The Cognitive Effect of Exercise Following Concussion in Children and Adolescents: When is Return-to-Play Safe?

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Abstract

Introduction

Traumatic brain injuries (TBI), including concussion, are among the most common injuries in children and can lead to lifelong disabilities and impairments. While the poor rate of recovery following severe TBI is well established for child and adolescent populations compared with adults, it is also important that we understand the post-concussion trajectory period in these populations. Furthermore, the effect of physical exertion on cognitive functioning of normal and injured children has yet to be identified. It is crucial to understand how the post-concussive course is affected by exercise in order to i) provide guidance regarding return to sports and ii) prevent further injury during the recovery of TBI. A thorough understanding of this will provide a basis for the development of appropriate return-to-play guidelines for the children and adolescent populations.

Rationale and Study Aims

This project aimed to examine the effect of exercise on the cognitive symptoms of concussion in children and adolescents over time following a concussive injury. More specifically, this study focused on changes in the information processing speed and attention in children and adolescents following an exercise routine during the post-concussive phase. The following four hypotheses were proposed: (1) participants with concussion will report increased physical symptoms and higher levels of cognitive impairment after exercise, (2) cognitive impairment and physical symptoms post-exercise will reduce from Day 2 (post symptom resolution) to Day 10, (3) at Day 10, physical and cognitive symptoms in the concussed group will be comparable to that of the non-concussed controls, both pre- and post-exercise, and (4) at Day 10, quality of life (QOL) will be predicted by post-concussive symptoms (PCS), as well as age, gender, and history of previous concussion.
Method

Thirty patients aged 10 to less than 18 years who presented to the emergency department of The Royal Children’s Hospital, Melbourne, with a concussion were recruited. A further 30 healthy controls were also recruited from the general public.

Once concussed participants reported that they were asymptomatic at rest, they were invited to attend the clinic (Day 2) and complete their first set of assessments. Subjective symptom report and cognitive function (using CogSport) were assessed, followed by an exercise routine, and then a repeat of the initial assessments. Quality of life (QOL) was also assessed at Day 10. This protocol was then repeated eight days later (Day 10) in order to better understand the effects of exercise and the pattern of recovery over time post-symptoms.

Results and Discussion

Results support the expected recovery pattern for PCS, regardless of exercise. Analysis of neurocognition found that recovery was dependent on the degree of cognitive demand, with an unexpected reduction from Day 2 to Day 10. Surprisingly, when compared to healthy controls, concussed individuals showed a reduction in PCS as well as faster reaction times on cognitive tasks.

This study supports the current return-to-play guidelines for children and adolescents, and suggests that the use of moderate exercise may be beneficial in the management of concussion post-symptom resolution.
Declaration

I, Vicky Manikas, declare that this thesis comprises only my original work towards the degree of Doctor of Philosophy and that due acknowledgement has been made in the text to all other material used.

This thesis is fewer than the maximum word limit in length, exclusive of tables, figures, bibliographies and appendices as approved by the Research Higher Degrees Committee.

Vicky Manikas
Preface

Chapter 5 of this thesis has been published as:


I, Vicky Manikas, was responsible for the data collection and analysis as well as the initial manuscript composition. V. Anderson, F. Babl and J. Dooley contributed to manuscript edits, and S. Hearps assisted with statistical data analysis.
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The Cognitive Effect of Exercise Following Concussion in Children and Adolescents: When is Return-to-Play Safe?

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Chapter 1 Traumatic Brain Injury

Preamble

Traumatic brain injuries (TBI) are among the most common causes of childhood death and permanent disabilities in developed countries (Sanchez & Paidas, 1999). The financial cost of TBI to society is significant and rising, with the total cost in the US being over $60 billion annually (Finkelstein et al., 2006). Mild TBI, which includes concussion, comprises 90% of all childhood TBI (Crowe, Anderson et al., 2012). Research has shown that concussion can lead to disruption in metabolic functions and ongoing cognitive and behavioural sequelae (Clapperton, Cassell & Wallace, 2003; Crowe, Catroppa et al., 2012; Wrightson & Gronwall, 1998).

Sports and recreational activities are the most common cause of concussion in children and adolescents (Crowe, Anderson et al., 2012), with millions of youth sustaining concussion each year. Although most fully recover following an isolated concussion, a significant minority develop prolonged symptoms and disability following injury (Blume & Hawash, 2012). Prolonged post-concussive symptoms (PCS) are likely due to interactions between the biological injury, pre-existing risk factors and psychosocial issues.

Studies indicate that premature return to active sport participation following a concussion presents an increased risk for more severe or prolonged PCS (McCrory & Berkovic, 1998). While the response to acute exertion may provide a marker for the individual’s readiness to return-to-play in adults, to date there has been no research examining the effects of exercise during recovery from concussion in child and adolescent populations. This study examined the effect of exercise on cognitive functioning, as well as subjective symptom complaints in children and adolescents following a concussion, in order to contribute to the development of appropriate return-to-play guidelines for this population.
Aims & Hypotheses

The aim of this project is to examine the effect of exercise on the cognitive functioning of children and adolescents following concussion. More specifically, this study will focus on changes in information processing skills (selective attention, reaction time) in children and adolescents following an exercise routine in the post-concussion period.

The following four hypotheses are proposed:

1. Participants with concussion will report increased physical symptoms and higher levels of cognitive impairment after exercise (Day 2).
2. Cognitive impairment and physical symptoms post-exercise, will reduce from Day 2 (post symptom resolution) to Day 10.
3. At Day 10, physical and cognitive symptoms in the concussed group will be comparable to that of the non-concussed controls, both pre- and post-exercise.
4. At Day 10, quality of life will be predicted by post-concussive symptoms, as well as age, gender, days post-injury, and history of previous concussions.

Part One: Defining Concussion

Definition and Classification Systems

While terminology in the fields of concussion, mild traumatic brain injury and mild (closed) head injury are fraught with ambiguity, each refers to a form of closed head injury. Closed head injury includes injuries that do not involve penetration of the skull and dural layer (these are called penetrating/perforating or open head injuries). The terms mild closed head injury and mild traumatic brain injury are often used interchangeably, however, it is important to note that only
mild TBI necessarily involves the presence of cerebral injury. ‘Concussion’ has been recognised for centuries. While historically it referred to a head injury of any severity, today it is often employed to describe a blow to the head involving a transient loss or alteration of consciousness without any associated structural damage, and has become particularly associated with sport-related head trauma. Of note, the term ‘concussion’ is often used interchangeably with ‘mild traumatic head injury’ or ‘mild traumatic brain injury’. Where, and if, there is a line to further discriminate these terms remains a topic of debate. In recent years, terminology has been further complicated by the introduction of a division between ‘complicated’ and ‘uncomplicated’ mild head injury, with the latter referring to instances where brain pathology is identified and/or where PCS persist (Yeates & Taylor, 2005).

The International Conference on Concussion in Sport consensus paper, resulting from an expert consensus meeting in Zurich in 2013, has attempted to provide a distinction between the definitions of concussion and mild TBI (McCrory, Meeuwisse, Aubry et al., 2013). This position paper acknowledges that these terms should not be used interchangeably as they refer to different injury constructs. It was unanimously decided by the panel that concussion should be defined as follows (McCrory, et al., 2013):

Concussion is a complex pathophysiological process which affects the brain and is a direct result of traumatic biomechanical forces. The various features of concussion, which include clinical, pathogenic, and biomechanical injury constructs include the following from the Zurich Consensus Statement of Concussion in Sport:
1. Concussion may be caused either by a direct blow to the head, face, neck, or elsewhere in the body with an “impulsive” force transmitted to the head.

2. Concussion typically results in the rapid onset of short-lived impairment of neurologic function that resolves spontaneously.

3. Concussion may result in neuropathological changes but the acute clinical symptoms largely reflect a functional disturbance rather than a structural injury.

4. Concussion results in a graded set of clinical symptoms that may or may not involve loss of consciousness. Resolution of the clinical and cognitive symptoms typically follows a sequential course; however, it is important to note that in a small percentage of cases, post-concussive symptoms may be prolonged.

5. No abnormality on standard structural neuroimaging studies is seen in concussion.

In previous years, concussion was often classified as either simple or complex, depending on the duration of the PCS following the injury (McCrory et al., 2004). However, this terminology has since been abandoned as it does not fully differentiate and describe the entities. Similarly, while the classification of complicated and uncomplicated mild head injury has emerged more recently, it is also unable to reliably differentiate the severity of injuries or to predict recovery outcomes.

After systematic review of the literature, and expert input, the Zurich panel has concluded that between 80-90% of all concussions are resolved within a 7-10-day period; however, this trajectory may be longer in children and adolescents. Clinically, when evaluating a person for a suspected concussion, the panel has recommended that one or more of the following clinical domains are assessed:
(a) Symptoms – somatic (e.g. headache), cognitive (e.g. feeling like in a fog), and/or emotional
(b) Physical signs (e.g. loss of consciousness, amnesia, poor balance)
(c) Behavioural changes (e.g. irritability)
(d) Cognitive impairment (e.g. slowed response times, attentional problems)
(e) Sleep disturbance (e.g. insomnia)

At their most recent conference in Berlin in October 2016, the Concussion in Sport Group focused on deepening the understanding of concussions specifically in sports. The Berlin expert panel modified definition of sports-related concussion from the previous Concussion in Sport Group as follows:

*Sport related concussion (SRC) is a traumatic brain injury induced by biomechanical forces.*

*Several common features that may be utilised in clinically defining the nature of a concussive head injury include:*

- SRC may be caused by either direct blow to the head, face, neck or elsewhere on the body with an impulsive force transmitted to the head.
- SRC typically results in the rapid onset of short-lived impairment of neurological function that resolves spontaneously. However, in some cases, signs and symptoms evolve over a number of minutes to hours.
- SRC may result in neuropathological changes, but the acute clinical signs and symptoms largely reflect a functional disturbance rather than a structural injury and, as such, no abnormality is seen on standard structural neuroimaging studies.
SRC results in a range of clinical signs and symptoms that may or may not involve loss of consciousness. Resolution of the clinical and cognitive features follows a sequential course. However, in some cases symptoms may be prolonged.

The clinical signs and symptoms cannot be explained by drug, alcohol, or medication use, other injuries (such as cervical injuries, peripheral vestibular dysfunction, etc) or other comorbidities (eg, psychological factor or coexisting medical conditions) McRory, et al., 2017)

Features of Concussion

There has been speculation regarding whether or not the symptoms of concussion are unitary and fall across a spectrum, or if different concussion sub-types exist. These subtypes may include differences in clinical manifestations (confusion, memory problems, loss of consciousness), anatomic localisation (e.g., cerebral versus brainstem), biomechanical impact (rotational versus linear force), genetic phenotype (ApoE4 positive versus ApoE4 negative), and neuropathological change (structural injury versus no structural injury). It is unlikely that these factors operate independently and several may interact with each other.

The immediate symptoms and indicators of a concussion, generally referred to as post-concussive symptoms (PCS), include: changes in athletic ability, vacant stare, fogginess, confusion, memory disturbance, loss of consciousness, increased emotionality, coordination difficulties, headache, dizziness, and vomiting. Typically, children and teenagers make a full recovery from a single concussion. However, the process of recovery can take time and neurobehavioural problems can persist in the days, weeks, or even months following a concussive injury, with 1.5-11% of concussed youth symptomatic for more than one month after injury (Blume & Hawash, 2012). PCS can be divided into three domains (Aubry et al., 2002):
1. **Somatic** – these symptoms include headaches, fatigue, sleep disturbance, nausea, vision changes, tinnitus, dizziness, balance problems, and sensitivity to light and noise.

2. **Cognitive** – slowed thinking or response speed, mental fogginess, poor concentration, distractibility, trouble with learning and memory, disorganisation, and problem-solving difficulties.

3. **Emotional/Behavioural** – lowered frustration tolerance, irritability, increased emotionality, depression, anxiety, clinging, and personality changes.

Research suggests that, while females have a higher risk of post-concussive headache, it is unclear if there is a gender difference in cognitive recovery (Blume & Hawash, 2012). Neuroimaging techniques have demonstrated that there is a correlation between PCS and functional neurological changes (Fay 2010). However, it has also been demonstrated that various pre-existing factors and psychosocial factors can affect risk for prolonged PCS.

**Somatic Symptom Report after Concussion**

The most common PCS include headache, the sensation of pressure on the head, dizziness, balance problems, fatigue, difficulty sleeping, restlessness, sensitivity to noise and light, blurred or double vision, nausea, and tinnitus (Broshek, De Marco & Freeman, 2014; Luce, 1986; Miller & Low, 2001). Studies have shown that headaches and balance problems are the most commonly reported physical symptoms five days post-injury, while drowsiness is most commonly reported at 30 days post-injury (Leddy, Sandhu, Sodhi, Baker & Willer, 2012).
There are a number of common sequelae of concussion which are the same in children and adults. These include reduced speed of information processing, poor attention, and impaired executive function (Anderson, 2001; Collie, Darby & Maruff, 2001; Echemendia & Jullian, 2001; Macciocchi, Barth, Alves, Rimel & Jane., 1996; Maddocks & Dicker, 1989). It is also recognised that concussion may have various secondary impacts on social and educational activities common in the child and adolescent populations, resulting in difficulties acquiring new knowledge and attending to school work. It has also been found that some children may experience various post-concussive behavioural sequelae even though their results on neuropsychological assessments are normal (Anderson, 2001).

Concussions that are sustained during childhood or adolescence differ to those which are sustained in adulthood. For example, the impact of a TBI is affected by the geometry of a child's developing skull and brain; there is a greater prevalence of diffuse injury and less incidence of focal injury within the child and adolescent populations (Aubry et al., 2002; Cook, Schweer, Shebasta, Hartjes & Falcone, 2006). This is because the skull of a child is less rigid and (particularly in younger children) is incompletely fused in comparison to the adult skull. Whilst the flexibility of the skull may have a cushioning effect, it can also result in greater shearing forces on impact, as well as in the stretching of nerve fibres in the underlying nerve matter (Ponsford et al., 1999) and in the cortex (Oddy, 1993). The brain of a child is also vulnerable to the effects of head injury forces, due to the large size and weight of the skull relative to the small neck supporting it and overall body weight, particularly in younger children.

Studies also show that the brain’s tolerance to biochemical forces differs between adults and children. Specifically, research shows that a 2-3-fold greater impact force is required to produce the same clinical symptoms in children as adults (Ommaya, Goldsmith & Thibault, 2002; Ponsford et al., 1999). This is a result of several factors, such as age dependent physiological response to
mechanical stress, the differing geometry of the skull and brain, and the constitutive structures of the head. Therefore, whilst the child may not display symptoms of the same severity as an adult, the physical effects on the child’s brain and the recovery period may in fact be greater due to the plasticity and underdeveloped nature of its skull and brain. This suggests that, while the immediate effects of a concussion may not be as obvious in children as they are in adults, the impact on the brain and the typical recovery patterns may differ as a result of age. It is therefore important that children and adolescents are not simply treated as though they are “little adults” since the mechanisms, response, and the recovery following a concussion are very different than that of adults (Cantu, 1986; Cook et al., 2006).

**Cognitive Symptoms Post-TBI**

As the brain of a child or adolescent is more vulnerable to the impact of TBI, the risk of functional impairment following concussive injuries is likely to be greater in younger populations than it is in adults (Anderson, 2001; Taylor et al., 2010). This proposition is supported by the observation that younger concussed athletes are reported to show a more prolonged neuropsychological recovery period than adults (Davis & Purcell, 2013).

Following a concussive injury, children are generally observed for a short period of time before being discharged without a hospital admission. In the days following injury, typical cognitive symptoms of concussion in children are reduced attention, headache, delayed response speed, nausea, impairment in memory, and emotional dysregulation (Taylor et al., 2010). Whilst adult literature suggests that these symptoms remit in 7-10 days (Broglio & Puetz, 2008; Guskiewicz, Ross, & Marshall, 2001; Iverson, Brooks, Collins, & Lovell, 2012), research suggests that recovery is more prolonged for children and adolescents (Field, Collins, Lovell, & Maroon, 2003; McCrory, Collie, Anderson, & Davis, 2004; Purcell, 2009). This view has been supported by more recent
research which found an increased risk of post-concussional symptoms in children and adolescents with mild TBI for at least three months post injury (Barlow, Crawford, Stevenson, Sandhu et al., 2010).

Research also suggests that complex cognitive functions are most affected following a concussion. For example, simple response speed has been found to show no difference at five days post-injury when compared with pre-injury levels, while impairments in decision-making are observed even at ten days post-injury (Crowe, Catroppa, Babl & Anderson, 2012; Tate, McDonald & Lulham, 1998). As these skills are important for common day-to-day activities in childhood (such as school work and learning), the period following a concussive injury is often quite difficult for children and adolescents, as their days often require learning new skills and acquiring knowledge.

Ponsford and Kinsella (1992) published one of the first studies to examine the effects of TBI in adulthood. They looked specifically at impaired attention and deficits in speed and/or accuracy of performance on tasks of increasing complexity in a sample of adults with varying injury severity. Results indicated that there was no evidence of deficits in focused attention, sustained attention, or supervisory attentional control, but they did identify a deficit in speed of information processing. Significant differences were found on both simple- and choice-response time tasks, suggesting the presence of reduced speed of processing for adult survivors of head injury. These results suggest that, where possible, participants tended to sacrifice speed in order to maintain accuracy. Where this was not possible, they made significantly more errors than controls. These results remain to be replicated in both child and adult concussion.

Also in adults, Dikmen and colleagues (2004) found that penetrating, moderate and severe injuries were associated with persisting cognitive deficits. In contrast, mild TBI has a complex trajectory that is difficult to understand by comparison. Sports medicine studies indicate that cognitive deficits associated with sports-related mild TBI generally resolve within days and rarely
persist more than three months (Bleiberg, Cernich, Cameron, Sun, Peck & Uhorchack, 2004; McCrea et al., 2003). It is important to note that the above research relates mostly to individuals who are generally motivated and performance driven, such as professional athletes; therefore, we are not able to generalise these findings to all patients who experience mild TBI. Furthermore, the presence of loss of consciousness or post-traumatic amnesia, which correlate with outcomes in more severe TBIs, is not a reliable predictor of cognitive deficits in concussive injuries. Sports medicine literature has found that following a mild TBI, cognitive impairments are most severe immediately following injury and typically resolve within 48 hours. Authors have therefore highlighted the importance of cognitive rest following a mild TBI (Brown, Mannix, O’Brien, Gostine, Collins & Meehan, 2014).

Impaired attention as a result of TBI is frequently reported in the adult literature, but only a limited number of studies have investigated these difficulties in the paediatric population. In an early study of attention deficits in children following TBI, Murray and colleagues explored this domain using an information processing model consisting of the following stages: (1) feature extraction; (2) identification; (3) response selection; and (4) motor adjustment (Murray, Shum & McFarland, 1992). They administered a visual-spatial choice reaction time (CRT) task to identify at which stage the attentional process was breaking down from a stimulus-response perspective. They found that children with severe injuries were more likely to be impaired in terms of response selection and also displayed slower motor execution. Performance of participants with milder injuries did not differ from that of healthy controls.

Similar results were found in a subsequent study by Kaufmann, Fletcher, Levin, Miner and Ewing-Cobbs (1993), who demonstrated that, at six months post-injury, severely injured children exhibited residual impairment in sustained attention, as measured by the continuous performance task. Performance of children with mild-moderate injuries did not differ from that of controls. Based on these studies, it has been argued that severe TBI, in particular, is associated with impaired
attentional function. Subsequent research has further confirmed this pattern of impaired attention and slowed speed of processing following TBI in childhood (Anderson & Catroppa, 2005; Anderson, & Pentland, 1998; Catroppa & Anderson, 2005), but few studies have investigated these skills in children sustaining mild head injury or concussion.

**Emotional and Behavioural Sequelae of TBI**

Emotional and behavioural sequelae of TBI consist of a spectrum of symptoms including both internalising and externalising features (Bloom et al., 2001; Max et al., 1998; Shwartz et al., 2003; Wade, Michaud & Brown, 2006). Research has also identified a link between elevated rates of clinical syndromes, including attention deficit hyperactivity disorder (Bloom et al., 2001; Max et al., 1998; Max et al., 2005; Wassenberg, Max, Lind-Gren & Schatz, 2004), oppositional defiant disorder (Bloom et al., 2001; Max et al., 1998), depression, and anxiety disorders (Grados et al., 2008; Max et al., 1998; Vasa et al., 2002; Wade, Michaud & Brown, 2006). Research in school-age children suggests that internalising problems are more likely to resolve over time than externalising problems (Bloom et al., 2001). There is, however, a limited amount of research which examines the long-term development and maintenance of behaviour problems among children with less severe insults, such as concussion.

**Epidemiology of Concussion**

TBIs are the most common cause of death and disability in children, accounting for approximately 7,000 deaths in the United States every year (Langolis, Rutland-Brown & Wald, 2006). TBI is a common childhood injury and is associated with high rates of long-term disability and even mild TBI can lead to ongoing cognitive and behavioural sequelae.
In Australia, early research indicated that there were 27,434 presentations to hospitals across the country with a diagnosis of TBI between July 1996 and July 1997, resulting in a rate of 149 per 100,000 population. The highest age-specific rate was for adolescents aged between 15 and 19 years (244 per 100,000 population). Following stroke, TBI is the most prevalent form of acquired brain injury, resulting in approximately 22,710 hospital admissions in Australia between 2004-2005 (Helps, Henley & Harrison, 2008). More recent epidemiological data in Australia have shown the annual incidence rate of TBI to be between 149-500 per 100,000 cases across the age spectrum, 43.8% of which occur in children and adolescents aged below 19 years (Crowe et al., 2012). With statistics on more severe TBI readily available, the frequency of mild head injury is difficult to assess. Meta-analytic studies indicate that definitions of mild head injury vary from a bump to the head to concussion, and furthermore, only a small proportion of victims with concussion ever present for medical attention.

Research addressing child injuries specifically, indicates that approximately 250 every 100,000 children experience TBI each year (Anderson, Beauchamp, Rosema & Soo, 2013). In fact, one out of every 30 newborn children will sustain a TBI, most often a concussion, before the age of 16 (Annegers, 1983). Hospital records tend to underestimate the number of cases of mild TBI/concussion that are treated, but not formally admitted. For example, Mitra et al., (2007) found 765 per 100,000 Emergency Department (ED) presentations compared to 75 per 100,000 hospital admissions to Victorian paediatric hospitals. This under-reporting was also demonstrated in a more recent Victorian audit at the Royal Children’s Hospital (RCH) in Melbourne, which found that the rate of paediatric presentations to the ED for concussion were more than 10 times greater than presentations for more severe injuries (Crowe et al., 2012). Of note, this figure is still likely to underestimate the actual occurrence of concussions, as a large number of TBI injuries are treated by general practitioners and do not result in either hospital presentation or admission (Crowe et al., 2012).
It is difficult to determine the main causes of childhood concussion; however, it has been suggested that a large proportion of reported concussions and mild TBI are sustained during participation in sport. Consistent with this, a review of paediatric admissions to Victoria’s tertiary referral hospital during 2004-2005 found that sports were the main external cause for head injury in children aged between 9 and 16, with Australian Rules football accounting for over 30% of sports-related TBIs (Crowe, Babl, Anderson & Catroppa, 2009).

**Age**

Causes of TBI within the child and adolescent population are often related to age and developmental level. For instance, trauma that is a result of falls or child abuse is more common among infants than older children. Research by Holloway, Bye and Moran (1994) found that 61% of non-accidental injuries (including but not limited to head injuries) occur in children less than 12 months old, commonly resulting in more severe injury and higher mortality and morbidity than accidental injuries. Children have also been found to be at a higher risk of TBI during the pre-school stage as a result of falls and pedestrian accidents. In comparison, school-aged children and adolescents are more frequently victims of sporting, cycling, or pedestrian accidents (Holloway, Bye & Moran, 1994).

There is also evidence that fatality rates from more severe injuries tend increase as age decreases. Michaud et al., (1992) found that 14% of injuries in children aged over 14 years resulted in a fatality, while the fatality rate for children under the age of 2 was 50%. Consistent with this, they found a more positive recovery trajectory with increasing age. These results have been replicated by the concussion research team at RCH (Anderson et al., 2005) and demonstrate a greater level of vulnerability, which may be a direct result of age at injury. This vulnerability may have great implications for the recovery time and potential permanent or long-term impairment.

To date, there is little or no evidence that this vulnerability is present in the context of milder
injuries and concussion (Anderson et al., 2005; Anderson et al., 2009), although some early studies do describe significant problems in young children sustaining mild TBI (Wrightson & Gronwall, 1989; McKinlay, Grace, Horwood, Fergusson, Ridder & MacFarlane, 2008).

Sex

Research has consistently found that there is an effect of sex involved in sustaining a TBI. Kraus (1995) found that school-aged males are more than twice as likely as aged-matched females to suffer TBI and to sustain severe trauma. However, girls have been found more likely to sustain TBI resulting from falls or accidents whilst being passengers in cars (Berney, Favier & Froidevaux, 1994).

Interestingly, rates of TBI have been found to increase in males throughout childhood and adolescents, while there appears to be a decline in TBI rates in females over the same developmental stages (Kraus, Fife, Cox, Ramstein & Conroy, 1986). It is possible that these sex differences may be due to males tending to be more physically active and prone to exploratory behaviour than females (Lehr, 1990).

A recent review by Abrahams, McFie, Patricos, Posthumus and September (2013) looked at 23 studies that investigated whether there was a difference in concussion risk between males and females. Ten studies showed that women had an increased risk of concussion, four suggested that males had an increased risk, and nine studies found no association with risk and gender. When breaking the samples up into sport type, these studies found that in sports where rules and physicality are more equal between sexes (such as basketball and soccer), women appear to be at greater risk. However, when all types of sports are collectively analysed, there is low level of certainty that sex is a risk factor for concussion. This review suggests that further research be conducted which includes measures of exposures, so that a reliable correlation between sex and concussion risk is identified.
**Psychosocial Factors**

Research investigating incidence rates of childhood TBI has consistently found that it is most likely to occur on weekends, holidays, and afternoons. This is because children are more likely to be involved in sports and leisure activities during these times. Many have suggested that these injuries are a result of reckless behaviour in poorly supervised environments (Chadwick, Rutter, Brown, Shaffer & Traub, 1981; Dalby & Obrzut, 1991). Research has also consistently found that TBI is more common in families where parents are socially disadvantaged, unemployed, or emotionally unstable (Anderson et al., 1997; Brown, Chadwick, Shaffer, Rutter & Traub, 1981; Rivara et al., 1993; Taylor et al., 1995).

Furthermore, parental neglect and poor supervision (Moyes, 1980), as well as childrens pre-existing learning and behavioural deficits (Asarnow et al., 1991; Brown et al., 1981; Craft, Shaw & Cartlidge, 1972), have been found to increase TBI incidence rates. It has also been suggested that recovery following a TBI may be directly influenced by premorbid cognitive, behavioural, and social disturbances in the child’s home, social, and personal environment; with continued debate about whether or not children who sustain TBI are different from the general population in pre-injury characteristics (Perrot, Taylor & Montes, 1991).

**Mechanics and Pathophysiology of Concussion**

Changes in an individual’s conscious state are used as the primary means of determining the severity of a TBI. Risk factors, which may lead to a more severe TBI, are often difficult to observe and measure. These include: (1) the magnitude of the force of impact; (2) the intracranial vectors of transmitted force (linear, rotational); (3) the thickness of the scalp and skull; (4) the site of the impact; and (5) the presence or absence of a skull fracture (Amacher, 1988).
There are also a number of common clinical, pathogenic, and biochemical features of concussion, and more serious head injury. The classification of the pathophysiology is traditionally determined by the initial insult: (1) primary impact injuries occur as a direct result of the application of force to the brain. This includes fractures, contusions, lacerations, and diffuse axonal damage. By definition, these symptoms are uncommon in milder head injury and concussion; (2) secondary injuries are a result of the primary injury and can include vascular disruption, which can lead to extradural, subdural, and intracerebral haemorrhage.

There are two major classes of TBI: penetrating (or open) head injury and closed head injury. As the term suggests, penetrating head injury involves the penetration of the skull by some form of “missile” such as a bullet, rock or knife, and usually leads to more severe injuries. Closed head injury accounts for the majority of paediatric TBI, and incorporates mild TBI and concussion. As the name suggests, in closed injury there is no penetration of the skull. Instead, the brain is shaken within the skull cavity. This can often result in multiple injury sites and diffuse axonal damage. The most common cause of closed head injury are motor vehicle accidents, which are associated with high-velocity deceleration forces. Compression and deformation of the skull can result in contusion or bruising at the point of impact and at other cerebral sites. Studies have shown that there are certain areas of the brain, such as the basal frontal regions and temporal lobes, which are particularly vulnerable to such injury-related contusions or bruising (Kupferman, 1991; Tranel, 1992).

In closed head injuries, the brain is shaken backwards and forwards and rotated, with the force of the impact during such an injury resulting in varying degrees of shaking. The associated injuries resulting from this shaking include damage to the cerebral areas opposite the site of damage and shearing injuries to white matter, as the nerve tracts are bent and torn. Diffuse axonal injury can also be associated with rotational forces which can cause the brain to “swirl and glide”
within the skull. This results in tears and stretching of the white nerve fibres that connect the brain stem to cortical areas, as well as neural tearing throughout deep cerebral structures. Rotational forces such as these are commonly associated with motor vehicle accidents and sporting accidents, as well in relatively minor head injuries and concussions.

Secondary injuries such as haematoma, cerebral oedema, and raised intracranial pressure may also occur. However, in general, such secondary injuries are more likely result following a more severe closed head injury rather than a mild TBI or concussion.

**Measuring Severity**

The assessment of concussion and mild head injury is problematic in both adults and children, as most measurement tools have been developed specifically to evaluate more severe injuries, and are not sensitive to the gradations within injuries falling at the mild end of the spectrum. When assessing TBI, most emergency departments refer to the Glasgow Coma Scale (GCS; Jennett & Teasdale, 1981) to assess injury severity and the degree of impairment of consciousness. It includes a number of categories in measuring the level of a person’s consciousness and responsiveness. It assesses eye opening, motor responses, and verbal responses, with total GCS scores ranging from 3 to 15. The higher the score, the less the impact on the individual’s level of consciousness, and the less impairment is present. Of note, the GCS was never intended to differentiate severity at the milder end of the severity spectrum, and so, is not sensitive to differences in severity within the mild head injury and concussion groups. Table 1 below presents the behaviours assessed by the GCS.
**Table 1: Glasgow Coma Scale**

<table>
<thead>
<tr>
<th>Behaviour</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Eye Opening (E)</strong></td>
<td></td>
</tr>
<tr>
<td>Spontaneous</td>
<td>4</td>
</tr>
<tr>
<td>In response to speech</td>
<td>3</td>
</tr>
<tr>
<td>In response to pin-prick (pain)</td>
<td>2</td>
</tr>
<tr>
<td>No response</td>
<td>1</td>
</tr>
<tr>
<td><strong>Motor (M)</strong></td>
<td></td>
</tr>
<tr>
<td>Follows commands</td>
<td>6</td>
</tr>
<tr>
<td>Can localise pain</td>
<td>5</td>
</tr>
<tr>
<td>Withdraws from painful stimulus</td>
<td>4</td>
</tr>
<tr>
<td>Abnormal flexion to pain</td>
<td>3</td>
</tr>
<tr>
<td>Extensor response to pain</td>
<td>2</td>
</tr>
<tr>
<td>No response</td>
<td>1</td>
</tr>
<tr>
<td><strong>Verbal (V)</strong></td>
<td></td>
</tr>
<tr>
<td>Oriented</td>
<td>5</td>
</tr>
<tr>
<td>Confused conversation</td>
<td>4</td>
</tr>
<tr>
<td>Inappropriate words</td>
<td>3</td>
</tr>
<tr>
<td>Incomprehensible sounds</td>
<td>2</td>
</tr>
<tr>
<td>No Response</td>
<td>1</td>
</tr>
</tbody>
</table>

Note: Coma score = E + M + V

Post-traumatic amnesia (PTA) is a further measure of injury severity which has been identified as linked to long-term sequelae. PTA is defined as the period of confusion and disorientation following a TBI, during which the patient has little organised memory or recall of events. There are several PTA scales available that provide information regarding the individual’s level of alertness and confusion following the injury, by assessing a range of symptoms and skills.
over several time points post-injury. A number of these are appropriate for administration with children and adolescents, such as, the Westmead PTA Scale (Marrosszeky, Ryan, Shores, Batchelor & Marrosszeky, 1997) and the Children’s Orientation and Amnesia Scale (Ewing-Cobbs, Levin, Flecher, Miner & Eisenberg, 1990).

As with the GCS, PTA scales are not able to fully assess milder forms of TBI, as they require multiple time points, which are generally unavailable for patients with mild TBI/concussion who are often not admitted to hospital or fail to present for medical care. Another widely used example of concussion assessments include the Sports Concussion Assessment Test 3 (SCAT3: McCrory et al., 2013), which as its name suggests, has been developed specifically to assess mild injuries and concussions. The SCAT3 is a standardised method for evaluating injured athletes and can be used in athletes aged 10 years and older. Currently there is no similar tool to assess younger children post-concussion.

In response to the measurement problems inherent in the classification of TBI severity, the Mayo Classification for TBI Severity was introduced (Malec, Brown, Leibson, Flaada, Mandrekar, Diehl & Perkins, 2007). This system (see Table 2, below) employs a multifaceted diagnosis system rather than focussing on a single dimension, such as GCS or PTA measures. This system has particular utility in the field of mild head injury/concussion, where patients are often not hospitalised and medical records are frequently limited.
Table 2: MAYO TBI Severity Classification System

A. Classify as Moderate-Severe (Definite) TBI if one or more of the following criteria apply:
   1. Death due to this TBI
   2. Loss of consciousness of 30 minutes or more
   3. Post-traumatic anterograde amnesia of 24 hours or more
   4. Worst Glasgow Coma Scale full score in first 24 hours <13 (unless invalidated upon review, e.g., attributable to intoxication, sedation, systematic shock)
   5. One or more of the following present:
      • Intracerebral hematoma
      • Subdural hematoma
      • Epidural hematoma
      • Cerebral contusion
      • Haemorrhagic contusion
      • Penetrating TBI (dura penetrated)
      • Subarachnoid haemorrhage
      • Brain Stem Injury

B. If none of Criteria A apply, classify as Mild (Probable) TBI if one or more of the following criteria apply:
   1. Loss of consciousness of momentary to less than 30 minutes
   2. Post-traumatic anterograde amnesia of momentary to less than 24 hours

C. If none of the Criteria A or B apply, classify as Symptomatic (Possible) TBI if one or more of the following symptoms are present:
   • Blurred vision
   • Confusion (mental state changes)
   • Dazed
   • Dizziness
   • Focal neurologic symptoms
   • Headache
   • Nausea

(Malec, Brown, Leibson, Flaada, Mandrekar, Diehl, & Perkins, 2007)

The Biomechanics of Concussion

There are various biomechanical forces that can have an influence on the impact of a concussion, however these are difficult to observe in clinical contexts. They include skull shape, size and geometry, density and mass of neural tissue, thickness of skull and shape, extent, nature and direction of the concussive blow, head-body relationships, and the mobility of the head and neck.
Irrespective of the many ways one can sustain a concussive injury, all concussions have one thing in common; they all involve the near instant transfer of kinetic energy. This will require either the absorption (acceleration) or release (deceleration) of kinetic energy by the head and brain.

An accelerative/decelerative injury can be sustained via two methods: impact or impulse. Impact is a result of the concussive blow making direct contact with the head. Impulse, however, refers to an accelerative force which sets the head in motion without directly striking it. A concussive insult results in a process of inertial (or accelerative) loading.

There are two components to inertial forces: translational or linear acceleration (or deceleration) and rotational or angular acceleration (or deceleration). Translational forces are often associated with a blow delivered directly to the face where movement is in a straight line passing through the head’s centre of gravity. In contrast, rotational forces occur when movement of the head is arc-like though its centre of gravity, for instance, when there is a swinging upward blow to the chin.

The brain is suspended inside the subarachnoid space of the skull surrounded by protective cerebrospinal fluid. This space allows the brain some freedom to move within the skull cavity. Therefore, if there is a sudden movement and impact, the brain can collide against the skull, leading to lesions on more than one side of the brain. This movement within the skull has been coined a “mechanical shake” due to the acceleration and deceleration forces which are transmitted to the head following impact.

This then results in a complex cascade of neurochemical and neurometabolic events. Immediately following an insult to the brain, the neuronal and axonal membranes are stretched causing an unsystematic flux of ions through ion channels that are normally regulated by a transient physical membrane (Barkhoudarian, Hovda & Giza, 2001: Farkas, Lifshitz & Povlishock,
2006). This is then followed by a widespread release of neurotransmitters, excitatory amino acids in particular (Faden, Demediuk, Panter & Vink, 1989; Katayama, Becker, Tamura & Hovda, 1990), which results in alterations of neuronal ionic homeostasis.

Research involving the anatomic abnormalities relating to concussive injuries has discussed the range of pathophysiological responses that occur. At the point of a head impact which causes concussion, the brain is violently moved within the skull, resulting in damage to cells and blood vessels, which then leads to the above-mentioned chemical cascade responsible for disruption in normal brain function. Studies involving animals have found that concussion can cause an overproduction of potassium and calcium ions, which can then lead to cell damage (Giza & Hovda, 2001). These ions then cause constriction of blood vessels within the brain, decreasing blood flow and reducing the glucose necessary for normal brain function. These abnormalities may persist and may account for ongoing symptoms presenting as post-concussive syndrome.

During this period of recovery, the brain may be more susceptible to further injury if there is another impact to the head. A second impact in a concussed child or adolescent before complete resolution of the first concussion can have significant results and lead to more prolonged and severe post-concussion symptoms or, in extreme and rare cases, permanent neurologic consequences or even death (Kirkwood, Yeates & Wilson, 2006). Figure 1 below, presents the period of vulnerability where further injury could lead to prolonged concussive symptoms and longer-term damage.
In summary, research indicates that TBI results in sudden biochemical changes, which begin immediately after injury, and can lead to the disruption of brain injury metabolism. Even concussion and mild head injury can lead to these significant biochemical changes (Tavazzi et al., 2005). The post-mild TBI “energy crisis,” synaptic plasticity, and subsequent cognitive deficits are a direct result of this metabolic derangement (Wu, Ying & Gomez-Pinilla, 2010).

**Neuropsychological and Functional Outcomes of Concussion**

In general, TBI can impact an individual in many ways. In identifying the various neuropsychological impairments that can develop following a TBI, both cognitive and social functioning can be severely impacted (American Psychiatric Association, 2013). Impairments in these areas of functioning can lead to a number of outcomes which can have an impact on a child’s...
behaviour, as well as their educational and adaptive abilities. While there is strong evidence for a ‘dose-response’ relationship between injury severity and neuropsychological impairment in more severe injuries, this pattern is less clear following concussion (Anderson & Catroppa, 2006; Anderson, Catroppa, Dudgeon, Morse, Haritou, & Rosenfeld, 2006; Anderson et al., 1997).

**Basic Cognition**

**IQ** - Whilst IQ may be impaired due to moderate and severe TBI, research has demonstrated that concussion and mild head injury have very little effect on IQ. A large number of TBI studies have assessed IQ as either an outcome measure or a sample descriptor (Anderson et al., 2005; Anderson et al., 2009; Anderson & Moore, 1995). Research findings indicate that there is little to no intellectual deficit associated with mild TBI in either the acute or chronic recovery stages. Following a moderate to severe TBI, however, studies have reported lowered IQ scores immediately post-injury. While studies indicate that changes in IQ are only evident in moderate and severe TBI, they also suggest that some neurobehavioural domains (such as attention, speed of processing, memory and learning) may be particularly susceptible to the impact of TBI (Anderson & Catroppa, 2006; Catroppa & Anderson, 2002; Catroppa & Anderson, 2003; Kaufmann et al., 1993).

**Language Skills** – Clinical reports and research studies following serious head injury often indicate impairments in communication, such as slowed speech, dysfluency, poor logical sequencing of ideas, and word finding difficulties (Dennis, 1989; Dennis, Wilkinson, Koski & Humphreys, 1995). In contrast, studies focusing on concussion and mild head injury generally detect little to no change in verbal abilities post-injury.
**Visual and Motor Skills** - Visual and motor deficits are common during the acute recovery stage following moderate and severe head injury, and rapid recovery occurs during the first few months post-injury. Such motor deficits have been found to be more persistent in children following a severe injury, while children with mild head injuries tend to display more subtle deficits (such as psychomotor slowness and reduced hand-eye coordination), which are more persistent (Mucha et al., 2014; Taylor et al., 2010). A child who is experiencing these difficulties may find day-to-day tasks and activities to be quite difficult. For instance, playing sport or academic activities, such as drawing and writing, may be very difficult and (in cases where symptoms are prolonged) may also lead to secondary issues with self-esteem, socialisation and academic development. Whist the above studies refer to more severe injuries in comparison to concussion, it is unclear what, if any, impact returning to sport or physical and cognitive demanding tasks will have on a recently concussed child or adolescent in respect to visual and motor functioning.

**Information Processing**

**Attention Skills** – Research by Catroppa, Anderson, Morse, Haritou and Rosenfeld (2007) highlights the long-term impact that TBI can have on children’s attention skills. These authors examined 70 children who had sustained a mild, moderate or severe TBI between the ages of 2 and 7 years, at 5 years post-TBI. Results indicate that attention deficits persisted to 5 years, particularly in more severe injury. However, some reduction in attentional skills were also identified after milder insults. Researchers concluded that skills children are developing at the time of injury (e.g., sustained attention, shifting attention, divided attention, and processing speed) are more likely to be impacted and may not develop at a normal rate following injury (Catroppa et al., 2007).
**Processing Speed and Reaction Time** – Reaction time has been established as particularly sensitive to the acute consequences of concussion and mild head injury, which are not readily detected on more traditional paper and pencil assessment tools. There are typically three ways to assess reaction time.

1) Simple reaction time tasks – these involve only one stimulus and one response.

2) Recognition reaction time tasks – these paradigms include stimuli that should be responded to (the ‘memory set’) and others that should elicit no response (the ‘distracter set’). There is only one correct response.

3) Choice reaction time tasks where participants must give a response that corresponds to the stimulus, such as pressing a key corresponding to a letter that appears on the screen.

Research indicates that mean reaction times for college-age individuals on such tasks are approximately 0.19 seconds (190 ms) for light stimuli and 0.16 seconds (160 ms) for sound stimuli (Brebner & Welford, 1980; Fieand, Kuhtala, Kullberg & Saarl, 1956; Welford, 1980). An early study by Donders (1968) found that simple reaction time is typically shorter than recognition reaction time, and that choice reaction time is the longest of the three. This is consistent with a number of later studies, which indicate that a complex stimulus (e.g., several letters in symbol recognition vs. one letter) elicits a slower reaction time (Brebner & Welford, 1980; Luce, 1986; Miller & Low, 2001). Miller and Low (2001) concluded that the time for motor preparation (e.g., tensing muscles) and motor response (e.g., pressing a key on a computer keyboard) was the same in all three types of reaction time tests. This suggests that the differences found in reaction time are in fact due to information processing capacity.
In concussion literature, reaction time measurement is frequently employed to evaluate recovery. Typically, measures are computer-based, for example, CogSport (Collie et al., 2003), which assesses reaction times across a series of simple and complex information processing tasks. Such studies often report slower reaction times post-injury at a group level (Lovell & Solomon, 2013; McCrea et al., 2013), although their capacity to accurately measure recovery trajectories is not clear (Crowe et al., 2015)

**Memory and Learning** – There may be serious implications if difficulties or delays occur in this domain. During childhood, many day-to-day activities centre on learning and acquiring new skills and abilities. Memory and learning difficulties during this period could significantly interfere with this process and may lead to academic failure or delays in age-appropriate development. While memory difficulties have been identified as one of the most likely cognitive domains to show impairment following a TBI, there is very limited research looking at post-concussion memory sequelae.

Summarising the key findings to date, there is a dose-response relationship between injury severity and degree of memory impairment, with more severe injury related to higher levels of memory deficit, and mild head injury survivors less impacted. A similar relationship has also been found between injury severity and recovery. Children who sustained mild/moderate TBI are more likely to achieve age-appropriate memory function 12 months post-injury. In contrast, children who sustained severe TBI displayed slower and less complete recovery (Catroppa et al., 2007; Levin & Eisenberg, 1979; Levin, Eisenberg, Wigg & Kobayashi, 1982; Levin, et al., 1988). Overall, research indicates that following severe TBI, persistent memory and learning deficits are common. In cases of mild TBI, impairments in these areas have been found to be more variable.
Executive Function

The concept of executive function (EF) is an umbrella term which is used to define the skills necessary for goal-directed behaviour (Stuss & Benson, 1986). EF refers to an individual’s capacity for directing modular activities, such as language, memory, motor skills, and perception. It is also an ability which is flexible to specific settings, and works to manage and achieve specific goals. Anderson (2002) identifies a range of skills as included under the EF umbrella: (a) attentional control (described above)/response inhibition; (b) concept formation (working memory, mental flexibility); (c) planning, organisation and metacognition. Research suggests that there is a strong relationship between severe TBI and great EF deficits (Catroppa et al., 2007; Dennis et al., 1995; Konrad et al., 2011; Levin, Song, Ewing-Cobbs & Roberson, 2001; Pentland, Todd & Anderson, 1998). However, there is limited information and research on EF deficits following concussion or their trajectory post-injury.

Functional Outcome of Concussion

It is common for children to make a full physical recovery following a mild TBI. However, they may still have ongoing academic, social and/or behavioural difficulties, despite their healthy appearance (Rosema, Crowe & Anderson, 2012). Children who experience mild TBI may perform adequately on a number of neuropsychological assessments, however they may encounter problems when faced with day-to-day living. The most common problem areas that are reported are learning and skill acquisition, and psychosocial functioning (Asarnow et al., 1991; Asarnow et al., 1995; Willmott et al., 2000).
Educational and behavioural development, as well as adaptive functions, are highly dependent on intact capacities of learning, attention, and EF. As detailed earlier, neuropsychological functions may be impaired following a TBI, even while reports from psychometric assessments appear intact.

**Educational Abilities** - Research into paediatric TBI has a strong interest in educational outcome. Studies have found that following concussion, many children experience reductions in attention, EF and processing speed, as well as excessive fatigue and headaches. These symptoms mean that the child’s capacity to participate in the classroom is reduced, and they may struggle to take in information and acquire new skills and knowledge until they have recovered (Catroppa & Anderson, 1999; Barnes, Dennis & Wilkinson, 1999; Berger-Gross & Shackelford, 1985; Kinsella et al., 1997). Many ‘slow recoverers’ find it difficult to manage a full-time school schedule and need to make a gradual return-to-school over the weeks and months post-injury. These problems are most significant for older children and adolescents, where school demands are greater and where they may need to complete important exams and assignments (Catroppa & Anderson, 1999; Goldstein & Levin, 1985; Greenspan & MacKenzie, 1994; Levin, Grafman & Eisenberg, 1987).

**Behaviour and Adaptive Abilities** - The levels of behavioural and adaptive impairments that result from TBI have been debated for quite some time. It has been suggested that these problems are not a direct result of a TBI, as many have suggested, but instead reflect premorbid behavioural and family problems (Donders, 1992; Farmer et al., 1996; Max et al., 1997; Wade et al., 1996). These conflicting reports may be a result of methodological issues and a lack of objective pre-injury measures of behavioural and adaptive functioning.
Clinical reports have often noted behavioural changes post-mild head injury, ranging from initial PCS of irritability and fatigue, to more persistent problems such as aggression, hyperactivity, sleep disturbance, poor impulse control, decreased levels of motivation, reduced self-esteem, anxiety and social difficulties. Often behavioural problems can be the most disabling aspect of TBI for many children and adolescents; they may grow to be more severe over time, and may even persist into adulthood (Cattelani, Lombardi, Brianti & Mazzuchi, 1998; Klonoff, Clark & Klonoffm, 1995). Of note, unlike cognitive, motor and academic problems, there is no clear dose-response relationship between injury severity and social and behavioural problems (Rosema et al., 2012).

**Predictors of Outcome**

Recovery following TBI, particularly concussion and mild head injury, is quite variable and difficult to predict. Typically, neurological symptoms are the first to stabilise. In more severe TBI, these symptoms can persist and may even lead to permanent impairment. Recovery from behavioural difficulties is even more difficult to predict. Often behavioural difficulties appear to stabilise early on, along with initial reductions of fatigue and irritability. However, many researchers have reported an increase in psychological problems and psychiatric disturbance. It is possible that the onset of these symptoms reflect secondary problems that the child may experience as a result of physiological and cognitive impairment.

A number of variables have been reported as having the potential to predict impairment post-TBI. Following mild TBI and concussion, PCS are generally measured to provide an index of recovery, and have been noted to be predicted by a range of factors including injury severity (mild vs mild-complicated injury and the presence or absence of abnormalities on neuroimaging) age at injury, and premorbid and psychological risk factors (e.g., anxiety, depression).
Management of Sport Related Concussion and Return-to-Play Guidelines

Mild TBI is complex, involving both neurological and psychological features, that need to be considered when planning clinical management. It is generally acknowledged that, given the wide variation in presenting features and recovery trajectories, clinical care should be tailored to the individual to appropriately suit their injury severity, developmental level, and other unique differences (Atabaki, 2006). In the majority of cases, individuals who sustain a mild TBI will recover quite quickly, with relatively few requiring ongoing long-term clinical management.

Kirkwood, Yeates, Taylor, Randolph, McCrea and Anderson (2008) discussed the management of mild TBI on preschool and school-aged children. This review examined management in three time periods: acute, post-acute, and long-term. Table 3 below presents their proposed clinical management model, taking into account time post-injury and domain of focus.

Table 3: Brain Injury Clinical Management Matrix Organised by Time Post-Injury and Domain of Focus

<table>
<thead>
<tr>
<th></th>
<th>Acute (injury through 3 days post-injury)</th>
<th>Post-acute (4 days through 3 months post-injury)</th>
<th>Long-term (4 months post-injury through recovery)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive or neuropsychological evaluation</td>
<td>Brief, standardised cognitive screening</td>
<td>Abbreviated neuropsychological assessment</td>
<td>Comprehensive neuropsychological assessment</td>
</tr>
<tr>
<td>Youth intervention</td>
<td>Provide developmentally appropriate education, advice, and reassurance about mild TBI</td>
<td>Provide psychoeducational consultation as needed</td>
<td>Validate patient’s injury experience</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Provide reassurance, ensure reasonable symptom attributions developed, and</td>
<td>Consider cognitive-behavioural psychotherapy, focused</td>
</tr>
<tr>
<td>Timeframe</td>
<td>Acute (injury through 3 days post-injury)</td>
<td>Post-acute (4 days through 3 months post-injury)</td>
<td>Long-term (4 months post-injury through recovery)</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td></td>
<td>recommend “behavioural prescriptions” as appropriate</td>
<td>on functional improvement</td>
<td>Reframe search for “cure” and help child develop more effective coping strategies</td>
</tr>
<tr>
<td><strong>Family intervention</strong></td>
<td>Ensure caregivers can identify and act upon neurological emergencies</td>
<td>Provide ongoing education and advice about symptoms</td>
<td>Correct dualistic mind-body misconceptions and develop clear management plan</td>
</tr>
<tr>
<td></td>
<td>Provide parent-focused education, advice, and reassurance about mild TBI</td>
<td>Emphasise preventing further injury while youth is still recovering</td>
<td>Explore post-injury family dynamics</td>
</tr>
<tr>
<td></td>
<td>Attend to caregiver anxiety in particular</td>
<td></td>
<td>Consider family problem-solving therapy as needed</td>
</tr>
<tr>
<td><strong>School intervention</strong></td>
<td>Consult around when student should return to school</td>
<td>Consider graduated transition back to school</td>
<td>Coordinate school-based services among educators and healthcare personnel</td>
</tr>
<tr>
<td></td>
<td>Ensure school is alerted to injury and monitors for neurological deterioration</td>
<td>Ensure school personnel have adequate knowledge of mild TBI</td>
<td>Consider non-injury related factors when developing educational plans</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Recommend accommodations and modifications as needed</td>
<td></td>
</tr>
<tr>
<td><strong>Athletics intervention</strong></td>
<td>Ensure earliest athlete returns to sports is when asymptomatic and neurological exam and neuroimaging (if</td>
<td>Attend to emotional toll restriction from sports may be having</td>
<td>Ensure individualised cost-benefit analysis conducted when considering return-to-play</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Recommend individual or group based</td>
<td></td>
</tr>
<tr>
<td>Acute (injury through 3 days post-injury)</td>
<td>Post-acute (4 days through 3 months post-injury)</td>
<td>Long-term (4 months post-injury through recovery)</td>
<td></td>
</tr>
<tr>
<td>------------------------------------------</td>
<td>--------------------------------------------------</td>
<td>--------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>conducted) are unremarkable</td>
<td>psychological support as needed</td>
<td>Keep in mind persistent symptoms often at least partially reflect non-injury related factors</td>
<td></td>
</tr>
<tr>
<td>Consider restricting from high risk sports for 1–2 weeks after asymptomatic</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Reproduced with permission from Kirkwood, Yeates, Taylor, Randolph, McCrea, & Anderson (2008)**

Guidelines regarding returning to play or to participate in high-risk athletic activities have been the focus of an increasing bout of research in recent years. There has been considerable debate due to the limited research to inform practice. However, it is generally acknowledged that the following three criteria need to be satisfied prior to childrens’ return-to-play:

1. The athlete is asymptomatic physically, cognitively, and behaviourally (at rest and exertion)
2. No adverse findings should be apparent upon neurological examination, and
3. Neuroimaging findings should be unremarkable (if conducted) (Kirkwood, Yeates & Wilson, 2006).

Once these criteria are satisfied, different opinions still remain regarding the best time to return-to-play. It has been suggested that all child and adolescent athletes are removed from play immediately on the day of injury, regardless of how minor the concussion (Guskiewicz et al., 2004). Kirkwood and colleagues (2008) adopt a conservative approach and suggest that such athletes should be restricted for a further one to two weeks after they are asymptomatic due to their relatively immature and actively developing brain.
A widely accepted return-to-play process was also proposed from the international conference on concussion in sport held in Zurich in 2012 (McCrory, et al., 2013). This paper presents the following graduated return-to-play protocol. However, it is important to note that this is specifically designed for adults (see Table 4 below).

**Table 4: Graduated Return-to-Play Guidelines**

<table>
<thead>
<tr>
<th>Rehabilitation Stage</th>
<th>Functional exercise at each stage</th>
<th>Objective of each stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. No activity</td>
<td>Symptom limited physical and cognitive rest</td>
<td>Recovery</td>
</tr>
<tr>
<td>2. Light aerobic exercise</td>
<td>Walking, swimming, or stationary cycling keeping intensity &lt;70% maximum permitted heart rate. No resistance training.</td>
<td>Increase HR</td>
</tr>
<tr>
<td>3. Sport-specific exercise</td>
<td>Skating drills in ice hockey, running drills in soccer. No head impact activities.</td>
<td>Add movement</td>
</tr>
<tr>
<td>4. Non-contact training drills</td>
<td>Progression to more complex training drills, e.g., passing drills in football and ice hockey. May start progressive resistance training.</td>
<td>Exercise, coordination and cognitive load.</td>
</tr>
<tr>
<td>5. Full-contact practice</td>
<td>Following medical clearance participate in normal training activities</td>
<td>Restore confidence and assess functional skills by coaching staff</td>
</tr>
<tr>
<td>6. Return-to-play</td>
<td>Normal game play</td>
<td></td>
</tr>
</tbody>
</table>


Leddy and colleagues (2016) argue that complete rest following a concussion may have a negative impact on recovery and that controlled exercise is beneficial to the recovery process. Based on their review, Leddy et al., (2016) argue that stage 1 of the recovery process in the Zurich return-to-play guidelines, should be limited to only the first few days following injury. However, there is not enough research to indicate what type of exercise and at what intensity, frequency or duration would be appropriate at this acute recovery stage.

It is also important to understand that children and adolescents who participate in contact sport do so at an amateur or recreational level. The management of the concussion and the return-to-play decision are often the responsibility of the individual’s general practitioner, who may have limited exposure to sports-related concussion.

Decisions regarding the return-to-play following a concussive injury remain a significant challenge. It has been suggested that a player who returns to training or competition before having fully recovered is at an increased risk for complications, such as prolonged concussive symptoms or symptoms of depression and cumulative cognitive deterioration.

Current consensus guidelines have been put in place in order to reduce such risks. These guidelines involve the monitoring of concussed players until signs and symptoms have resolved, using brief cognitive tests to objectively assess the recovery of brain function, and then returning the player to sport in a graded, step-wise fashion. To date, surprisingly little attention has been directed to consideration of more ‘direct’ functional assessments as a marker of readiness to return to sports post-concussion. This is surprising, given the somewhat disappointing findings associated with use of either cognitive recovery indices or PCS symptom trajectories.
One promising domain yet to be adequately investigated post-concussion is the child’s response to exercise. Application of structured exercise protocols, and pre- and post-exercise evaluation of key domains (e.g., PCS, reaction time) may offer a potential index of how the child will respond to increased exertion and assist in guiding return-to-play and even return-to-school.

Recent concussion research has explored the notion of ‘controlled exercise’ as a way to speed up the recovery process (Hanna-Pladdy, Berry, Bennet, Phillips & Gourvier, 2001; Kowalski, Graham, Devinney-Boymei & Willer, 2013; Leddy, Baker, Kozlowski, Bisson & Willer, 2011). In normal, physically fit individuals, exercise is known to generally improve cognitive function (Audiffren, Tomporowski & Zagronik, 2008).

In contrast, a number of adult studies within the concussion literature focused on the potential negative effect that such activities may have; that exercise might unmask or exacerbate ongoing symptoms that may otherwise not be identified by self-report or neurocognitive measures (Audiffren, Tomporowski & Zagronik, 2008; Hanna-Pladdy et al., 2001; Kowalski, Graham, Leddy, Devinney-Boymei & Willer, 2013; Majerske et al., 2008). These results suggest that adults with a recent concussion, who are asymptomatic and exposed to intense physical and cognitive exertion, show an increase in PCS and reaction time, as well as subtle memory deficits. These findings were supported and extended by Majerske et al., (2008), who found that in the post-concussion phase, athletes who participated in intense physical activity reported an increase of symptoms.

However, Majerske et al., (2008) also identified that those who engaged in moderate exercise did not report symptom increase. Other researchers have suggested that the introduction of light exercise during the early recovery phase, may positively influence the recovery process (Audiffren, Tomporowski & Zagronik, 2008; Baker, Freitas, Leddy et al., 2012; Darling, Leddy, Baker, et a., 2014; Hanna-Pladdy, Berry, Bennet, et al., 2001; Leddy & Willer, 2013).
An increasing number of studies have identified that not only physical, but mental exertion can also aggravate and prolong concussion symptoms (Brown, Mannix, O’Brien, Gostine, Collins & Meehan, 2014; Gioia, Vaughan, Reesman, et al., 2010; Majerske, Mihalik, Ren, et al., 2008). Baker, Rieger, McAvoy, et al., (2014) argue that guidelines should also be considered for the graduated return-to-learn in order to ensure sufficient cognitive rest. These recommendations and research highlight not only the importance of physical, but also adequate cognitive rest following concussive injury.

The 2017 Concussion in Sport Group (CISG: McCrory, 2017) developed a graduated return-to-school strategy, which ensures that the concussed athlete receives adequate cognitive rest as well as physical rest. This is the first concussion management guideline specifically designed for the child and adolescent athlete. The CISG highlighted the lack of concussion research in the child and adolescent population, and they put these guidelines forward to encourage families and schools to introduce sports-related concussion (SRC) policies for returning to school. They also highlight that the concussion guidelines for returning to sport following a concussion should be applied after gradually returning to school. This strategy for returning to school is detailed in Table 5 below.
Table 5: Graduated Return to School Strategy

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

Conclusions

This chapter has defined key terminology in the field of concussions, outlined the physiological and biochemical effects of head injuries on the brain and the functional outcomes reported. Clinical management and return-to-play guidelines were outlined, and the limited research in the child and adolescent population regarding the development of these guidelines was highlighted. The return-to-play guidelines presented above are suitable for an adult athlete rather than a child or adolescent. It is therefore important for more explorative and detailed research to investigate the recovery period following a concussive injury in this younger population. This will help to develop safe return-to-play guidelines while limiting the risk for secondary injury and prolonged symptoms in the child and adolescent populations.
Chapter 2 – The Present Study

Rationale

The financial cost of TBI to society is significant and rising, with the total cost in the US being over $60 billion in 2004 (Finkelstein, 2006). Mild TBI, which includes concussion, comprises 90% of all child TBI (Crowe, Anderson & Babl, 2010). Research has shown that the effects of concussion can lead to ongoing cognitive and behavioural sequelae, as well as disruption in metabolic functions (Crowe et al., 2010; Wrightson & Gronwall, 1998; Clapperton et al., 2003), which in turn lead to poorer participation in normal daily activities (school, sport), and increased risk of secondary emotional and psychological problems.

Sports and recreational activities are the most common cause of concussion in children and adolescents (Crowe, et al., 2012). Studies indicate that the premature return to active sport participation following a concussion in childhood or adolescence presents an increased risk for additional injury, including a subsequent concussion, with potentially fatal consequences (Kirkwood et al., 2008; McCrory & Berkovic, 1998).

While the response to acute exertion may provide a marker for the individual’s readiness to return-to-play in adults (Majerske et al., 2008), to date there has been little research examining the effects of exercise during recovery from concussion in child and adolescent populations. A recent study by Sivlerberg and colleagues (2016) explored how concussive symptoms in children can worsen abruptly due to exertion. This study found sudden increases in cognitive demand, such as returning to school or extracurricular activities, did increase the risk of concussive symptom ‘spikes.’ However, these findings were not consistent and it was noted that the participants who did experience increases in symptoms were more symptomatic on initial presentation. Whilst this
research is in support of current return-to-play guidelines, further research is necessary to
determine if these ‘spikes’ in symptom return are detrimental to overall recovery or if they can put
the child at risk of further injury.

Sporting clubs and schools are becoming increasingly aware of the potential consequences
of early return-to-school and play and, in particular, the risk of sustaining a second concussion.
However, the majority of guidelines have been developed for adult athletes and currently few such
guidelines have been specifically developed for the child and adolescent populations (Davis &
Purcell, 2014; Giza et al., 2013; Kirkwood et al., 2008; McCrory et al., 2004). Given the structural
and developmental differences between the brain of an adult and the brain of a child, the protocols
developed for the adult athlete would not necessarily be suitable for younger populations. A recent
systematic review by Davis, Anderson, Babl et al., (2017), evaluated the management of sports
related concussion in children and adolescents aged 5-18 years. It was concluded that there should
be age-specific paradigms for the management of sports-related concussion in children. Children
were found to have a longer recovery time than adults, taking up to 4 weeks to recover (Davis, et
al., 2017).

It is crucial to better understand the post-concussive course of the younger population. In
particular, the effect of physical exertion on cognitive functioning needs to be identified to limit the
risk of further injury during the recovery of a concussion. A thorough understanding of this will
provide a basis for the development of appropriate return-to-play guidelines for the child and
adolescent populations.
Methodological Issues

There are a number of important factors that require consideration when designing brain injury research, particularly if the injuries are sports-related. These include determining what constitutes a ‘significant change’ in cognitive function. There has been considerable debate regarding this issue and there is a lack of appropriate normative data. Traditional pen and paper neuropsychological tests are limited, as their psychometric properties do not account for a test/retest study design methodology which is required to assess recovery in concussed athletes (McCaffery & Westervelt, 1995). In addition, these tests are typically not sufficiently sensitive to detect the subtle changes that are expected following a mild head injury (Erlanger et al., 2003, Makdissi et al., 2010), and may also not detect performance change related to practice effects (Rasmussen et al., 2001). Spreen and Strauss (1998) have noted that practice effects are evident in a number of pen and paper tests commonly used in post-concussive assessments, such as the Digit Symbol, Trail Making, Stroop and Paced Auditory Serial Attention Test.

The current study aims to utilise a design, and assessment tools, that take account of these important methodological issues, by including sensitive, computer-based tools, which can accurately tap reaction times and also account for serial practice effects. The use of a control group, matched for age, cognitive function and history of prior concussions, was used to compare the exercise effect on symptom report and cognitive functioning between concussed (CON) and healthy controls (HC).
Aims & Hypotheses

The overarching aim of this project is to examine the effect of exercise on the cognitive functioning following a concussion, and over time post-injury, in children and adolescents. More specifically, this study will focus on changes in information processing skills (selective attention and reaction time) in children and adolescents following an exercise routine in the post-concussion period.

The following four hypotheses are proposed:

1. Participants with concussion will report increased physical symptoms and higher levels of cognitive impairment after exercise (Day 2).
2. Cognitive impairment and physical symptoms post-exercise will reduce from Day 2 (post symptom resolution) to Day 10.
3. At Day 10, physical and cognitive symptoms in the concussed group will be comparable to that of the non-concussed controls, both pre- and post-exercise.
4. At Day 10, quality of life will be predicted by post-concussive symptoms, as well as age, gender, days post-injury, and history of previous concussions.
Chapter 3 – Method

Design

This single site study employed an experimental, case-control (concussed versus healthy controls), repeated measures (test-exercise-test) design, with the exposure being completion of an intensive exercise session.

Setting

This project was conducted at the RCH, Melbourne, in collaboration with The University of Melbourne and the Murdoch Children’s Research Institute.

Participants

Participants included 30 patients aged between 10 and less than 18 years, who presented to the ED of the RCH with symptoms of concussion following an injury to the head, between June and November 2011.

A further 30 healthy control participants aged between 10 and less than 18 years old were recruited from the general public. These participants acted as a control group to identify differences between the concussed and non-concussed participants, and were matched for age, cognitive functioning and prior concussion. This project was granted ethical approval by the RCH Human Research Ethics Committee (see Appendix A).
The research questions and aims of this project led to the submission of two separate research papers, one of which had been accepted for publication at the time this thesis was submitted (chapter 5) and the other still under review (chapter 6). It is important to clarify that the concussed group data was the same data set of 30 concussed participants used in both papers, with the control group data being used in the second paper only.

**Recruitment**

**Concussed Group**

Participants were identified via the electronic visits database of the RCH ED, and eligibility was verified with the treating clinician, prior to the research team approaching the patient and family regarding the study.

Information was also provided to medical and other research staff with recruitment instructions regarding identifying and recruiting potential participants. This information detailed the purpose of the study and provided step-by-step instructions to be followed (see Appendix B). Eligibility screening forms were also used to identify if potential participants met all selection criteria (see Appendix C1). Consistent with the Zurich Consensus statement, concussion was defined as a blunt injury to the head associated with an altered mental state or any of the following symptoms: headache, dizziness, fatigue, drowsiness, nausea/vomiting, poor balance, memory, or concentration problems.

Interested and eligible participants, and their parents/guardians, were provided with information statements about the project and given the opportunity to ask questions about the study before deciding whether or not to take part. See Appendix D for information statements and consent forms for the concussed participants.
Participants were included if they presented to the ED with head/neck/face trauma resulting in any of the following: (i) loss or altered consciousness; (ii) post-impact confusion and disorientation; and (iii) development of acute concussion symptoms including headache, dizziness, gait unsteadiness or blurred vision. These symptoms were assessed upon presentation to the ED by triage staff as part of a routine ED assessment and management. Patients who presented with GCS below 13 were excluded as these are considered moderate to severe injuries. The following exclusionary criteria were used: (i) GCS below 13; (ii) evidence of pre-existing physical, neurological, or psychiatric disorder; (iii) history of chronic substance abuse; and (iv) insufficient English to complete protocol.

Participants and parents/guardians who agreed to take part in the study were asked to sign the consent form and were given the initial questionnaires and assessments to complete whilst the injured child/adolescent was in the ED under observation. Arrangements were then made for the follow-up calls and further assessments.

**Participation and Drop Out**

Of the 48 families and children approached for recruitment into the study, 30 agreed to participate (62.5% recruitment rate), with all 30 completing all stages of the assessment protocol (100% participant retention). Those who declined to participate stated family time commitments, distance from home to RCH, or lack of interest as reasons for not participating.

**Control Group**

The control group included 30 non-concussed children/adolescents, and were a convenience sample recruited from the general public and from the registered list of families who had previously agreed to be contacted for research undertaken on the RCH campus. Families who had previously signed a permission to be contacted for further research were sent a brief letter
about the project, along with a Permission to Contact form they could complete and post back if they wished to be given further information about the study (see Appendix F). They were then contacted by the primary researcher to explain the study in more detail. The researcher also completed the eligibility screening form via telephone (Appendix C2) to ensure that all participants met the inclusionary requirements. If happy to be enrolled in the study, a suitable time was then scheduled to complete the assessment. Participant Information Statements and Consent Forms were also completed by the parents/guardians and participants over 12 years old (Appendix E).

**Measures**

**Descriptive/Demographic**

**Concussed Group - Eligibility Screening Form 1** (enrolment only). This was administered to all potential concussed participants while in the ED to determine their eligibility to participate in the study. The information collected included participant age, an indication of the presence of concussion symptoms, Glasgow Coma Score, any relevant medical or physical information, and English proficiency (See Appendix C1).

**Control Group - Eligibility Screening Form 2** (enrolment only). This was administered to all control group participants to determine their eligibility to participate in the study. The information collected included participant age, relevant medical and physical information, and English proficiency (See Appendix C2).

**Demographic, Medical and Injury** (enrolment only – concussed group). This questionnaire consisted of an assessment of the participants’ demographic characteristics, parental education and occupation, as well as the details of the participants’ current concussive injury (see Appendix G).
Children’s Health Questionnaire (CHQ: Waters, Salmon, Wake, Hesketh, & Wright, 2000): questionnaire measuring functional health status and well-being with scores referenced to Australian normative data. The CHQ was administered to all participants at baseline.

Descriptive Measures: Cognitive and Behavioural Skills

The Wechsler Abbreviated Scale of Intelligence (WASI: Wechsler, 1999) (Day 10 only). The WASI is individually administered, and is designed to assess intellectual abilities in individuals aged from 6 to 89 years. The WASI consists of four subtests: Vocabulary, Block Design, Similarities and Matrix Reasoning. For the purposes of this study the two-subtest form of the WASI was completed. This form includes verbal (Vocabulary) and non-verbal (Matrix Reasoning) subtests, and yields a Full-Scale IQ score (M=100, SD = 15).

Behavioural Rating Inventory of Executive Function – Parent Form (BRIEF: Guy, Isquith & Gioia, 2004) (Day 10 only). The BRIEF is a questionnaire for parents and teachers of school age children, which assesses executive function behaviours in the home and school environments. The BRIEF was developed for children aged 5 to 18, and examines behavioural aspects of attention, planning, reasoning and organisational skills that are evident in everyday function, and that are also vulnerable to concussion.

The current study used the parent form of the BRIEF, which consists of 86 items within eight theoretically and empirically derived clinical scales that measure different aspects of executive functioning: Inhibit Shift, Emotional Control, Initiate, Working Memory, Plan/Organise, Organisation of Materials, and Monitor. These clinical scales form two broader Indices, Behavioural Regulation and Metacognition, and an overall score, the Global Executive Composite (M=50, SD=10). The BRIEF is a reliable and valid behaviour rating scale of executive functions in children.
and adolescents (Guy, Isquith & Gioia, 2004). Parent (pre-injury) ratings of the BRIEF were collected and used as a measure of quality of life (QoL).

Exercise Routine and Child Exertion Ratings

**Exercise routine** (*Days 2 and 10*). This routine was used to determine the cognitive changes of sub-maximal physical exercise after cycling on an exercise bike. Participants were assessed using a modified version of the McMaster All-Out Progressive Continuous Cycling Test (Bar-Or, 1983). This test was selected as it has been shown to be suitable and safe for a range of childhood groups.

Typically, this test would require participants to exercise to the point of exhaustion and is implemented in such a way to ensure it lasts for between 8 and 12 minutes. However, as we did not require participants to reach the point of exhaustion, we used a modified version of the test that required participants to exercise at a sub-maximal level for 8 minutes. During this assessment participant heart rate was measured via a heart rate monitor strapped to their chest and monitored on a portable device held by the examiner (Polar FS1 Heart Rate Monitor – Model: 7258822716; Polar Electro Oy, 90440 Kempele, Finland).

**Warm up.** The routine began with a two-minute warm up on a stationary exercise bike – In Sight, Magnetic Upright Trainer (Model: B870P; Condell Park, NSW Australia). Participant height was used to determine at what resistance level each child should begin. Table 3.1 below summarises this:
Table 6: Exercise Routine Completed at Day 2 and Day 10

<table>
<thead>
<tr>
<th>Height</th>
<th>&lt;160cm</th>
<th>&gt;160cm</th>
<th>&lt;160cm</th>
<th>&gt;160cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warm up</td>
<td>1 (50)</td>
<td>1 (50)</td>
<td>25</td>
<td>50</td>
</tr>
<tr>
<td>Stage 1</td>
<td>6 (75)</td>
<td>9 (100)</td>
<td>25</td>
<td>50</td>
</tr>
<tr>
<td>Stage 2</td>
<td>9 (100)</td>
<td>13 (150)</td>
<td>25</td>
<td>50</td>
</tr>
<tr>
<td>Stage 3</td>
<td>11 (125)</td>
<td>15 (200)</td>
<td>25</td>
<td>50</td>
</tr>
</tbody>
</table>

Once on the bike and the appropriate resistance level was selected, each participant was read the following instructions:

“In a minute I am going to ask you to do a 2-minute warm up. To do this you will ride the bike at a speed that keeps the rotations per minute (indicate the measure on the bike) at 60. This should not be too fast so that you get tired, but not too slow either. Keep both feet on the pedals, and both hands on the handles. Ready? ...Go!”

Stages 1 – 3: Submaximal exercise routine. After the 2-minute warm up, the resistance level was then increased by either 25 or 50 watts based on the participant height (See Table 5 above, for more detail).
Child ratings of exercise. At the end of each stage the participants were asked to rate how difficult the routine felt on the CERT scale (detailed below):

“For the next 6 minutes I would like you to keep riding the bike just like you did in the warm up, not too fast but not too slow – keeping the rotations per minute at 60. While you do this I will be measuring how fast your heart is beating and will also be asking you some questions about how you feel and how hard it is for you. Keep both feet and both hands on the bike the whole time and try not to stop until I tell you to. If you start to feel like you can’t keep going or you start to feel unwell in any way, like your head hurts or your stomach doesn’t feel good, I want you to let me know. Is that ok? Ready?....Go!”

Throughout this 6-minute period the researcher monitored each participant’s heart rate and recorded it every 2 minutes. Also, at each of the 2-minute intervals, the participants were asked to indicate their perceived level of exertion using the following rating of perceived exertion scale.
The Children's Effort Rating Scale (*Days 2 and 10*). This was used to measure the participants' perceived level of exertion while completing the exercise routine. At two-minute intervals the participants were asked to indicate their effort level using the following rating of perceived exertion scale (see Figure 2; adapted from Bar-Or & Rowland, 2004).

<table>
<thead>
<tr>
<th></th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Very, very easy 😊😊😊</td>
</tr>
<tr>
<td>2</td>
<td>Very easy 😊😊</td>
</tr>
<tr>
<td>3</td>
<td>Easy 😊</td>
</tr>
<tr>
<td>4</td>
<td>Just feeling a strain 😖</td>
</tr>
<tr>
<td>5</td>
<td>Starting to get hard 😖</td>
</tr>
<tr>
<td>6</td>
<td>Getting quite hard 😖😊</td>
</tr>
<tr>
<td>7</td>
<td>Hard 😖😊😊</td>
</tr>
<tr>
<td>8</td>
<td>Very hard 😖😊😊😊</td>
</tr>
<tr>
<td>9</td>
<td>Very, very hard 😖😊😊😊😊</td>
</tr>
<tr>
<td>10</td>
<td>So hard I’m going to stop 😖😊😊😊😊</td>
</tr>
</tbody>
</table>

*Figure 2: The Children's Effort Rating Scale (CERT) (adapted from Bar-Or & Rowland, 2004)*
Participants were also reminded at each interval to inform the researcher if they started to feel any physical pain or if they began to feel unwell (such as dizziness, headache, or nausea). On two occasions participants indicated they were feeling unwell. The exercise routine was stopped immediately and the participant was assisted to sit down.

**Outcome Measures: Information Processing**

**Information processing** (*Enrolment, Days 2 and 10*). This consisted of a series of neuropsychological tests and a symptom rating scale. These were completed by the participant via a computerised administration protocol, a written questionnaire and questions asked by the researcher. This test protocol required approximately 30 minutes to complete and was administered to participants immediately before and after the exercise protocol. The test protocol included:

**Sports Concussion Assessment Test** (*SCAT*: Collie et al., 2003) – used to measure subjective concussive symptoms. This version of the SCAT is incorporated into the CogSport assessment (detailed in Figure 3), and presents a number of common concussive symptoms. Participants were asked to rate themselves on a six-point scale, indicating how much they were experiencing each symptom at the time of the assessment.
### Sports Concussion Assessment Test (SCAT)

#### Questions

Please score yourself on the following symptoms based on how you feel now:

<table>
<thead>
<tr>
<th>Symptom</th>
<th>None</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Headache</strong></td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>Pressure in head</strong></td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td><strong>Numbness</strong></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td><strong>Balance problems or dizzy</strong></td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td><strong>Nausea or vomiting</strong></td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>Vision problem</strong></td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td><strong>Hearing problems/loud</strong></td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>Dizzy or off balance</strong></td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td><strong>Feeling “drugged” or “drunk”</strong></td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>Confusion</strong></td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td><strong>Feeling slowed down</strong></td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>Feeling like ”out of it“</strong></td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td><strong>Dizziness</strong></td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>Fatigue or low energy</strong></td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td><strong>Moody or emotional than usual</strong></td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>Inability to concentrate</strong></td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td><strong>Difficulties sustaining attention</strong></td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>Sensitivity to noise</strong></td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

---

*Figure 3: Sports Concussion Assessment Test (SCAT)*
**CogSport.** *(Days 2 and 10: Collie, Maruff, Darby & McStephen, 2003).* All participants completed CogSport (Collie et al., 2003), which comprises of six computerised tasks. Each task is an adaptation of standard neuropsychological and experimental tests that assess cognitive functions vulnerable in the context of head injury, including speed of processing, attention and working memory (Babikan, McArthur & Asarnow, 2012; Baillargeon, Lassonde, Leclerc & Ellemberg, 2012; McCrea et al., 2013). CogSport has been found to be a reliable cognitive test which can be repeatedly administered without practice effects (Collie, et al., 2003).

CogSport was presented on a laptop computer fitted with headphones. All tasks were in the form of card games that were presented in succession on a green background, and participants provided responses by pressing either the ‘Yes’ or ‘No’ key on the laptop. In order to aid individuals with the task, written instructions were presented to the left of the screen to indicate the rule for each new task. Participants were then given an interactive demonstration. Once the child had successfully completed a single complete practice trial and had demonstrated their awareness of the task rules, the task began. The participant started each task by pressing the ‘Yes’ key. For each task, 30 correct responses were required before proceeding to the next task.

*Brief descriptions of each task are provided below, in the order of task presentation.*

**Detection Task – Processing Speed.** A card is presented face down at the centre of the computer screen. The participant is instructed to ‘Press Yes’ as soon as a card turns face up. After a randomised delay, the next card flips face up, and the participant must press the ‘Yes’ key as quickly as possible.
Identification Task - Decision Making. A card is presented face down at centre screen, and the participant is asked: ‘Is the face-up card red?’ and responds by pressing ‘Yes’. After a randomised delay, the next card flips face up, and the participant must respond ‘Yes’ (red card) or ‘No’ (other colour).

One Back Task - Working Memory. A card is presented face up at centre screen. The participant is asked ‘Does the face-up card exactly match the one before?’ The card then goes to the back of the pack and after a randomised delay the next card is revealed. If the card is identical to the card before it, the participant presses the ‘Yes’ key, if not, ‘No’.

One Card Learning Task - Learning / Memory. A card is presented face down at centre screen. The participant is asked ‘Have you seen this card before in this task?’ After a randomised delay, the card flips face up. For each card, participants must decide whether they have seen that card before in the task and respond ‘Yes’ or ‘No’.

The computerised testing was completed immediately before and after the exercise protocol and took 8 minutes to complete. These measures are highly reliable when administered to healthy adults and children (Makdissi et al., 2004; Mollica et al., 2005), and have documented sensitivity to sports-related head injury (Marosszeky et al., 1997; Moriarty et al., 2004). See Figures 4 - 8.
HAS THE CARD TURNED OVER?

You are now going to do a practice.

You will still need to use the YES button for this task.

In this task, a playing card will appear in the center of the screen.

Press the YES button when the card turns face-up as fast as you can.

If you make a mistake you will hear an error sound. This means you have responded too soon.

Try to make your responses as accurate and fast as possible after a card turns face-up.

Are you ready to start?

(Press ENTER to begin.)

Figure 4: CogSport: Instruction Screen for Simple Reaction Time Test

Figure 5: CogSport: Simple Reaction Time Test
Figure 6: CogSport: Instruction Screen for Real Test for Simple Reaction Time Test

HAS THE CARD TURNED OVER?
You are now going to do the real test.
(Press ENTER to begin.)

Figure 7: CogSport: Instruction Screen for Choice Reaction Time Test

IS THE CARD RED?
You are now going to do a practice.
You will need to use both the YES and NO buttons for this task.
In this task, a playing card will appear in the center of the screen.
As soon as it turns face-up you must decide: is the color of the card red?
If it is red, press the YES button.
If it is not red, press the NO button.
If you make a mistake you will hear an error sound.
Try to make your responses as accurate and fast as possible after a card turns face-up.
Are you ready to start?
(Press ENTER to begin.)
**Procedure**

Concussed participants were recruited acutely on admission to the RCH ED (Day 0), and assessed at 2 time-points: Days 2, and 10. These days were chosen as they enabled a comparison of recovery from concussion during the acute post-injury period of concussion. Day 10 was selected, based on data from the RCH longitudinal concussion study regarding average time to symptom resolution (4 days), and from published management guidelines and which suggest normal recovery occurs within 2 weeks of injury. Thus, on average Day 2 would be 6 days post injury and Day 10 would be 2 weeks post injury, as per Zurich guidelines (Crowe et al., 2015).
Day 0 represented the day the child or adolescent presented to the ED at RCH with a concussion. Day 2 represented the first day following the concussion that the participant was asymptomatic at rest. Day 10 assessments were conducted eight days following the assessments undergone at Day 2. This allowed for a comparison of the effects of exercise over time (after symptom resolution) following a concussive injury.

**DAY 0.** Participants were screened for their eligibility to take part in this study upon presenting to the ED by the researcher, who then invited them to join the study. All parents/guardians, as well as adolescents over the age of 12, were provided with an information statement outlining the purpose of the study and what would be asked of them if they chose to participate. They were also given a statement of informed consent, which they were asked to sign once they had a full understanding of the project and agreed to participate. Adolescents over the age of 12 years were also asked to sign a consent form along with their parent/guardian.

Whilst in the ED, parents/guardians were asked to complete measures of pre-morbid cognitive functioning as well as demographic questionnaires documenting previous medical history and general health (CHQ). Participants were asked to return to the exercise laboratory for their Day 2 assessment once they were asymptomatic at rest (based on self-report).

The researcher telephoned the parent/guardian daily following the child’s discharge from the ED in order to determine when the participant was asymptomatic and to arrange an appropriate day and time to meet for their Day 2 assessment.
Upon returning on Day 2, participants were greeted by the researcher who then administered the cognitive symptom protocols, followed by the exercise protocol and a second administration of the cognitive assessments. The cognitive and exercise testing took approximately 45 minutes in total. At the completion of this assessment, a time was then arranged for the participants’ Day 10 assessment (eight days later). This assessment was a repeat of the Day 2 assessment, but also included a measure of the participants’ general health (GHQ), intellectual functioning (WASI), and behavioural regulation (BRIEF).

Healthy controls were assessed at one time point, during which their parent/guardian completed the CHQ and BRIEF, while the participant was administered the WASI, followed by the SCAT and CogSport, the exercise routine and CERT, and a repeat of SCAT and CogSport. See flow charts of assessment procedures for concussed and control groups in Figures 6 and 7 below.
**GCS = Glasgow Coma Score, CHQ = Child Health Questionnaire, SCAT = Sports Concussion Assessment Test, CERT = Children’s Effort Rating Scale, WASI = Wechsler Abbreviated Scale of Intelligence, BRIEF = Behavioural Rating Inventory of Executive Function.**

Figure 9: Flow Chart of Recruitment and Assessment Procedures for Concussed Group
Data Analysis

Data were analysed using Stata SE v14.0, and employed a significance level of $\alpha = 0.05$. Since this project is divided into two studies, the analyses are listed below as they relate to each study. Model effect sizes for both studies were also reported, with 0.10 presenting a small, 0.25 a medium, and 0.40 a large effect size (Selya, Rose, Dierker, et al., 2012).

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**SCAT = Sports Concussion Assessment Test, CERT = Children’s Effort Rating Scale, WASI = Wechsler Abbreviated Scale of Intelligence, BRIEF = Behavioural Rating Inventory of Executive Function.**

---

**Figure 10: Flow Chart of Recruitment and Assessment Procedures for Control Group**
Study one (chapter 5) – concussed group data only, at Day 2 and Day 10

Summary statistics were initially calculated for demographic and injury-related variables. Repeated mixed models were then conducted to examine the effects of pre- and post-exercise, days post-concussion (Day 2 and Day 10), and the interaction of these two variables on the four CogSport subtasks. Due to its distribution (heavy positive skew), CogSport SS data were modelled using Poisson repeated mixed model. Repeated observations were clustered on the individual random variable, and day post-concussion was entered as a random slope. Estimated model RT means were plotted to illustrate the effect of pre- and post-exercise at Days 2 and 10. RT is often (log10) transformed to better satisfy the assumption of normality (Whelan, 2008). However, for these data a sensitivity analysis between log10 and raw RT models did not yield differing results, model fit was not improved, and no noteworthy change to regression diagnostics was identified. As such, raw RT outcomes were modelled and presented to aid estimate interpretation.

Study 2 (chapter 6) – concussed (Day 2) and healthy controls

Analysis of injury characteristics, demographic data and sample descriptions (IQ, GEC, QoL) were initially completed to explore potential group differences. We then conducted 2 x 2 repeated measures analysis of variance (ANOVA) models to examine the effects of pre- and post-exercise, and group membership (CON, HC) and the interaction of these two variables (Whelan, 2008). The CogSport SS data was modelled using a mixed effects Generalised Estimating Equation (GEE) with a negative binomial distribution, emulating the RT 2x2 ANOVA models.
A mixed effects GEE model was applied to a combined RT model, exploring the influence of subtest order of difficulty (DET = 1, ID = 2, OB = 3, OCL = 4) on group and time effects on RT. All possible interactions were explored, and a planned comparison of adjacent contrasts joint test was conducted. Finally, multiple regression analysis applied to the concussed group explored the prediction of functional health (CHQ) from CogSport SS post-exercise and composite RT scores, as well as age, sex, days to symptom resolution, previous concussion, and baseline QoL. To achieve the most parsimonious model, fit improvement through predictor addition was tested using both likelihood ratio tests, and comparisons of Akaike information criterion (AIC).

Definitions

Table 7 below presents the definitions used throughout the following chapters relating to the times of assessment and phase of recovery of the concussed participants.

Table 7: Definitions of Time of Assessment and Phase of Recovery

<table>
<thead>
<tr>
<th>Time Since Injury</th>
<th>Phase of Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Day 0</strong></td>
<td></td>
</tr>
<tr>
<td>Day of injury / day presented at emergency department</td>
<td>Injury</td>
</tr>
<tr>
<td><strong>Day 2</strong></td>
<td></td>
</tr>
<tr>
<td>First day asymptomatic at rest</td>
<td>Acute period</td>
</tr>
<tr>
<td><strong>Day 10</strong></td>
<td></td>
</tr>
<tr>
<td>8 days after Day 2</td>
<td>Sub-acute period</td>
</tr>
</tbody>
</table>
Chapter 4 – Characteristics of Sample

Sample Characteristics

A total of 60 participants were included in this study. During the recruitment of the concussed group, 18 families did not express interest in participating in the study and from the remaining 30 who were approached, all agreed to participate and all 30 attended both day 2 and day 10 assessments.

Table 8 presents the number of male and female participants in each group. Table 9 presents the total number of concussed and control group participants, their ages and the mean ages and standard deviation of age in each group.

Table 8: Male and Female Participants in Concussed and Control Groups

<table>
<thead>
<tr>
<th></th>
<th>Concussed Group</th>
<th>Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males (%)</td>
<td>25 (83.3%)</td>
<td>16 (53.3%)</td>
</tr>
<tr>
<td>Females (%)</td>
<td>5 (16.7%)</td>
<td>14 (46.7%)</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>30</td>
</tr>
</tbody>
</table>
Table 9: Age Range, Means and Standard Deviations (SD) of Control and Concussed Participants

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Age Range</th>
<th>M</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Group</td>
<td>30</td>
<td>10.2-17.8</td>
<td>13.9</td>
<td>2.2</td>
</tr>
<tr>
<td>Concussed Group</td>
<td>30</td>
<td>10.0-17.0</td>
<td>13.0</td>
<td>2.2</td>
</tr>
</tbody>
</table>

Table 10 provides details on the mode of injury in concussed participants. These data suggest that a large proportion of these injuries were sustained in the context of sporting activities with specific mechanisms, including being hit or struck by an object (ball hitting head, or being tackled by another player and colliding with objects or body parts) and by falling while moving (running, playing sport, etc.).

Table 10: Mode of Injury

<table>
<thead>
<tr>
<th>Mode of Injury</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor Vehicle Accident (bike)</td>
<td>1</td>
</tr>
<tr>
<td>Motor Vehicle Accident (car)</td>
<td>2</td>
</tr>
<tr>
<td>Fall (stationary)</td>
<td>5</td>
</tr>
<tr>
<td>Fall (moving)</td>
<td>10</td>
</tr>
<tr>
<td>Kicked/Struck by object or person</td>
<td>12</td>
</tr>
</tbody>
</table>
In order to identify individual differences that may have an impact on study findings, screening measures of cognitive ability (WASI) and behaviour (BRIEF) were administered to all participants. Table 11 presents the means and standard deviations for the two groups in the behavioural regulation, metacognition and global executive composite of the BRIEF. Table 12 presents the means and standard deviations for the two groups in the WASI full scale IQ.

Table 11: Means and Standard Deviations (SD) of BRIEF in Both Groups

<table>
<thead>
<tr>
<th></th>
<th>Behavioural Regulation T-Score</th>
<th>SD</th>
<th>Metacognition T-Score</th>
<th>SD</th>
<th>GEC T-Score</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concussed</td>
<td>50.2</td>
<td>9.9</td>
<td>53.7</td>
<td>10.3</td>
<td>52.5</td>
<td>10.1</td>
</tr>
<tr>
<td>Control</td>
<td>51.6</td>
<td>12.3</td>
<td>52.9</td>
<td>31.6</td>
<td>52.0</td>
<td>12.9</td>
</tr>
</tbody>
</table>

No significant group differences

Table 12: Full Scale IQ and Standard Deviations (SD) in Both Groups

<table>
<thead>
<tr>
<th></th>
<th>Full Scale IQ Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concussed</td>
<td>107.1</td>
<td>14.2</td>
</tr>
<tr>
<td>Control</td>
<td>108.4</td>
<td>13.3</td>
</tr>
</tbody>
</table>

No significant group differences

Based on these descriptive statistics, there were no major differences between the two groups in age distribution, behaviour, or intelligence level; suggesting these factors did not play an influencing role in participants’ performance on the assessments.
Baseline concussion symptom scores were compared to identify differences in the self-reporting of symptoms (SCAT) between the concussed and control groups. Means and standard deviations are presented in Table 13 below. Whilst at Day 2 concussed participants reported being asymptomatic, it is interesting that they did report more symptoms than the control group. It is important to note that the requirement of being “asymptomatic” on the Day 2 of testing meant this is what each participant reported that morning when they woke up. Symptoms may have worsened as the day progressed, and this could explain why this baseline measure for the concussed group was higher than the controls at this time.

Table 13: Means and Standard Deviation for Baseline SCAT (Day 2 Pre-Exercise) in Both Groups

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concussed</td>
<td>7.73</td>
<td>8.1</td>
</tr>
<tr>
<td>Control</td>
<td>6.23</td>
<td>8.3</td>
</tr>
</tbody>
</table>

No significant group differences

Table 14 presents the frequencies and percentages of the developmental, medical and educational history provided by parents in the Injury and Demographic Questionnaire at Day 0.
| Table 14: Frequencies and Percentages of Developmental, Medical and Educational History in Concussed Participants |
|---------------------------------------------------------------|---------------------------|
|                                                               | Yes (%) | No (%) |
| Problems During Pregnancy and Birth                           | 8 (26.7) | 22 (73.3) |
| Developmental Milestones Reached Normally                     | 28 (93.3) | 2 (6.7) |
| Childhood Illnesses                                            | 9 (30.0) | 21 (70.0) |
| Previous Hospital Admissions                                   | 23 (76.7) | 7 (23.3) |
| Psychiatric Diagnosis                                          | 3 (10.0) | 27 (90.0) |
| Current Medication                                             | 5 (16.7) | 25 (83.3) |
| School Issues or Concerns                                      | 6 (20.0) | 24 (80.0) |
| Assistance Required at School                                  | 5 (16.7) | 25 (83.3) |
| Previous Head Injuries                                         | 7 (23.3) | 23 (76.7) |
| Returned to School at Day 2                                    | 0        | 30 (100) |
| Returned to School at Day 10                                   | 2 (6.1)  | 28 (93.3) |
| Days Post-Injury to Symptom Resolution M (SD)                  | 5.4      | (4.3)   |
Chapter 5

Impact of exercise on clinical symptom report and neurocognition following concussion in children and adolescents
Impact of Exercise on Clinical Symptom Report and Neurocognition after Concussion in Children and Adolescents

Vicky Marikas,1,3 Franz E. Babi,2,5 Stephen Hearps,1 Julian Dooley,1,6 and Vicki Anderson1,3,4

Abstract

Recovery from concussion in childhood is poorly understood, despite its importance in decisions regarding return to normal activity. Resolution of post-concussive symptoms (PCS) is widely employed as a marker of recovery in clinical practice; however, it is unclear whether subtle impairments persist only to re-emerge in the context of increased physical or cognitive demands. This study aimed to examine the effect of strenuous exercise on clinical symptom report and neurocognition in children and adolescents after PCS resolution after concussion. We recruited children and adolescents with concussion (n = 30) on presentation to an Emergency Department (ED). At Day 2 and Day 10 post-self-reported symptom resolution, participants completed a strenuous exercise protocol, and pre- and post-exercise assessment of PCS and neurocognition. Results demonstrated an overall reduction in PCS from Day 2 to Day 10 post-symptom resolution, with no evidence of symptom increase after strenuous exercise at either time point. Neurocognitive performance was linked to task complexity: on less cognitively demanding tasks, processing speed was slower post-exercise and, unexpectedly, slower on Day 10 than Day 2, while for more demanding tasks (new learning), Day 2 exercise resulted in faster responses, but Day 10 processing speed post-exercise was slower. In summary, we found the expected recovery pattern for PCS, regardless of exercise, while for neurocognition, recovery was dependent on the degree of cognitive demand, and there was an unexpected reduction in performance from Day 2 to Day 10. Findings provide some suggestion that premature return to normal activities (e.g., school) may slow neurocognitive recovery.

Keywords: cognitive function; head trauma; outcome measures; pediatric brain injury; recovery

Introduction

MILD TRAUMATIC BRAIN INJURY (TBI), which includes concussion, comprises 90% of all TBI in children and adults.1,2 Of the reported incidence of mild TBIs, 15–16% are sustained during participation in sport.3 The majority of concussion victims recover within weeks of injury, but a significant proportion experience persistent physical, cognitive, and behavioral sequelae. Such delayed recovery is associated with ongoing use of health services (e.g., medical, allied, and mental health) and delayed return to normal activities including work, school, and sport. The financial cost to society is significant and rising.4

While evidence is scarce, there are several consensus driven return-to-play (RTP) concussion guidelines for athletes, primarily adult-based, which recommend that post-concussive symptoms (PCS) are monitored, that the athlete is asymptomatic at rest before beginning to return to normal activities, and that a gradual return to play process is undertaken.5-9 These guidelines are derived from findings that premature return to active sport participation, before full symptom resolution, presents an increased risk of further injury and the potential for worse outcomes.10

In child and adolescent concussion, there is evidence that recovery may be more protracted than the 7–10 days often quoted for adults.11,12 If so, there are important implications for post-concussion management in these younger age groups, because current guidelines, informed primarily by adult recovery patterns, may lead to early return to normal activities and thus increased risk of further injury.

One means of reducing risk of premature return to normal activities is to base decisions on reliable measurement tools, rather than subjective clinical opinions. There are various methods for assessing PCS, including: (1) traditional severity indices (e.g., Glasgow Coma Score [GCS])13, with limited sensitivity to concussive injuries; (2) sideline tools (e.g., Sports Concussion...
Assessment Tool [SCAT], which tap into orientation, attention, memory, balance, and co-ordination; (3) self- and parent-report questionnaires, rating presence and severity of symptoms (e.g., Health and Behavior Inventory, Post-Concussion Symptom Index, which may not account for pre-existing symptoms, common in the general population; and (4) standard neuropsychological assessment tools, which can be both long and costly, and are often insensitive to change.

Recently, research has explored the potential for controlled exercise to contribute to decisions regarding return to play and to quicker recovery. In the normal population, and in physically fit individuals, exercise has been shown to improve neurocognitive function, including reaction times (RTs). In contrast, within the concussion literature, several adult studies have explored whether such activity post-concussion may actually unmask ongoing symptoms not evident on self-report or neurocognitive testing. Preliminary findings suggest that post-concussion, asymptomatic adults exposed to intense physical and cognitive exertion show increases in PCS and processing speed, and subtle memory deficits. Majerse and associates have extended these findings, showing that athletes who engaged in intense activity demonstrated increased symptoms post-exercise. In contrast, moderate level exercise (e.g., school activity, slow jogging, or domestic chores) resulted in no such drop in performance. Others have reported that introduction of light exercise early in recovery may accelerate return to pre-concussion function.

Given these conflicting findings and population findings that exercise improves neurocognition, we set out to examine the effect of strenuous exercise in children and adolescents with a recent concussive injury. We were particularly interested to identify whether strenuous exercise results in the re-emergence of previously resolved PCS or unmasking persisting neurocognitive inefficiencies, and thus may assist in more accurately determining full recovery and guide safer return to normal activity. No previous research has examined these relationships in children and adolescents, despite the high frequency of concussive injuries and the reported delayed recovery trajectories in these younger age groups.

Using a standardized exercise regimen, with a test-retest design, we assessed a sample of children and adolescents with concussion recruited on presentation to an Emergency Department (ED) and explored the effect of exercise on PCS and neurocognition once PCS had resolved. Specifically, we examined the impact of exercise on PCS and neurocognition at two time points—Days 2 and 10 post-symptom resolution. We predicted that, following self-reported PCS resolution: (1) exercise would result in increased PCS and reduced neurocognition; and (2) these effects would decrease from Day 2 to Day 10 post-symptom resolution.

Patients and Methods

Design

This study employed an experimental, repeated measures (test-exercise-test) design with three time points: Day 0, presentation to The Royal Children’s Hospital (RCH) ED; Day 2, two days after self-reported full symptom resolution; Day 10, 10 days after self-reported full symptom resolution.

Participants

The study comprised 30 children and adolescents (25 males), aged between 10.9 to 17.1 years, presenting to the RCH ED, Melbourne, within 24 h of sustaining a concussive injury. The study investigator (VM) identified ED presentations with concussion through surveillance of the electronic visits database of the RCH ED. Eligibility was then verified with the treating clinician, before the research team approached the patient and family regarding the study.

Consistent with the Zurich Consensus statement, concussion was defined as a blunt injury to the head associated with an altered mental state or any of the following symptoms: headache, diziness, fatigue, drowsiness, nausea/vomitting, poor balance, memory or concentration problems. Participants were included if they presented with: (1) loss or altered consciousness; (2) post-impact confusion and disorientation; and (3) two or more acute concussion symptoms including headache, diziness, gait unsteadiness, and blurred vision. These symptoms were assessed by ED staff as part of routine clinical assessment and management. Exclusion criteria were: intubated patients, need for neurological operative intervention or general anesthesia for injury management, presence of structural/hemorrhagic intracranial injury on computed tomography (CT) scan, clinical evidence of cerebrospinal fluid leak, injury resulting from child abuse or assault, alcohol or drug intoxication at time of ED presentation, multiple trauma, GCS <14 below 13, pre-existing physical, neurological, or psychiatric disorder.

Once eligibility was confirmed, the researcher then approached potential participants and their families in the ED and provided detailed information on the study protocol. Of the 48 young persons approached, 30 agreed to participate (62.5% recruitment). Reasons for refusal included family time commitments, residing at a distance from the RCH, and lack of interest. Of those who agreed to participate, all completed all study requirements.

Measures

A. Screening and demographic information

Screening questionnaire. The young person (or parent) completed a questionnaire in the ED to determine study eligibility. Information collected included participant age, post-concussion symptoms, English proficiency, demographic characteristics, and developmental history.

Injury characteristics. GCS, injury details, and clinical symptoms were extracted from medical histories.

Sample descriptors: Intellectual ability (Day 10). The Wechsler Abbreviated Scale of Intelligence (WASI), two-subtest form provided a Full-Scale Intelligence Quotient (IQ) score estimate (M = 100, standard deviation [SD] = 15).

Everyday Executive Function (Day 10). The Behavior Rating Inventory of Executive Function–Parent Form (BRIEF) consists of 86 items and provided an overall score, the Global Executive Composite (GEC) (M = 50, SD = 10). A score of >60 is indicative of clinical level executive problems.

Quality of life (Days 0 and 10). The Children’s Health Questionnaire–Parent Form (CHQ) was administered at Day 0 to determine any pre-injury health or psychosocial problems.

B. Outcome measures (pre-post exercise)

CogSport. This is a computerized tool, commonly used to assess PCS and cognitive function post-concussion. The symptom scale (CogSport SS) comprises 24 items describing common PCS (e.g., headache), scored on a seven-point Likert scale from 0
(none) to six (severe) and divided into symptom clusters: arousal, somatic, cognitive, emotional, and sleep dysregulation. Based on International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) criteria, symptom resolution is defined as endorsement of ≤3 PCS with less than moderate intensity (rating 0–2). Participants completed the CogSport SS in the ED and then immediately before and after completing the exercise protocol on Days 2 and 10.

CogSport also includes a computerized assessment tool, commonly used to examine multiple aspects of information processing and new learning. Four CogSport subtests were administered in this study: (1) detection (DET); simple RT/processing speed; (2) identification (ID); simple decision-making; (3) One Back (OB); working memory; and (4) One Card Learning (OCL); learning/memory. After an initial practice session on Day 2, to control for practice effects, CogSport was completed immediately before and after the exercise protocol on Days 2 and 10. Each administration took approximately 8 min. The RT scores were used in analyses.

C. Exercise protocol. Participants completed an adapted version of the McMaster All-Out Progressive Continuous Cycling Test,42 which has been shown to be suitable for children. The protocol required participants to exercise at a submaximal level for 8 min. During this assessment, heart rate was monitored on a portable device (Polar FS1 Heart Rate Monitor–Model: 7258822716).

Warm-up. The protocol began with a 2 min warm up on a stationary exercise bicycle. In stages 1–3 (submaximal exercise routine) after the 2 min warm-up, the bicycle’s resistance level was increased by 25 or 50 W, based on participant height (Table 1). Participants were instructed to keep rotations per minute constant. Throughout a 6 min exercise period, the researcher monitored participants’ heart rate every 2 min, and participants were asked to rate their level of exertion using the Children’s Effort Rating Scale (CERS),42 which has a 10 point scale where 1 = very easy and 10 = hard I’m going to stop.

Procedure

This study was approved by the RCH Human Research Ethics Committee. Participants were initially identified via ED database surveillance and approached, in the RCH ED, by the primary researcher (VM), at which time the project was explained in detail. Consenting participants/parents completed a screening questionnaire while under observation in the ED (Day 0). In the following days, the research team made phone contact with participants each morning until they reported being asymptomatic at rest. Once two consecutive asymptomatic days had passed (Day 2), participants then attended morning appointments at an outpatient clinic and again eight days later (Day 10).

<table>
<thead>
<tr>
<th>Table 1. Exercise Routine Completed at Day 2 and Day 10</th>
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<tbody>
<tr>
<td><strong>Resistance level (rotations per min)</strong></td>
</tr>
<tr>
<td><strong>Increment (resistance level)</strong></td>
</tr>
<tr>
<td>Height</td>
</tr>
<tr>
<td>Warm-up</td>
</tr>
<tr>
<td>Stage 1</td>
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<tr>
<td>Stage 2</td>
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<tr>
<td>Stage 3</td>
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</table>

On presenting to the exercise laboratory on Day 2 and Day 10, participants completed the CogSport SS and CogSport, followed by the exercise protocol and a second administration of the CogSport SS and CogSport (Fig. 1). Testing was completed within 45 min in total.

**Statistical analysis**

Summary statistics were initially calculated for demographic and injury-related variables. Repeated mixed models were then conducted to examine the effects of pre/post-exercise and days post-concussion (measured at Days 2 and 10), and the interaction of these two variables on the CogSport four subtasks. Because of its distribution (heavy positive skew), CogSport SS data were modeled using a Poisson repeated mixed model. Repeated observations were clustered on the individual random variable, and day post-concussion was entered as a random slope.

Estimated model RT means were plotted to illustrate the effect of pre/post-exercise at Days 2 and 10. The RT is often (log_{10}) transformed to better satisfy the assumption of normality.42 For these data, however, a sensitivity analysis between log_{10} and raw RT models did not yield differing results, model fit was not improved, and there was no noteworthy change to regression diagnostics. As such, raw RT outcomes were modeled and presented to aid estimate interpretation. Model effect sizes (Cohen’s F) were also reported, with 0.10 representing a small, 0.25 a medium, and 0.40 a large effect size.44

All analyses were conducted using Stata SE v14.0, and employed a significance level of α = 0.05.

**Results**

**Demographic and medical characteristics**

Participants comprised 25 males and five females, with a mean age at injury of 14.0 years (SD = 2.1, range: 10.1–17.7 years). Concussions were primarily as a result of sporting injuries (n = 27, 59.0%) and seven (23.3%) participants reported a history of previous concussion. No participant presented with abnormal neurological signs, 28 reported normal early development, and 6 (20%) noted school/learning problems (Table 2).

Days to resolution of post-concussive symptoms varied across the sample (M = 5.4 days, SD = 4.3; range: 0–24 days). On presentation at Day 2 post-symptom resolution, CogSport SS scores for the group had a mean of 7.7 (SD = 8.1) and a range of 0–43.

The IQ scores were within the average range for all participants (M = 107.1, SD = 14.2) as were everyday executive skills (BRIEF-GEC: M = 52.5, SD = 10.1) and pre-injury quality of life: CHQ physical (M = 46.5, SD = 8.9) and psychosocial (M = 54.6, SD = 8.2).

**Post-concussive symptoms**

**CogSport SS.** Results for the CogSport SS are provided in Table 3. Overall, a significant model was found for PCS on the CogSport SS, Wald χ²(3) = 131.55, p < 0.001, Cohen’s f² = 0.33. This appeared to be driven by a significant main effect of time from post-symptom resolution (Day 2 vs. 10) (Poisson beta coefficient [β] = −1.03, p < 0.001). No significant effect of exercise (β = −0.31, p = 0.06), or interaction effect (β = −0.17, p = 0.39) was found (Fig. 1).

**Neurocognitive performance.** (Results for the CogSport measures are provided in Table 3)

**Detection.** A significant model was found for Detection RT, Wald χ²(3) = 45.97, p < 0.001, f² = 0.43. Both exercise and time
effects were significant. Effects of exercise indicated that participants performed worse after completing the exercise routine (unstandardized beta coefficient $\beta = 3.145, p = 0.001$). For time post-symptoms, there was a decline in performance from Day 2 to 10; that is, increased RTs ($\beta = 3.133, p = 0.001$). A non-significant interaction term ($\beta = 2.90, p = 0.82$) suggested parallel lines of change between the two observation days (Fig. 1).

Identification: A similar pattern was found in Identification RT as seen in Detection (Fig. 4). Overall, the model was significant, Wald $\chi^2(3) = 45.97, p < 0.001$, and significant main effects for exercise ($\beta = 66.90, p < 0.001$), and time post-symptoms ($\beta = 3.10, p < 0.001$). Again, the interaction was not significant ($\beta = -20.61, p = 0.32$).

One-Back. No significant main effect of exercise ($\beta = 5.47, p = 0.82$), or time post-symptoms ($\beta = 4.45, p = 0.86$), was found (Fig. 1). There was no observed interaction effect ($\beta = 0.55, p = 0.99$), and the overall model was not significant (Wald $\chi^2(3) = 0.18, p = 0.98, r^2 = 0.002$).

One Card Learning. For One Card Learning, all terms were significant (model Wald $\chi^2(3) = 8.56, p = 0.04$): exercise $\beta = -78.00, p = 0.02$; time-post symptoms $\beta = -79.01, p = 0.01$; and interaction effect $\beta = 121.87, p = 0.01$. There was a decrease in RT from pre- to post-exercise on Day 2, but an increase in RT from pre- to post-Exercise on Day 10 (Fig. 1).

Effort ratings. Participant effort ratings suggest that the routine was challenging, with Children's Effort Rating Scale scores at Level 3, "getting quite hard" (mean = 5.57, median 6) at Day 2 and "starting to get hard" (mean = 4.97, Median = 5) at Day 10.

Discussion

The aim of this study was to examine the effect of exercise on PCS and neurocognitive function in children and adolescents with a recent concussive injury to determine whether additional stress post-symptom resolution could result in re-emergence of symptoms. Specifically, we investigated whether strenuous exercise precipitated recurrence of PCS and neurocognitive impairment in the 10 days after self-report of symptom resolution.

PCS

Despite participants reporting resolution of PCS for two days before testing, on formal measures of PCS they continued to rate
TABLE 2: Sample Demographics and Injury Details

<table>
<thead>
<tr>
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<th>Concussed participants (n = 30)</th>
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<tr>
<td><strong>Demographics</strong></td>
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<tr>
<td>Males n (%)</td>
<td>25 (83.3)</td>
</tr>
<tr>
<td>Age at onset (years)</td>
<td>14.0 (2.1)</td>
</tr>
<tr>
<td><strong>Injury factors</strong></td>
<td></td>
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<tr>
<td>Cause of injury</td>
<td></td>
</tr>
<tr>
<td>Sports n (%)</td>
<td>27 (90%)</td>
</tr>
<tr>
<td>Motor vehicle accident n (%)</td>
<td>3 (10%)</td>
</tr>
<tr>
<td>Previous concussion n (%)</td>
<td>7 (23.3)</td>
</tr>
<tr>
<td><strong>Pre-injury function</strong></td>
<td></td>
</tr>
<tr>
<td>Normal early milestones n (%)</td>
<td>28 (93.3)</td>
</tr>
<tr>
<td>School/learning problems n (%)</td>
<td>6 (20.0)</td>
</tr>
<tr>
<td>Pre-injury CHQ M (SD): Physical M (SD)</td>
<td>55.5 (4.6)</td>
</tr>
<tr>
<td>Psychosocial M (SD)</td>
<td>55.6 (5.8)</td>
</tr>
<tr>
<td><strong>Study data</strong></td>
<td></td>
</tr>
<tr>
<td>Days post-injury to symptom resolution M (SD, range)</td>
<td>5.4 (4.3, 0-24)</td>
</tr>
<tr>
<td>Returned to school Day 2 n (%)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Returned to school Day 10 n (%)</td>
<td>28 (93.3)</td>
</tr>
<tr>
<td>PCS Day 2: CogSport SS M (SD)</td>
<td>7.7 (8.1)</td>
</tr>
<tr>
<td>IQ: WASI M (SD)</td>
<td>107.1 (14.2)</td>
</tr>
<tr>
<td>Executive function: BRIEF: GEC M (SD)</td>
<td>52.5 (10.1)</td>
</tr>
<tr>
<td>Day 10 CHQ M (SD): Physical M (SD)</td>
<td>46.5 (8.9)</td>
</tr>
<tr>
<td>Psychosocial M (SD)</td>
<td>54.6 (8.2)</td>
</tr>
</tbody>
</table>

SD: standard deviation; CHQ: Child Health Questionnaire; PCS: post-concussive symptoms; SS: symptom scale; IQ: intelligence quotient; WASI: Wechsler Abbreviated Scale of Intelligence; BRIEF: Behavioral Rating Inventory of Executive Function; GEC: Global Executive Composite.

SDs, standard deviation: CHQ: Child Health Questionnaire; PCS: Post-concussive symptoms; SS: Symptom scale; IQ: Intelligence quotient; WASI: Wechsler Abbreviated Scale of Intelligence; BRIEF: Behavioral Rating Inventory of Executive Function; GEC: Global Executive Composite.

Our overall finding that while exercise did not impact PCS, it had a significant negative impact on more simple neurocognitive functions (simple decision making, RTs) at both Day 2 and Day 10, is in contrast to research with healthy persons, which suggests that exercise has a positive effect on processing speed and increases the ability to inhibit responses and reduce the time required to make decisions. Rather, our findings suggest that, in the presence of a concussive injury, this normal response is not evident. Further, the continued decline in post-exercise neurocognitive performance (but not PCS) at Day 10 was unexpected. Interestingly, similar results have also been reported in other studies of child and adolescent concussion.

One explanation for these unexpected findings is that reduced neurocognitive performance is related to return to school and other normal activities. While no participant in our study had returned to school at Day 2 assessment, most were involved in regular pre-injury school and normal routines by Day 10 testing (n = 28, 93%), arguably before full recovery, which may have led to an increase in physical and mental fatigue and thus poorer test performances. This suggests that, for children and adolescents, self-reported resolution of PCS may not be an accurate index of full recovery, and neurocognitive inefficiencies may persist. This has important implications for return to cognitively demanding activities, such as school. To facilitate full neurocognitive recovery, a longer recovery period may be beneficial.

Results from our study must be considered in the context of some methodological limitations. While we report unique longitudinal data, which incorporated an experimental design, the study sample was relatively small. Despite this, large effect sizes were found. With respect to generalizability of results, mean time to symptom resolution is less than has been reported in the previous literature.

TABLE 3: Reaction Time Results for Sports Concussion Assessment Tool and CogSport

<table>
<thead>
<tr>
<th></th>
<th>Pre-exercise</th>
<th>Post-exercise</th>
<th>Pre-exercise</th>
<th>Post-exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M (SD)</td>
<td>M (SD)</td>
<td>M (SD)</td>
<td>M (SD)</td>
</tr>
<tr>
<td>SS</td>
<td>7.7 (8.1)</td>
<td>6.3 (6.6)</td>
<td>2.8 (5.7)</td>
<td>1.9 (4.0)</td>
</tr>
<tr>
<td>DET</td>
<td>307.9 (74.4)</td>
<td>339.3 (70.5)</td>
<td>339.4 (75.0)</td>
<td>373.8 (107.6)</td>
</tr>
<tr>
<td>ID</td>
<td>486.1 (85.3)</td>
<td>555.0 (123.2)</td>
<td>545.2 (114.1)</td>
<td>594.0 (149.2)</td>
</tr>
<tr>
<td>OB</td>
<td>760.9 (159.8)</td>
<td>766.3 (175.4)</td>
<td>765.3 (218.4)</td>
<td>771.3 (206.8)</td>
</tr>
<tr>
<td>OCL**</td>
<td>997.0 (201.8)</td>
<td>919.0 (197.4)</td>
<td>917.9 (175.3)</td>
<td>961.8 (261.5)</td>
</tr>
</tbody>
</table>

M: mean; SD: standard deviation; SS: CogSport Symptom Scale (mean symptoms); DET: detection; ID: identification; OCL: One Celt Learning; OB: One Back; OMP: Composite Score (all in milliseconds).

* Time effect (Day 2 vs Day 10); ** exercise effect (pre- vs. post-exercise); *** interaction (time×exercise).
although more in keeping with recent ED-recruited samples than those reporting on patients attending follow-up clinics. We do note that follow-up demonstrated that mean group IQs were within the normal range, as were parent ratings of executive abilities and quality of life.

Primary outcome measures were limited to self-reported clinical symptoms and computer-based testing of neurocognitive skills, and may not be sufficiently sensitive to detect functional difficulties. The subjectivity of self-report of clinical symptoms and whether they accurately represent PCS is a common issue in concussion research. Further, the recommended cut-off for symptom resolution (that is, ≤3PCS, ICD-10), while supported by population studies, is yet to be validated against robust outcome measures, and so may incorrectly classify some concussed persons. Finally, the exercise protocol used a submaximal exercise routine, and it may be that more strenuous exercise is necessary to illicit neurocognitive and clinical symptoms. Participant ratings, however, indicate that the routine was challenging, with Children’s Effort Rating Scale scores for Level 3 of “getting quite hard” at Day 2 and “starting to get hard” at Day 10.

Conclusions

Study results suggest different recovery trajectories for PCS and neurocognition after child and adolescent concussion. PCS appeared unaffected by exercise and demonstrated the expected reduction in symptoms with time post-injury. In contrast, neurocognitive function was more susceptible to strenuous exercise and, contrary to our predictions, poorer neurocognitive performances were recorded at Day 10, when most participants had returned to normal activities. Our results provide preliminary evidence that subtle neurocognitive impairments may be present even once PCS have resolved, and support the need for ongoing monitoring in the weeks after symptom resolution.

Acknowledgments

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Author Disclosure Statement

No competing financial interests exist.

References


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Chapter 6

Impact of exercise on post-concussive symptoms and cognitive function after concussion in children and adolescents compared to healthy controls

Preamble

Resolution of post-concussive symptoms (PCS) is a marker of recovery, however it is unclear if subtle impairments re-emerge in the context of increased demands. This study examined the effect of strenuous exercise on clinical symptoms and cognitive efficiency in children and adolescents after PCS resolution following concussion. We recruited concussed children and adolescents (n=30) on presentation to an Emergency Department (ED) and compared them to non-injured controls (n=30), matched for age, cognitive function and prior concussion. At Day 2 post symptom resolution, concussed participants (and controls) completed an exercise protocol, and pre- and post-exercise assessments of PCS and cognitive efficiency. Findings demonstrated that, compared to controls, participants with recent concussion showed a reduction in PCS post-exercise, and faster reaction times on cognitive tasks, even where cognitive demands were high. These results provide preliminary support for the use of moderate exercise in the management of concussion post-symptom resolution.

Introduction

Concussion and mild TBI account for more than 85% of all TBI (Crowe, Babl & Anderson, 2009), with 1/5 children sustaining a concussive injury before age 16 (Barlow et al., 2014). Approximately 1/2 of these injuries are sustained during sports and leisure activities (Crowe, Anderson, Catroppa,
& Babl, 2010; Crowe et al., 2015). While most adult victims recover completely within two weeks, there is concern that the developing brain may be more vulnerable, even to mild injury, resulting in children and adolescents demonstrating more protracted post-concussion recovery (Anderson, Spencer-Smith, & Wood, 2011). While this vulnerability has been demonstrated in the context of more severe brain injury (Anderson et al., 2009), it remains to be tested in milder, concussion. To date, such confirmation is limited due to a lack of objective markers of complete recovery. We do know that, when delayed recovery occurs, it is associated with debilitating symptoms for the child that disrupt normal activities, including participation in school and sport. There are also significant economic and psychological consequences for children and families due to ongoing use of health services, missed school and workdays for parents, and family disruption and distress (Finkelstein, Corso, & Miller, 2006).

Consensus-based guidelines for return-to-play and school following concussion recommend a gradual, increase in activity and exercise levels associated with monitoring of PCS, which include physical, cognitive and behavioural symptoms (Davis, Anderson, Babl et al., 2017; Davis & Purcell, 2014; Giza et al., 2013; Kirkwood, Petersen, Connery, Baer, & Forster, 2016; McCrory et al, 2017; Schneider et al., 2017). This approach to clinical management has emerged from several strands of evidence demonstrating that: i) unnecessary rest and inactivity may be detrimental and extend the duration of PCS (Thomas, Apps, Hoffmann, McCrea, & Hammake, 2014); and ii) early paced return to activity is beneficial (Leddy & Willer, 2016; Schneider et al., 2017). In contrast, other research has demonstrated that premature return to active sport participation or intense exercise prior to full symptom resolution is associated with increased risk for further injury, including subsequent concussion, and psychological distress (Collins et al., 2002; Hanna-Pladdy, Berry, Bennet, Phillips, & Gouvier, 2001; Majerske et al., 2008; McCrea et al., 2003). Thus, accurate measurement of full recovery is critical to safe and timely return to normal activities.
One approach to ensuring speedy recovery, while balancing risk of premature return-to-play and school, is to base management on reliable recovery indices. One such approach is to monitor performance in a context which simulates day-to-day situations, for example, strenuous exercise. A number of studies report that intensive physical and cognitive exertion may lead to re-emergence of PCS and neurocognitive deficits (decreased processing speed, subtle memory deficits) in previously asymptomatic concussed participants (Hanna-Pladdy et al., 2001; Kowalski, Graham, Leddy, Devinney-Boymei, & Wiler, 2013; Majerske et al., 2008), suggesting that these individuals had not fully recovered, despite reporting no symptoms. In contrast, moderate levels of exercise have been shown to have no effect in asymptomatic concussed adults and even beneficial effects in healthy controls (Kowalski et al., 2013; Leddy, Baker, Kowalski, Bisson, & Willer, 2011).

Monitoring the individual’s response to acute exertion post-concussion, in particular, evidence of increased PCS or cognitive inefficiency, may provide the opportunity to simulate return-to-play conditions in a safe context. This may then contribute to decisions around complete recovery and the safe return to normal activities, including participation in sports and leisure activities. We were interested to explore whether, following remission of PCS, participation in strenuous exercise would result in increased PCS and decreased neurocognitive efficiency in concussed versus healthy participants. To examine this, we assessed concussed participants two days after self-reported symptom resolution, to approximate timing of management decisions regarding return to normal activities (McCrorry et al., 2013; 2017), and compared results to healthy controls. We predicted that, following an intensive exercise routine, asymptomatic concussed participants would report elevated PCS, and reduced neurocognitive efficiency, increasing with level of cognitive demand, compared to healthy controls. In addition, for the concussed sample, we were interested in exploring factors that contributed to functional recovery and wellbeing, and predicted that both injury and non-injury factors would contribute to these outcomes.
Method

For details on methodology, procedure, and statistical analysis see chapter 3.

Results

Demographic and medical characteristics

As illustrated in Table 15, there were no group significant differences identified for age, previous concussions, baseline quality of life, or post-injury executive function and IQ (p>0.05). In keeping with sex distributions for concussion, there were more males in the CON group (p=0.012).

For the CON group, 90% of participants had sustained sports-related concussions, and seven had a history of prior concussion. Time to self-reported symptom resolution was 5.4 days (range: 4.3-24). No participant had returned to school or play at Day 2 assessment, while 93% (n=28) had returned to school at Day 10 follow-up.
Table 15: Between-group demographic and injury characteristics.

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<tr>
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<th>Concussed</th>
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<th>Healthy Controls</th>
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Demographics

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<tbody>
<tr>
<td>Males, n (%)*</td>
<td>25 (83.3)</td>
<td>16 (53.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at testing (years), M (SD)</td>
<td>13.9 (2.1)</td>
<td>13.0 (4.3)</td>
<td></td>
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<tr>
<td>Normal development/medical history n (%)</td>
<td>28 (93.3)</td>
<td>29 (96.7)</td>
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Pre-injury function

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<tbody>
<tr>
<td>CHQ: Physical M (SD)</td>
<td>55.5 (4.6)</td>
<td>56.08 (5.37)</td>
<td></td>
<td></td>
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<tr>
<td>CHQ: Psychosocial M (SD)</td>
<td>55.6 (5.8)</td>
<td>54.12 (6.10)</td>
<td></td>
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<tr>
<td>Prior concussion n (%)</td>
<td>7 (23.3)</td>
<td>5 (16.7)</td>
<td></td>
<td></td>
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<tr>
<td>Currently involved in sports n (%)</td>
<td>23 (76.7)</td>
<td>20 (67.7)</td>
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Cause of injury

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<tr>
<td>Car/bicycle n (%)</td>
<td>2 (6.7)</td>
<td>-</td>
<td></td>
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<tr>
<td>Fall/blow n (%)</td>
<td>14 (46.7)</td>
<td>-</td>
<td></td>
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</tr>
<tr>
<td>Kicked/struck by object n (%)</td>
<td>7 (23.3)</td>
<td>-</td>
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<tr>
<td>Other n (%)</td>
<td>7 (23.3)</td>
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Symptom recovery post-concussion

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<tbody>
<tr>
<td>PCS Day 2: SCAT (pre-exercise) M (SD)</td>
<td>7.7 (8.1)</td>
<td>6.2 (8.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCS Day 2: SCAT (post-exercise) M (SD)</td>
<td>6.3 (6.6)</td>
<td>9.1 (10.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back at school at Day 2 n (%)</td>
<td>0 (0.0)</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back to school Day 10 n (%)</td>
<td>28 (93.3)</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptom resolution (days) M (SD)</td>
<td>5.4 (4.3)</td>
<td>-</td>
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Day 10 outcomes

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<tbody>
<tr>
<td>WASI-2 M (SD)</td>
<td>107.7 (14.2)</td>
<td>108.4 (13.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BRIEF: GEC M (SD)</td>
<td>52.5 (10.1)</td>
<td>52.0 (12.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHQ: Physical M (SD)</td>
<td>46.5 (9.0)</td>
<td>-</td>
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<td>CHQ: Psychosocial M (SD)</td>
<td>54.6 (8.2)</td>
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* p = 0.01
Self-reported clinical symptoms

Table 3 reports the summary statistics of raw RT for the CogSport SS and the four CogSport RT subscales, and the composite of these pre- and post-exercise. A significant interaction was found in the negative binomial GEE model for the CogSport SS Composite score \( p=0.022 \). Examination of mean symptoms shows that, contrary to expectations, on average, the HC group increased in almost 3 symptoms from pre- to post-exercise, whereas the CON group decreased by almost 1.5 symptoms (Figure 11, Table 16).
Table 16: Mean Symptom Severity and raw Cogsport RT (milliseconds) between groups.

<table>
<thead>
<tr>
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<th>Normative data(^a) (n=321)</th>
<th>Healthy Controls (n=30)</th>
<th>Concussed group (n=30)</th>
<th>Group</th>
<th>Time</th>
<th>Group* Time</th>
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<td>-</td>
<td>7.2 (4.1 – 10.3)</td>
<td>10.1 (6.2-13.9)</td>
<td>8.7 (5.7 11.8)</td>
<td>7.3 (4.8 – 11.8)</td>
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<tr>
<td>DET</td>
<td>330 (184)</td>
<td>333 (299 - 370)</td>
<td>345 (318 – 375)</td>
<td>301 (279 -324)</td>
<td>333 (310 – 358)</td>
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<tr>
<td>ID</td>
<td>547 (156)</td>
<td>527 (490 - 568)</td>
<td>586 (539 – 636)</td>
<td>479 (449 – 511)</td>
<td>543 (501-588)</td>
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<td>OCL</td>
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<td>1108 (1036-1186)</td>
<td>1082 (971-1207)</td>
<td>978 (908 – 1054)</td>
<td>899 (823 – 872)</td>
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<td>OB</td>
<td>723 (166)</td>
<td>856 (791 – 926)</td>
<td>802 (724 – 888)</td>
<td>744 (606-807)</td>
<td>746 (682 - 716)</td>
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<td>2833 (2588-3100)</td>
<td>2522 (2376-2676)</td>
<td>2539 (2371-2719)</td>
<td>0.006</td>
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</table>

CSS: CogSport Symptom Scale; DET: Detection; ID: Identification; OCL: One Card Learning; OB: One Back

\(^a\)Williams et al, 2015, provides normative data for healthy 13-14-year-olds (n=321), using identical CogSport protocol

p-value=Between-group main and time, and interaction effects p-values. RT Subtest models: 2x2 repeated measures ANOVA models with log-transformed outcomes, adjusting for sex; Symptom Scale mode: 2x2 repeated negative binomial mixed effects Generalised Estimating Equation model, adjusting for sex
Cognitive efficiency

Significance values from ANCOVA models for CogSport RT were inconsistent. For the overall Composite, there was a significant group difference (p=0.006), with the CON group demonstrating faster RTs than HCs. A similar result was found for the two more demanding CogSport subtests (OCL: p=0.002; OB: p=0.036). For the ID and DET subtests both CON and HC groups recorded slower RTs post-exercise, with this effect significant only for the ID subtest (p<0.001). No group or interaction effect was present (Figures 12 and 13).
Figure 12: Composite Reaction Time Pre- and Post-Exercise

Figure 13: Reaction Times: CogSport Subtests Pre- and Post-Exercise
Cognitive demand

A mixed effects GEE model explored the moderating effect of subtest difficulty on a combined analysis of all subtests. Results showed that both degree of cognitive demand and exercise had significant main effects (p<0.001 and p=0.035, respectively) and a significant interaction between the two (p=0.044).

As illustrated in Figure 13, there was a two-fold increase in reaction times between less (Identification and Detection) and more demanding CogSport subtests (One Card Learning, One Back), for both groups as well as an increase in reaction time after exercise (more evident on less demanding subtests).

Effort ratings

Children’s Effort Rating Scale scores were all at Level 3, ‘getting quite hard’ or above (Mean = 5.57, Median 6).

Discussion

The primary aim of this study was to explore whether, following remission of PCS, strenuous exercise would result in a re-emergence of PCS and cognitive symptoms in concussed versus healthy participants, indicating that subjective symptom report may be an inadequate index of full recovery, and may lead to at-risk children and youth returning to sports and school prematurely. In keeping with the limited literature available, we expected that, following a strenuous exercise session, asymptomatic concussed participants would report increases in PCS, and decreases in cognitive functioning, compared to HC. We also expected that functional wellbeing would be dependent on both injury and non-injury factors. Our predictions were largely unsupported.
PCS

Both CON and HC groups reported presence of PCS prior to exercise, with the CON group reporting a mean of 7.8 symptoms, compared to 6.2 symptoms in HC. This is consistent with previous research which suggests that PCS are present in the general population, even without exposure to injury (Iverson & Lange, 2003).

Contrary to current evidence, which suggests that physical and cognitive exertion may lead to re-emergence of PCS (Hanna-Pladdy et al., 2001; Kurowski et al., 2017), while the HC group demonstrated an average increase of almost three symptoms post-exercise, the CON group recorded a decrease in symptoms. These results suggest that participation in strenuous exercise once PCS have remitted may be therapeutic in this post-symptom period, providing an opportunity for re-conditioning prior to return to active participation.

Cognitive performance

Once again, study results did not conform to predictions. Overall, the CON group recorded faster reaction times than the HC group on CogSport, both pre-and post-exercise, with this effect most evident on cognitively demanding subtests (OB, OCL). Exercise appeared to have little impact on reaction times for either group, with the exception of the ID subtest, where reaction times slowed significantly for both groups post-exercise. This finding may relate to the timing of the ID subtest, which is one of the early CogSport subtests conducted immediately post-exercise, where exercise impact may be greatest. Additional research is needed to further explore this possibility.
Finally, and as might be expected, cognitive demand was identified as an important factor for performance, with slower reaction times on more demanding tasks (e.g., simple response time versus learning and working memory) for all participants, both pre- and post-exercise, and with the impact of exercise exacerbating this effect (Auddifren, Tomporowski, & Zagronik, 2008; Baker, Freitas, Leddy, Kawolski, & Willer, 2012; Darling et al, 2014). However, group comparison demonstrates that the CON group continues to respond more quickly than HCs, even in the context of increasing cognitive demand.

A number of study limitations need to be considered when interpreting these results. Firstly, the sample size is modest, and low power may have led to lack of sensitivity in our analyses. We do note, however, that our findings were generally consistent and suggest an overall benefit of exercise for participants with concussion. Second, and also related to small sample size, generalisability of our results needs to be considered. We compared baseline neurocognitive performances on CogSport of our two groups with those from a large normative study (Williams et al., 2016), and found comparable reaction times across measures, supporting the validity of our findings. Further, there may have been group differences in symptoms and performance that we did not measure. Of note, we identified no differences in age, cognitive function, concussion history or pre-injury quality of life, and all participants were active in sports and competent using computers.
Lastly, in the context of contradictory evidence regarding the intensity of exercise and its impact on PCS and cognitive inefficiencies post-concussion, we employed an exercise routine considered to be of high intensity (Bar-Or, 1983). However, participants rated the exercise routine in ‘moderate’ intensity range, possibly reflecting a high fitness level. Taking participant ratings into account, the lack of evidence for exercise to negatively impact PCS or cognitive efficiency, and some evidence for benefits, provides support for use of moderate exercise in concussion management immediately post self-reported symptom resolution.

In summary, we found no evidence that exercise results in the re-emergence of clinical symptoms or cognitive deficits following symptom resolution in young people post-concussion. Compared to healthy controls, participants with recent concussion showed a reduction in PCS following exercise, and consistently recorded faster reaction times on cognitive tasks, even where cognitive demands were high. Acknowledging that our sample may represent a group more fit and active than population expectations, these results may be best interpreted as supporting the use of moderate exercise in the management of concussion post-symptom resolution.
Chapter 7 – Discussion Summary

Preamble

The aim of the current study was to determine the effect of exercise on cognition in children and adolescents in the acute and sub-acute period following a concussive injury. The above two studies aimed to better understand the post-concussive course of the child and adolescent populations, and the effect that physiological stress (exercise) can have on functioning in the days following a concussive injury. The aim of this study was to gain a better understanding of the recovery path post-concussion in children and adolescents, and thus contribute to the evidence base for effective clinical management.

In summary, our results showed the expected reduction in PCS over time following concussion, but limited evidence that these symptoms are affected by strenuous exercise. However, for cognition, there was a decline in performance over time post-concussion on simple tasks only, with worse performance 10 days post-symptom recovery and some evidence that exercise further reduces these skills. Compared to healthy controls, concussed participants showed few impairments; rather controls exhibited slower information processing. However concussed participants tended to be more negatively affected by exercise.

Summary of Current Study Aims

Study one (chapter 5) aimed to examine the effect of exercise on the cognitive and PCS in children and adolescents once asymptomatic from a concussion. This study focused on identifying what changes occur, both in symptoms and in information processing skills (selective attention,
processing speed), in children and adolescents following an exercise routine once asymptomatic from a concussion.

Based on previous literature, which suggests differences in recovery between children and adults (Aubry et al., 2002; Cook et al., 2006; Makdissi et al., 2013), the current study hypothesised that exercise in this early, but asymptomatic, phase of recovery (Day 2) would lead to an increase in concussive symptoms and have a detrimental effect on cognitive ability.

Study two (chapter 6) aimed to explore the recovery trajectory following a concussive injury in the child and adolescent populations. Once again, based on previous literature (Aubry et al., 2002; Cook et al., 2006), this study assumed that by Day 10 of testing, recovery would be complete; that the detrimental effects of exercising on cognitive functioning and on concussive symptom report would no longer be apparent, and that children with concussion would be functioning similarly to non-concussed controls (Broglio & Puetz, 2008; Carney et al., 2014; Guskiewicz, Ross & Marshall, 2001; Iversen, Brooks, Collins & Lovell, 2006).

As detailed in the methodology chapter, participants were assessed at two points in time. The first assessment (Day 2) occurred once the child was asymptomatic at rest. This was the first day that the child did not display or experience any symptoms of concussion upon waking. The second assessment occurred eight days later (Day 10) when most children had returned to normal daily routine, such as school and other activities.

**Summary of Study Results**

Comparison of Day 2 and Day 10 PCS and cognition provided partial support for our hypotheses. For PCS, as expected, symptoms of concussion decreased from Day 2 to Day 10, but did not change significantly following exercise. These results support previously documented
recovery at the symptom level over time, but also show that recovery continues even after self-reports of resolved symptoms. Results were unexpected on neurocognitive measures, with reaction times slower at Day 10 than Day 2. The slowest reaction times were recorded pre-exercise on Day 2, with better performance post-exercise, and more surprisingly Day 10 reaction times post exercise were slower than pre-exercise and slower than those for Day 2.

Study 2 compared the healthy control participants’ performances with those of the concussed group at Day 2. Results for PCS were not in line with study hypotheses. Firstly, exercise failed to significantly impact symptom report at Day 2, with healthy controls reporting an average increase of three symptoms post-exercise and the concussed group recording a significant decrease in symptoms.

For cognitive measures, we found that, while there were no group differences for simple cognitive tasks, concussed participants tended to perform faster than controls in the more complex tasks at both test days. As predicted, effects of exercise were greater at Day 2 for the concussed group, however, the cognitive performance of the control group was also affected by exercise. Interaction effects indicated that, while the concussed group tended to be slower after exercise, the controls were less affected.

In an attempt to better understand the impact of concussive injuries on day-to-day function, we surveyed quality of life (QOL) and explored whether factors previously identified as relevant would contribute to outcomes. We considered both physical and psychosocial domains of QOL, finding that higher PCS post-exercise were a significant predictor of poorer QOL. Child factors (age, gender), cognitive status, history of prior concussion, and composite RT were not identified as impacting QOL suggesting that contributions to concussion outcomes are likely to be complex and multi-determined. Larger samples are required to further explore this area.
Strengths and Limitations of Study Results

This study has a number of methodological strengths. Firstly, the repeated-measures design provides the opportunity to accurately document acute levels of function and to follow recovery trajectories to symptom resolution and, potentially, beyond. Further, the inclusion of a comparison group of healthy children and adolescents allows us to place our results in the context of healthy performances. Interestingly, such comparisons showed that healthy controls endorse PCS, perhaps more frequently than the recovered concussed child, and also demonstrate a trend for slower reaction times on cognitive tasks.

Our standardised, and graded, exercise protocol was safe to administer post-concussion and ensured that all children experienced the same physiological stress levels. Further, cognitive measures were developed specifically for use in concussion, and thus, were able to accurately and objectively measure subtle differences in cognitive performance. They also included elements to reduce practice effects, which is key for serial assessments required when monitoring recovery post-concussion.

Whilst this study yielded important and some unexpected results, there were a number of limitations that may have impacted the findings. The modest sample size of 30 concussed and 30 controls, may have limited the power of the study to detect group differences and exercise effect for PCS and cognitive functioning. To minimise this risk, we have reported effect sizes. It is also important to note that the current sample size is comparable to similar studies in concussion literature. Common limitations in child concussion research include, sample size, and lack of matched control groups or comparisons (Kirkwood & Yeates, 2012).
Our control group also provides some limitations. As mentioned earlier, the control group in the current study reported significantly higher symptoms of concussion after exercise. It is unclear if this was because controls were less athletic and fit than the concussed group, and thus were more dramatically affected by strenuous exercise. Utilisation of comparison groups matched for fitness and sports participation should be considered in future research. When comparing the results of the two studies, it is noted that there are some inconsistencies, and as a result, findings need to be interpreted cautiously. It may be that, despite published psychometrics of CogSport (Collie et al, 2003), there may be problems with test-re-test reliability. Further research is needed with larger samples and case-control design to replicate these findings.

In this study, QOL was surveyed through a parent questionnaire and not completed by the concussed participant, so may not have accurately characterised outcomes. Use of self-report is strongly recommended for future research.

Another potential limitation of this study is the difference in gender balance between the control and concussed groups. However, sex differences were controlled for in our analysis and consistent with previous TBI research, no effect of sex differences was found.

**Clinical Implications: Recommendations for Return-to-play Guidelines**

Whilst study hypotheses were not fully supported, our findings are important and warrant further investigation. As highlighted above, the long-term impact that concussive injuries can have on the child and adolescent populations is yet to be fully understood and requires further research (Makdissi et al., 2013). Of particular significance, there was an unexpected decline in cognitive functioning of concussed participants from Day 2 to Day 10; a time when most children return to “normal” daily activities (such as school and recreation), and are assumed to be functioning
normally. In our sample, most children had indeed returned to school by Day 10 assessment and poorer results for information processing may reflect the negative impacts (fatigue, poor concentration) of premature return-to-school. These findings are consistent with those of previous studies in adult populations, which have found that returning-to-play prematurely can lead to decline in information processing and in psychomotor function. Of note, a recent child concussion study has reported similarly poor results at 10 days post-concussion (Crowe et al., 2015). These researchers report that 30-40% of concussed participants experienced ongoing somatic, arousal and cognitive symptoms to Day 30 post-injury. These findings support the review by Davis, et al., (2017) which found that recovery time in children can take up to 4 weeks. This review also stated that the definition of recovery needs to be better defined. This is evident in the current study, which found that even healthy controls presented with a number of symptoms. It is important that future research, with larger sample sizes and broader assessment, explores these findings further.

At the level of clinical management, our findings support the current return-to-play guidelines for the child and adolescent populations. However, while PCS appear to have resolved, performance on neurocognitive tasks appears to be dependant on the degree of cognitive demand suggesting that premature return to daily activities may slow neurocognitive recovery.

**Increasing Awareness: Community Perspectives**

There has been a significant increase in research as well as media attention in the area of sports-related concussion and the long-term implication on athletes. Whilst, this study supports the current return-to-play guidelines, it is suggested that further research be conducted to ensure that these guidelines are not promoting premature return-to-play for the younger populations. Research by White et al., (2013) aimed to assess whether key messages from current guidelines, as well as the severities of repeated concussions, are understood and reflected in sporting club
practices. This study involved the assessment of coaches and trainers in Australian Rules Football and Rugby League, and included a total of 916 trainers and coaches who completed the online survey. Findings indicated that trainers had a higher level of knowledge than coaches. While most were able to correctly identify concussive symptoms, fewer than 50% understood the increased risk for a second concussion. What was most concerning was that fewer than 25% recognised, and less than 40% were uncertain, that younger players typically take longer to recover than adults. Whilst it is acknowledged this comparison to adult athletes is beyond the scope of the current study, further education for trainers, coaches and parents is strongly recommended, in order to limit the risk of athletes returning-to-play too soon and putting themselves at risk for further injury.

**Conclusion**

This study identified the expected reduction in PCS over time post-concussion, but limited impact was seen following strenuous exercise. For cognition, there was a decline in information processing skills over time post-concussion on simple tasks only, with worst performance 10 days post-symptom recovery, and some evidence that exercise further reduces these skills. Compared with healthy controls, concussed participants showed faster information processing (pre- and post-exercise) and fewer concussive symptoms post-exercise.

Further research, with a larger sample size and which addresses the above limitations, is required in order to develop effective return-to-play guidelines for this population. In addition, sporting clubs, schools, and families should be further educated regarding the long-term impact of concussion and the risks associated with returning-to-play prematurely.
References


## Appendix A – RCH Human Research Ethics Committee Approval

The Royal Children's Hospital Melbourne

### RCH Human Research Ethics Committee Approval

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<td>APPROVED PROTOCOL:</td>
<td>Protocol v5 dated 24 November 2010</td>
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<td>PRINCIPAL INVESTIGATOR:</td>
<td>Vicky Manika</td>
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<td>DATE OF REVISION APPROVAL:</td>
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### Approved Subject to the Following Conditions:

**ALL PROJECTS**

2. Any proposed change in the protocol or approved documents or the addition of documents (including forms, brochures, advertising material etc) must be submitted to the Human Research Ethics Committee (HREC) for approval prior to implementation.
3. The Principal investigator must notify ethics & Research of:
   - Any serious adverse effects of the study on participants and steps taken to deal with them.
   - Any unforeseen events (e.g. protocol violations or complaints).
   - Investigators withdrawing from or joining the project.
4. A progress report must be submitted annually and at the conclusion of the project.
5. RCH HREC approval must remain current for the entire duration of the project. If the project is not completed in the allocated time a renewal request must be submitted to the Ethics & Research Department. Investigators undertaking projects without current HREC approval risk their indemnity, funding and publication rights.

### CLINICAL TRIALS

7. Must report all serious adverse events (SAEs) to the sponsor and the RCH HREC within 72 hours of occurrence.
8. Must report all Unexpected Serious Adverse Reactions (USARs) to the Therapeutic Goods Administration (TGA) for sponsored studies the sponsor may take this responsibility.
24 December 2010

Prof Vicki Anderson
Psychology
RCH

Dear Prof Anderson,

RE: HREC 29047 B
The Cognitive Effect of Exercise Over Time Following a Concussive Injury in Children.

Please find attached the RCH HREC Approval Certificate for the above project.

Also, please note the conditions of ethics approval which have been listed on the certificate.

The Committee wishes you well with your research study.

Yours sincerely

[Signature]

Ethics and Research Department, on behalf of the
RCH Human Research Ethics Committee

The Royal Children’s Hospital Human Research Ethics Committee (RCH HREC) is constituted according to the National Health and Medical Research Council’s “National Statement on Ethical Conduct in Human Research (2007). The committee operates in accordance with these guidelines and is registered with the NHMRC.
Appendix B – Project Information for Emergency Department Medical and Research Staff

RCH / MCRI Concussion Study

Childhood CONCUSSION!

Project Information Folder

Email vicky.manikas@mcri.edu.au for more information

or call 0423 124 453 or 9090 5239
What is the exercise and head injury study about?

The exercise and head injury study is examining the effect that exercise has on the cognitive functioning of children aged between 10 and below 18 years of age in the month after they sustain a head injury.

This is an important study as head injuries are among the most common injuries in children and can lead to long term impairments. There is also a relatively poor rate of recovery following head injury for a child compared to that of an adult, so a clearer understanding of the post head injury trajectory is crucial.

Exercise also plays an important role. We currently have very little information about the effect of exercise on the head-injured child’s brain. Current return-to-play guidelines for children are modelled on those of adults. This is problematic as a child’s brain is more vulnerable and reacts differently to an adult’s following a head injury. This study will help establish more appropriate return-to-play guidelines for children by monitoring the effect of exercise in the period following the injury.

Who are the researchers?

- Ms Vicky Manikas, PhD Candidate, Child Neuropsychology, University of Melbourne. The results of this project will be written up as a PhD thesis.
- Professor Vicki Anderson, Director of the Department of Psychology, The Royal Children’s Hospital
- Dr Franz Babl, Honorary Research Fellow, Emergency Research, The Royal Children’s Hospital

Who do I contact if I need more information?

For further information contact

Vicky Manikas
Phone: 0423 124 453 or 9090 5329   Email: vicky.manikas@mcri.edu.au
**Who will take part in the study?**

We are recruiting 50 patients aged 10-18 who present to the ED at the RCH with a head injury.

**Inclusion criteria:**

Presentations to the ED with a head/neck/face trauma resulting in any of the following:

- Loss or altered consciousness
- Post-impact confusion and disorientation
- Development of acute concussion symptoms including headache, dizziness, gait unsteadiness and blurred vision
- Glasgow Coma Score of 13 and above

**What will participants be asked to do as part of the study?**

Once consented if the researcher is present in the ED, parents/guardians will be asked to complete measures of pre-morbid cognitive functioning as well as demographic and medical questionnaires. If Vicky is not available, these measures will not be completed at this time.

Following the patient’s discharge, Vicky will contact the participants and arrange an assessment time at the concussion exercise laboratory (located at 369 Royal Parade). This assessment will occur approximately 2 days following discharge.

This assessment will take approximately one hour during which Vicky will administer various cognitive symptom protocols and a short exercise protocol, followed by a second administration of the cognitive protocol.

This assessment will then be repeated eight days later in order to identify any changes over time.
There is a concussed patient in the ED, what do I do?

The following points indicate what steps you should take if you notice a patient in the ED with a concussion and you think he/she may be suitable for the concussion project.

1. **Determine the patient’s eligibility.** Use the screening form located in the concussion study draws in the fishbowl to determine if the patient meets the criteria to take part in the project (see a copy of form in Appendix A).

2. **Contact Researcher.** If the researcher, Vicky Manikas, is not in the ED, notify the RA working in the ED that day. Vicky can also be contacted on 0423 124 453. Vicky will aim to be in the ED as much as possible during recruitment however there will be times when she is not available.

3. **Researcher not available – obtaining participant consent or interest.** If Vicky is unable to come to the ED to speak to the patient you are able to obtain the patients consent or interest in the project.

   Participant Information forms (Appendix B) are also located in the concussion draws in the fishbowl. These also include consent forms (appendix 3) and permission to contact forms (Appendix D).

   - As the patient and his/her parent/guardian if they would be interested in hearing more about the study. If they would like more information, provide them with a copy of the Information Package (which includes all the forms mentioned above).

   - Once they have read the form if they are happy to consent to the project, ask them to sign the consent form. Make a copy of the consent form for the patient and place the original in the research box in the fishbowl.

   If the patient is interested in the project but is unsure if they want to consent without further information, ask them to sign the permission to contact form and place this in the research box. The researcher will then be in contact with the patient over the next 24 hours to discuss the project in more detail.
Appendix C1 – Eligibility Screening Form: Concussed Group

RCH EXERCISE AND HEAD INJURY STUDY

ELIGIBILITY SCREENING FORM 1

Enrolment Number (to be entered by researcher only): ______

Date: __/__/__ Form completed by: ________________

PLEASE ATTACH PATIENT LABEL TO THIS SHEET AND
ATTACH THIS SHEET AT TRIAGE TO ALL PATIENTS WITH LIKELY CONCUSSION / MILD TBI

1. Inclusion criteria (please tick) – both criteria required to be included
   - □ Age: between 10 and <18 years
   - □

2. Exclusion criteria (please tick) – any one = excluded
   - □ Glasgow Coma Score below 13
   - □
   - □ Pre-existing physical, neurological, or psychiatric disorder
   - □
If any of the exclusion criteria are selected – DO NOT PROCEED – place this form in the research box in the fishbowl.

If all inclusion criteria and no exclusion criteria are present please obtain participant interest or consent for the study by:

1. Alert researcher Vicky Manikas on 0423 124 453

2. Give parents/guardians Parent Information Form If patient is over 12 years old, give them the Child Information Form also (forms are located in the Head Injury Study research box in the fishbowl)

Enrolment Number (to be entered by researcher only):

Interest or Consent: given by parent / guardian (please circle)

YES

NO – please return this form to fishbowl

If interested and/or consented,
• ensure parent/guardian completes the permission to contact form and/or consent form on the back of the information statement

• give copies of consent and permission to contact forms to the parent / guardian and to children aged 12 years and over

• place **ORIGINAL** consent and permission to contact forms in the research box in the fishbowl (ensure to staple together any forms if both parent/guardian and patient have signed separately)
Appendix C2 - Eligibility Screening Form: Control Group

RCH Exercise and Concussion Study

Eligibility Screening Form 2

Enrollment Number (enter only if consented): ____________________

Date: __/__/__ Form completed by: ______________________

1. Inclusion criteria (please tick) – both criteria required to be included

☐ Age: between 10 and <18 years

2. Exclusion criteria (please tick) – any one = excluded

☐ History of head trauma or current head trauma

☐ Pre-existing physical, neurological, or psychiatric disorder
If any of the exclusion criteria are selected – DO NOT PROCEED – please return the form to the researcher.

3. If all inclusion criteria and no exclusion criteria are present please read the information statement and consent form carefully.
Appendix D – Concussed PIS and Consent Form

PARENT/GUARDIAN INFORMATION STATEMENT
AND CONSENT FORM

HREC Project Number: 29047

Research Project Title: The Cognitive Effect of Exercise Over Time Following a Concussive Injury in Children

Thank you for taking the time to read this Information Statement. This Information Statement and Consent Form is 5 pages long. Please make sure you have all the pages.

If you wish to participate in this study please complete and return the consent form on page 5 of this Information Statement. If you would like further information about this project before you decide to participate, please complete and return the Permission to Contact Form attached to the back of this Information Statement.

You and your child are invited to participate in a research project that is explained below.

What is an Information Statement?
This Information Statement tells you about the research project. It explains to you clearly and openly all the steps and procedures of the project. The information is to help you to decide whether or not you would like you and your child to take part in the research.

Please read this Information Statement carefully. You can ask us questions about anything in it. You may want to talk about the project with your family, friends or health care worker.

Participation in this research project is voluntary. If you don’t want to take part, you don’t have to. You can withdraw from the project at any time without explanation and this will not affect their access to the best available treatment options and care from The Royal Children’s Hospital.

Once you have understood what the project is about, and if you would like you and your child to take part please sign the consent form at the end of this information statement. You will be given a copy of this information and consent form to keep.

1. What is the research project about?
Concussion is a kind of brain injury that can result from either a direct hit to the head or a hit to the torso or neck that can lead to impact upon the head and brain. We know that people who have concussion can later on have different kinds of cognitive (thinking) problems, for example, problems with remembering and paying attention. We also know that during the one-month period following a concussion the brain is very sensitive. If another brain injury occurs it may lead to more severe and long term problems.

We do not know enough about how these cognitive functioning problems affect children and adolescents who have a concussive injury. We don’t know what effect physical exercise might have on the cognitive functioning of children and adolescents in the month following a
2. **Who are the researchers?**

The researchers conducting this study are:

- Ms Vicky Manikas, PhD Candidate, Child Neuropsychology, University of Melbourne. The results of this project will be written up as a PhD thesis.
- Professor Vicki Anderson, Director of the Department of Psychology, The Royal Children’s Hospital
- Dr Franz Babl, Honorary Research Fellow, Emergency Research, The Royal Children’s Hospital
- Dr Julian Dooley, Senior Research Fellow, Child Health Promotion Research Centre, Edith Cowen University, WA.

3. **Who is funding this research project?**

This project is being undertaken as a PhD thesis and is fully funded by The University of Melbourne and the Murdoch Children’s Research Institute.

4. **Why is my child being asked to be in this research project?**

We are asking your child because he/she came to the Emergency Department of The Royal Children’s Hospital with a concussive head injury and is aged between 10 and below 18 years old.

5. **What does my child need to do to be in this research project?**

**In the Emergency Department**

*What you will be asked to do:* As a parent/guardian we will ask you to complete a short questionnaire about your child. It asks things like how your child is going at school, if your child has been sick or had a head injury before. This will take about 15 minutes. We will collect the completed questionnaire before you leave the Emergency Department.

*What your child will be asked to do:* We will ask your child a few questions about how they are feeling and about their general health. This will take approximately 15 minutes to complete.

*Please note – these questionnaires will only be completed if the researcher is present in the Emergency Department, in order to answer any questions you may have. If the researcher is not present, these questionnaires will be posted out to you should you choose to participate in the study.*

*What happens after my child is discharged from the Emergency Department?*
A member of the research team will phone you each day after your child is discharged from the Emergency Department. We will ask if your child had any signs of concussion when he or she woke up that morning (such as headache or dizziness). This is because we need your child to not be showing any symptoms in order to begin the assessment phase of the project.

Once your child is not showing concussive symptoms we will ask you both to return for two assessment visits at our research laboratory, which is located on Level 8, 369 Royal Parade, Parkville (near the hospital). Each assessment will take approximately 60 to 90 minutes. We will try to make sure visits are at times that suit you.

Visit 1

*Parent/guardian:* We’ll ask you to complete a short questionnaire asking how your child is coping since the concussion, as well as neurobehavioral symptoms such as attention difficulties, poor memory, and difficulties with planning and decision making. This will take approximately 20 minutes. You can do these while your child is doing his/her assessment.

*Your Child:* We will ask your child to do some activities with us. These will include some assessments of memory and attention which are mostly done on a computer. These will allow us to see how well he/she can respond to and pay attention to things. These tasks will take approximately 15 minutes to complete.

After this, your child will do 11 minutes of physical activity on a stationary bicycle. Then we will repeat the earlier computer activities again to see if there is any change as a result of the physical exercise.

Visit 2 – approximately 1 week after visit 1

You will complete the same questionnaires that you did at Visit 1, along with another questionnaire looking at any cognitive or educational changes in your child since the head injury. Together these will take about 1 hour.

Your child will also complete the same assessments as visit 1 as well as some additional tests measuring their general cognitive and educational functioning which will take approximately 30 minutes. This visit will take about 90 minutes in total.

6. **What are my child’s alternatives to taking part in this project?**

You and your child don’t have to be in this project if you do not want to. If you start and change your mind, you and your child can stop at any time without telling us why. If you and your child withdraw from the project we will use any information collected, unless you tell us not to.

Your decision to not take part or withdraw will not affect any treatment or care your child gets; or your child’s relationship with The Royal Children’s Hospital.

7. **What are the possible benefits for my child?**

The benefits of being involved in the study will be that rather than only returning to the hospital or to your GP for a check on your child’s recovery, you will receive the added assessment and support during the two assessment visits. We will also give you individual feedback on your child’s progress during the follow-up assessments.
8. **What are the benefits for other people in the future?**
This study may help us understand more about the effects of exercise on concussion. The things that we learn may help us know how to better manage and support children and adolescents during the month following a concussion. This information may also help us develop guidelines for when children should return to sport or physical exercise after a concussive injury.

9. **What are the possible risks, side-effects and/or discomforts?**
We feel that there are minimal risks or side effects associated with being involved in this study. There is a possibility that some participants may experience an increase in the symptoms of concussion, such as head ache, drowsiness and difficulty concentrating. These are anticipated to be very minor. If you have any questions about the study, please ask us.

10. **What are the possible inconveniences?**
We understand that we are asking a lot of time from you and your family to help us with this study. Where possible we will try to make sure that assessment sessions are booked for a time that is good for you and your child.

11. **What will be done to make sure my child’s information is confidential?**
Any information we collect from you and your child will remain confidential. We will use your information only for this research project. Only the researchers involved with this project and The Royal Children’s Hospital Ethics Committee can have access to this information. We can disclose the information only with your permission, except as required by law.

You and your child have the right to look at, and ask correction of, the information in accordance with the Freedom of Information Act 1982 (Vic).

The information will be re-identifiable. This means that we will remove your names and give the information a special code number. Only the research team can match your names to the code number, if it is necessary to do so.

All information will be stored securely in a locked filing cabinet in the Department of Psychology at the Murdoch Children’s Research Institute. Information will also be stored on a password-protected computer database.

We will keep the information until the youngest participant in this project turns 25 years old. After this time, we will destroy the information.

When we write or talk about the results of this project, we will report information about the whole group of participants. This means that no one will be able to identify you or your child.

12. **Will we be informed of the results when the research project is finished?**
At the end of the whole study we will send you a summary about what we found from the results. We will also be able to provide individual feedback on your child’s individual results if requested.

If you would like more information about the project or if you need to speak to a member of the research team in an emergency please contact:

**Name:** Ms Vicky Manikas

**Contact telephone:** 9090 5239 or 0423 124 453
If you have any concerns about the project or the way it is being conducted, and would like to speak to someone independent of the project, please contact:

Head of Department
Ethics and Research Department
Human Research Ethics Committee
The Royal Children’s Hospital.
Telephone: (03) 9345 5044
CONSENT FORM FOR PARENT/GUARDIAN TO GIVE INFORMED CONSENT
FOR THEIR CHILD TO TAKE PART IN A RESEARCH PROJECT

HREC Project Number: 29047

Research Project Title: The Cognitive Effect of Exercise Over Time Following a Concussive Injury in Children

I (Parent/Guardian name) ____________________________________________________
of (child’s name) _______________________________________________________

voluntarily consent for me and my child to take part in the above research project

• I believe I understand the purpose, extent and possible effects of my child’s involvement in this project.
• I have had an opportunity to ask questions and I am satisfied with the answers I have received.
• I understand that this project has been approved by The Royal Children’s Hospital Human Research Ethics Committee and will be carried out in line with the National Statement on Ethical Conduct in Human Research (2007).
• I understand I will receive a copy of this Parent/Guardian Information Statement and Consent Form.

Parent/Guardian Signature __________________________ Date ________________

Participant Contact Number (1)_________________________ (2)________________________

Print name of witness to parent/guardian’s signature
______________________________________________

Witness Signature __________________________ Date ________________

I have explained the project to the parent/guardian who has signed above, and believe that they understand the purpose, extent and possible effects of their child’s involvement in this project.

Person Obtaining Consent __________________________

Researcher Signature __________________________ Date ________________

Note: All parties signing the Consent Form must date their own signature
Appendix E – Control Group PIS and Consent Form

PARENT/GUARDIAN INFORMATION STATEMENT

AND CONSENT FORM

HREC Project Number: 29047

Research Project Title: The Cognitive Effect of Exercise Over Time Following a Concussive Injury in Children

Thank you for taking the time to read this Information Statement. This Information Statement and Consent Form is 4 pages long. Please make sure you have all the pages.

If you wish to participate in this study, please complete and return the consent form on page 4 of this Information Statement using the pre-paid envelope provided.

You and your child are invited to participate in a research project that is explained below.

What is an Information Statement?

This Information Statement tells you about the research project. It explains to you clearly and openly all the steps and procedures of the project. The information is to help you to decide whether or not you would like you and your child to take part in the research.

Please read this Information Statement carefully. You can ask us questions about anything in it. You may want to talk about the project with your family, friends or health care worker.
Participation in this research project is voluntary. If you don’t want to take part, you don’t have to. You can withdraw your child from the project at any time without explanation and this will not affect their access to the best available treatment options and care from The Royal Children’s Hospital.

Once you have understood what the project is about, if you would like your child to take part please sign the consent form at the end of this information statement. You will be given a copy of this information and consent form to keep.

13. What is the research project about?

Concussion is a kind of brain injury that can result from either a direct hit to the head, or a hit to the torso or neck, which can lead to impact upon the head and brain. We know that people who have concussion can later on have different kinds of cognitive (thinking) problems, for example, problems with remembering and paying attention. We also know that during the one-month period following a concussion the brain is very sensitive. If another brain injury occurs it may lead to more severe and long term problems.

We do not know enough about how these cognitive functioning problems effect children and adolescents who have a concussive injury. We don’t know what effect exercise might have on the cognitive of children and adolescents in the month following a mild concussion. We hope to find out more about the time after a concussion and how the brain of a child and adolescent reacts to physical exercise during this time. This will help us develop standards for children and adolescents who have concussion to help people decide when they can return-to-playing sport or engaging in physical activity.

A total of 100 children and adolescents aged between 10 and below 18 years old will participate in this project. 50 of these participants will have recently received a concussion and 50 will be used as a control group to compare the results with the concussed group.

14. Who are the researchers?

The researchers conducting this study are:

- Ms Vicky Manikas, Psychologist, PhD Candidate, Child Neuropsychology, University of Melbourne. The results of this project will be written up as a PhD thesis.
15. Who is funding this research project?

This project is being undertaken as a PhD thesis and is fully funded by The University of Melbourne and the Murdoch Children’s Research Institute.

16. Why is my child being asked to be in this research project?

You and your child are being asked to participate in this study as part of a control group as your child is above 10 and below 18 years old and may meet the criteria to take part. This means your child’s results and performance on any questionnaires or tasks that are completed will be used to compare with another group of clinical participants known as the experimental group. These participants will have recently had a brain injury leading to a concussion.

17. What does my child need to do to be in this research project?

You and your child will be asked to come to our research laboratory, which is located on Level 8, 369 Royal Parade, Parkville (near the hospital), and you will be asked to do the following:

As the parent/guardian you will be asked to complete a short questionnaire about your child. This asks various things about your child such as how they are going at school and will take approximately 30 minutes. This can be done while your child is completing the assessment.

Your child will be asked to do some activities with us; these will include some memory and attention tests mostly done on a computer. These activities will allow us to see how well your child can respond to and pay attention to things.
After this, your child will do 11 minutes of physical activity on a stationary bicycle. Then we will repeat the earlier activities again to see if there is any change as a result of the physical exercise.

18. What are my child’s alternatives to taking part in this project?

You and your child don’t have to be in this project if you do not want to. If you start and change your mind, you and your child can stop at any time without telling us why. If you and your child withdraw from the project we will use any information collected, unless you tell us not to.

Your decision to not take part or withdraw will not affect any treatment or care your child gets; or your child’s relationship with The Royal Children’s Hospital.

19. What are the possible benefits for my child?

The benefits of being involved in the study will be that your child will receive an individual report on their cognitive functioning before and after exercise. This may be of use to you if you would like to know how participation in sports may affect your child’s cognitive functioning and behaviour at home and at school.

20. What are the benefits to other people in the future?

As results will be compared to a group of children/adolescents who have had a concussion, this research may give us more information about the effects that exercise has on people who have concussion. The things that we learn may help us know how to better manage and support children and adolescents during the month following a concussion. This information may also help us develop guidelines for when children should return to sport or physical exercise after a concussion.

21. What are the possible risks, side-effects and/or discomforts?

We feel that there are minimal risks or side effects associated with being involved in the study. If you have any questions about the study, please ask us.

22. What are the possible inconveniences?

We understand that we may be inconveniencing you and your family to help us with this study. Where possible we will try to make sure that the assessment session is set at a time that is good for you and your family.
23. **What will be done to make sure my information is confidential?**

Any information we collect from you and your child will remain confidential. Only the researchers involved with this project and The Royal Children’s Hospital Ethics Committee can have access to this information. We can disclose the information only with your permission, except as required by law.

You and your child have the right to look at, and ask correction of, the information in accordance with the Freedom of Information Act 1982 (Vic).

The information will be re-identifiable. This means that we will remove your names and give the information a special code number. Only the research team can match your names to the code number, if it is necessary to do so.

All information will be stored securely in a locked filing cabinet in the Department of Psychology at the Murdoch Children’s Research Institute. Information will also be stored on a password-protected computer database.

We will keep the information until the youngest participant in this project turns 25 years old. After this time, we will destroy the information.

When we write or talk about the results of this project, we will report information about the whole group of participants. This means that no one will be able to identify you or your child.

24. **Will I be informed of the results when the research project is finished?**

At the end of the whole study we will send you a summary about what we found from the results. We will also be able to provide individual feedback on your child’s results if requested.

If you would like more information about the project or if you need to speak to a member of the research team in an emergency please contact:

**Name:** Ms Vicky Manikas

**Contact telephone:** 9090 5239 or 0466 481 341
If you have any concerns about the project or the way it is being conducted, and would like to speak to someone independent of the project, please contact:

Head of Department
Ethics and Research Department
Human Research Ethics Committee
The Royal Children’s Hospital
Telephone: (03) 9345 5044
CONSENT FORM FOR PARENT/GUARDIAN TO GIVE INFORMED CONSENT
FOR THEIR CHILD TO TAKE PART IN A RESEARCH PROJECT

HREC Project Number: 29047

Research Project Title: The Cognitive Effect of Exercise Over Time Following a Concussive Injury in Children

I (Parent/Guardian name)

of (child’s name)

voluntarily consent for my child to take part in the above research project

• I believe I understand the purpose, extent and possible effects of my child’s involvement in this project.
• I have had an opportunity to ask questions and I am satisfied with the answers I have received.
• I understand that this project has been approved by The Royal Children’s Hospital Human Research Ethics Committee and will be carried out in line with the National Statement on Ethical Conduct in Human Research (2007).
• I understand I will receive a copy of this Parent/Guardian Information Statement and Consent Form.

Parent/Guardian Signature ___________________________ Date ___________

Parent/Guardian Contact Number (1)____________________ (2)____________________

Print name of witness to participant’s signature __________________________
I have supplied an Information Statement and Consent Form to the participant

Person Obtaining Consent  Ms Vicky Manikas

Note: All parties signing the Consent Form must date their own signature.
Appendix F – Permission to Contact Form

Dear Parent/Guardian,

Research Project 29047: The cognitive effect of exercise over time following a concussive injury in children

Our research team from the Department of Psychology at The Royal Children’s Hospital is studying the immediate effects of exercise on the cognitive functioning (attention and information processing speed) of children and adolescents that have recently sustained a concussion.

We plan to recruit 50 children and adolescents, aged 10-18 years, who have had a concussion, and compare their results with a group of 50 children and adolescents, who have not had a concussion (a comparison group).

We would like to invite you and your child to take part in this study as a comparison participant. We have asked your child’s school to forward this letter and the attached information statement and consent form to you. Please be assured that your child’s school has not given us your names or any contact information.

Please read the information statement and consent form. If you and your child are interested in taking part in this study, please complete and sign the consent form and send it to us in the reply-paid envelope provided. Don’t forget to give us your contact phone number! When we receive the consent form, we will call you to arrange a suitable time and day for the study assessment.

If you would like more information, please contact Vicky Manikas on (03) 9090 5239.

Thank you for your assistance.

Ms Vicky Manikas (PhD Candidate)
Australian Centre for Child Neuropsychology Studies
Murdoch Children’s Research Institute
The Royal Children’s Hospital
Parkville 3052
vicky.manikas@mcri.edu.au
PERMISSION TO CONTACT FORM

The Cognitive Effect of Exercise over Time Following a Concussive Injury in Children

RCH HREC 29047

If you and your child are interested in taking part in this project or would like more information about the project please complete this form and a member of the research team will contact you.

Yes, you can phone me to tell me more about this research project.

The phone call is to give me more information about this research project and to check whether my family and child want to be in the project.

The phone call does not mean I agree to be in the project.

I can decide to be in the project, or not, after the phone call.

I understand that my contact details are confidential. They will only be used to tell me about this research project that is currently being done at The Royal Children’s Hospital, Melbourne.
I agree to be phoned by one of the research team to discuss the project

Name (parent/guardian): _________________________________

Child’s Name: _______________________________________

Signed ________________

Date ________________

I can be phoned at this phone number/s _____________________________

_____________________________________________________

The best days and times to phone me are _____________________________
Appendix G – Injury and Demographic Questionnaire

RCH EXERCISE AND CONCUSSION STUDY

DEMOGRAPHIC, MEDICAL AND INJURY INFORMATION

Enrolment Number: __________________

Date of Birth: __/__/__  Date of Injury: __/__/__

Age at Insult: ______ Years _______ Months (see below)

HISTORY

Name: __________________________________________________________

Address: ________________________________________________________
Parent / Guardian Telephone/s:  
Home __________________

Work __________________

Mobile __________________

Family Information

Family tree:

Father’s Occupation: ________________________________

Father’s Level of Education: _________________________

Mother’s Occupation: ______________________________

Mother’s Level of Education: _________________________

Child’s Development and Medical History
Any problems during pregnancy or birth:
_________________________________________________________________________
________________________________________________________________________

Developmental milestones:

Reached at appropriate age? Y/N/U___

Details________________________________________________
________________________________________________________
________________________________________________________
________________________________________________________
________________________________________________________

Has your child had any major childhood illnesses? Y/N/U___

Details___________________________________________________
________________________________________________________
________________________________________________________
________________________________________________________
________________________________________________________

Has your child had any previous hospital visits / admissions? Y/N/U ___

Details___________________________________________________
________________________________________________________
________________________________________________________

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Has your child ever had a psychiatric diagnosis? Y/N/U ___
Details

Is your child currently taking any medication? Y/N/U ___
Details

Educational Information

What school does your child attend? ______________________________

Year level_____  

Does your child have any school related issues or concerns? ____________________________

__________________________________________________________________________

__________________________________________________________________________

__________________________________________________________________________

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How would you describe your child on the following academic skills (e.g., average, above average, below average)?

Reading______________________________

Writing______________________________

Spelling______________________________

Math______________________________

Has your child repeated any year levels? _____________________

What are your child’s strengths and weaknesses? _____________________

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

Does your child receive any extra assistance with schoolwork? If so, what?

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

Social Development
Does your child get along with siblings? Y/N __

Does your child get along with other children? Y/N __

How would you describe your child’s level of social interaction? ___________
________________________________________________
________________________________________________
________________________________________________

1. Injury Type (please circle appropriate number):

1 MVA (car)
2 MVA (pedestrian/bike)
3 Fall (stationary: e.g. tree, roof)
4 Fall (Moving: e.g. bike, trampoline, running)
5 Kicked/Struck by object
6 Other (specify) ________________________________

Please provide brief description of incident
2. Glasgow Coma Score

Initial GCS on presentation to RCH: __________

How long after the injury: _____hours _____minutes

3. Neurological Signs (please circle all that apply)

1 = none

2 = focal neurology

3 = seizures

4 = dysarthria / speech difficulties

5 = ataxia
6 = incontinence

7 = hemiplegia

8 = gait disturbance

9 = numbness / sensory disturbance

10 = photophobia

11 = blurred / altered vision

12 = transient / permanent hearing loss

13 = other (please describe)________________________________________

4. Loss of Consciousness (LOC)

1 = none

2 = LOC of < 5 min

3 = LOC > 5 min < 30 min
4 = LOC > 30 min < 60 min

5 = LOC > 60 min < 2 hrs

6 = LOC > 2 hrs

7 = Unknown / No Documentation
Author/s: 
Manikas, Vicky 

Title: 
The cognitive effect of exercise in children and adolescents: when is return to play safe 

Date: 
2015 

Persistent Link: 
http://hdl.handle.net/11343/194169 

File Description: 
Complete Thesis 

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Terms and Conditions: Copyright in works deposited in Minerva Access is retained by the copyright owner. The work may not be altered without permission from the copyright owner. Readers may only download, print and save electronic copies of whole works for their own personal non-commercial use. Any use that exceeds these limits requires permission from the copyright owner. Attribution is essential when quoting or paraphrasing from these works.