pm$ SD)	Mean ( $\pm$ SD)
Percentage Correct	70.12 ( $\pm$ 13.87)	76.62 ( $\pm$ 12.11)	81.16 ( $\pm$ 13.5)	88.31 ( $\pm$ 12.95)
				Effect Size
				Partial Eta Squared ( $\eta^2$ )
				0.276

**Table 19:** Displays the Means ( $\pm$  SD) and also the Effect Size for the Visual Short Term Memory assessment within the Exercise-Fatigue study



**Figure 14:** Visual Short Term Memory. The above graph shows the difference in percentage correct scores on the Visual Short Term Memory task. There was a significant difference between baseline and session 3 and also session 1 and session 3 ( $p < 0.05$ ) where scores significantly improved. Error bars represent  $\pm$ SD, \* represents significance between Baseline and Exercise Session 3 whilst † demonstrates significance between Exercise Session 1 and Exercise Session 3.

## **Chapter 4 – Discussion**

This thesis sought to determine the reliability of a new computerized neurocognitive assessment (RESET) over a specified test-retest period. Moreover, this thesis looked to determine the reliability of a shortened battery of RESET assessments, under the constraints of fatigue, and thus determine the plausibility of RESET to be used during a pitch-side concussion assessment.

The results on the reliability of RESET over a clinically relevant interval, baseline and day 45 (Broglia et al., 2007), was found to display ICC values ranging from 0.64 to 0.78 resembling good to strong reliability during this test-retest interval. In addition, between day 45 and day 50 all composite ICC values ranged from 0.47 to 0.88 demonstrating moderate to strong reliability. However, these results did not support our hypothesis that all the composites of RESET would attain ICC values of equal to or more than 0.80 (Nunally et al., 1994). Ensuing analysis revealed that only one composite elicited an ICC value over 0.80 throughout both test-retest intervals.

Nevertheless, all of the composite values for the baseline to day 45 test-retest interval exceeded the minimal acceptable reliability value, 0.60 (Anastasi, 1998). Further, the attention composite displayed excellent reliability and acceptable test-retest reliability (Portney & Watkins, 1993), whilst the visual perception battery, memory composite, PRO and executive functioning composite were all found to have good reliability (Cicchetti, 1994). Additionally, the test-retest interval for day 45 to day 50 revealed that two composites (memory composite and the visual perception battery) were below the minimally accepted reliability value suggested by Anastasi (1998). Regardless, two categories ‘attention’ and the ‘PRO’ were found to have excellent reliability over this period and therefore acceptable test-retest reliability (Portney, 1993). Meanwhile, the executive functioning composite was found

to have good reliability whilst both the visual perception battery and the memory composite were found to have fair reliability values over this five day period (Cicchetti, 1994).

Equally, between baseline and day 45 there was no significant difference in all five of the neurocognitive domains used within RESET. However, between day 45 and day 50, a shorter time interval, there was a significant difference in the Visual Perception composite score. Upon further analysis, the percentage correct scores in six out of the seven assessments that form the Visual Perception composite increased linearly between baseline and day 50 (Table 8). Therefore, the significant increase in cognitive performance score in the Visual Perception composite between day 45 and day 50 could be the subject of a learning effect. Nevertheless, there was no significant differences in the other four composite scores.

In a further study, a shortened RESET battery was administered to determine the plausibility of such a computerized neurocognitive test to be used pitch-side. This study looked to assess the reliability of using a computerized neurocognitive test pitch-side. Through examining a total of six tests that could be conducted within the timeframe provided for a pitch-side assessment, we exercised participants to a state of fatigue to determine whether this would influence the participant's cognitive performance, identified by RESET. Results showed that none of the six assessments were negatively affected by exercise-induced fatigue. Although, contrary to our hypothesis we found that the performance of three out of the six assessments post-exercise significantly increased post-fatigue. This did not support our hypothesis that none of the applied assessments would be significantly affected post-fatigue.

However, as there was no negative influence of fatigue on the computerized neurocognitive tests administered it displays positive signs that a computerized test could be employed pitch-side, thus reducing subjectivity in diagnosing a concussion. In addition, fatigue did not result

in the performance of the neurocognitive test scores to diminish and thus display results that may be evident in a concussed individual and therefore result in a possible misdiagnosis of concussion. As a direct result of the tests administered and the ability to administer RESET on applications such as Tablets, computerized tests now have the potential to be used pitch-side and subsequently can be an effective tool that can be used to reduce the subjectivity in diagnosing a concussion.

#### **4.1. Test-Retest**

In all, RESET is formed of a hybrid of tests; a mix between conventional neurocognitive assessments and computerized neurocognitive assessments, and is composed of a total of 15 assessments. These assessments span an array of neurocognitive domains, and thus have a higher probability of outlining any possible cognitive deficits. As a result of this large array of tests and good to excellent reliability over a 45 day period, RESET displays the potential to be a reliable neurocognitive test.

In an attempt to present precise reliability values of RESET over this test-retest interval, we looked to control for a number of factors that could cause confounding effects. The study attempted to control external confounds inflicting on results through controlling for random errors, maintaining the same lab environment upon every visit and also completing the exact same procedure on each session along with carrying out each session for the participant at approximately the same time of day. This ensured that we controlled for as many factors as possible which could potentially skew our results. Thus, through mirroring the same environment during each session it ensured that the ICC values obtained were due to cognitive performance only and the results were not predisposed to conflicting variables.

However, potential confounding factors such as the quantity of sleep individuals sustained the night before and any caffeine intake, both of which could potentially directly influence the individuals neurocognitive performance were not controlled for within this study. Equally, the current study did not control for the quantity of effort established throughout the assessment to ensure participants were engaged at all times. Thus, it is possible that these factors may have influenced neurocognitive performance. Nevertheless, these factors are present in an everyday environment and therefore if RESET was used as a concussion tool it is likely that these factors will also play a role.

Another potential limitation to our study could be an ordering effect. Within the test-retest study we did not randomise the order of any of the assessments and thus this could have played a potential role in the reliability values sustained over both baseline and day 45 and also between day 45 and day 50. Once again there are external factors such as effort and concentration in which may have played a role in influencing cognitive performance especially at day 50 (third RESET assessment) and also towards the end of all sessions themselves. Therefore, even though our overall results display moderate to strong test-retest reliability we must also consider that a lack of randomisation of these assessments may have affected the reliability values sustained.

The findings of reliability of other computerized neurocognitive tests have been variable, aforementioned. Through comparing our results to previously identified computerized neurocognitive ICC values over a 45 and 50 day test-retest interval, the ICC values displayed by RESET are equally, or more, reliable. Over a 45 day test-retest interval, ICC values for CogState, ImPACT and HeadMinder have ranged from 0.15 to 0.78 (Broglia et al., 2007; Resch et al., 2013; Nelson et al., 2016). Whilst another study found ImPACT to have reliability values of 0.67 to 0.87 after 45 days (Nakayama et al., 2014). However, the ICC

values identified within RESET in this study ranged from 0.64 to 0.78, after a 45 day test-retest interval. These reliability values are dramatically higher than other reliability values reported in literature on current neurocognitive tests (Broglia et al., 2007; Resch et al., 2013; Nelson et al., 2016). Further, the reliability values presented from RESET are similar to the values displayed by Nakayama et al. (2014), who reported the highest ICC values for a 45 day test-retest period for ImPACT.

Although, the RESET ICC reliability values displayed within this study, between day 45 to day 50, revealed a larger range of ICC values across all composites (0.47 to 0.88). This is potentially suggesting that over a shorter time interval RESET is less reliable compared to a clinically relevant time period (45 days), due to two composites not meeting the minimally accepted ICC value to be reliable (Anastasi, 1998) and also having a larger range of ICC values. Nevertheless, when comparing the results of RESET over this 5 day interval to similar test-retest intervals reported in literature, the reliability values of RESET were higher than some neurocognitive tests, 0.36 to 0.66 (HeadMinder) and 0.39 to 0.61 (ImPACT) (Broglia et al., 2007) and also contained very similar findings to other studies, 0.45 to 0.76 and 0.6 to 0.85 respectively (Resch et al., 2013; Nakayama et al., 2014).

Therefore, these preliminary findings on the reliability of RESET as a computerized neurocognitive test to be used over a clinically relevant time period used to assess a concussion, are very encouraging. Further, between baseline and day 45 the ICC values for the Visual Perception Battery (0.64), PRO (0.67), Memory (0.68), Attention (0.78) and the Executive Functioning test battery (0.66) were all above the 0.60 value, which has been found to be a “cut-off” value used to distinguish “acceptable” reliability (Anastasi, 1998). In addition to this, the reliability of RESET was found to be higher than that reported by Broglia et al. (2007), Resch et al. (2013) and Nelson et al. (2016). Whilst also having obtaining

similar reliability scores as those reported by Nakayama et al. (2014). This reinforces RESET's potential to be used as an accurate, reliable neurocognitive test subject to high reliability values over a clinically relevant time period for a concussion.

Further, when analysing the range of ICC values found within RESET to the range of composite values found within CogState (0.38 to 0.93), HeadMinder CRI (0.36 to 0.90) and ImPACT (0.23 to 0.91) the range of ICC values for the composites between baseline and day 45 for RESET (0.64 to 0.78) fall within the "higher bracket" of the ICC composite values found within these other neurocognitive tests. In addition, the ICC composite values found for RESET between day 45 and day 50 (0.47 to 0.89) fall between the middle to higher range of ICC values found by the other neurocognitive tests.

One concern of our results is that two of the composites between day 45 and day 50 did not meet the minimal acceptable reliability value (Anastasi, 1998). This provides a cause for concern when using the test over a much shorter interval of time. Thus, further studies should look at the influence of a range of test-retest intervals on RESET to determine the reliability value for various test-retest intervals. However, concussions typically occur within a month to a year period after the baseline examination. Therefore, this time interval (5 days) is not of clinical relevance. Nevertheless, this test-retest interval was conducted in order to examine the reliability values over a shorter period of time, which many previous studies have equally looked to address (Falleti et al., 2006; Collie et al., 2003; Louey et al., 2014; Iverson et al., 2003; Register-Mihalik et al., 2012; Resch et al., 2013; O'Brien et al., 2015; Nelson et al., 2016).

In line with test-retest reliability, it is also important to determine whether the assessments used within RESET have any ceiling effects and thus the true reliability of the test is being

masked. Using the tables provided in Section 2.7 we can look at the means and standard deviations of each assessment during each session in order to determine whether any ceiling effects are present. Upon the analysis of assessments within the Visual Perception battery such as the Visual Discrimination, Visual Closure and the Visual Short Term Memory tests there is a plateauing of score values which is likely to be due to a ceiling effect. Moreover, after repeated assessments the scores of all Visual Perception tests increase, this is likely due to a learning effect taking place. As a result of analysing the percentage correct of these test scores, it is plausible that these tests could have a ceiling effect, especially when measured repeatedly over a short period of time. Equally, the test-retest reliability of assessments such as Reaction Time may also be experiencing ceiling effects as there will be a physiological limit to the speed at which healthy individuals will be able to respond. Our results showed that across the three test-retest intervals reaction time deviated by 0.02 seconds. Therefore, when used within a healthy cohort there could be a ceiling effect in performance of reaction time. Another assessment that may have experienced a ceiling effect within some of the variables assessed is the Go/No-Go assessment. One evaluation of the Go/No-Go task is correct responses, although as this assessment has a set number of responses before completion, it limits the performance of the individual. This is reflected within our study in which across the three time points the correct responses deviated by 1. A final assessment which could be considered to have a ceiling effect is Line Crossing. Due to its use within more severe TBI, applying it to a healthy cohort may produce high performance scores due to the assessment being formed for severe injury and not used in healthy individuals. Although, not present within our means it is plausible that through repetitive testing the performance on Line Crossing would reach a ceiling effect.

Further, several of the RESET assessments are adaptations of conventional neurocognitive tests such as the Card Sort test and the TMT. However, these components of the RESET computerized assessment battery are yet to be analysed for their validity to the original assessments. Thus, studies should seek to rectify this discrepancy in order to distinguish whether these two conventional assessments used within RESET remain valid even though they are now computerized assessments.

Further, alternative factors such as the population assessed could potentially create the various reliability findings seen within other computerized neurocognitive assessments. The present study looked at the use of RESET in physically active University students. Thus, the population assessed are likely to have greater cognitive performance competencies than the standard Rugby player as a direct result of being educated to a higher level. Therefore, the results displayed within this study are obtained from individuals that are likely to have higher cognitive competencies than the athletes that the assessment is designed to assess. As a result of this, the reliability values found within this study may differ to those found within a study looking to address the test-retest reliabilities of athletes, or those that are not as highly educated. Therefore, it is essential that future studies look to explore the reliability of RESET within a cohort of professional Rugby players, or sportsman, in whom would regularly use concussion assessments. This would determine the reliability values of the RESET assessment in a population of athletes in whom it is targeted at. Thus, the reliability values recorded from such a study would carry more authority, as the protocol administered is more representative of how the test would be administered in a typical environment.

Nevertheless, these are preliminary findings. Thus, more extensive reliability assessments should be conducted on RESET to indisputably determine its reliability over different time intervals and between authors. This is key due to the range of findings currently reported

within literature on the reliability of the current computerized neurocognitive tests used. However, the reliability values obtained within this study on RESET displays its potential to be used effectively over a clinically relevant time period. Nevertheless, future studies should look to examine similar and varying test-retest intervals to generate a better representation of the reliability of RESET. Through multiple authors examining the reliability, it allows for judgement over alternative factors such as experimenter variances in reliability. The reliability of cognitive performance has differed dramatically within other computerized neurocognitive assessments, questioning the intra-experimenter reliability of these assessments. Thus, the reliability of RESET should equally be examined by multiple experimenters, allowing for judgement over the influence of experimenter differences on the reliability of RESET. If the variance of ICC values between these experimenters remains low whilst still above the acceptable reliability value to be used clinically, then the reliability and also the potential of RESET as a clinically used assessment tool is very high.

Once the reliability of RESET has been further established through varying test-retest intervals, future studies should subsequently look to determine RESET's sensitivity to concussion. Examining the sensitivity of RESET should be conducted after the reliability for RESET has been established. This would therefore determine both the reliability and the sensitivity of the RESET concussion battery. Thus, outlining the ability for RESET to be used as a concussion assessment tool.

Further, when studies are looking to assess RESET's sensitivity to concussion, it would be interesting to address the ability of RESET to be used as a protocol within RTP. When individuals are diagnosed with a concussion they follow the RTP (Section 1.4), however computerized neurocognitive tests are not considered a necessity during this protocol.

Although, studies have found neurocognitive tests during this period can help outline when an individual is fit to RTP (Chermann et al., 2014; McGrath et al., 2013). As of yet computerized neurocognitive tests are not an essential protocol used within the RTP assessment. The current RTP protocol proposed by McCrory et al. (2013) allows for athletes to begin the following stage when asymptomatic. However, this generally is a subjective interpretation. Further, athletes maybe likely to suppress their signs and symptoms in order to expedite their RTP progress. Nevertheless, a previous study found that both cognitive and balance deficits post-concussion returned to baseline levels after 7 and 5 days, respectively (McCrea et al. 2003). Therefore, it would be assumed that these neurocognitive deficits would be eradicated by the time the individual had finished the RTP process anyway. However, a recent study analysed the RTP process and assessed individuals on a computerized neurocognitive test throughout. When analysing asymptomatic individuals who were about to complete the RTP, they identified that 28% of athletes still displayed neurocognitive deficits compared to their baseline results after they had exercised (Zaring et al., 2015). This study clearly displays that the current RTP procedure, using subjective interpretations of self-report symptoms, is inadequate in assessing the athlete's neurocognitive performance along with their inability to help determine when the individual has fully recovered cognitively from the effects of concussion. Thus a more objective approach is warranted.

Without this objective approach, athletes may be being put at further risk of a secondary injury, through returning to play prematurely. Furthermore, the findings of studies such as Zaring et al. (2015) reinforce the importance of using computerized neurocognitive tests during the recovery of a concussion. The findings of this study indicate that without the use of a computerized neurocognitive test during the RTP protocol of a concussion, there is the potential of 28% of athletes returning to play prematurely and being exposed to further

concussive impacts, which can be detrimental (Section 1.3.4 - Second Impact Syndrome). Therefore, enforcing computerized concussion tests over this period as an essential protocol to assess the recovery of the concussion could further enhance the safety of the athlete and ensure they return to play when they have completely recovered from the concussion. Further, as there is a demand for athletes to return to play as quickly as possible, the use of a computerized assessment has great beneficial use to clinicians in indisputably identifying whether athletes are still experiencing any neurocognitive deficits due to the concussion or whether they have recovered. Subsequently, this will reduce the pressure on the clinicians in allowing an athlete to return to play or not. In addition to this, computerized neurocognitive tests are known to have high objectivity and excellent sensitivity rates to concussion and thus the use of these during the recovery of a concussion is unquestionable. Consequently, like when assessing for a concussion pitch-side, a multi-faceted approach should be used during this RTP in order to track the athlete's progress from recovery of the concussion throughout. In all, this questions the current reliability in assessing an athlete's progress of recovery from a concussion.

Further, a recent study was conducted in Rugby players in regards to improving the current return-to-play guidelines and further limit the incidence and risk of sustaining a concussion in the following months through individualising the RTP process and also incorporating a neurocognitive assessment. Through incorporating CT/MRI scans, the use of SCAT-2 to analyse symptoms, along with assessing the severity of the concussion and conducting a cognitive assessment they then allowed the individual to slowly follow a graded exercise regime. Subsequently, through taking into account these varying aspects it makes the RTP guidelines more individualised to each athlete. When the individual's symptoms had disappeared during this RTP protocol, another cognitive assessment was conducted and if the

symptoms had disappeared then the athlete was allowed to continue playing the sport (Chermann et al., 2014). Interestingly, following this adjusted protocol they found that it took 21 days on average for players to return to the sport, which is dramatically longer than proposed by McCrory et al. (2013), with 60.6% of participants returning after 21 days. More importantly they found that only one individual who followed this RTP guideline suffered a further concussion within 3 months. Further, via the use of a neurologist a further two individuals were advised to stop playing rugby all together.

Thus, a study looking to provide a follow up neurocognitive assessment on concussed individuals during this RTP protocol would be able to provide essential information to the clinicians about the mental status of the athlete. Further, the use of RESET or other computerized neurocognitive assessments within the RTP protocol would significantly enhance the safety of the athlete through individualising the RTP and therefore only allowing the athlete to return to play when they are fully recovered from the concussion. In addition, it could potentially reduce the amount of musculoskeletal injuries that have been found to be evident in individuals post-concussion. In all, future studies should look at implementing an assessment such as RESET in an environment such as the RTP. However, this test should be applied after both the reliability and the sensitivity of RESET has been definitively determined.

#### **4.2. Exercise**

As a direct result of no assessments of RESET being negatively influenced by fatigue it demonstrates a promising potential to be used during a pitch-side diagnosis of a concussion and reduce the subjectivity that is currently present during the diagnosis of a concussion. This is the first study to our knowledge that has looked to develop a shortened computerized

neurocognitive test that can be administered pitch-side. The results of which provide convincing evidence to support the notion that such a test can be administered pitch-side which will ultimately improve the objectivity in diagnosing a concussion.

Nevertheless, Reaction Time, Visual Short Term Memory and Figure Ground scores all significantly improved in one or more of the exercise-induced fatigue sessions whilst Card Sort, TMT and Form Constancy did not significantly differ throughout. Even though findings have found these tasks to not significantly differ post-exercise, conversely other findings suggest that performance within these tasks can be facilitated post-exercise.

Reaction Time post-exercise in the present study significantly improved compared to baseline within all three sessions. Further to this, the raw results display a total of 16 out of the 24 participants experiencing enhanced reaction time scores post-fatigue compared to baseline. Equally, other studies such as Hogervorst et al. (1996) have examined the influence of reaction time post-exercise. Through a strenuous exercise protocol, they exercised individuals at 75% of their maximal work capacity until they had completed the equivalent of an hours exercise as fast as possible. They then examined the participant's reaction time post exercise and compared this to baseline data. Their results showed that after fatiguing exercise, simple reaction time significantly improved compared to baseline. Further, at a lower exercise intensity of 50% max  $\text{VO}_2$ , participants were equally found to significantly improve their reaction time compared to baseline (Davranche & Audiffren, 2004). This facilitation in reaction time has been found to occur due to U Shape hypothesis proposed by Levitt & Gutin (1971) whom exercised participants at specific heart rates (115bpm, 145bpm and 175bpm), then assessed the reaction time compared to performance at rest. Results show that the reaction time scores peaked at 115bpm and remained stable at 145 bpm, however decrease at 175bpm exercise. Subsequently, this association between heart rate and performance on

reaction time could be the underlying factor within this study as to why performance for reaction time significantly improved post-exercise. Even though the participants exercised at 70% of their predicted  $\text{VO}_2$  max, by the time they completed the reaction time assessment their heart rate would have been around this 115bpm value. Thus, this could potentially be the facilitating factor as to why reaction time significantly increased post-exercise.

The TMT of the RESET assessment battery was found to be unaffected by the influence of exercise-induced fatigue. However, there was a trend in which, post-exercise the difference in performance between TMT-B and TMT-A was reduced and thus performance improved. Nevertheless, studies have equally identified that performance on the TMT to be uninfluenced by factors such as fatigue after aerobic exercise, in terms of performance during the TMT-B test alone (Alves et al., 2012) and also in the TMT B-A difference (Harveson et al., 2016). Thus, supporting our findings that the TMT was uninfluenced by fatigue and further illustrating the reliability of the TMT and its potential use to be incorporated into a neurocognitive test “pitchside” as a result of its high reliability and sensitivity to concussion.

Another encouraging finding was that the Card Sort task revealed non-significant findings on all eight variables assessed. Previous studies have demonstrated similar findings, when assessing a set-switching task after moderate exercise for thirty minutes there was no significant differences in performance post-exercise compared to baseline (Kubesch et al, 2003). Further, Coles & Tomporowski (2008) replicated these findings, in which they concluded that acute aerobic exercise did not significantly influence the set-shifting task used. Thus, our findings imitate those reported in current literature, in which a set-shifting task such as Card Sort is not significantly affected post-exercise. Coinciding with its sensitivity to concussion (Matser et al., 1999 & Downs et al., 2002), Card Sort is a very robust test that could be used as a pitchside assessment.

Thus, the findings within this study suggest that executive functioning is not significantly affected by exercise-induced fatigue. This is due to the results displaying that both the TMT and Card Sort, which are used to assess executive functioning, revealed non-significant differences post-fatigue compared to each individual's baseline results. Executive functioning is an umbrella term used to cover a range of cognitive processes that help athletes organise and act on information provided to them. As a result of both the TMT and Card Sort being uninfluenced by external factors such as fatigue, whilst also being found to be sensitive to concussion, executive functioning could be a vital component of a computerized concussion assessment tool.

However, the Visual Short Term Memory assessment was found to be significantly enhanced after the third post-exercise session compared to both the baseline and also the first exercise session. In addition, there was a consistent trend in increased performance scores from baseline through to the third exercise session (*Figure 14*). This trend was also present within the raw data in which the majority of individuals experienced higher performance scores in the Visual Short Term Memory task post-fatigue, with the remaining participants not differing at all. The trend in enhanced memory performance post-exercise was equally found by Coles & Tomporowski et al. (2008). They administered a 30 minute exercise intervention at 60% of the participants'  $\text{VO}_2$  max before completing a short term memory task. The performance from this task was then compared to the baseline performance of the respective individual, acquired previously. Results revealed that, although non-significant, short-term memory performance improved post-exercise. These findings reflect those found within this study. In that short-term memory improved, from baseline, post-exercise. The reason for the final exercise session producing significant differences compared to both baseline and the first exercise session however is not definitively known. Although, it can be hypothesised that due

to the exact same images being displayed to the participants to memorise approximately three days apart, that after each session the participants memory of that specific image was slightly more vivid. Thus, by the final exercise induced fatigue session the image displayed was embedded within their memory therefore allowing the participants to select the most appropriate response resulting in an enhanced performance. Consequently, a learning effect has potentially taken place within the visual short-term memory assessment, subsequently equating to an enhanced cognitive performance within this task.

The two remaining tests were the visual perception tasks, Form Constancy and Figure Ground. These two tests were incorporated into this reduced battery of tests due to the newfound desire to use such visual tasks “pitch-side” (McCrory et al., 2013). So far there are no such tests that can integrate these visual assessments into their neurocognitive battery, therefore the use of these tests in an environment resembling a pitchside assessment was revolutionary. As their use pitch-side is currently found wanting, there is a lack of studies that have examined the influence of such tests to factors such as fatigue. Our results display that within the Form Constancy assessment there is a trend in improved performance across each assessment, however this did not reach significance. Whilst Figure Ground experiences a similar trend in improved performance at each assessment point, however performance is significantly higher at exercise sessions two and three compared to baseline. This enhanced performance on Figure Ground is the result of an improvement in scores compared to baseline in the majority of individual’s analysed rather than a few participants resulting in skewed data. Further, as a result of the lack of studies examining the impact of fatigue on visual perception tasks which could be used to address a possible concussion, it makes it difficult to define whether these findings are common.

The exercise induced within this study is one possible explanation as to why some of the RESET assessments displayed facilitating effects on the cognitive performance of individuals within our study. Assessments such as Reaction Time are likely to improve post-exercise due to heightened physiological factors caused by exercise such as elevated heart rate and adrenaline, thus improved reaction time. Whilst other assessments, such as Visual Short Term Memory, have been equally suggested in previous studies to be facilitated post-exercise. However, it must be noted that this is only a possible explanation as to why cognitive performance in some of the assessments significantly improved. There is a variety of other external factors which could equally have played a role in influencing cognitive performance post-exercise. One of which is the likelihood that learning/practice effects may have taken place, due to repeated short-term exposure to these tests, which could have similarly significantly improved cognitive performance. Therefore, it is difficult to indisputably argue that the reason for the significant improvement in cognitive performance in RESET post-exercise is due to the exercise itself or rather the protocol of the study.

Nevertheless, some previous findings present a plausible link towards the possibility that exercise may facilitate cognitive performance post-exercise, although within this study we must also consider the influence of practice effects. All the assessments, apart from Card Sort, display findings resembling improvement in cognition after each exercise session. However, it must also be considered whether this improvement is not due to exercise itself but due to the time interval between each session. The time interval between sessions within this study was between three to five days and therefore by the fourth session it is plausible that the repeated assessments within such a short period of time caused a learning effect and thus increased cognitive score. As a result of this, it is not known whether exercise itself resulted in the facilitation of cognition. It could be similarly argued that due to such short intervals between

repeated sessions of RESET that a learning effect may have masked the true influence of the exercise. Therefore, not only is it unknown as to whether exercise was the reason as to why cognitive performance significantly increased, but it is also unknown as to whether exercise had any kind of influence of cognitive performance at all, and if it did whether practice effects concealed the true effect of the exercise. Consequently, studies looking to conduct a similar protocol should increase the time interval between sessions to nullify the plausibility of a learning effect taking place and influencing cognitive performance and thus indisputably determine the influence of exercise alone.

There had only been one other study, to date, that assessed the reliability of a computerized neurocognitive test post-exercise. Covassin et al., (2007) assessed the influence of a maximal exercise test, inducing fatigue, on the performance of an ImPACT test. As previously mentioned, they found that there was no significant change in performance post-exercise in the visual memory, motor processing speed and reaction time composites, whilst verbal memory was significantly inhibited post-exercise. Firstly, due to verbal memory being impaired post-exercise in a healthy cohort, this will result in the clinician not knowing whether the decrement in performance observed when assessing someone pitchside is due to fatigue itself or a possible concussion, and therefore is unreliable. Further, ImPACT is known to take 25 minutes to administer. Thus, the influence of fatigue on the first cognitive tests would be dramatically more than its influence on the tests at the end of the ImPACT test battery. In addition, the first ImPACT composite to be assessed post-exercise was the verbal memory composite, which coincidentally was the only test found to be significantly impaired post-exercise. Equally, by forming composite values it masks the effect of fatigue on each individual assessment. Further, it is unlikely that the tests conducted were randomized in order for fatigue to influence all ImPACT assessments administered. Therefore, as ImPACT

takes 25 minutes to complete, in which the influence of fatigue will diminish, the tasks not being randomized and also the formation of composite scores it generates doubt as to whether their findings are reliable. As a result the findings that which verbal memory was the only composite to be significantly affected by fatigue becomes more clear. This is likely due to the effects of fatigue wearing off before the whole of ImPACT was completed and also due to the lack of randomization, therefore the verbal memory composite experienced the full effect of fatigue compared to the other composites analysed.

Further, as previously mentioned the current neurocognitive assessment applied pitch-side is SCAT-3. However, the results of the SCAT-3/SAC can be perceived as subjective. This essentially creates a “cloud of uncertainty” in terms of an accurate diagnosis of a concussion, thus potentially putting the athlete at further risk of injury if they are misdiagnosed. Thus, in order to diminish this uncertainty in the diagnosis of a concussion and also to reduce intra-experimenter differences, we applied an objective neurocognitive assessment that could be administered as a replacement of the SAC. This would therefore aid the clinician in their diagnosis of a concussion through the use of an objective assessment. These preliminary results of using a new computerized neurocognitive test (RESET) as a pitchside assessment is promising as no assessments used within this shortened RESET battery were negatively influenced by fatigue, thus demonstrating its plausibility to be used pitch-side.

Using RESET, we administered a shortened protocol that could be completed within a ten minute timeframe, and therefore applicable within a HIA. Further, due to the reduction in time taken to complete the assessments used, it is likely that all, if not most of the assessments were effected by fatigue within each session, unlike previous research. Nevertheless, to further strengthen our protocol we randomized the order of these tests anyway, this ensured that after completion of all three exercise-induced fatigue sessions all cognitive tasks

experienced the influence of fatigue for each participant. Subsequently, the results found are all due to the direct influence of fatigue. Further, we analysed each individual assessment without forming composites allowing us to clearly identify assessments that were more or less influenced by fatigue than others. This is important as it is essential that the neurocognitive tests used pitch-side are unaffected by fatigue so that the accuracy in diagnosing a concussion is as high as possible.

To further strengthen our findings we conducted multiple exercise-induced fatigue sessions. This would subsequently nullify the effects of confounding factors that could influence both fatigue and also performance on neurocognitive tests, such as caffeine which has been found to significantly improve reaction time (Kruk et al., 2001) and has also been found to significantly improve performance stroop tasks and visual information processing tasks (Hogervorst et al., 2008). Along with the after effects of any recent additional exertional exercise, the time of the day, hormones and the athlete's hydration status, which if diminished has been found to result in short term memory and perception task deficits (Masento et al., 2014). Thus, examining the effects of performance after a single exercise bout may not be accurate due to potential factors directly influencing performance and skewing results. Therefore, through the use of multiple assessments we were able to eradicate the effects of these factors and thus have a better knowledge of the direct influence of fatigue on RESET cognitive performance.

In addition, the practicality in completing the RESET assessment pitch-side is unarguable. The RESET software can be used on portable devices such as Tablets, ensuring that these neurocognitive tests can be applied pitch-side in an effective manner. Further, the results that are obtained are instantly saved to an online database which when accessed clinicians are able to directly compare scores within-individuals with graphs produced to outline their

performance on specific tasks across time. Combined, this all aids the clinician in making a fast, accurate non-subjective assessment when diagnosing a potential concussion.

However, the testing environment used within this study was not a replica of the environment in which you would apply the RESET neurocognitive pitch-side. The test was completed within lab conditions and therefore was not directly related to the factors that are exhibited pitch-side and cannot be repeated within a lab. Further, the quantity of exercise that the participant had undergone that day and the hydration level of that athlete was also not controlled for throughout all three sessions. This may have led to slight discrepancies between each testing condition.

Future studies should look to address this issue. Through taking the shortened RESET assessment battery pitch-side, and addressing the effect of fatigue on cognitive performance scores, it will resemble a more accurate environment in which the RESET assessment may be used. Thus, providing more honest data on the reliability of the RESET cognitive battery. Further, no studies have physically implemented a computerized neurocognitive assessment pitch-side. Thus, if future studies would pursue this potential protocol it would instigate the first findings in the reliability of a computerized neurocognitive test pitch-side.

Therefore, there are many questions still to be answered by the RESET assessment battery. It must be noted that the exercise study conducted here was an additional assessment on the reliability of RESET itself, and not to be interpreted as a potential current pitch-side concussion protocol as it has not yet been assessed for its sensitivity to concussion. Further, the most appropriate computerized assessments to be used pitch-side needs to be defined. These assessments must be fast to administer, sensitive to concussion itself and reliable against confounding factors such as fatigue. The tests used within this study were based

around other tests identifying their reliability within a similar environment and also previous tests finding them to be sensitive to concussion. Due to time constraints, both the exercise-induced fatigue and the RESET test-retest studies were carried out alongside one another. This meant that the reliability of the RESET assessments was not known before beginning the exercise-induced fatigue examination. Thus, in order to decipher the best tests to be used pitch-side, or in this case after exercise, previous studies' findings on similar assessments and also current protocols (SCAT-3) were used to best select the tests that could be used pitch-side.

Thus, due to this some assessments of RESET maybe more reliable and potentially more beneficial to be used pitch-side. Therefore, all assessments of RESET should be analysed in future research within similar conditions to indicate their reliability post-exercise. This would define the tests that are most reliable and from here the sensitivity of those tests can be examined to determine the efficiency of these tests in identifying a concussion. Subsequently, this would provide a group of RESET tests that are not affected by exercise (highly reliable) and also sensitive to concussion creating the best assessment of concussion pitch-side possible.

Another possible limitation to our study is our means to establishing each individuals  $\text{VO}_2$  max. We used a submaximal exertion test to then predict each individuals  $\text{VO}_2$  max which was then used to establish the subsequent power output used to establish 70%  $\text{VO}_2$ . However, using this prediction we may have under or overestimated the wattage provided to the individual. The gold standard of identifying an individuals  $\text{VO}_2$  max, and therefore wattages used to elicit a certain percentage of the individuals  $\text{VO}_2$  max, is through the use of an actual  $\text{VO}_2$  max test which is the only way to accurately determine an individual's maximum aerobic capacity. Nevertheless, our study set out to exercise individuals to fatigue, therefore even if

the submaximal  $\text{VO}_2$  max test used did under or overestimate individuals maximal aerobic capacity, we were still able to establish a state of fatigue which was identified through the RPE scale, the inability to maintain RPM and voluntary exhaustion. The only aspect that this affected is the wattage cycled at, this is the only factor that would be slightly altered as a result of the predicted  $\text{VO}_2$  max test used.

Further, we used a cycle ergometer to complete the exercise sessions. Once again this is not specific to sports such as Rugby, and therefore to the type of exercise in which RESET would likely be used to assess. Nevertheless, a meta-regression analysis recently found that both running and cycling improved cognitive performance post-exercise (Lambourne et al., 2010). Moreover, cycling resulted in significantly higher cognitive performance than running. Therefore, this could be a factor as to why we found significant improvements in three of the assessments post-fatigue compared to baseline. Nevertheless, running was also found to improve cognitive performance post-exercise, although not to the same extent. Therefore, post-fatigue performance should once again not be influenced negatively by fatigue. However, this should be examined within future research to undoubtedly determine if more sport-specific tasks such as running results in significant alterations in neurocognitive performance. Thus, further illustrating RESET's reliability to be used pitch-side further.

Equally, the type of format of exercise assessed was not sport-specific. We incorporated an endurance exercise test in order to assess the influence of fatigue. However, many sports are not endurance tests and commonly are formed of short-intermittent sprints between phases of play instead (Rugby). Therefore, rather than exercising at a given output and intensity over a prolonged period of time, a more high intensity sprint protocol maybe more appropriate to ensure that the exercise conducted was sport specific.

Additionally, in order to be a neurocognitive pitch-side assessment used by professional athletes, it should firstly be assessed within this population. Even though we examined physically active participants, it needs to be established whether this non-significant effect of fatigue on cognitive performance is also found within elite athletes. Studies should look to establish this prior to determining the sensitivity of such tests in order to undeniably define the reliability of these tests in both population's, athlete and non-athlete, due to its probability in being used within both.

Future studies should look to expand the results found presently. Through assessing various exercise intensities such as a sport-specific exercise protocol, it would further strengthen the reliability of RESET. Through exercising individuals in a sport-specific manor it will ensure that the reliability values obtained are very accurate to a sporting environment. Thus, providing further information on the reliability of the RESET assessment battery and develop the knowledge of its ability to be used as a concussion assessment tool. Further, studies have found other cognitive assessments to be influenced by exercise dependent on the intensity of the exercise elicited. Therefore, through examining a range of exercise intensity values it will provide us with more knowledge of the influence of these exercise intensities on specific RESET assessments and may allow us to identify the best tests to be used within the pitch-side assessment.

In addition, once the reliability of RESET has been determined, it would be intriguing to examine the influence of a training and/or match environment on neurocognitive performance in professional players after the reliability of RESET had been further established pitch-side. The assessment of training and/or matches would enable the RESET test battery, to be scrutinised for its reliability within a situation that the athletes are experiencing impacts/subconcussive blows to the head. Further, a training environment will be more

representative of a sport-specific situation, not only in terms of physical fatigue but mental fatigue also. Whilst competing in sport, athletes regularly have to think about various aspects such as tactical plays, positioning and often have to carry out problem solving tasks. As a result of this it could be considered that athletes may be experiencing mental fatigue whilst completing the concussion assessment, therefore it is important to determine if mental fatigue has any effect on the reliability of the RESET test battery. Thus, administering a computerized neurocognitive, pitch-side concussion test within a training environment will determine a more accurate and representative reliability score of the cognitive assessment in healthy individuals. Applying such a test during a training or match environment will allow for a more in depth test of reliability of the cognitive test (RESET) through determining its reliability against both mental and physical fatigue and thus it's potential use in a more representative pitch-side environment. Therefore, if future studies look to apply this protocol it will enhance the understanding of RESET or any other computerized cognitive tests to be used pitch-side and would indisputably determine its reliability as a concussion tool, due to it examining individuals in a sport-specific environment who are open to head impacts and also suffering from physical and potentially mental fatigue. Subsequently, this will determine RESET's overall potential to be used as a pitch-side test in terms of reliability, prior to determining it's sensitivity to concussed athletes.

After all of these reliability assessments have been examined; sport-specific environment (training/matches), assessing varying exercise modalities and intensities it is then important to examine RESET for its sensitivity to identify concussed individuals. It is important to ensure the reliability of RESET first as a concussion assessment battery, as if unreliable in different situations and under different constraints then the sensitivity of RESET itself is trivial.

## **Chapter 5 – Conclusion**

The purpose of our study was to evaluate the plausibility of a new computerized neurocognitive assessment (RESET) to be used during a pitch-side diagnosis of a concussion. In order to determine the credibility of RESET to be administered pitch-side, the influence of fatigue was assessed to determine its reliability to be used pitch-side. However firstly, the reliability of RESET had to be established over a clinically relevant time period that is a common interval to test for concussion. This would therefore define the general capability of RESET to be used as a test for concussion, as if it was not reliable from a common interval used to examine baseline performance to a test for a potential concussion, then it would not be acceptable to be used pitch-side.

The results of this preliminary study found that RESET had moderate to strong reliability over a clinically relevant time period to test for concussion. Further, RESET displayed better or similar reliability values to findings on the reliability of other computerized neurocognitive assessments. Thus overall, the reliability of RESET over a clinically relevant time period suggests that it can be used as a reliable neurocognitive tool (Anastasi, 1998).

A further study was conducted in order to determine whether RESET could be used as a pitch-side concussion assessment and therefore reduce the subjectivity of a concussion diagnosis. Through incorporating a shortened RESET battery we looked to form a more objective concussion tool that could be used within the timeframe given to conduct a pitchside assessment. As this was the first study to our knowledge to incorporate a computerized neurocognitive assessment pitch-side and within the ten minute HIA period provided by the Rugby Federation, we looked to assess RESET's reliability under fatiguing circumstances. Results found that no cognitive performance scores were negatively affected during fatigue.

Thus, RESET is reliable pitch-side and could therefore be used within this environment and under these time constraints provided within Rugby.

Future research needs to look at assessing the sensitivity of the RESET assessment battery to a diagnosed concussion. Equally, research should look at the influence of fatigue on the other assessments used within the RESET test battery that were not examined within this study. This would ultimately determine the most reliable tests to be used pitch-side. Corresponding with the RESET tests that have been found to be the most sensitive to concussion, a new condensed battery of tests can be formed to assist in the diagnosis of a concussion.

Overall, RESET therefore displays the potential to be used as an alternative computerized neurocognitive assessment which can be used both over a long test-retest interval to assess for a possible concussion and also be used pitch-side to help aid the clinician in the diagnosis of a concussion. Nevertheless, the reliability of RESET over a shorter-time interval within this study was found to be reduced. Thus, future studies should conduct further assessments into the reliability of RESET over various intervals. However, RESET does provide a more objective measurement of cognitive performance pitch-side and therefore could potentially assist in the diagnosis of a concussion.

## Chapter 6 – References

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## Chapter 7 – Appendix

### Screening Form

#### Screening Form- The Learning Brain (RESET) Study

I understand what is required of me within this study and I consent to participation in the study. The details provided below are answered to the best of my knowledge.

Exclusion Criteria	Yes	No
Are you current/have you recently been experiencing any lower extremity pain when you are exercising or when at rest		
Have you experienced a concussion within the last 12 months		
Have you got a cardiovascular illness? (If so, what?) .....		
Have you got a respiratory illness? (If so, what?) .....		
Do you suffer from any visual impairments (i.e. Colour blind) – if so what? .....		
Do you suffer from any learning disabilities? (If so, what?) .....		
Do you suffer from any attention deficit disorders?		
Do you have any cognitive deficiencies? (If so, what?) .....		
Is English your first language?		
How often do you exercise per week? What is your current physical fitness level?		
<div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;"> <input type="checkbox"/> Low (0-1 times per week)         </div> <div style="text-align: center;"> <input type="checkbox"/> Moderate (2-3 per week)         </div> <div style="text-align: center;"> <input type="checkbox"/> High (5+ per week)         </div> </div>		

Have you read, and understand all information provided to you and answered all the questions to the best of your knowledge? Yes/No

Name :  
Signed :

Date :

**Neuroplasticity and Neurorehabilitation Laboratory  
School of Sport, Exercise and Rehabilitation Sciences**

## **INFORMED CONSENT**

Participant Identification for this study:

### **The Learning Brain**

**Name of Researcher:**

**Please  
initial**

I confirm that I have read and understood the information sheet detailing the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

☐

I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reasons.

☐

I understand that where it is relevant to my research participation, data acquired may be analysed by responsible individuals from the University of Birmingham, or from regulatory authorities. I give permission for these individuals to have access to my data records.

☐

I agree to participate in submaximal exercise in different study sessions as outlined in the participant information sheets.

☐

I agree to attend four session at the Neuroplasticity and Neurorehabilitation Laboratory at the University of Birmingham's School of Sport, Exercise and Rehabilitation Sciences.

☐

I understand that All information collected about me during the course of the study is kept strictly confidential.

☐

I agree to take part in the above study.

☐

\_\_\_\_\_  
Name of Participant

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Researcher Name

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

(File: 1 for participant, 1 for researcher)

All information collected will be stored in accordance with the Data Protection Act 1998

### RPE Scale

rating	description
6	NO EXERTION AT ALL
7	
8	EXTREMELY LIGHT
9	
10	VERY LIGHT
11	
12	LIGHT
13	
14	SOMEWHAT HARD
15	
16	HARD (HEAVY)
17	
18	VERY HARD
19	
20	EXTREMELY HARD
	MAXIMAL EXERTION